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Table of contents

South African Family Practice 2019; 61(2):S2-S3

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NW REFRESHER COURSE

Morphine spinals: ICU or ward?

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History

Josef Wang first described the use of intrathecal morphine in 1977.[1] He injected 8 rats (weighing between 400–500 g) with 25 µg intrathecal morphine. The tail-flick response was monitored. He concluded that intrathecal morphine might become a predictable modality of pain relief.

Yaksh followed 2 years later with a study looking at the use of intrathecal morphine in parturition in rats and rabbits.[2] Gravid rats and rabbits had intrathecal catheters inserted. After the initiation of nest building, the rats were injected with 15, 45 and 100 µg of intrathecal morphine and the rabbits with 80 µg. Analgesia was tested in the rats with a hot plate as well as a tail flick test. In rabbits it was tested with a hot probe. The animals were well analgesed and there was no difference compared to controls with the onset of delivery as well as the percentage of pups alive after 150 minutes. Alper in the editorial of the same journal in which Yaksh's article was published, described intrathecal morphine as "potentially revolutionary".[2] Intrathecal morphine provided analgesia in gravid rats and rabbits, had no effect on parturition and seemed safe for both the mother and the child.

Josef Wang was at this stage, also exploring the use of intrathecal morphine for the treatment of intractable pain of inoperable cancer.[3]

Pharmacology

Opioid receptors are found in the brain (periaqueductal grey matter, rostral ventral medulla and medial thalamic limbic system). In addition, opioid receptors are also found in the spinal cord (Rexed laminae II and V and substantia gelatinosa). Of the 4 opioid receptors, 3 (µ, K and δ) are found in the spinal cord.[4] Theoretically, because intrathecal morphine acts at specific opioid receptors it provides analgesia without actions on other sensory or motor functions.[5]

Opioids can be classified according to their solubility. Morphine is a hydrophilic opioid and remains in the cerebrospinal fluid for longer than the lipophilic opioids (fentanyl and sufentanil). This is advantageous as this allows the drug to remain in the intrathecal space as it crosses the dura poorly. This results in a prolonged duration of action and little drug should be found in maternal and foetal blood.[5]

Effectiveness

It has been shown that for postoperative pain relief and time to first analgesic request following spinal anaesthesia, the duration of intrathecal bupivacaine ranges from 90–190 minutes and is up to 184 (+/- 20) minutes for intrathecal fentanyl and bupivacaine.[6]

Intrathecal morphine (in a dose of 0.1mg) results in an least 11 hours of effective analgesia and a significant reduction in postoperative analgesic requirements.[7]

Adverse effects

Adverse effects include pruritus, nausea and vomiting and respiratory depression.[7] Of these, respiratory depression is the most feared. The difficulty in reviewing the literature is that the term "respiratory depression" has no clear definition.[8] Consequently determining the exact incidence is not a perfect science.

The reported incidence of respiratory depression ranges from 0–0.9%.[9]

The incidence of respiratory depression correlates with the dose of intrathecal morphine. Meta-analysis indicates a reduced frequency of hypoxaemia when lower doses (vs. higher doses) of single-shot intrathecal opioids are used.[10] The optimal dose (balancing effective analgesia and a low incidence of adverse effects) most probably is between 75–150 µg.[11]

In one study, neither 100 µg nor 250 µg intrathecal morphine affected minute ventilation or the ventilator responses to CO_2, whereas both measurements were depressed for 3 hours after 8 mg subcutaneous morphine.[12]

Bailey et al. explored the effects of 300 µg of intrathecal morphine versus 0.14 mg per kilogram of body weight on ventilator drive.[13]He found that the depression of the ventilator response to hypoxia after the administration of intrathecal morphine is similar in magnitude to, but longer lasting than, that after an equianalgesic dose of intravenous morphine.

The mechanisms of respiratory depression include[9]:

- Vascular uptake by the epidural or subarachnoid venous plexuses and circulation to brainstem respiratory center.
- Arachnoid penetration and movement into the spinal cord.

- Rostral spread via the aqueous cerebrospinal fluid to the brainstem.
- Rostral spread via direct perimedullary vascular channels.

Patients at risk[9]

- Obstructive sleep apnoea
- Morbid obesity
- Elderly
- Cardiopulmonary disease
- Preoperative opioid tolerance
- Hypermagnesemia (in obstetric patients)

Guidelines

The American Society of Anesthesiologists has published guidelines for the post operative monitoring of patients who have had intrathecal monitoring.[10] This should be done hourly for the first 12 hours and then 2 hourly for the next 12 hours. Monitoring should include respiratory rate as well as level of consciousness. Pulse oximetry is not more sensitive than clinical monitory. Capnography is sensitive but has severe practical limitations.

Conclusions

Intrathecal morphine has the advantages of:

1. Simplicity
2. Reliability
3. Prolonged duration without a catheter in situ

With all interventions in anaesthesia, one must weigh up the benefits versus the risk. The most dreaded risk of intrathecal morphine is that of respiratory depression. This risk is dose-dependent. Doses of 100 µg are effective for analgesia with very little risk of respiratory depression. However, respiratory depression is potentially fatal. Therefore the patient at risk for respiratory depression must be recognized and adequate monitoring put in place. Over-sedation and respiratory depression should be treated proactively.

If a patient does not have any risk factors for respiratory depression and receives low dose intrathecal morphine (< 300 µg), it would seem that the risk for respiratory depression is the same or even less than the same patient receiving parenteral opioids. There are no data to support the use for extended monitoring of patients receiving low dose intrathecal morphine.[14]

In conclusion, if the patient has no risk factors for respiratory depression and you are happy to prescribe parenteral opioids in the ward, you should be happy to send the patient to the ward post low dose (< 300 µg) morphine spinal. Sound evidence-based medicine must be followed as opposed to dogma.

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NW REFRESHER COURSE

Perioperative Management of Pacemakers (PM) and Implantable Cardioverter Defibrillators (ICD) in South Africa

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Summary

PMs and ICDs are cardiac implantable electronic devices (CIEDs) that are becoming increasingly sophisticated and the perioperative management of these devices is changing along with this development. Traditionally, PM functions have been changed to asynchronous modes during surgery because of the fear of electromagnetic interference (EMI) from diathermy causing oversensing and subsequent loss of pacing. ICDs have been switched to off mode to prevent inadvertent shocks during EMI. This may lead to patient harm, due to R-on-T phenomenon in PM set in asynchronous mode and undiagnosed perioperative v-tach or v-fib in patients who have ICDs in off mode. PM-on and ICD-on strategies are becoming more acceptable, depending on the site of surgery. Intraoperative magnet use is currently underutilised and may have advantages to changing PM and ICD settings in patients who may otherwise have had the CIED functions switched off. Reversal of functions to preoperative settings may be achieved in the operating theatre without the need of a PM technologist.

Background

Approximately 7500 PMs and ICDs are implanted every year into patients in South Africa. Discovery Medical Aid submissions for PMs and ICDs number 7200 per year, but this figure includes new devices, temporary pacemaker insertion, generator replacement for end of service (EOS) or end of life (EOL) and lead changes or repositioning (see Figure 1).[1,2] With patient longevity rates increasing, it is becoming more likely that anaesthetists will encounter patients with PMs and ICDs, especially in the elderly. The medical technologists who specialise in CIEDs provide an important service in interrogating these devices and anaesthetists need to work closely with them in providing the optimum perioperative care when patients with devices present for surgery. All patients presenting for surgery need a recent interrogation of their device and the information presented to the surgical team. The anaesthetist should make decisions regarding pacemaker management in conjunction with the technologist, cardiologist and surgeon (see Figure 4).

Modern PMs and ICDs

PM technology was developed 60 years ago and recent advances, especially over the last 10 years have taken a relatively crude device that initially provided an asynchronous pacing beat to the right ventricle as a life saving procedure for patients with complete heart block to the sophisticated modern device that paces on demand, reacts to exercise by increasing the heart rate to a pre-set level and in the operating environment can distinguish between a sensed beat and EMI. Many of the guidelines for the management of PMs and ICDs were published at the beginning of the current decade and could do with a complete revision, taking into account the developments of these devices over the last 10 years.

Perioperative considerations

PMs The anaesthetist has to weigh up the pros and cons of either leaving a PM with its usual settings (PM-on) or asking the technologist to change the settings to asynchronous mode (either DOO or VOO). The problem that may be experienced with a PM left in DDD mode is oversensing due to electromagnetic interference (EMI) when the PM senses the EMI as electrical activity of the heart and inhibits the generation of a paced beat. This may result in periods of asystole while diathermy is being used. Modern PMs have algorithms that can distinguish between EMI and normal electrical activity in the heart and may ignore diathermy induced EMI completely or change the PM setting temporarily to DOO. The problem of a PM changed to asynchronous mode is that an R-on-T phenomenon may occur, which may result in ventricular fibrillation if an asynchronous beat is delivered during the refractory period of the cardiac cycle. The benefits of a PM-on protocol are that the chances of an undiagnosed R-on-T phenomenon occurring perioperatively are reduced and in addition, that the PM settings do not have to be reset by a technologist postoperatively. If the anaesthetist is planning to follow a PM-on protocol, the preoperative interrogation should include the PM response to magnet application as well as the ability to apply a magnet intraoperatively to manage oversensing if it occurs due to EMI (see Figure 7).

Many pacemakers are implanted today for disease of the sinu-atrial node (Sick sinus syndrome - SSS) where the patient experiences syncope due to bradycardia associated with SSS. These patients have normal atrioventricular conduction and the PM is set on AAI. Changing the PM to DOO or VOO may result in asynchronous ventricular contraction because the ventricular

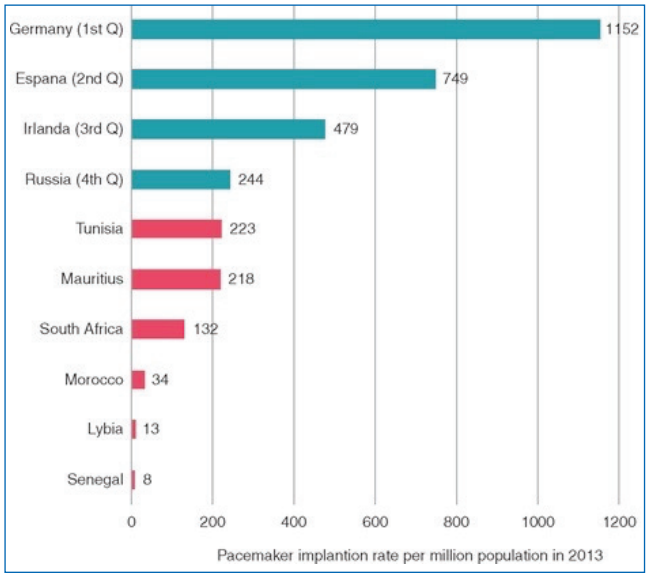

Figure 1: Implantation rate estimated to be 138.25/million in 2016 (total population 54146735, total number 7485) US rates are double Germany

lead is usually placed in the right ventricle. The left ventricular conduction and contraction is delayed and this may result in reduced left ventricular efficiency. These patients would benefit from a PM-on protocol.

ICDs are potentially problematic in that an ICD-on protocol may result in unwanted and repeated shocks due to EMI being misinterpreted by the device as ventricular fibrillation. This can lead to myocardial damage and depletion of battery life. It has been shown that ICDs do not respond to EMI if the operation site is below the iliac crest and that the diathermy dispersive pad is placed at a site to lead current away from the ICD.[3] If an ICD-on protocol is to be used, the anaesthetist should be aware of the response to application of a magnet to the specific device (see Figure 8).

An ICD-off protocol may result in undiagnosed v-tach or v-fib in the perioperative period and case reports have been published where patients have died at home after the device was not checked and turned on postoperatively. International literature is clear that the responsibility for resetting the ICD belongs to the anaesthetist and not to the technologist.[4] An ICD-off protocol may result in unnecessary external cardioversion for v-tach because anti-tachy pacing (ATP) is disabled. ATP reduces the need for shocks in patients who develop v-tach as many tachyarrhythmias can be terminated by the rapid pacing before the device has to deliver a shock (see Figure 3).

The standardised pacemaker codes are depicted in Figure 2.[5] Multisite ventricular pacing refers to cardiac resynchronisation therapy (CRT) for the left and right ventricles. It is utilised in patients with left bundle branch block to resynchronise left and right ventricular contraction to occur simultaneously. This may improve cardiac output by up to 15% in patients with heart failure due to reduced ejection fraction. Multisite atrial pacing is used experimentally to treat atrial fibrillation.[6]

Revised NASPE/BPEG Generic (NBG) Pacemaker Code

I	II	III	IV	V
Chamber(s) Paced	Chamber(s) Sensed	Response to Sensing	Rate Modulation	Multisite Pacing
O = None	O = None	O = None	O = None	O = None
A = Atruim	A = Atrium	T = Triggered	R = Rate Modulation	A = Atrium
V = Ventricle	V = Ventricle	I = Inhibited		V = Ventricle
D = Dual (A + V)	D = Dual (A + V)	D = Dual (T + I)		D = Dual (A + V)

Pacing Clin Electrophysiol. 2002 Feb;25(2):260-4

Figure 2: Pacemaker Codes

Implantable Cardioverter Defibrillator (ICD) and Anti-Tachycardia Pacing (ATP)

Patients with recurrent ventricular tachycardia and/or ventricular fibrillation or those at risk for developing these arrhythmias may have an implantable cardioverter defibrillator (ICD) placed in the left subclavian region. The ICD senses the R-R interval and if the interval reduces to a predetermined level, the device algorithm reads this as ventricular tachycardia and can deliver a repetitive sequence of eight rapid paced beats to try to break the re-entry condition of v-tach. If this fails to cardiovert the v-tach, a high voltage shock is delivered (see Figure 3). The shock is delivered from the coils to the generator in a triangulated vector to incorporate the left ventricle. (The high voltage coils around the pacemaker leads act as the cathode and the pulse generator acts as the anode). ICDs recognise supraventricular tachycardias (SVTs, AF and sinus tachycardia) via atrial sensing, but cannot cardiovert them. This is designed to prevent unnecessary shocks. ICDs may deliver anti-bradycardia therapy if required to do so.[7] A magnet applied to an ICD will generally disable the anti-tachycardia therapy while it is in situ, but will have no effect on anti-bradycardia therapy or rate responsiveness.

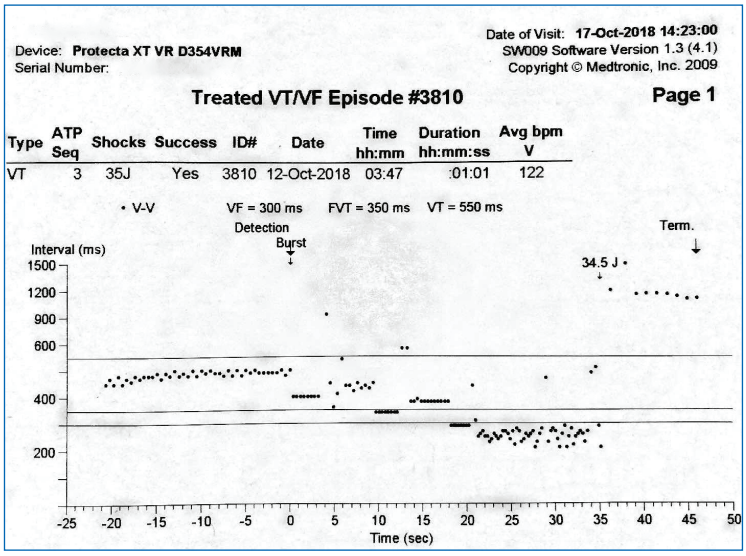

Figure 3: De-Identified printout from a patient's ICD showing an episode of V-Tach with attempted anti-tachy pacing (ATP) followed by successful 34.5 J defibrillation. Image supplied by Medtronic SA.

Preoperative Pacemaker Interrogation is Considered Standard of Care: Individual Prescription ℞

Is Tech available:
1. Type PM/ICD/CRT-P or D
2. Manufacturer and Model
3. Indication and date of insertion
4. Pacemaker Dependency
5. Battery Life (BOL/EOL/RRT) – replace prior to surgery
6. Pacemaker Settings and thresholds checked if new leads
7. Recent Activity
8. Effects of magnet application (and removal)
9. Reset rate if scope of operation requires
10. Device or Lead Alert/Recall status

Is Tech unavailable in an emergency:
1. CXR
2. ECG for dependency
3. Patient Card
4. Cardiologist
5. Manufacturer 24 hour helpline
6. Last Interrogation PM <12 months, ICD < 6 months, CRT-D or P <3 months
7. Magnet application preoperatively to assess PM rate changes or ICD Tones
8. Blind magnet application not recommended unless emergency

Figure 4. Preoperative Pacemaker and ICD Interrogation

Preoperative pacemaker interrogation is considered to be the standard of care and should be scheduled during the week prior to surgery. The PM technologist should provide the information as shown in Figure 4 and in consultation with the technologist and cardiologist and taking into account the planned surgery, the anaesthetist should decide on the perioperative PM management (see Figure 7).

If a PM-on strategy is to be followed, it is vitally important that the effects of magnet application and removal to the specific PM are known. It may be advantageous to reset the base rate of the pacemaker, even though a PM-on protocol is followed. For example, a base rate of 60 may be increased to 70 or 80 if haemodynamic challenges are expected, such as blood loss or neuraxial anaesthesia.

If the PM settings are to be changed, this should be done on the day of surgery and preferably reversed to the preoperative settings as soon as possible after the ESU is no longer required.

If an ICD-on strategy is to be followed, it is important to note that placing a magnet over the ICD will not change the underlying PM function and this has to be changed independently of the anti-tachyarrhythmia function. This should be considered in PM dependent patients if the surgery is close to the ICD and/or leads.

	CIED	Response to Magnet Application
PM	Pacemaker	85 beats per minute (65 BPM if RRT) DOO, VOO or AOO and disables rate responsiveness
ICD	Implantable Cardioverter-Defibrillator	Suspends Anti- Tachyarrythmia Therapy and Anti-Tachycardia Pacing (ATP) and has no effect on PM functions. 10s even tone in Med
CRT	Cardiac Resynchronisation Therapy	85 beats per minute (65 BPM if RRT) DOO
CRT-D	Cardiac Resynchronisation Therapy with Cardioverter-Defibrillator	Suspends Anti- Tachyarrythmia Therapy and Anti-Tachycardia Pacing (ATP) and has no effect on PM functions
Leadless PM	VVI implanted directly into RV	Depends on Manufacturer: Medtronic – no effect St Jude - VOO

Figure 5: Response to magnet application in Medtronic PM and ICDs

CRT devices need to be checked within 3 months because the coronary sinus leads have poorer contact compared to the right ventricular leads and higher thresholds are accepted. This may result in faster battery drain and thus reduce longevity.

Response to magnet application

The response to magnet application in Medtronic PM and ICDs is shown in Figure 5. It is important to note that there is no uniformity across the industry, and each manufacturer has a different set of responses to magnet application. This makes it imperative that the anaesthetist is aware of the specific response of the patient's device before applying a magnet. An indication of the enormity of this issue, is that in the USA, there are 1440 different types of device models across the different manufacturers.[7,8] Modern PM and ICDs respond in a determined manner to magnet application, and many of the problems associated with application have been dealt with. Examples include resetting device programming under the influence of a magnet and concurrent EMI, and switching off anti-tachy functions in ICDs which do not return once the magnet is removed. These problems do not occur in modern devices.

During surgery, magnet application needs to be carefully monitored. This is easily done in the patient with a PM, because magnet application will result in a fixed rate change, which is specific to the manufacturer. For example, Medtronic pacemakers change from the patient's usual settings to a rate of 85 beats per minute while the magnet is applied. This rate is 65 if the battery life is shortened (EOL) and the generator needs to be replaced (RRT). Therefore, as long as the heart rate is 85 bpm, the anaesthetist can be reassured that the magnet is correctly applied.

It is less clear in the case of ICDs. The Medtronic ICDs emit a tone for 10 seconds when the magnet is applied, but after this initial signal, there is no indicator to the anaesthetist whether or not the magnet is still in place and exerting its effect on the ICD. The magnet has no effect on the PM function of the ICD, so heart rate changes cannot be used as an indicator. It would make sense for the manufacturers to provide the anaesthetist with an ongoing signal to determine correct placement of a magnet over an ICD. Modern devices have Bluetooth functionality and an elegant

Operating Theatre Requirements

Monitoring and Emergency Measures:
1. ECG with filters on pacemaker detection
2. Pulse Oximeter trace
3. Arterial Line trace
4. Capnography
5. Acid Base status and electrolytes
6. CVC Guide Wire Insertion (Coronary sinus lead in CRT PM)
7. Temporary Pacemaker
8. Defibrillator Pads (paddles)
9. Magnet available

Defibrillator/ Pacing Pads should be placed front to back for maximum efficiency. In open heart surgery, pads will have to be placed side to side.

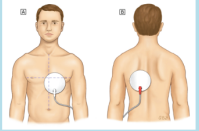

Figure 6: Operating Theatre Requirements

way of dealing with this problem would be to have a smartphone application that can read the wireless signals from the device.

PM-on or CRT-P-on protocol suggests that the PM settings are not changed during the standard preoperative technologist interrogation of the device. PM-on protocol will avoid inadvertent development of R-on-T phenomenon and implies that magnet application is possible if the situation of oversensing caused by EMI develops. In addition to this, the anaesthetist is able to remove the magnet when EMI is no longer being used. It takes away the need for postoperative high dependency unit care and a repeat call out by the technologist to reset the PM. The successful PM-on protocol requires the anaesthetist to follow the algorithm in Figure 7. A magnet can disable the rate responsiveness function in a PM and this is useful to prevent unwanted increases in heart rate, for example when the sternal saw is used in open-heart procedures, as the vibration of the saw may be misinterpreted as patient movement (see Figure 7).

ICD or CRT-D-on protocol suggests that the anti-tachycardia therapy of the ICD is not switched off perioperatively and that the device is allowed to sense tachyarrhythmias and deliver anti-tachycardia pacing (ATP) and shock if necessary. This provides protection to the patient in the event of V-Tach and/or V-fib, which may occur at anytime perioperatively. In order to prevent unnecessary ATP or shocks due to EMI being incorrectly read by the generator, a magnet should be available to place over the ICD to change the setting to ATP and Shock off. It is important to note that the anaesthetist should know exactly what happens to the specific ICD under the influence of magnet application and removal, that the patient position is such that the magnet can be properly secured during surgery and that the tone emitted by the generator is recognised. There are certain operating sites where it is safe to leave the ICD on and generally these are more that 15 cm (6 inches) from the generator and leads and below the umbilicus or ileac crest, as long as the ESU dispersal pad is sited away from the surgical site so that EMI is not directed towards the ICD.[3] For example, hip surgery is safe to proceed without switching off the anti-tachy therapy, as long as the dispersal pad is placed on the ipsilateral thigh.

The anaesthetist should consider switching off the anti-tachy therapy of the ICD if:

1. The operation site is within 15 cm of the generator or leads, especially if long bursts of unipolar diathermy are to be used. The argon beam ESU cannot be used in short bursts and may cause long periods of EMI.
2. A magnet cannot be reliably secured over the generator, such as in the prone position.
3. Certain operations such as hand surgery and ophthalmic operations where inadvertent shocks may lead to patient or operator harm. This would include operations at these sites performed under local anaesthesia. Thoracic operations would require the ICD-off because left chest procedures would render the anti-tachy functions ineffective because of poor tissue shock transfer due to high impedance when the chest is open. Also, in right chest procedures, it would be difficult to ensure proper application and security of the magnet if it was required.[9]

If the patient is pacemaker dependent, the anaesthetist may consider asking the PM tech to change the PM settings to DOO as in the PM-on protocol. It is also advisable to turn off rate responsiveness, as this function is not changed by magnet application in ICDs.

It is important to note that if the anti-tachy function has been turned off (ICD-off), the settings must be restored as soon as possible after the procedure and the patient has to be observed in a high dependency unit until this has been achieved.

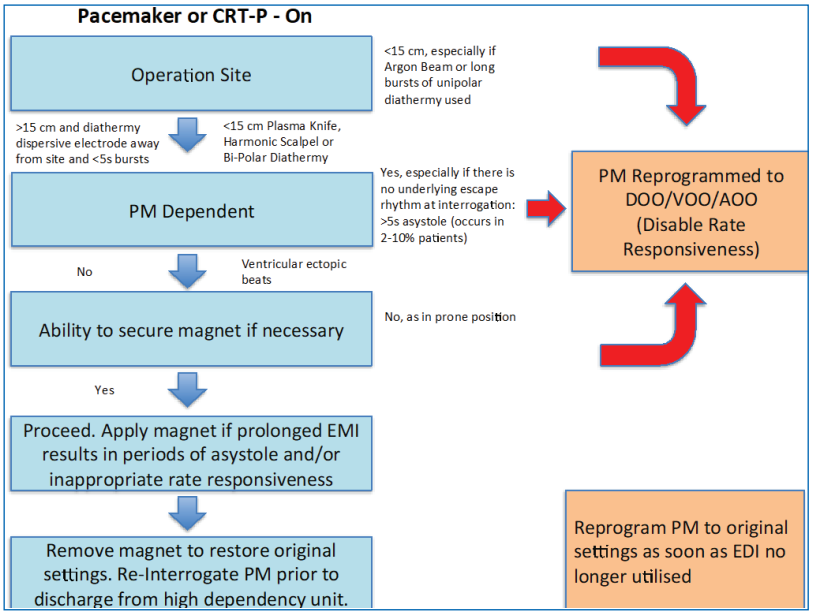

Figure 7: PM-on algorithm

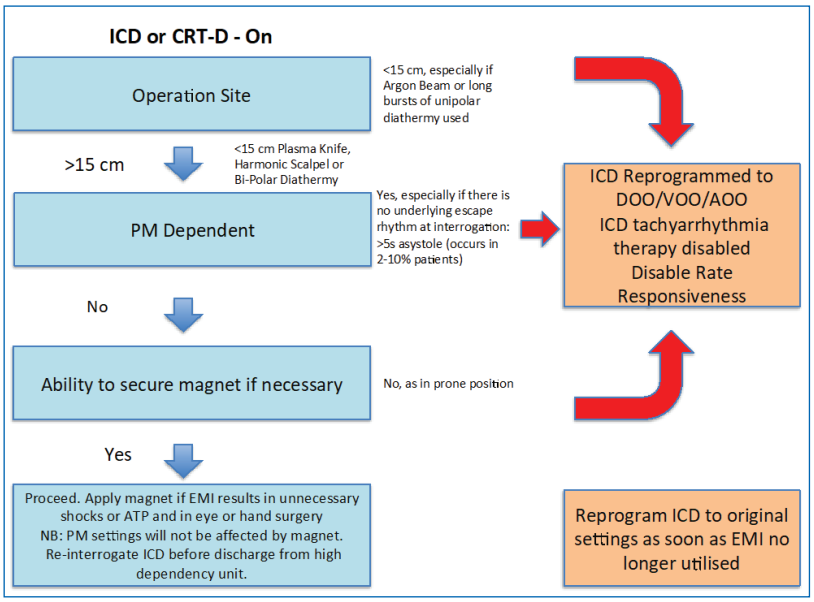

Figure 8: ICD-on algorithm

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Glossary of terms, abbreviations and acronyms

ATP – Anti Tachycardia Pacing

BOL –Beginning of Life

CIED – Cardiac Implantable Electronic Device

CRMD – Cardiac Rhythm Management Device

CRT – Cardiac Resynchronisation Therapy

EOL – End of Life

EOS – End of Service (same as RRT)

ESU – Electrosurgical Unit

ICD – Implantable Cardioverter Defibrillator

IPD – Implantable Pulse Generator

PM – Pacemaker

RRT – Recommended Replacement Time

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NW REFRESHER COURSE

The elderly with a fractured hip – analgesia

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Introduction

The rate of patients with hip fractures is increasing every decade[1] with the numbers expected to double from 2.2 million to 4.5 million between the years 2017 and 2050.[2] The elderly population represents the majority of these patients. The incidence rises exponentially with age,[3] with females being more affected than males due to Osteoporosis.[4] Almost 30% of these elderly patients suffer from some form of cognitive dysfunction[5] and other comorbidities like hypertension, diabetes, and cardiac diseases, which have been increasing over the years.[1] It must be borne in mind that the fall leading to the hip fracture might be caused by an acute cardiac or neurological event. Overall, hip fractures are associated with poor outcome with 5% of patients dying during their hospitalisation[4] and up to 10% within 30 days of the hip fracture.[4,6] Pre-existing medical conditions are the cause of death in 75% of the patients rather than the fracture itself.[1] Treatment is either by immobilization with skin traction which is becoming more and more rare, with the majority of patients receiving open reduction with internal fixation or hip arthroplasty. Mortality rate in hip arthroplasties is significantly higher where the indication for surgery is a fracture, compared to those patients who need elective hip replacements for chronic arthritic conditions, with men having a higher mortality than women.[1]

The anaesthetic role should ideally start preoperatively, with optimising the patient for surgery, along with assessing and managing pain, continuing intraoperatively, and extending into the post-operative period.

Pain assessment

Pain is subjective and health care practitioners depend on patients to report their pain, verbally in most instances. This presents a challenge in patients with cognitive dysfunction who might have difficulty in expressing themselves. The Universal Pain Assessment Tool (Figure 1) which is a commonly used pain assessment scale is very useful, but poses a challenge in the cognitively impaired. Cognitive impairment and communication difficulties are stated as the most common barriers to appropriate provision of analgesia in the elderly.[6] Fortunately, there are a number of pain assessment tools currently available for those patients with cognitive impairment that can aid in this regard. One of the scales that can be used is the Pain Assessment in Advanced Dementia (PAINAD) score[7] which is graded from 0 to 10 and simplifies managing this potentially challenging group of patients (Table 1).

Pain management

Following a hip fracture, pain is amongst the major physiological stressors that patients will face together with the blood loss associated with surgery.[8] Inappropriate management of these physiological stressors is associated with significant morbidity and mortality. Appropriate analgesics not only aid in nursing care of the patients but also in positioning during the imaging studies which are mandatory before surgery. Thus, it is important to administer appropriate forms of analgesia in all patients with suspected hip fracture as soon as they arrive in a hospital setting. In fact, analgesics should be instituted before the patients are transferred to a health care facility. This has mainly been through

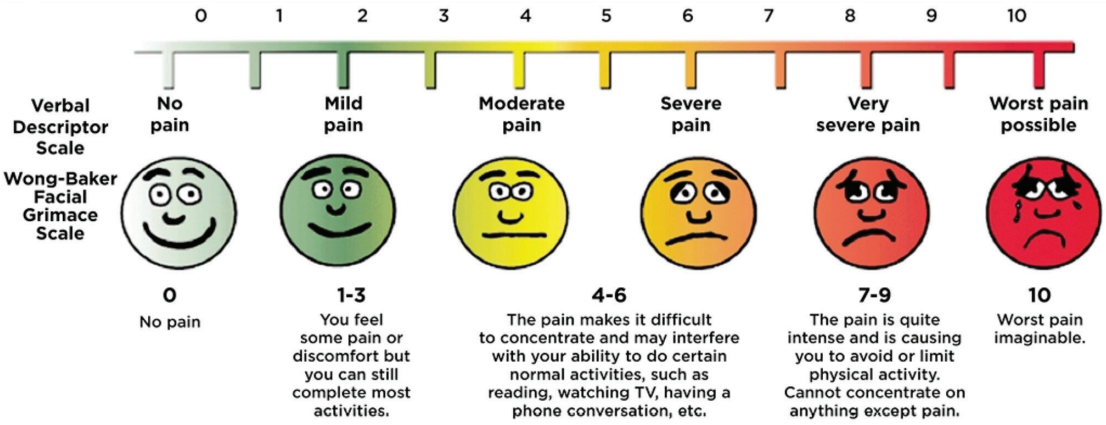

Figure 1. Universal pain assessment tool

Table 1. PAINAD scale

Pain Assessment in Advanced Dementia (PAINAD)				
	0	1	2	Score
Breathing Independent of vocalization	Normal	Occasional labored breathing. Short period of hyperventilation.	Noisy labored breathing. Long period of hyperventilation. Cheyne-Stokes respirations.	
Negative Vocalization	None	Occasional moan or groan. Low-level speech with a negative or disapproving quality.	Repeated troubled calling out. Loud moaning or groaning. Crying.	
Facial expression	Smiling, or inexpressive	Sad. Frightened. Frown	Facial grimacing	
Body language	Relaxed	Tense. Distressed pacing. Fidgeting.	Rigid. Fists clenched. Knees pulled up. Pulling or pushing away. Striking out.	
Consolability	No need to console	Distracted or reassured by voice or touch.	Unable to console, distract or reassure.	
				TOTAL

opioids which are either given orally or parenterally, but this approach is suboptimal[3] and is associated with considerable morbidity. Most guidelines recommend the use of paracetamol, opioids and the avoidance of nonsteroidal anti-inflammatory drugs (NSAIDs) because of their side effect profile, especially in this patient population, with peripheral nerve blockade being an optional extra provided the prior modalities are inadequate.[9]

Treatment options

It is well established that pain itself is a multifactorial phenomenon involving both the peripheral and central nervous system with multiple pain pathways contributing to the ultimate perception of pain.[3] Treatment therefore should follow this pattern and target the multiple implicated areas through multimodal analgesia. A comprehensive approach would involve targeting pain at tissue level, the peripheral and central nervous systems. This could be achieved with common analgesics like paracetamol, NSAIDs, opioids, local anaesthetics, and the less commonly used drugs like alpha-2-agonists, N-methyl-D-aspartate (NMDA) antagonists, anticonvulsants and antidepressants.[3] It is difficult to achieve optimal pain relief using a single drug without significant side effects, hence the combination of different drugs at lower doses, for their additive and synergistic effects.[10]

Recently, there is an increase in the use of peripheral nerve blockade throughout the perioperative period.[11] This includes, but is not limited to, femoral nerve and fascia iliaca blocks for patients with hip fractures. Neuraxial blocks are also an option, with the setback for intrathecal injections being motor blockade and the need for intensive monitoring, which makes titrated epidural injections more desirable, especially because their use can extend into the postoperative period. Regional anaesthesia has a myriad of advantages, which include less sedation resulting in patients being more cooperative, further aiding postoperative rehabilitation. Motor blockade with peripheral nerve blockade can pose a challenge to postoperative mobilisation. However, this can be minimised by the use of lower local anaesthetic drug concentrations. Pure sensory nerve block like the lateral femoral cutaneous nerve block does preserve motor function, but alone it is inadequate to treat hip fracture pain.

Unfortunately there is limited evidence comparing the different pain management interventions that are currently available in terms of effectiveness, benefits and adverse events.[12]

Conclusion

In a nutshell, it must be acknowledged that hip fractures are painful. Patient profile, especially the impaired cognition aspect, may make it difficult to assess this, but it is the health care providers' responsibility to equip themselves with at least one pain assessment tool for this population group. With the array of treatment options available, pain associated with hip fracture and its surgery is manageable. Adequate pain management spanning from preoperatively through to the rehabilitation period avoids cardiopulmonary and mental state complications, restoring ambulation and independence.[12] Above all, adequately treating pain is a humanitarian obligation.

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NW REFRESHER COURSE

A practical approach to perioperative anticoagulation

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More than half of US citizens over 65 consume drugs impacting coagulation on a chronic basis. This excludes those using non-prescribed supplements and herbal preparations. About two thirds of agents impact platelet function. The remainder fall in the category of anticoagulants. Novel oral anticoagulants (NOACs) are also known as direct acting oral anticoagulants (DOACs) and are newer additions to our current armamentarium of heparin, LMWH, pentasaccharides and warfarin. NOACs provide more efficacious anticoagulation than current agents with a lower incidence of major and life threatening bleeding. Of the NOACs currently available in SA, rivaroxaban and apixaban are factor Xa inhibitors and dabigatran is a thrombin (Factor II) inhibitor. Although there are some differences between NOACs in this respect, the range of indications for NOACs continues to expand and includes:

1. VTE (venous thrombo-embolism) prophylaxis in orthopaedic and general surgery
2. Treatment and long term prevention of VTE – DVT or PTE – in medical and surgical patients
3. SPAF (stroke prevention in atrial fibrillation)
4. Anticoagulation for any indication in patients with current, or a history of, HIT (heparin induced thrombocytopaenia)
5. Anticoagulation in acute coronary syndromes, percutaneous coronary interventions (PCI), stents and stable coronary artery disease

Commencement of anticoagulation for postoperative prophylaxis rarely poses challenges beyond choice of an appropriate drug and dose for the patient demographic and health profile and timing of initiation, based on surgical bleeding risk. As a general rule, for effective VTE prophylaxis with acceptable bleeding risk, the t_{max} of the anticoagulant should not be achieved < 8 hours after surgery (commencement > 6 hours post-surgery) nor > 24 hours after surgery (commencement on the morning after surgery).

It is the patients on long-term anticoagulation presenting for surgery, particularly urgent or emergency surgery (whether or not related to bleeding), and those bleeding intra- and postoperatively that produce our major challenges. It is important to note that the mere presence of the drug does not imply that bleeding will occur, nor that bleeding that occurs relates to the drug. However, several factors increase the likelihood of drug related bleeding and complicate management of such bleeding:

1. The clinical duration of effect of the drug being taken (warfarin > fondaparinux > dabigatran > rivaroxaban > apixaban)
2. The dose of drug being taken and overdosage
3. Temporal proximity of the dose to the surgical procedure
4. Combinations of agents impacting coagulation
5. Organ function, particularly renal (greatest impact on dabigatran)
6. Age
7. Lean body mass
8. The nature of the surgery

WHICH DRUG IS ON BOARD?

DRUG	ACTION	HOW TO MEASURE	CLINICAL DURATION OF BLEEDING RISK
Heparin / LMWH	Anti II / Xa	aPTT; aCT; anti Xa activity	4 – 24 hours
Warfarin	Anti II / VII / IX / X	INR	3 – 7 days
Dabigatran (Pradaxa)	Anti II	aPTT etc – non-linear	24 – 48 hours
Rivaroxaban (Xarelto)	Anti Xa	INR – non-linear	18 – 36 hours
Fondaparinux (Arixtra)	Anti Xa	Anti Xa activity; INR – non-linear	1 – 3 days
Aspirin	Anti-platelet	Bleeding time; PFT	3 – 7 days
Clopidogrel / Ticagrelor	Anti-platelet	Bleeding time ; PFT	3 – 7 days

When dealing with true emergency surgery, in the absence of antidote availability (idarucizumab for dabigatran; andexant alpha for Xa inhibitors or ciraparantag for both), there is little that can be done to reverse drug effect. We need to ensure open lines of communication to the laboratory and blood bank, use point of care monitoring, have procoagulants available, defend the clotting milieu (temperature, calcium, etc.) and encourage limited and meticulous surgery.

With less emergent surgery, we can consider several factors to mitigate both the risks of thrombotic events and of major bleeding[1]:

1. The gravity of the indication for anticoagulation (active/recent VTE; high grade thrombophilia; artificial mitral valves; AF with high CHADS-VASC score) – hence the need for perioperative anticoagulant cover
2. The bleeding risk of the envisioned surgery
3. The clinical duration of effect of the drug on board
4. Safe discontinuation interval for anticoagulants
5. Age and co-morbidity
6. Bridging strategies
7. Anticoagulant reversal
8. General/non-specific prothrombotic strategies
9. Appropriate perioperative monitoring

The strength of indication for anti-coagulant in atrial fibrillation is described in terms of the CHA_2DS_2-VASc scoring system. A score of 2 or more mandates life-long anticoagulation.

Figure 1 below summarises the recommendations for pre-procedural discontinuation of NOACs to ensure no residual anticoagulant effect.

In situations where the clotting risk is considered high to prohibitive but the bleeding risk of the procedure is also significant, it is considered prudent to use shorter-acting anticoagulants as **bridging** options in the perioperative period. These situations include the active phase of VTE treatment (within about 3 weeks of the acute event), mechanical mitral valves, severe thrombophilias with strong clotting history and AF with high risk scores. As a general rule, if we employ the principle that we should wait 2–3 half lives of clinical effect to ensure insignificant anticoagulation, no bridging is required with heparins, LMWH or NOACs. **The risk of a thrombotic event during drug interruption is lower than that of a bleeding event from bridging.** Bridging of NOACs must, however, be considered if there is a prohibition on oral medication intake in the postoperative period. In this instance, LMWH is recommended in a prophylactic dosing regimen (e.g., enoxaparin 40 mg s/c daily), with the first dose corresponding to the next due dose of NOAC and the final dose of LMWH 24 hours before the first postoperative dose of NOAC. No overlap is required on resumption of NOAC treatment. Warfarin therapy with its long duration of clinical effect does, however, require bridging. The recommended approach with warfarin is as follows:

- Stop warfarin 4–7 days prior to surgery
- Following day, LMWH 0.5–1 mg/kg lean body mass bid (or equivalent in IU/kg). Lower dose with maintenance anticoagulation for VTE or AF; higher dose for the obese, mechanical mitral valves and active VTE
- Last dose the night before surgery (at least 12 hours pre-op) plus measure INR – if normal:
- Proceed with surgery
- Resume LMWH > 6 but < 12 hours postoperatively

Table 1: Stroke and bleeding risk stratification with the CHA_2DS_2-VASc and HAS-BLED schemas

CHA_2DS_2-VASc	Score	HAS-BLED	Score
Congestive heart failure/LV dysfunction	1	Hypertension i.e. uncontrolled BP	1
Hypertension	1	Abnormal renal/liver function	1 or 2
Aged ≥75 years	2	Stroke	1
Diabetes mellitus	1	Bleeding tendency or predisposition	1
Stroke/TIA/TE	2	Labile INR	1
Vascular disease [prior MI, PAD, or aortic plaque]	1	Age (e.g. >65)	1
Aged 65-74 years	1	Drugs (e.g. concomitant aspirin or NSAIDSs) or alcohol	1
Sex category [i.e. female gender]	1		
Maximum score	**9**		**9**

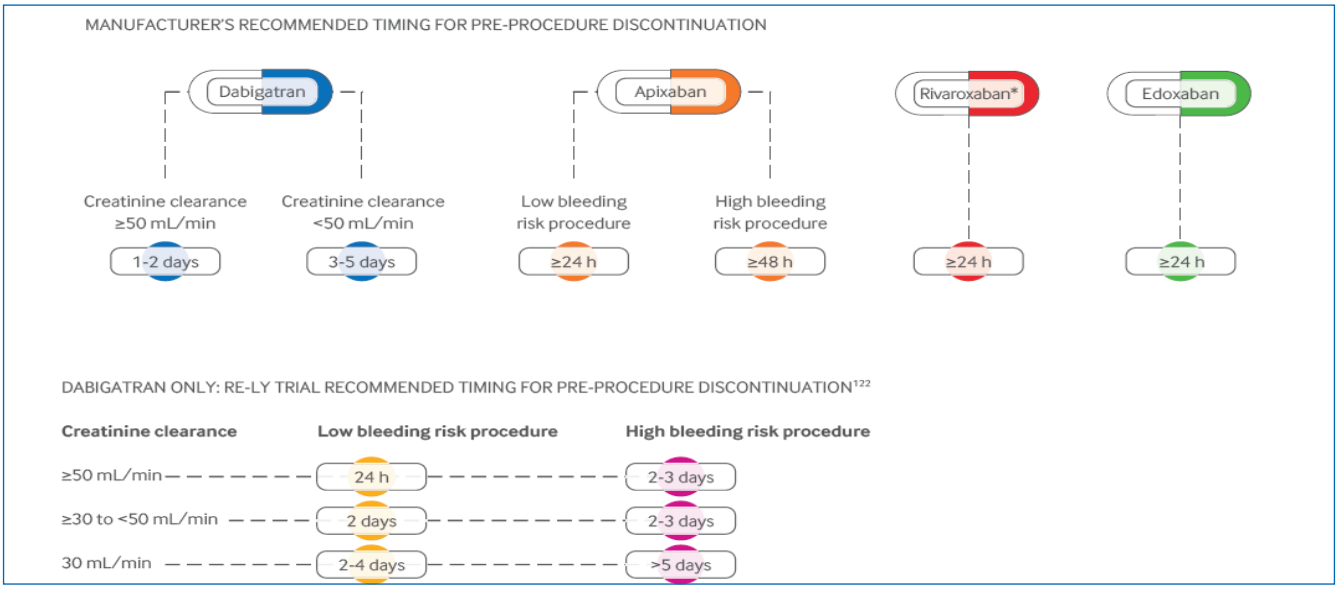


Figure 1

- Resume routine warfarin dose when feasible
- Stop warfarin, measure INR – if therapeutic:
- 2 day crossover with LMWH
- Measure INR on day 3 of warfarin therapy and, if therapeutic, suspend LMWH
- Otherwise continue LMWH and check INR daily, suspending LMWH when INR therapeutic

Reversal of anticoagulants may be necessary under the following circumstances[2]:

1. Surgery to manage a consequence of excessive anticoagulation
2. Significant intra- or postoperative bleeding as a proven consequence of anticoagulant therapy
3. Emergency surgery with a high bleeding risk, particularly in patients with a non-critical indication for anticoagulation
4. Effective reversal strategy available.

Reversal of agents except warfarin is rarely necessary or appropriate in the absence of bleeding, given that the surgery can be delayed for 2–3 drug (or drug effect) half lives. Warfarin is, however, frequently implicated in bleeding complications necessitating surgical intervention, because of its variable and fluctuating therapeutic effect, drug and food interactions, long duration of clinical effect and the relatively high concentrations of factor VII present in and required for haemostasis in the GIT and CNS. Depending on the urgency of surgery, severity of bleeding and degree of derangement of the INR, a variety of reversal options for warfarin are available. The following guidelines assist in management of warfarin-induced hypocoagulability:

- In the absence of bleeding or imminent surgery, an abnormal INR can be managed merely by omitting warfarin doses and regular INR assessment until the patient reaches the upper limit of the target INR range. Warfarin can then be resumed and a dosage titration carried out against regular INR assessments. This avoids the hypercoagulability that is inevitable with reversal.
- The presence of significant haemorrhage mandates a combination of IV vitamin K and prothrombin complex concentrate (PCC) – in SA this is marketed as Haemosolvex – or fresh frozen plasma to achieve an INR around or below 1.6. The doses of the drugs/agents are determined by the severity

Anticoagulant	Reversal agent
Heparin	Protamine sulfate
	Protamine sulfate is strongly basic and combines with acidic heparin forming a stable inactive complex
	1mg per 100 units of heparin, *not to exceed 50 mg*
	Max infusion rate - 5mg/min
	Check aPTT 5-15min after initial dose and then at 2-8 hours
Enoxaparin	Protamine sulfate
	1mg per mg of enoxaparin if last injection <8hrs 0.5mg per mg of enoxaparin if last injection >8hrs 0.5mg per mg of enoxaparin if bleeding persists after 4 hours of first dose
	Single dose not to exceed 50mg
	Max infusion rate – 5mg/min
Warfarin	4F-PCC (KCentra, Octaplex)^
	If INR 2 to <4 25 units/kg; *not to exceed 2500 units*
	If INR 4 to 6 35 units/kg; *not to exceed 3500 units*
	If INR >6 50 units/kg; *not to exceed 5000 units*
	Single dose only OR If 4F-PCC is not available Fresh Frozen Plasma: 10-20mL/kg*
	PLUS
	Vitamin K: 5-10mg IVPB (20-60 minutes) with either PCC or FFP
	Repeat INR in 30-60 minutes after administration
Fondaparinux	4F-PCC (KCentra, Octoplex)^*
	50 units/kg; *not to exceed 5000 units*
	Single dose only

Anticoagulant	Reversal/treatment options
Dabigatran	Idarucizumab (Praxbind) 50mg total dose (given as divided doses of 25mg, 15 minutes apart)
	Alternatives if idarucizumab is unavailable
	Hemodialysis
	Activated charcoal 100g po/NG if ingestion time <2 hours
	4F-aPCC (FEIBA)# 50 units/kg IV; *not to exceed 5000 units* (single dose only)
	Tranexamic acid 25mg/kg IV
	Desmopressin 0.3mcg/kg SQ or IV; limit to 2 IV doses given Increased risk of tachyphylaxis
	FFP: Not recommended rFVIIa: Not recommended
Apixaban	Activated charcoal 100g po/NG if ingestion time <6 hours
	4F-PCC (KCentra / Octaplex)#^ 50 units/kg IV; not to exceed 5000 units (single dose only)
	Tranexamic acid 25mg/kg IV
	Desmopressin 0.3mcg/kg SQ or IV; limit to 2 IV doses given Increased risk of tachyphylaxis
	Andexant alfa* 400mg IV bolus at 30mg/min followed by continous infusion at 4mcg/min for 120 minutes
	FFP: Not recommended rFVIIa: Not recommended
Rivaroxaban	Activated charcoal 100g po/NG; if ingestion time <8 hours
	4F-PCC (KCentra / Octaplex)#^ 50 units/kg IV; not to exceed 5000 units (single dose only)
	Tranexamic acid 25mg/kg IV
	Desmopressin 0.3mcg/kg SQ or IV; limit to 2 IV doses given Increased risk of tachyphylaxis
	Andexant alfa* 800mg IV bolus at 30mg/min followed by continuous infusion at 8mcg/min for 120 minutes
	FFP: Not recommended rFVIIa: Not recommended

of the derangement of INR. PCC or FFP produce a reduction in INR within 60 minutes.

- Where surgery is required for indications other than bleeding, the urgency of envisioned surgery determines the appropriate route for vitamin K administration and whether additional PCC or FFP is indicated; and the extent of INR disturbance determines the dose needed.
- Oral vitamin K produces significant reversal of warfarin toxicity in 24–48 hours and the IV route about 12 hours faster.

Reversal strategies for NOACs remain non-specific until specific antidotes and assays are available in SA. They are outlined in the following table:

It should be noted that, in correcting excessive NOAC-related anticoagulation:

- Desmopressin and tranexamic acid form part of the algorithm for reversal of excessive anticoagulation with NOACs and should be used only
  - Where urgent major/trauma surgery is envisaged and
  - The patient is bleeding clinically or
  - NOACs have been taken in the last 12 hours in therapeutic doses or
  - Renal function is significantly impaired
  - Essentially, however, they mitigate bleeding from other causes
  - PCC is recommended for more specific prophylaxis in the same situations
  - Further perioperative management of NOAC-related bleeding requires blood products guided by TEG monitoring and other specific tests (haematologist)
  - Concerns about procoagulant complications with rVIIa; FBG; PCC; products

Surgery and invasive procedures, depending on their nature and patient co-morbidity especially renal function, can be carried out safely when more than 3 half-lives of non-warfarin anticoagulants have passed or laboratory evidence reveals adequate reversal.

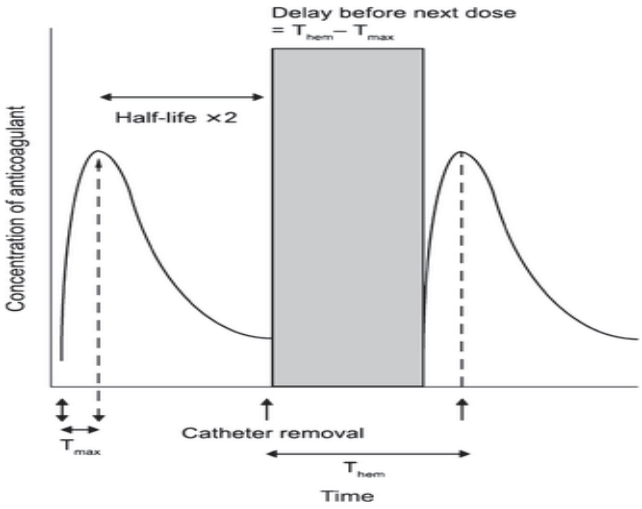
Although, in reality, seldom the domain of the anaesthesiologist, it should not be forgotten that the postoperative phase is associated with a shift in haemostatic balance towards clotting and is acknowledged to produce an incidence of VTE of 5–50% and a significant incidence in the risk and severity of adverse arterial thrombotic events compared with a non-surgical population. It is therefore absolutely mandatory, particularly in patients already at increased thrombotic risk, to resume anticoagulation and/or anti-platelet therapy as soon as safety permits and to bridge patients with short-acting. Far more patients suffer morbidity and mortality related to postoperative hypercoagulability than peri-operative bleeding. The following guidelines apply to postoperative resumption of anticoagulation:

- Stable clot is generally present 8 hours after surgery in systemically healthy patients (longer with organ dysfunction)
- Can resume the anticoagulant 1 t_{max} before this following surgery with low bleeding risk
- Higher bleeding risk surgery
  - Lower thrombotic risk patients – delay for up to 48 hours (mechanical prophylaxis)
  - Higher thrombotic risk – delay until bleeding risk is considered acceptable but bridge with LMWH, commenced > 6 hours postoperatively
- Resuming warfarin
  - If bridging indicated preoperatively, bridging also indicated postoperatively until INR is in target range

Implications for regional anaesthesia and pain therapy

The 2018 ASRA guidelines[3] have been released to expand and update guidelines and recommendations for regional anaesthesia and pain interventions in patients on all available antithrombotic and thrombolytic agents. Little has changed in terms of nature and strength of recommendations. The major highlights include:

1. Review of neuraxial haematoma reports – several case reports of provoked and unprovoked haematomas after thrombolytics; single case reports with fondaparinux and rivaroxaban. Good evidence that increased awareness of antithrombotic kinetics, guidelines and patient risk factors have dramatically reduced the incidence of haematomas since the 1999 closed claims analysis. The Rosencher model remains the reference point for calculation of safe intervals from drug to neuraxial procedure and from procedure drug resumption. Evidence (but not yet guidelines) suggests that risk decreases meaningfully from epidural catheter techniques, through single shot epidural to single shot spinal to pencil point spinal.



Rosencher model for epidural catheter removal (or neuraxial procedure in patients on chronic prophylaxis) and redosing of prophylactic anticoagulant. T_{haem} – time to formation of a stable clot – 8 hours in a normal patient

2. Inclusion of recommendations for NOACs – essentially deferring of neuraxial and deep blocks (lumbar plexus/paravertebral) and pain interventions for a minimum of 2 half-lives after prophylactic doses of oral Xa inhibitors (rivaroxaban, apixaban & edoxaban) and 3 half lives after therapeutic doses.

Anticoagulant	Recommendations to minimize risk of hematoma following regional analgesic/anesthetic procedures[a]				
	$T_{1/2}$	Anticoagulant type	AC-RA/CM	RA/CM-AC	Monitoring and precautions
Heparin (unfractionated) intravenous	1.5–2 hours	Pro-antithrombin III (anti II, X)	2–4 hours, or aPTT WNL	1–2 hours nontraumatic; 6–12 hours if traumatic	aPTT, anti-Xa/IIa, ACT
Heparin SQ BID ≤10,000 U/d	1.5–2 hours	Pro-antithrombin III (anti II, X)	None; Caution: peaks 1–4 hours postdose	No restriction	Platelets for HIT
Heparin SQ TID ≥10,000 U/d	1.5–2 hours	Pro-antithrombin III (anti II, X)	Insufficient data and caution advised, >6 hours[b]	Insufficient data (many choose nadir of effect at >6 hours[b])	Platelets for HIT
Enoxaparin (Lovenox) QD prophylaxis (0.5 mg/kg) (40 mg daily)	3–6 hours	LMWH Anti-Xa	12 hours	2 hours; 24 hours posttraumatic needle puncture	Anti-Xa–[c]
Enoxaparin (Lovenox) BID prophylaxis (0.5 mg/kg) (30 mg BID)	3–6 hours	LMWH Anti-Xa	12 hours	Not recommended with catheter. Initiate ≥2–4 hours postremoval	Anti-Xa–[c]
Enoxaparin BID therapeutic dose (≥0.5 mg/kg)	3–6 hours	LMWH Anti-Xa	24 hours	Not recommended with catheter. Initiate ≥10–12 hours postremoval	Anti-Xa–[c]
Warfarin (Coumadin)	20–60 hours	Vitamin K-dependent factor inhibition	INR ≤1.5, 4–5 days	INR <1.5	INR
Aspirin	6 hours	Antiplatelet	None	No restrictions	
Clopidogrel (Plavix)	6–8 hours	Irreversible platelet aggregation inhibitor	5–7 days; may be OK for superficial PNA SSRA without discontinuation	Not recommended with catheter. Initiate ≥2 hours postcatheter removal[b]	
Ticlopidine (Ticlid)	4–5 days	Irreversible platelet aggregation inhibitor	14 days	Not recommended with catheter. Initiate ≥2 hours postremoval[b]	
Prasugrel (Effient)	7–8 hours	Irreversible platelet aggregation inhibitor	7–10 days	6 hours	
Ticagrelor (Brilinta)	7–8.5 hours	ADP reversible receptor blocker	5–7 days	6 hours	–[d]
Abciximab (ReoPro)	0.5 hour	Glycoprotein IIb/IIIa inhibitor	48 hours	Not recommended with catheter. Initiate ≥2 hours postremoval	
Eptifibatide (Integrilin)	1–2.5 hours	Glycoprotein IIb/IIIa inhibitor	8 hours	Not recommended with catheter. Initiate ≥2 hours postremoval	
Tirofiban (Aggrastat)	2 hours	Glycoprotein IIb/IIIa inhibitor	8 hours	Not recommended with catheter. Initiate ≥2 hours postremoval	
Bivalirudin (Angiomax), lepirudin, desirudin	0.5–3 hours	Thrombin (II) inhibitor	Not recommended for neuraxial/deep-PNB Insufficient data	Not recommended for neuraxial/deep-PNB Insufficient data	aPTT
Argatroban	35–40 minutes	Thrombin (II) inhibitor	Not recommended for neuraxial/deep-PNB Insufficient data	Not recommended for neuraxial/deep-PNB Insufficient data	aPTT
Dabigatran (Pradaxa)	12–15 hours	Thrombin (II) inhibitor (oral)	4–5 days	6 hours	aPTT–[c]
Fondaparinux (Arixtra)	17–21 hours	Anti-Xa through binding to antithrombin III	3–4 days; SSRA only	Contraindicated for indwelling catheters. Initiate ≥12 hours postremoval[b]	Anti-Xa
Rivaroxaban (Xarelto)	5–9 hours	Anti-Xa	3 days	6 hours	Anti-Xa, PT–[c,d]
Apixaban (Eliquis)	10–15 hours	Anti-Xa	3–5 days	6 hours	Anti-Xa, PT–[d]

Dabigatran package insert specifically contra-indicates the use of neuraxial anaesthesia after dabigatran use. No specific recommendations are made regarding deep blocks.

3. Emphasis on the risk factors for reduced anticoagulant clearance and prolongation of half life – renal function; advanced age and low lean body mass – particularly relevant for the highly renally cleared dabigatran.
4. Emphasis that, barring those with artificial mitral valves and active thrombo-embolic disease, bridging is more harmful than beneficial and has largely been abandoned.
5. There is a shift in focus from early postoperative chemical prophylaxis to mechanical means or early mobilization in moderate to low risk procedures and patients, enhancing RA safety.

The Table on the next page summarises the delays between last anticoagulant dose and RA/neuraxial block. There are substantial differences between recommendations of various societies.

Rules of thumb include:

1. Decide on the need for/nature of the RA based on the merits of the case.
2. If the risk of not doing RA – either physiologically or in terms of pain relief – is substantial, plan to do the most superficial/peripheral possible RA.
3. If a neuraxial/deep block is essential, follow the timing guidelines/specific exclusions rigorously.
4. If the RA/deep block must be performed within an "unsafe" time period, preferentially opt for a single shot spinal anaesthetic with a small bore pencil point needle over a deep block, a deep block over a single shot epidural and a single shot epidural over an epidural catheter technique.
5. Monitoring for the development of a neuraxial haematoma (or a major deep compartment bleed) should continue for 48–72 hours after the last intervention in the neuraxis or deep compartment (irrespective of whether timing rules were followed or not). Continuous epidural analgesic techniques should be with solutions sufficiently dilute to allow monitoring of motor function.
6. Aspirin is thought not to confer added risk.
7. Informed consent regarding bleeding and possible neural compression complications of deep and neuraxial blocks should be obtained before embarking on these procedures, despite the relative rarity of these adverse events.
8. It is of the utmost importance to resume anticoagulation as soon as safe after your RA (as per Rosencher model) and, in the case of epidural infusions and very high thrombotic risk situations, to bridge with LMWH.

For a practical way of planning your RA in patients on anticoagulants, download the ASRA Coags 2.0 App

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NW REFRESHER COURSE

Two medicolegal issues of concern

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Unnatural Deaths: are we signing them off as "natural" deaths?

Health Professions Amendment Act No 29 of 2007[1]:

"Death of a person undergoing a procedure of therapeutic, diagnostic or palliative nature or of which any aspect of such procedure has been a contributory cause, shall not be deemed to be a death from natural causes as contemplated in the Inquests Act, 1959, or the Births, Marriages and Deaths Registration Act, 1963".

Regulation 359 (March 2018) of the National Health Act 2003[2]:

These Regulations are called Regulations Regarding the Rendering of Forensic Pathology Service, 2018.

"Unnatural death" for the purposes of the medico-legal investigation of death, the following shall be deemed to be deaths due to unnatural causes, as contemplated in the Inquests Act 1959 (Act No. 58 of 1959):

(a) Any death due to physical or chemical influence, direct or indirect, or related complications;

(b) Any death, including those deaths which would normally be considered to be a death due to natural causes, which may have been the result of an act of commission or omission which may be criminal in nature;

(c) Any death as contemplated in section 56 of the Health Professions Act, 1974 (Act No. 56 of 1974) *See amendment to the Act above*; and

(d) Any death which is sudden and unexpected, or unexplained, or where the cause of death is not apparent.

Unnatural Deaths in Health Establishments[2]:

1. A person in charge of a health establishment, where a person has been declared dead and the cause of death appears to be due to unnatural causes must:

   (a) Immediately notify the South African Police Service and the Service of such death;

   (b) Preserve, provide access to and or make available of all the relevant medical paraphernalia, exhibits and applicable specimens, especially biological fluid specimens in the case of suspected toxicology cases;

   (c) Ensure access to and availability of all the deceased's full medical records including laboratory and investigative reports;

   (d) Not hand over the body or items referred to in paragraphs (b) and (c) to an undertaker;

2. The medical records and or relevant completed clinical forms must accompany the deceased to the designated facility.

The patient using/abusing Anabolic Steroids…..is he/she at risk for sudden death postoperatively?

An increasing number of young people are taking performing enhancing drugs, particularly regular gym attendees and recreational body-builders. The commonly used anabolic steroids comprise two main groups of drugs: the 17α alkyl derivatives taken orally, and the parenteral 17β-ester derivatives.[3]

These agents may have the following effects, which may impact on anaesthesia[3]:

1. Cardiovascular:
   - Hypertension
   - Left ventricular hypertrophy (resulting in diastolic dysfunction);
   - Irreversible focal myocardial fibrosis (may act as a focus for malignant arrhythmias);
   - Atheromatous coronary artery disease as a result of an abnormal lipid profile.

2. Blood components:
   - Polycythemia
   - Hypercoagulopathy (may result in cerebral thrombosis, left ventricular mural thrombus, thrombosis in peripheral arteries)

3. Hepatic:
   - Liver dysfunction
   - Hepatotoxicity

4. Large muscle mass and high caloric intake:
   - May lead to increased oxygen consumption and carbon dioxide production.

5. Neuropsychiatric effects, which may modify behaviour, as well as emergence from anaesthesia.

When assessing these patients preoperatively, it is important to check if they are also taking nutritional supplements and "accessory" drugs, such as ephedra, insulin, diuretics and growth hormone.[3]

Thus, despite a young body builder being assessed as an ASA 1 patient, if he/she is using or abusing anabolic steroids and other drugs, the anaesthetic may be fraught with problems.

1. No 29 of 2007: Health Professions Amendment Act 2007

2. No R359. No 61 of 2003: National Health Act

3. Kam PCA, Yarrow M. Anabolic steroid abuse. Anaesthesia. 2005;60:685-92.

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A Practical Approach to Anaesthesia for the Child with Musculoskeletal Disease

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This article aims to provide the reader with a practical and brief approach to managing or avoiding the many issues associated with anaesthesia for children with a muscular or skeletal abnormality or disease.

The disorders mentioned in this note are some of the more common to present for anaesthesia management. They are not comprehensively described below, instead, the major areas of concern for anaesthesia providers are set down in each case.

Cerebral Palsy

Cerebral palsy is a non-progressive encephalopathy which manifests as varying degrees of motor, sensory and intellectual deficit. It is estimated to affect approximately 1 in 500 live births and (contrary to much belief) is related to an intra-uterine event during foetal development in around 80% of cases. Of all cases of CP identified, birth complications make up less than 10% of all causes and no cause is ever identified in around 30% of cases.

Most children suffering from CP will have an increase in muscle tone and much of the surgical work done involves mitigating the effects of spasticity.[1]

Main Areas of Concern

Neurological System and Sensation

- Many CP children have impaired vision or hearing. Cognitive deficits are common, and they are frequently unable to understand or make themselves understood. They require sensitive and compassionate handling and bright lights, rapid changes in environment, loud noises and large groups of people are to be avoided.
- Spastic posturing often makes for difficult IV access; scoliosis similarly complicates regional anaesthesia.
- Many of these children are epileptic and are typically quite brittle. The omission of medications prior to surgery is to be avoided.

Gastrointestinal, Nutritional and Respiratory

- CP children frequently manifest difficulties with swallowing and gastro-oesophageal reflux which complicate their feeding. They are prone to clinical or subclinical aspiration and often have poor respiratory function and frequent chest infections.
- Another result of the poor feeding performance is that they are frequently undernourished (despite the best efforts of the caregivers) resulting in low muscle and body fat bulk. Care must be taken to ensure adequate warming during anaesthesia, and careful history around feeding as well as current respiratory health must be taken.
- Finally, a tendency to more bleeding is frequently mentioned, particularly in the severe malnourished CP child. Care and attention to the application of tourniquet where applicable and vigilance for uncontrolled haemorrhage is important.

Polypharmacy

- CP children are frequently on a number of medications which may include anticonvulsants, antispasticity medications, antireflux medications and even behavioural modifiers. Drug interactions should be carefully considered.
- Anaesthesia drug effects are unpredictable. Children with severe deficits and those receiving anticonvulsants may have a considerably decreased MAC. Chronic respiratory disease may increase sensitivity to depressant medications, such as opiates and sedatives.[2]

Dwarfism

Children with abnormally short stature frequently present for surgery either related or unrelated to their underlying problem. Achondroplasia is the commonest heritable form of dwarfism and affects around 1:7500 individuals.[3]

Main Areas of Concern

Airway Management

- All dwarfism is noted to present an airway of increased difficulty ranging from mildly increased in the case of achondroplasia to massively difficult in the case of the mucopolysaccharidoses.
- Abnormalities include abnormal facial anatomy causing poor mask fit, macroglossia and micrognathia, tracheal stenosis and abnormal laryngeal anatomy.
- Great care must be taken in examining the airway and planning airway management ahead of time. A second pair of experienced hands to assist will also be essential should more advanced manoeuvres prove necessary.
- Instability of the cervical spine features prominently in dwarfism and as little as possible manipulation should be performed.

Sleep Apneoa and Respiratory Function

- Most forms of dwarfism suffer from some degree of sleep apnoea. In the case of achondroplasia, this is thought to be related to pressure as a result of the smaller than usual space afforded the medulla and is of the central apnoea type. In other forms, macroglossia and abnormal airway anatomy predispose to the usual obstructive type sleep apnoea.
- In both cases, care must be taken when dosing medications which worsen sleep apnoea.

Skin, MSK and regional

- Achondroplasia may cause excess thick skin which may make IV access difficult.
- Careful positioning may be necessary to avoid the formation of abnormal pressure points.
- Regional anaesthesia is an attractive option in these patients, however titratable methods such as epidural are favoured, and while peripheral regional anaesthesia is certainly possible, anatomy may make this route considerably more challenging than usual.[4]

Osteogenesis Imperfecta

Osteogenesis imperfecta is the commonest heritable skeletal dysplasia and affects around 1 in every 20 000 people. Most OI involves some aberration in the formation of type I collagen.

Main Areas of Concern

Airway and Handling

- As with the dwarfism syndromes, considerable care should be exercised when manipulating the cervical spine and jaw as they are prone to dislocation and fractures.
- All joints are prone to subluxation and bones can fracture with minimal force. Great care must be taken when transferring to and from the operating table and padding pressure points.

Cardiac anomalies

- As collagen is the foundation of the fibrous cardiac skeleton, cardiac disease has an increased frequency in OI. Valve regurgitation is common as well as dilatation of the aortic root. These problems are infrequent in children with the disorder, however.

Bleeding

- Platelet related bleeding and clotting factor deficiencies have both been observed in patients with OI. Avoidance of anticoagulant medications seems sensible.
- Cryoprecipitate, factor concentrates and platelet infusions have all been tried with some success.

Hyperthermia

- Another reported complication of anaesthesia in OI is the "malignant hyperthermia-like" syndrome of hyperthermia and hypermetabolism.
- While there is not an association between true MH and OI, there is an increased propensity of these patients to manifest in a similar fashion.
- Pathogenesis of this feature is unknown but suggested mechanisms involve abnormal central temperature regulation, abnormal muscle metabolism (CK levels are raised in patients with this problem) and a potential link to abnormal thyroid function (elevated thyroid hormone concentrations in 50% of OI).
- Current evidence supports the avoidance of MH trigger agents, and treatment as for malignant hyperthermia seems reasonable if this complication arises.[5]

Muscle Disorders

This section is potentially larger than all the sections which have come before in this article. Each of the disorders mentioned below has its own peculiarities and particular features, symptoms and signs. In the interests of applicability, however, they will be treated together as a group to give a unified "catch-all" approach to the management of a child with a suspected or known muscle disorder.

This section includes a practical guideline for the following muscle disorders:

- Beckers and Duchenne muscular dystrophies (dystrophinopathies)
- Congenital myopathies (Central core, mitochondrial, multicore, mini-core and nemaline rod)
- Myotonias (Dystrophic and Congenital type)[6]

The following points are appropriate in all children:

1. Children with no previous medical history must be regarded as potentially having a muscle disorder and the features which are suggestive must be actively sought. **Table 1** includes common findings which should raise suspicion of a muscle disorder.
2. Children with a known muscle disorder will frequently not be able to name their disorder, nor will their parents.
3. A serum creatine kinase is extremely useful in guiding management of these cases
4. Muscle diseases almost always affect the cardiac and respiratory systems, and energy metabolic processes are frequently also involved.

Table 1 - Clinical signs and symptoms associated with muscle disease, adapted from Brandom, B (2013)

Family History	Muscle disease in the family
Personal History	Hypotonia
	Arthrogryposis
	Delayed motor development
	Painful muscle cramps
	Dark urine following exercise or anaesthesia
Examination	Firm enlarged calves
	Contractures
	Amyotrophy
	Myopathic facies
	Walking like a duck
	Tachycardia at rest
Investigations	Asymptomatic elevated CK or AST
	ECG – conduction abnormality

Main Areas of Concern

Potential for malignant hyperthermia or anaesthesia-induced rhabdomyolysis

- It should be noted that of children who manifest a hyperpyrexial or rhabdomyolytic episode under anaesthesia, less than 10% give a family history of such an issue and 50% of such patients have undergone at least 2 previous anaesthetics with trigger agents without incident. Such history is, therefore, no guarantee of safety.
- It is reasonable that all children with a known or suspected muscle disease should undergo a trigger agent free anaesthetic with a clean anaesthetic machine. This should include all children with an elevated serum CK unless a plausible alternative cause is found.
- It is reasonable that all children with any form of known or suspected muscle disease should NOT receive suxamethonium.
- Unless the child in question is known to have a condition that is strongly associated with either AIR or MH. A gas induction with sevoflurane is reasonable before converting to a total intravenous technique.
- Anaesthesia providers should familiarise themselves with the appropriate action should an attack of MH/AIR be suspected. In particular, surgery must be terminated, dantrolene administered, intensive care informed. As little as possible delay should be allowed before critical care is instituted.
- Temperature management should aim for normothermia at all times. It is tempting to avoid active warming in order to aid in identifying hyperpyrexia, but low temperatures are harmful and particularly so in myotonias where they reliably precipitate spasms.

Cardiovascular Disease

- As mentioned above, cardiovascular and respiratory complications are frequently encountered in these children.
- Cardiac manifestations can range from abnormally high resting heart rate to full-blown cardiac failure and arrhythmias.
- Cardiac disease can occasionally be more marked than the accompanying muscle disease.
- Avoidance of negatively inotropic drugs and a low threshold for CVS support is recommended.
- Dystrophinopathies are particularly notable for their CVS manifestations and this can even include female carriers of the gene (who also have an elevated CK).

Respiratory Compromise

- As a result of muscle weakness involving the respiratory system, these children manifest frequent chest infections and may have a poor cough.
- Subclinical aspiration due to poor pharyngeal muscle function has been seen. Sleep apnoea is also a consideration.
- Preoperative workup should include chest X-rays, pulmonary functions as appropriate and night oximetry to detect sleep apnoea if suspected.
- Postoperative ventilatory support should be considered in major surgery or severely affected individuals

Other systems

- Gastrointestinal tract issues are also frequently seen with most of the diseases mentioned above which may complicate postoperative nutrition.
- Carbohydrate intake and energy balance must be carefully controlled particularly in the mitochondrial myopathies and periodic paralyses.
- Muscle disorders are associated with dysmorphisms and other congenital abnormalities which should be considered, particularly the challenges they might add to airway management.[7,8]

In conclusion, musculoskeletal disorders are an inhomogeneous group of conditions, each of which brings distinct challenges to the anaesthesia provider. Although far from comprehensive, it is the author's hope that this note will serve as a useful guide in the practical management of these children during the many anaesthetics they will certainly require in their lifetime.

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Opioid Free Anaesthesia: a paradigm shift

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Introduction

Opioids have been the cornerstone of analgesia under anaesthesia since the 1960's and were introduced to provide haemodynamic stability in this setting.[1] The routine use of synthetic opioids, although rarely questioned, should be supported with evidence which favours patient outcomes in the perioperative period.[2] As physicians, best practice evidence guides our hand in rendering favourable outcomes to our patients. Therefore, it is prudent to question whether or not there are alternative methods to managing pain in the perioperative setting.

Why opioid free anaesthesia?

Opioids have served anaesthesiologists well in rendering haemodynamic stability and reduced nociception to their patients, but have also caused many complications because of their side effect profile and the candid nature with which they are used. This unconsidered use of opioids has led to the so called 'opioid crisis'.[3,4]

What is the opioid crisis?

In the United States, doctors prescribe and patients consume a staggering 80% of the world's supply of opioids despite only making up approximately 4.4% of the world's population.[5]

In just over a decade, opioid prescriptions quadrupled and opioid related deaths surpassed motor vehicle accidents as the leading cause of accidental death.[6,7]

Since the treatment of pain is constitutionally a basic human right, and costs nations millions in medical treatment and loss of productivity, there has been a pendulum swing unintentionally towards the increased use of opioids. However, this has led to the overwhelming overuse and abuse of opioids that is now deemed to be 'in crisis'.[5]

As Anaesthetists, we play an important role in the promulgation of this crisis through postsurgical pain management. Retrospective studies show that between 3% and 7% of opioid naïve surgical patients still use opioids their first year after surgery.[8,9] The risk of chronic opioid abuse is significantly increased in surgical patients when compared to non-surgical patients[10] and it is therefore the responsibility of the perioperative physician to add good governance to prescription practices so as to curve the added risk of potential addiction to postoperative patients. To reduce the burden of hospital discharge, doctors are incentivised to overprescribe post hospital opioids. This results in up to 72% of the pills prescribed going unused by general surgical patients.[11] It has been shown that this strategy leads to opioids falling into the wrong hands and exacerbates drug addiction problems.[12,13]

Therefore, opioids are under the spotlight as a leading cause of morbidity and have consequences that are not only patient specific, but affect society and the economy.

The reason behind opioids being so addictive and propagating this knock-on effect is because of the pathophysiological process known as neuroadaptation.

Neuroadaptation

The major features of opioid addiction are tolerance, withdrawal and compulsive use and relapse. These are thought to be brought about by a large range of neuroadaptations in response to chronic opioid exposure.[14]

Adaptations to opioid exposure are considered to occur at different levels in the nervous system and include:

- tolerance at the mu-opioid receptor
- cellular tolerance and withdrawal in opioid-sensitive neurons
- systems tolerance and withdrawal in opioid-sensitive nerve networks
- synaptic plasticity in opioid-sensitive nerve networks

Tolerance to opioids is characterised by a reduced clinical response to opioid agonists, manifesting as increasing dose requirements to achieve the desired effect. Mechanisms of receptor regulation appear to be enhanced as a result of *receptor* tolerance and include desensitisation and internalisation.[14]

Cellular tolerance is more complex and several processes are involved which include the upregulation of cAMP/PKA and cAMP response signalling as well as the mitogen PK cascade.[14]

The complex neuropharmacology of neuroadaptation is out of the scope of this discussion, but is important to the understanding of why opioid free anaesthesia (OFA) may offer better anaesthetic care in the face of the opioid crisis. Furthermore, neuroadaptation is just one of many consequences to opioid use peri-operatively and thereby supports efforts to seek alternative perioperative analgesic practices.

The threat of opioids

The consequences of opioid administration intra- and postoperatively are not benign or uncommon and include:

- Nausea and vomiting
- Sedation
- Ileus
- Confusion/delirium
- Respiratory depression
- Increased postoperative pain and morphine consumption[15]
- Immunodepression
- Potential hyperalgesia
- Chronic postoperative pain
- Addiction

Hypoxaemia, ileus and confusion/delirium are among the most commonly seen complications, which are associated with significant morbidity.[1]

Hypoxaemia

This is a frequent complication post-anaesthesia and occurs within minutes after extubation. Patients undergoing abdominal surgeries have a high incidence of postoperative hypoxaemia, between 20%-40%[16,17] which is attributed largely to the use of drugs such as opioids.[18] In the USA, it is well described that a large majority of closed claims are the result of severe postoperative respiratory depression occurring within the first 24 hours post-surgery.[19]

Ileus

Postoperative ileus and its sequelae are one of the most important causes of prolonged hospitalisation from abdominal surgery. This is further complicated by the use of opioids that are often needed to manage pain.[1] More serious complications of ileus include:

- Gastrointestinal perforation
- Nosocomial infections
- Malnourishment
- Muscular atrophy

Complications exacerbated by the concomitant use of opioids in patients with ileus include:

- Bowel dysfunction
- Postoperative ileus in non-abdominal procedures
- Prolonged recovery

The incidence of ileus can be as high as 10%, as shown in recent reviews and was higher when higher doses of morphine was used.[1,20]

Delirium and postoperative cognitive dysfunction (POCD)

Delirium and POCD are common in geriatric patients (5%-15% and 25%-40%, respectively), especially those coming for arthroplasty procedures. Delirium is associated with further cognitive decline that may lead to accelerated onset of dementia.[21,22] Furthermore, they are associated with a longer length of stay and discharge to monitored care environments. Overall, the incidence of 1 year mortality is higher in this patient population. Postoperative opioid analgesic practice in this group of at-risk patients is of particular concern, as the administration of intravenous opioids has been shown to significantly increase the risk of elderly arthroplasty patients developing POCD.[20] Krenk et al.[23] showed that fast track set ups that disallow for prolonged hospital stays and utilise opioid-sparing or opioid-free practice, avoids the development of delirium post operatively and hence reduces the risk of POCD and mortality.[23]

Acute tolerance/hyperalgesia

The more opioids given intraoperatively, the more the postoperative analgesic requirements: this is termed the 'opioid paradox' and can be explained through acute tolerance and neuroadaptive processes caused by short acting opioids or chronic opioid use. It has therefore been suggested by several authors that the fewer opioids given intraoperatively the less opioid will be required postoperatively, because mu-receptor integrity is maintained.[24]

Therefore, the revolutionary status that opioids have held because of their usefulness in creating a balanced anaesthetic now appears to be under duress. The rising evidence in favour of opioid restricted or non-opioid anaesthesia, although scarce, appears promising. Furthermore, in the context of enhanced recovery programmes, there is congruency and synergism with OFA that negates the negative effects opioids have had in abdominal procedures. OFA has therefore been pushed into the spotlight as a potential solution to perioperative analgesic management that extends beyond its use in only abdominal surgeries.

Opioid Free Anaesthesia

The basis of successful fast-track surgery is the use of efficacious multimodal analgesia and anaesthesia, and has been recommended for over a decade now to negate the potential deleterious effects of opioid overuse/abuse. These multimodal, opioid avoiding drug regimens aim to decrease intraoperative and postoperative opioid requirements, decrease postoperative pain, and hence hasten recovery through avoidance of potential side effects caused by opioids.[25]

Opioid-free anaesthesia (OFA) is a multimodal anaesthetic practice that utilises:

- Hypnotics
- Gabapentinoids
- N-methyl-D-aspartate (NMDA) antagonists
- local anaesthetics
- anti-inflammatory drugs
- alpha-2 agonists

The abovementioned OFA drugs were discussed in last year's North West Refresher notes and hence will not be repeated here.[26] Instead, the focus of this discussion is to inform about specific OFA protocols and debate whether we should be practicing them.

Concerns over providing haemodynamic stability with OFA are abated by evidence provided in the first studies concerning OFA, which focused on bariatric patients. The use of dexmedetomidine, was shown to significantly reduce postoperative pain and opioid requirements in this patient population, without causing respiratory depression.[27,28] Furthermore, the use of dexmedetomidine permits haemodynamic stability under anaesthesia, due to its unique spinal and supraspinal mode of action. Several studies[27,28] have gone on to show the positive effects of OFA with dexmedetomidine, which include:

- sparing of other anaesthetic agents
- improved haemodynamic stability
- reduced bleeding
- prevention of shivering
- non-delayed emergence
- attenuated postoperative pain
- reduced postoperative opioid consumption
- reduction in postoperative nausea and vomiting
- prevention and treatment of hyperalgesia

The significance of hypotension and bradycardia caused by dexmedetomidine is yet to be determined, as there is no evidence currently on the consequences of the use of alpha-2 agonists intraoperatively.[2]

Loco-regional anaesthesia also forms part of OFA principles, as they negate the need for intraoperative and postoperative opioids. Peripheral nerve blocks and epidurals improve pain management significantly. Furthermore, epidurals have been shown to prevent, independently from the use of opioids, postoperative hyperalgesia.[29] Local anaesthetic adjuncts now also include alpha-2 agonists in their armamentarium, and thus provide safer block prolongation without the unwanted side effects of opioids.[2]

Ketamine has an important role in OFA, as its use improves the management of postoperative pain, through its analgesic, anti-hyperalgesic properties and haemodynamic safety profile.[2]

To further abate concerns over providing a haemodynamically stable anaesthetic with OFA, adding magnesium sulphate to OFA protocols, is shown to not only augment the analgesic action of lignocaine and ketamine, but importantly reduces heart rate variability without causing hypotension.[2]

The abovementioned drugs form part of most OFA regimens and are not complete without the mention of intravenous lignocaine. Lignocaine use intravenously is advocated in major surgeries, especially abdominal surgeries, because of its complimentary effects to enhanced recovery programs i.e. anti-inflammatory properties, pro-peristaltic action, sympathetic blockade and acute analgesic action.

Although scarce, the available evidence advocating opioid sparing techniques is in favour of their use. However, it is not clear whether there is overall benefit to completely abdicating the use of opioids. The Postoperative and Opioid Free Anaesthesia (POFA) randomised-controlled trial is underway (NCT03316339)[1], and hopes to test the superiority of OFA techniques, but to also test non-inferiority and safety of OFA.[1]

Perhaps the most famous protocol to date is the Bruge Protocol developed at Sint Jan Bruge to treat patients coming for major bariatric surgeries.

OFA Protocol Sint Jan Brugge with Dex

Three drugs (Dex 200ug, Ket 50 mg, Lid 300 mg, add H20 to 20 ml) given at 1 ml/10 kg IBW and followed by 1 ml/10 kg IBW/h adapt to HR/MAP

- Dexmedetomidine 0,5 to 1 ug/kg IBW followed by 0,5 to 1 ug/kg IBW/h
- Ketamine 0,125 to 0,25 mg/kg followed by 0,125 to 0,25 mg/kg IBW/h
- Lidocaine 1,5 mg/kg IBW followed by 1,5 to 3 mg/kg IBW/h

Magnesium sulphate 40 mg/kg IBW followed by 10 mg/kg IBW/h

Propofol is given at 2,5 mg/kg IBW followed by inhalation anesthesia at 0,6 - 0,8 MAC with BIS around 40%.

Rocuronium 0,6 - 1 mg/kg IBW followed by infusion 1 mg/ kg IBW/h and based on TOF PTC (if NMB is needed).

Postoperative analgesia

Non-steroidal anti-inflammatory agents

- Paracetamol 2 g loading 1 g/6h
- Diclofenac 150 mg loading, 2x75 mg/day
- Or Keterolac 40 mg loading, 3 x 10 mg/day

Local wound infiltration (calculate toxic dose!)

Choice between:

- Continue with clonidine 2 x 75 ug/day or give low dose morphine

OR

- Keep infusion of sympatholytic mixture (ket dex lido Mg) at low dose without deep sedation
  - Ketamine 0,05 mg/kg/h
  - Lidocaine 1 mg/kg/h
  - MgSO4 10 mg/kg/h
  - Dexmedetomidine 0,1 - 0,2 ug/kg/h

Monitoring and ensuring safe OFA

One of the valid concerns, regarding OFA, is the lack of adequate tools to monitor nociception (sympathetic/parasympathetic balance). This, however, brings into question how accurate any nociceptive monitoring is, especially since it is not routine and anaesthetists rely mainly on the haemodynamic status to address 'pain' under anaesthesia.[24]

Noxious stimuli from surgical stress induces neuro-humoral activation and therefore cardiovascular and pulmonary effects that can be objectively monitored and documented through standard ASA monitoring under anaesthesia. This is effective in monitoring opioid-based anaesthetic practice, but is not specific to surgical stimulus and nociceptive activation exclusively.[24]

The 'pain matrix' or brain network responsible for the sensory processing of nociception and pain is associated not only with cortical activity but sub-cortical activity too, thus making it a highly complex network. Therefore, monitors such as BIS or Entropy, which monitor processed cortical EEG brain activity,

do not asses the effects of nociception. This is corroborated by Lichtner et al. who demonstrated that propofol cannot alter noxious stimuli effects at the spinal level nor at midbrain level, even at burst suppression doses.[24]

What tools do we have then, to monitor the stress response effects, when using OFA?

Autonomic system evaluation

The measurement of sympathetic activity and heart rate variability through skin conductance methods as well as surgical plethysmography index tools have shown some promise in detecting acute pain in anaesthetised patients, however their accuracy clinically has never been shown to be clinically significant.[30] More recently, a French company, Metrodoloris, has been promoting the use of the Analgesia Nociceptive Index (ANI), which is promoted as a potential tool to aid the assessment of acute nociception and pain.[24]

ANI works on the basis of raw ECG data that is derived from the use of two ANI electrodes that are applied in the V1 and V5 positions on the chest. Frequency domain-based analysis of the high frequency component of HRV combined with respiratory rate computes the ANI, which is displayed as a number from 0-100. The values reflect predominance in parasympathetic tone, with low numbers being low tone and high numbers being high parasympathetic predominance.[31,32]

Despite there being a large number of publications regarding ANI-guidance for intraoperative opioid administration, there is weak evidence supporting that it improves pain post-operatively. This makes it less likely to be useful as a tool for monitoring pain in the setting of OFA anaesthesia.[24]

Conclusion

In conclusion, the scarcity of evidence supporting the use of OFA in place of opioid based anaesthetic practice means that the obvious feasibility of OFA is not sufficient to be recommended formally. Yet, specific adverse outcomes from OFA in the literature are absent. This calls into question the added value of opioid use at all, since the use of opioids have such potential for adverse events postoperatively. The lack of research in a wide range of surgical procedures means that opioids still form the basis of perioperative analgesia, however, they have fallen out of favour in enhanced recovery programmes, due to the obvious benefits of OFA. This see-saw is where we are currently at determining the place of OFA and the POFA trial hopes to shed more light on this controversial topic.

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NW REFRESHER COURSE

Difficult paediatric airway

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Introduction

Evidence from the ASA Closed Claim Database shows that respiratory events are more common in children than adults (43% vs 30% respectively; p ≤ 0.01) with the commonest cause of morbidity and mortality due to the inability to ventilate rather than to intubate.[1, 2] Contributing factors are the anatomical and physiological differences which exist between the neonate, infant, child and adult.[3] These make the normal paediatric airway potentially difficult particularly in children under the age of one year. Repeated attempts at securing the airway may potentiate tissue trauma, bleeding and mucosal oedema which can transform an airway that can be ventilated into one that cannot (cannot intubate, cannot oxygenate situation). The difficult airway in the paediatric population is a rare (incidence of about 0.15 – 1.4 %)[4] and challenging entity, which is often devastating if inappropriately managed.

A difficult airway is defined as a 'clinical situation in which a conventionally trained anaesthesiologist experiences difficulties with facemask ventilation, tracheal intubation or both'. The recommendation is that subsequent attempts use alternate devices. This represents a complex interaction between **patient factors, the clinical setting and the skills of the practitioner**.[5]

The 1993 ASA guidelines defined a difficult intubation as 'when proper insertion of the tracheal tube with conventional laryngoscopy requires more than three attempts or more than 10 min'.[6] The 2013 updated report has revised this, and now defines difficult tracheal intubation simply as 'requiring multiple attempts'. Difficult facemask or supra-glottic ventilation is defined as an inability to provide adequate ventilation because of inadequate seal, leak, or excessive resistance to the ingress or egress of gas.[5] An alternate definition of difficult mask ventilation, is the inability of an unassisted anaesthesiologist to maintain the measured oxygen saturation as measured by pulse oximetry > 92% or to prevent or reverse signs of inadequate ventilation during positive pressure ventilation under general anaesthesia.[7] The incidence of unexpected difficult bag mask ventilation may be as high as 6%.[4,8]

Guidelines

In 2012, the Guidelines Group, supported by the Association of Paediatric Anaesthetists of Great Britain and Ireland, the Difficult Airway Society and liaising with the Royal College of Anaesthetists developed guidelines following an exhaustive process which involved a Delphi analysis and extensive literature review. They found that there was little grade 1 evidence to support good practice in the management of the difficult paediatric airway, and guidance must therefore be essentially a clinical issue. The target audience for these guidelines is the anaesthetist working in the non-specialist paediatric setting who wishes to learn or maintain paediatric airway skills, rehearse unexpected difficult airway scenarios and teach good practice.[8,9] Three algorithms were chosen based on the clinical scenarios that would benefit most from the straightforward plans:

- Difficult mask ventilation (MV) – during routine induction of anaesthesia in a child aged 1 to 8 years.
- Unanticipated difficult tracheal intubation (TI) – during routine induction of anaesthesia in a child aged 1 to 8 years (Figure 1).
- Cannot intubate and cannot ventilate (CICV) in a paralysed anaesthetised child aged 1 to 8 years.

The assumptions made are that children older than eight years of age could use the adult Difficult Airway Society (DAS) guidelines; anticipated airways are predictable and therefore can be adequately prepared for; and more importantly that practice guidelines are systematically developed recommendations that assist the practitioner and patient in making decisions. They may be adopted, modified or rejected according to clinical needs and constraints and are not intended to replace local institutional policies.[5] The question then is **do we have local institutional policies on the management of paediatric airways**?

It has been recognised that factors influencing performances can be broadly divided into those relating to **preparation** (guidelines, training, experience, consultation and planning) and those relating to **implementation** (impaired decision making, fixation, omission or failure to act and the inability of teams to function effectively) of the airway plan.

The Vortex (Figure 2) was thus developed as a cognitive tool that may be effective in reducing implementation errors of the difficult airway algorithms. The information-dense, text-based presentation of the major airway algorithms, despite being technically accurate, makes it more strenuous for teams to use the information within them during the stress and uncertainty of an evolving airway emergency. A simple, low-content, context-independent, predominantly graphic design of the Vortex

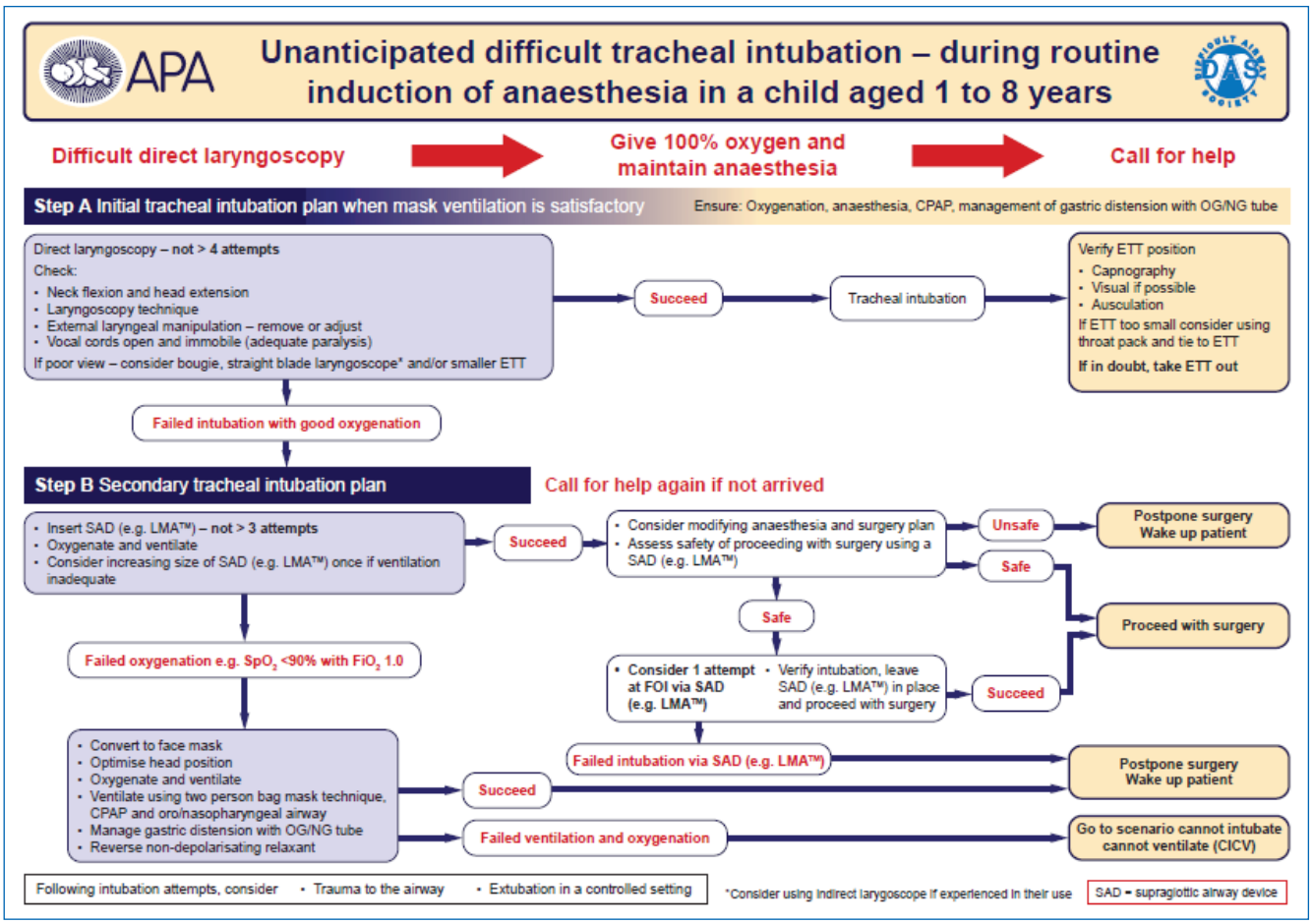

Figure 1. Unanticipated difficult tracheal intubation during routine induction of anaesthesia in a child aged 1 to 8 years

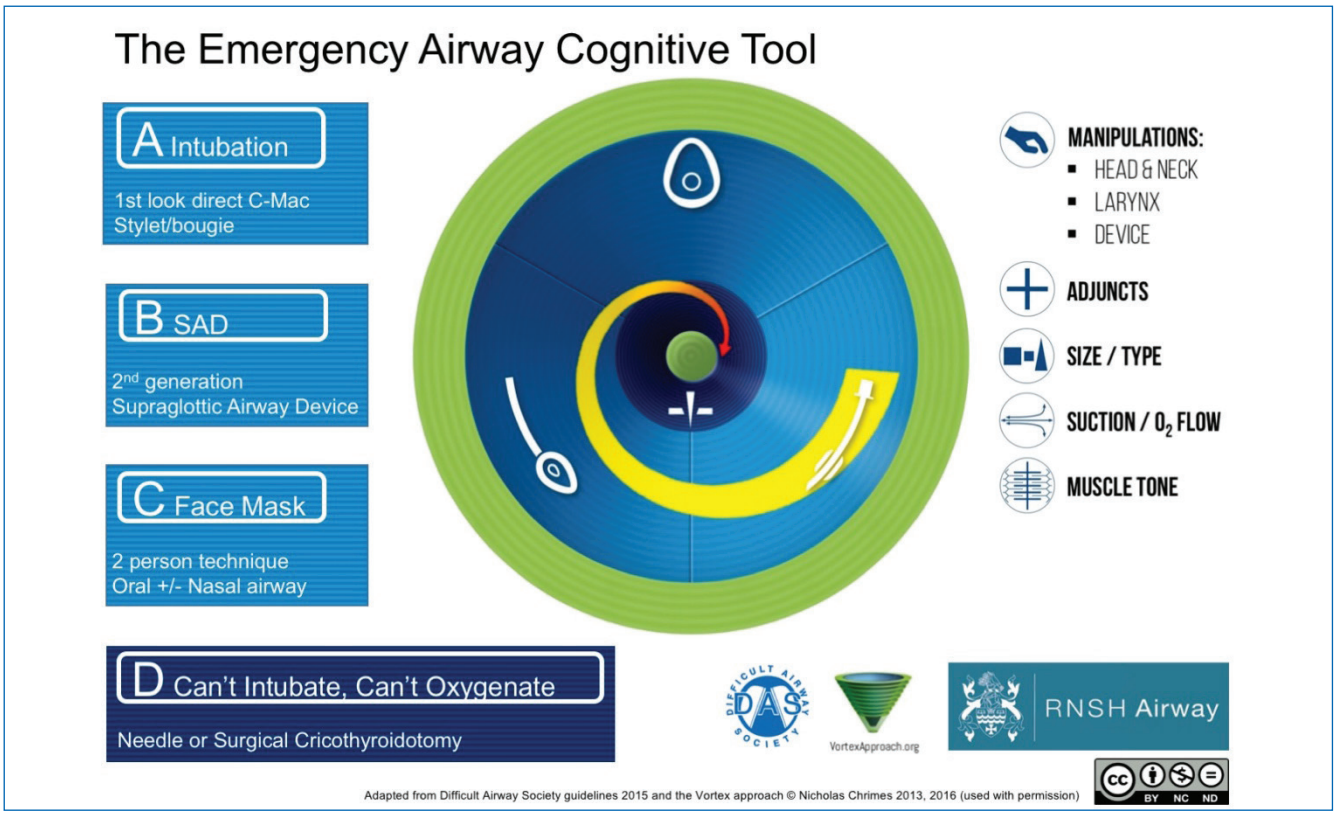

Figure 2. Vortex implementation tool (superior and lateral aspects)

Green zone – adequate alveolar oxygen delivery[11]

approach makes it more suited to real-time use during crisis situations irrespective of the clinical background of the user.[10]

Usage is based on the principle that there are three none surgical techniques to establish a patent airway: face mask, a supraglottic device, or an endotracheal tube. Inability to achieve adequate alveolar oxygenation after a best effort at any or all of the three lifelines mandates spiral movement inwards by initiating the can't intubate can't oxygenate (CICO) rescue plan, i.e. surgical airway. Any attempt at a lifeline must incorporate optimisation that has previously not been implemented in the form of manipulations (of head, neck, larynx or device), usage of adjuncts, changing sizes and types of device, usage of suction and supplemental oxygen and ensuring that airway muscle tone is not a hinderance. The Vortex should not be considered an alternative to the existing algorithms, but rather a complementary tool intended to place emphasis on a shared, simplified mental model enhancing situational awareness, team performance and minimising error.[10]

Literature around the paediatric airway

In 2011, the Fourth National Audit Project (**NAP4**) of the Royal College of Anaesthetists and the Difficult Airway Society was established with the aim of estimating the incidence of and contributing factors to major complications of airway management during anaesthesia in the United Kingdom. Some of the significant findings were: (i) more than half the patients were ASA 1-2, during elective surgery under the care of anaesthetic consultants, (ii) aspiration was the most frequent cause of mortality, (iii) many reports showed evidence of poor planning of primary and subsequent rescue techniques, (iv) cricothyroidotomy by anaesthetists was associated with high rate of failure, (v) omission or incorrect interpretation of capnography led to undiagnosed oesophageal intubation, (vi) elements of poor management were observed in the majority of airway complications and most deaths. Thus, there was a significant **'human factor'** contribution.[12] Several system recommendations were made. These included development of local intubation algorithms modified from DAS' plan with clear pathways for airway escalation, standardisation of approach and equipment, universal use of the pre-intubation checklist, universal use of the end-tidal capnography to confirm correct endotracheal placement and multidisciplinary training (anaesthesia, ED and ICU) in airway technical and nontechnical skills.

Secondary analysis of airway and ventilation management of the Anaesthesia Practice in Children Observational Trial (**APRICOT**) looked primarily at the incidence of difficult airway management, and secondarily at the associations between difficult airway management, known pre-existing respiratory risk factors and the occurrence of critical respiratory events. There was a strong association between severe respiratory critical events and the number of attempts to secure the airways, the airway management device, the presence of preoperative respiratory risk factors and young age (neonates and children < 1 year of age). Multiple tracheal intubation attempts were reported in the presence of CL grades 1 and 2, which may reflect on planning and practitioner technique. The use of video laryngoscopy was surprisingly low, indicating a poor availability of the device or a principle use as a rescue tool during unexpected difficult tracheal intubation (TI). These last 2 points (difficult TI with CL grade 1 and 2, and low use of VL) are in stark contrast to the findings of the PeDI study.[13]

While APRICOT was enrolling patients in Europe, the **Pediatric Difficult Intubation (PeDI)** registry was collecting data on > 2000 difficult airway events from the USA. Both APRICOT and PeDI found an increased likelihood of airway difficulty in younger children (particularly < 1 year of age). They also noted significantly increased respiratory events in patients with 3 or more attempts at intubation, suggesting the morbidity may be decreased by reducing the total number of tracheal intubation attempts.

The multicentre PeDI registry tried to characterise risk factors for difficult TI, establish success rates of various techniques, catalogue the complications associated with difficult TI, and establish the effect of more than 2 TI attempts. The most frequently attempted first TI techniques were direct laryngoscopy (46%), FOB (28%) and indirect video laryngoscopy (18%), with first attempt success rates of 3%, 54% and 55% respectively. The most severe complication was cardiac arrest (which occurred in 2%). Temporary hypoxaemia was the most frequent non-severe complication. Interestingly oxygen was rarely given during tracheal intubation attempts. 80% of difficult tracheal intubations were anticipated which allowed for appropriate planning. The occurrence of complications was associated with more than 2 TI attempts, a weight < 10 kgs, short thyromental distance, abnormal airway physical examination, and 3 direct laryngoscopy attempts before an indirect technique.[14] Suggestions from the study were:

1. Practitioners should 'actively pursue opportunities to deliver supplemental oxygen throughout the process of difficult airway management'. Preoxygenation is practised but few (10% in PeDI registry) oxygenate during the attempt. When hypoxaemia occurs during TI the intubation attempt is interrupted to ventilate and oxygenate the patient. Passive oxygenation should be instituted.
2. Derive and implement a standardised airway checklist.
3. Transition to the most experienced clinician should happen quickly.
4. Use extraglottic airway device early.

A sub-analysis of the PeDI registry looked at video laryngoscopy (VL) versus fibreoptic bronchoscopy (FOB) intubation through a supraglottic airway device (SAD) in children with a difficult airway. The main finding was that FOB-SAD and VL have similar rates of first attempt success in children with difficult airways. However, FOB-SAD as the first technique was associated with significantly fewer intubation attempts and changes in airway management strategies, as demonstrated by a higher overall success rate. Furthermore, in infants < 1 yr, FOB-SAD had a significantly higher success rate (54%) compared to VL (36%). Hypoxaemia was significantly less common during FOB-SAD technique when

continuous ventilation was used throughout the intubation attempt. Where both these techniques failed, tracheal intubation was eventually achieved with DL, FOB without SAD, flexible FOB with video laryngoscopy, rigid bronchoscopy and very rarely a surgical airway was required.[15]

Some recommendations are that the paediatric specific guidelines from DAS should be updated to emphasise:

1. Children < 10 kg represent a high risk population. In this population supplemental oxygen should be considered.
2. Direct laryngoscopy (DL) should be limited to less than 2 attempts with an early transition to an advanced alternative airway technique (e.g. VL, FOB with or without SAD).
3. A SAD should be readily available and inserted if difficult ventilation is encountered, or if rescue oxygenation is needed.
4. Structured teaching and practice (e.g. simulation) with advanced airway devices should take place in normal patients.[16,17]

Approach to difficult airway[18]

Assessment

Recognising the patient with a potentially difficult airway is an opportunity that allows you to prepare ahead with appropriate equipment, personnel and a backup plan. Many methods exist for evaluating and predicting difficult airway in adults; no comparable methods have been forthcoming in children. Characteristics that may warn one of a difficult laryngoscopy and intubation include (Table 1):

- specific syndromes
- maxilla-facial malformations
- anomalies of the mouth, tongue or teeth
- cervical spine pathologies
- oropharyngeal space occupying lesions [19]
- previous history of difficult airway.

The lower airway passages can be accessed via the mouth, nose or neck. The most viable options should be reviewed. Thereafter can you align the 3 airway axes (oral, pharyngeal and laryngeal axes) sufficiently to bring the larynx into view if direct laryngoscopy is the plan of choice. Perhaps even more important than recognising a challenging intubation, is identifying the patient who will be difficult to ventilate

Teamwork and communication

Key factors in making problem solving and crisis management successful is teamwork and communication. One needs to take stock of the situation and self, there needs to be a co-ordinated team effort with a shared mental model. Everyone needs to know what the problem is, the intended plan in resolving it and what their individual role is going to be. As part of the team, there needs to be an individual dedicated to situational monitoring, i.e. patient condition, vitals and time lapse during attempts.

Figure 3. Patient for cardiac surgery with undiagnosed syndrome with features suggestive of difficult airway

Table 1. Predictors of an expected difficult airway[4,19]

Predictors of an expected difficult airway	
Soft tissue pathologies	Tumours Abscess Scars Post radiation therapies Burns, trauma
Maxilla-facial malformations	Hypoplasia of the mandible Retrognatia/micrognatia Facial asymmetries (including ear anomalies) Mandibular joint ankyloses (reduced mouth opening)
Mouth, tongue and teeth anomalies	Microstomia Macroglossia Cystic hygroma Overbite
Cervical spine pathologies	Reduced movement, e.g. Klippel-Feil syndrome Instability, e.g. Downs syndrome, rheumatoid arthritis, mucopolysaccaridosis
Airway obstruction	Obstructive sleep apnoea Stridor Infective processes, e.g. epiglottitis, laryngotracheitis, abscess Bleeding post tonsillectomy Anaphylaxis Airway foreign body
Specific syndromes, e.g. Pierre Robin, Treacher Collins, Goldenhar	
History of difficult airway	

Careful documentation of all measures taken during the airway management should be detailed in file, and patient or parents notified of pertinent facts.[18]

Planning (PREPARE FOR FAILURE)

Intubation is usually uneventful, thus we are lulled into a false sense of security. Take no intubation for granted, always prepare for failure! Realistically assess if you are the optimal person or institution to manage the airway. You may have to refer to a specialised unit with appropriate equipment and capability for support from the otorhinolaryngologist (ENT surgeon). Ensure intravenous access is well secured and working prior to embarking on the difficult airway, where necessary an intra-osseous line may be an alternative. Position is critical, ensure it is optimised before starting.

The first choice in the management of a potentially difficult airway, whether the child is sedated or under general anaesthesia, is to maintain spontaneous ventilation. The reasons for maintaining spontaneous gaseous exchange are that neuromuscular blockade may result in total airway obstruction owing to loss of tone of the tongue, pharyngeal and laryngeal muscles and suspensory ligaments which may not be alleviated by manual ventilation. Secondly, if a child is paralysed, the loss of spontaneous breathing leads to earlier onset of apnoea and hypoxemia, and it eliminates a technique useful in locating the glottis (see 'following the bubble'). There has been some shift in practice to paralysing children with difficult airways with non-depolarising muscle relaxants where it is felt that muscle tone is the major contributor to inability to visualise and intubate the airway, or where there is a fear of airway activation (laryngospasm, bronchospasm, coughing). This can only occur after confirming easy mask ventilation. Rocuronium is often used due to the availability of sugammadex to reverse the paralysis should the emergency situation arise.[14,20]

A simplified approach to the airway should be outlined as in Table 2. This is not prescriptive as to which specific technique should be employed with each attempt, rather the focus is on preparation, assessment, team skills and communication of the airway plan between the team and team leader, and the avoidance of fixation error.[21]

Table 2. Simplified airway algorithm[21]

PREPARATION – ASSESS, CHECK, PLAN, OPTIMISE
PLAN A – INITIAL INTUBATION STRATEGY
- direct or indirect laryngoscopy, e.g. video laryngoscopy assisted by usage of bougie, stylet or wand
PLAN B – SECONDARY INTUBATION STRATEGY
- fibreoptic bronchoscopy ± supraglottic airway device - rigid bronchoscopy
PLAN C – MAINTAIN OXYGENATION & VENTILATION
- facemask with oropharyngeal or nasopharyngeal airway - supraglottic airway device - high flow nasal cannula or modified Trumpet manoeuvre
PLAN D – RESCUE TECHNIQUE FOR 'CAN'T INTUBATE, CAN'T VENTILATE
- needle or scalpel cricothyroidotomy - surgeon prepped and ready for surgical airway

Stressful situations make even the most skilled providers forget crucial steps. Checklists help to eliminate the weaknesses of human factor. The Difficult Airway Society has an intubation checklist developed for use in the critically ill adult patient which can be sampled and modified for use in the paediatric population (Table 3).[22]

Preparation (equipment)

A wide array of equipment is available, however resources and skill may restrict what may be used to rescue the airway. Have a prepared difficult airway trolley with all the necessary equipment in a central area. There should be knowledge of many alternative intubation and ventilation equipment as each has limitations depending on the clinical scenario, e.g. high rates of first pass failure using video laryngoscopy include blood in airway, limited mouth opening, airway oedema or a mass. Practise with your devices during routine intubations to become proficient; this encourages competency with what is available. Remember it is the operator's expertise rather than a certain technique or equipment which leads to successful management.

Based on the literature published, video laryngoscopy (VL) and fibreoptic bronchoscopy (FOB) have revolutionised the management of the difficult airway and are accepted as primary techniques.[14,15] Supraglottic airway devices are perhaps the most important rescue devices for clearing an obstructed airway as well as providing a conduit for fibreoptic intubation, while

Table 3. Suggested intubation checklist[21,22]

TEAM	EQUIPMENT	PATIENT
1. Verbalise indication for intubation 2. Allocate roles - team leader - 1st/2nd intubator - intubators' assistant - drugs administrator - monitoring patient - runner - who will perform surgical airway 3. Confirm intubation plan - PLAN A, B, C, D Who do we call for help? Time keeper	1. Check equipment - tracheal tubes - oro- and nasopharyngeal airway - direct/indirect laryngoscope - suction - supraglottic device - flexible fibreoptic - surgical access kit 2. Apply monitors (SpO_2, waveform $ETCO_2$, ECG, NIBP) 3. Check drugs - reliable IV/IO access - induction agent, relaxant, pressor/inotrope, sedation	1. Airway assessment 2. Optimise position - < 1 yr: towel under shoulders - > 8 yr: towel under head 3. Optimise preoxygenation - 3 mins or ETO_2 > 85 % - consider other forms of supplemental oxygenation 4. Optimise patient - fluid/pressor/inotrope - aspirate NGT

delivering adequate anaesthesia and maintaining oxygenation. In particular the air-Q laryngeal airway offers many advantages over traditional laryngeal masks when used as a conduit in intubation.

Novel techniques to consider where FOB or VL are not available:

- Optimal external laryngeal manipulation is particularly helpful in children with immobile or short necks.
- 'Follow the bubble' – in the spontaneously breathing patient or even if apnoeic (may need to apply gentle chest compression) air bubbles at the glottis opening may assist in the visualisation of the airway.
- Shaping the endotracheal tube into a 90-degree angle with a stylet, then placing the tip thereof behind the epiglottis (or the centre of the base of the tongues if the epiglottis is not visible) and then tracking the capnography as one blindly locates the glottis opening and trachea.[20]
- Retromolar, lateral or paraglossal approach using a straight blade[3,23] is particularly useful in children with a large tongue or small mandible.
- Blind nasal intubation.

Don't forget the patient attached to the airway

Consideration must be taken of the patient's pre-existing condition, e.g. many of the syndromic conditions have a co-existing cardiac lesion, and drugs given may render the child haemodynamically unstable. Designate an assistant solely tasked with monitoring and treating the patient while the airway is being dealt with. The speed of onset of critical hypoxia due to apnoea in children is faster. This can be prolonged by supplemental oxygenation. Routine preoxygenation must take place, followed by some passive (apnoeic) oxygenation techniques. This can be provided by:

- Nasal prong oxygen.
- High flow, positive-pressure, humidified oxygen via nasal cannula (e.g. Transnasal Humified Rapid Insufflation Ventilatory Exchange - THRIVE) at 1-2L/kg/min.[24]
- Modified Trumpet manoeuvre (Figure 4) – insufflation into the hypopharynx via an endotracheal placed while other orifices not being used are occluded.[25]
- During FOB via SAD.
- Tracheal tube attached to a laryngoscope, e.g. Truview PCD videolaryngoscope.[26]

Elective or emergency surgical access

We all fear the catastrophic 'can't intubate can't oxygenate' scenario, yet we practise as though it will never happen to us. If an airway looks difficult, consider an awake intubation. Paediatric anaesthetists often avoid this due to fears of lack of patient cooperation, discomfort and lack of experience. Awake intubation with sedation is possible with proper preparation, well functioning intravenous access and where possible topicalisation of the airway. Topicalisation can take place via nebulised lignocaine; topical application of local anaesthetic sprays, jellies, or ointments; translaryngeal delivery of lignocaine; spray as you go through the suctioning channel of the FOB; or less rarely via a superior laryngeal nerve block.[20]

Important to note, sedate cautiously and be patient! Oversedation can lead to loss of airway muscle tone. It is best to rely on good airway local anaesthesia, rather than just sedation.

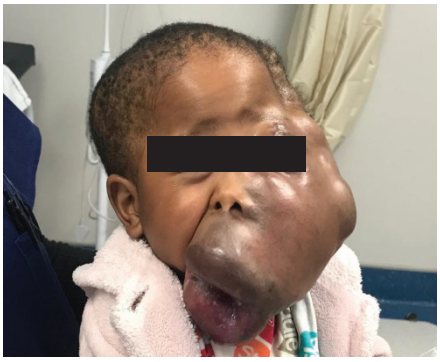

Figure 5. Patient with Sturge-Weber syndrome sedated with dexmedetomidine 3 ug/kg + ketamine 0.25-0.5 mg/kg IV followed by an awake tracheostomy

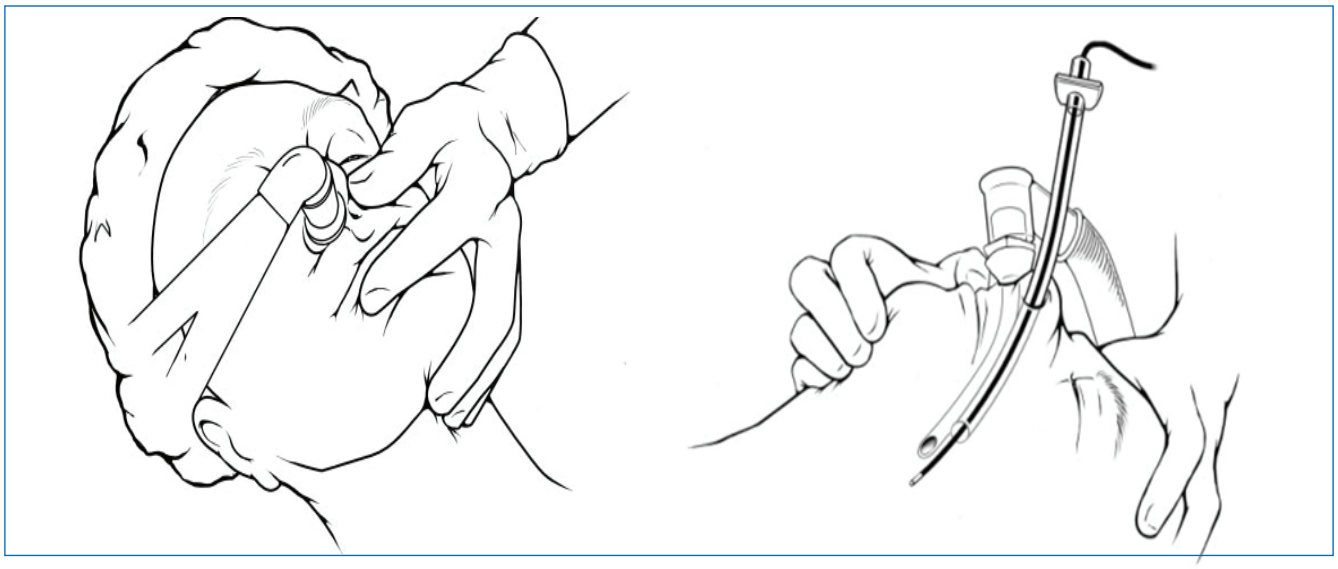

Figure 4. Modified Nasal Trumpet manoeuvre[25] – controlled or assisted ventilation through the right nostril (with other orifices firmly occluded) while the other nostril is used for intubation via a fibreoptic scope

Many alternatives exist with dexmedetomidine and ketamine having favourable outcomes.

The need for an emergency surgical airway in infants is very rare. There is a paucity of literature in this patient population and very little equipment developed in this area. Moreover, the cricothyroid membrane is difficult to identify and expeditious performance of a surgical airway is challenging even for the most skilled paediatric otolaryngologist. In a crisis, the fastest option to oxygenate is most likely through needle cricothyroidotomy (Figure 6). However this is performed with the risk of perforation of the posterior tracheal wall.[17] There is currently insufficient evidence to prescribe one specific surgical airway technique over another, the biggest debate being whether to use a scalpel, a needle (cannula) cricothyroidotomy, a large bore catheter or the emergency cricothyroidotomy set.[27] There is a suggestion that the current best practice in neonates and smaller children remains the needle cricothyroidotomy in the CICO situation[17] due to the size of the cricothyroid membrane (CTM). Furthermore, in neonates and infants, full extension of the head and neck may not allow a flat enough approach to the CTM, and identification of landmarks may be technically difficult. Under these circumstances, a cannula tracheostomy may be necessary to avoid damage to the cricoid and thyroid cartilages.[28] The APA Guidelines for the CICV paralysed child aged 1–8 years recommend the use of a cannula cricothyroidotomy/tracheostomy.[9] Evidence suggests that the more distal along the trachea front of neck access (FONA) is attempted, the lower the success rate for both cannula and scalpel techniques (i.e. cricothyroidotomy preferred to tracheotomy). In a semi-urgent scenario, ultrasound may be used to identify the CTM[27, 29] (Figure 7 and 8). The appropriate equipment should ideally be prepacked and ready for use in the event of this much feared scenario.

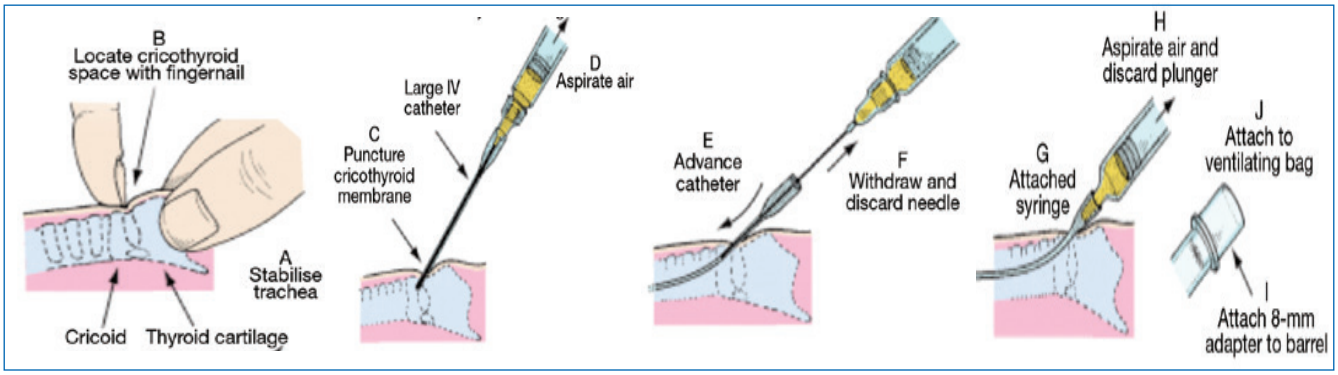

Figure 6. Technique of percutaneous needle cricothyroidotomy[3]

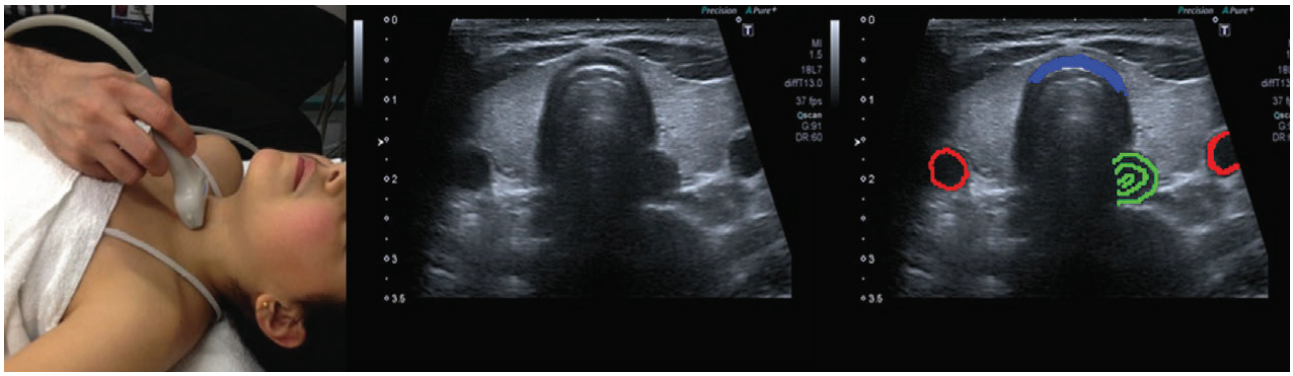

Figure 7. Ultrasound of transverse view of trachea
Tracheal ring (blue), oesophagus (green) and carotid arteries (red)[29]

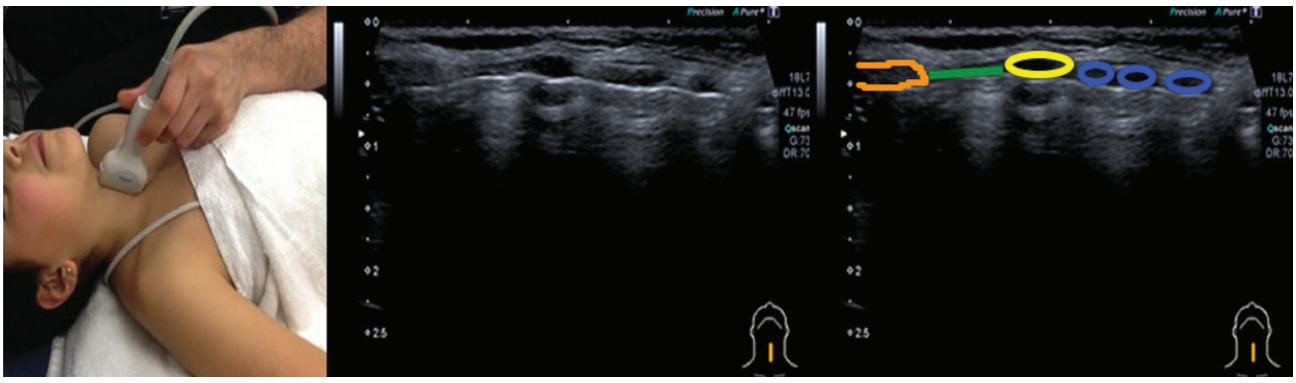

Figure 8. Ultrasound of the longitudinal view of the trachea
Thyroid cartilage (orange), CTM (green), cricoid cartilage (yellow), tracheal rings (blue)[29]

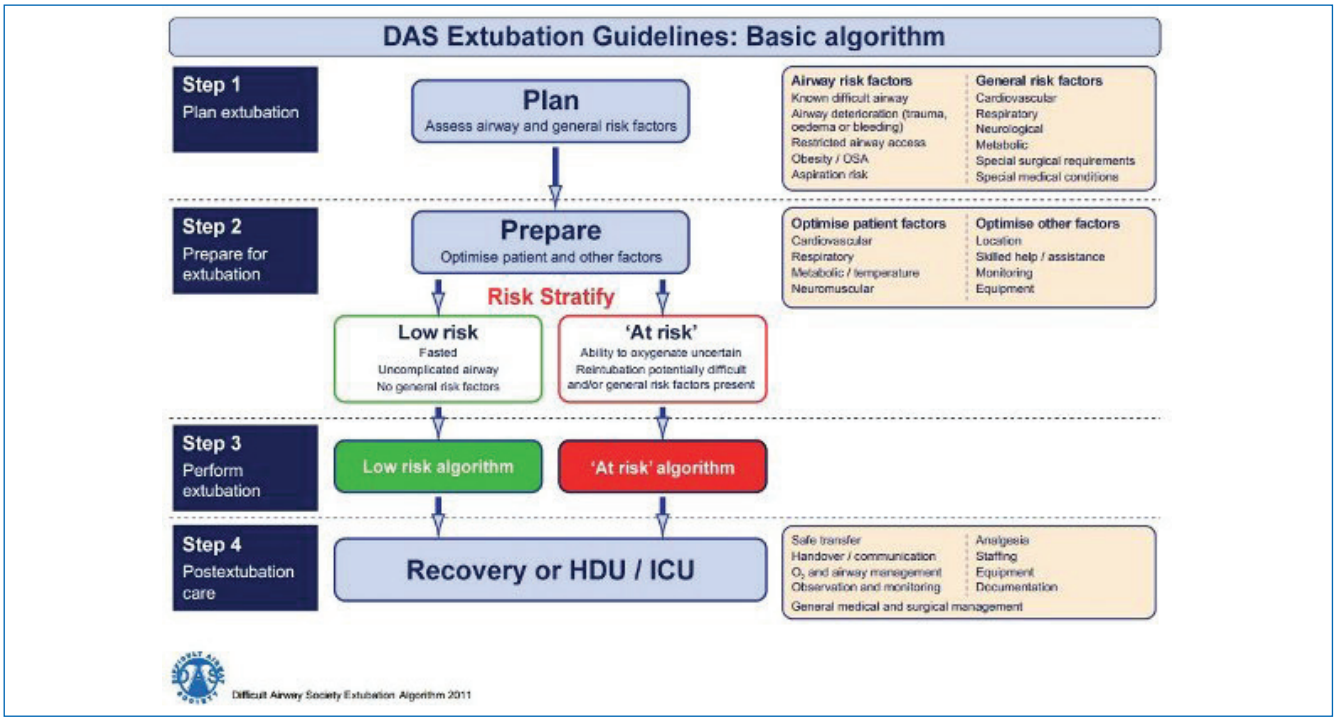

Figure 9. DAS Extubation Guideline

Extubation (plan for the end at the beginning)

Extubation after a difficult intubation should be performed under defined precautions, optimise your patient prior to extubation. If concerned about airway oedema, consider direct examination of the airway with a laryngoscope or fibreoptic scope. Alternatively, perform a leak test (deflate cuff and listen for leak around tube when patient exhales). Where possible, the patient should be monitored for at least 2–3 hours postoperatively. If there is any doubt a plan for re-intubation should also be in place.[4,30]

Remember re-intubation is often more difficult than at initial attempt due to intubation trauma, surgical insult, intravenous fluids. Figure 9 is the basic algorithm for extubation in adults as suggested by the Difficult Airway Society.

Conclusion

Local institutional policies on the management of the difficult paediatric airway need to be developed based on the extensive evidence available in adult and paediatric literature. Recognition of the difficult airway, expertise and corresponding infrastructure (team, communication and equipment) are vital in ensuring positive outcomes. The aim should be to plan and prepare in the non-emergency situation, e.g. healthy patients, workshops or simulation, as it is noted that practice develops muscle memory which can be used in the emergency situation. Emphasis must be made on the emerging importance of video laryngoscopy and fibreoptic bronchoscopy in the management of the difficult airway. However, as important are the role of supraglottic airway devices, supplemental oxygenation during attempts and optimal external laryngeal manipulation.

Human error is unavoidable. The onus is on us as practitioners to actively pursue avenues to make these errors less frequent and less damaging.

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NW REFRESHER COURSE

Peripartum Cardiomyopathy

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Introduction

Maternal morbidity and mortality are a major issue in South Africa with the country currently reporting a maternal mortality rate of 132.9 deaths per 100 000 births. This far exceeds the target of 35 deaths per 100 000 as set out in the Millennium Development Goals. The top five causes of death are: non-pregnancy related infections, hypertension, haemorrhage, medical and surgical conditions, and pregnancy related sepsis.[1]

In the 2014 Saving Mothers report,[1] 11.4% of maternal deaths were due to medical or surgical conditions. Cardiac disease accounted for one-third of these deaths. While the exact number of patients who died due to cardiomyopathy is unclear it does remain a significant contributor towards maternal morbidity and mortality.

Definition

Peripartum cardiomyopathy (PPCM) has been defined by the Heart Failure Association of the European Society of Cardiology Working Group on PPCM[2] as: an idiopathic cardiomyopathy presenting with heart failure secondary to left ventricular dysfunction towards the end of pregnancy or in the months following delivery, where no other cause of heart failure is found. It is a diagnosis of exclusion. The left ventricle may not be dilated but the ejection fraction is nearly always reduced below 45%.

The key features of this definition are that the presenting patient should have been previously well with new onset shortness of breath in the last month of pregnancy or up to 5 months postpartum with no other cause for the shortness of breath being found. Other causes of heart failure should be ruled out by an extensive history, physical examination and diagnostic testing.[3]

Epidemiology and risk factors of peripartum cardiomyopathy

The current incidence of PPCM around the world is not known and the data that does exist shows a wide variation in the incidence of PPCM. In the United States of America, the incidence of PPCM ranges from 1 in 1149 to 1 in 4350 live births. In South Africa the incidence of PPCM is 1 in 1000 births. There are also some countries that show a uniquely high incidence of PPCM with rates in Haiti of 1 in 299 live births and 1 in 100 deliveries in certain tribes in Nigeria.[3-5]

The large variation in the incidence of PPCM is due to many factors: genetic and geographical differences, reporting rates and access to diagnostic testing, as well as differences in cultural practices surrounding the peripartum period which may contribute to the development of PPCM. Indeed the practice of postpartum consumption of dried lake salt and lying on heated beds after delivery may contribute to the high incidence of PPCM in Nigeria.[4]

Risk factors for PPCM include: increased maternal age, multiparity, preeclampsia, multiple gestation, African descent, use of tocolytics, poverty, tobacco use, malnutrition and anaemia during the presenting pregnancy.[4]

Pathophysiology

The pathophysiology of PPCM is complex and multifactorial with a number of proposed theories. It is important to first understand the significant cardiovascular changes that occur during pregnancy and the stress that these changes cause to the myocardium.

The most important physiological changes during pregnancy are a combination of increased blood volume and decrease in systemic vascular resistance which lead to an increase in cardiac output. Vasodilation is mediated by the actions of oestrogen, progesterone and relaxin. This vasodilation causes the activation of the renin-angiotensin-aldosterone system leading to sodium and water retention. Cardiac remodelling occurs with an increase in left ventricular mass and increased angiogenesis.[6]

These changes are important in allowing the parturient to adapt to the metabolic needs of the foetoplacental unit as well as to prepare her for the upcoming labour and delivery. Failure or aberrations of these cardiovascular changes can lead to a variety of problems in the pregnancy, one of which is PPCM. The proposed contributory pathophysiological mechanisms will be discussed briefly.

Viral myocarditis

Viral infections have been proposed as the cause of PPCM in various investigations. Goulet et al.[7] and Melvin et al.[8] proposed it as the main mechanism for PPCM. Implicated viruses are parvovirus B19, cytomegalovirus, herpes virus 6 and Epstein-Barr virus.[4] However, the evidence is conflicting with myocarditis being found on endomyocardial biopsy in ranges of 9 to 62%.

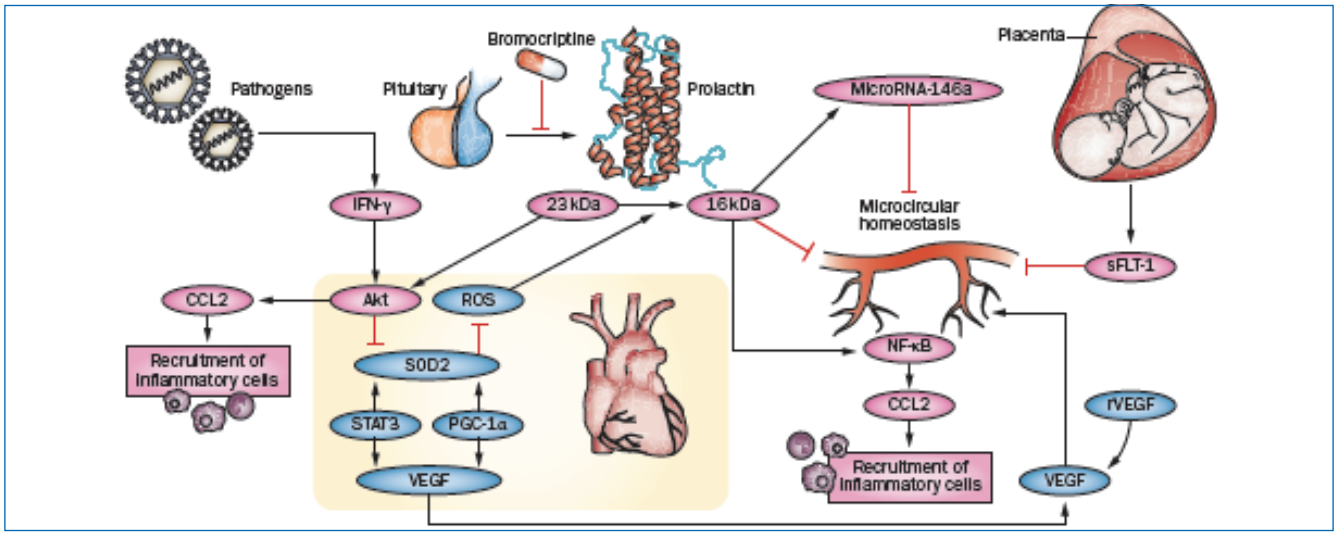

Figure 1. Pathophysiological mechanisms in PPCM[5]

Evidence of myocarditis has not been conclusively shown in the majority of women with PPCM.[4,9]

Oxidative stress and angiogenic imbalance

An imbalance between the production of reactive oxygen species and the ability of an organism to repair such damage leads to oxidative stress.[5] Mice that lack cardiac peroxisome proliferator-activated receptor gamma coactivator 1-alpha, a regulator of angiogenic vascular endothelial growth factor (VEGF), develop severe PPCM.[10] Toward the end of pregnancy the placenta secretes soluble fms-like tyrosine kinase (sFlt1) which inhibits VEGF. Higher levels of sFlt1 occur in women with preeclampsia and multiple gestations. This may explain the association between preeclampsia and multiple gestations with PPCM.[4,5]

Abnormal autoimmune response and inflammation

Circulating auto-antibodies to the myocardium have been reported in up to 50% of patients with PPCM. These auto-antibodies cause increased levels of cytokines such as tumour necrosis factor alpha, interleukin 6 and soluble Fas receptors, which may cause myotoxicity and myocarditis.[11] This auto-immune response may be due to previous exposure from a prior pregnancy or exposure to paternal major histocompatibility complex antigens.[4, 12]

Genetic susceptibility

The increased incidence of PPCM in certain geographical areas suggests a genetic predisposition to the disease and cases have been reported of multiple women in one family developing PPCM.[13] However, a conclusion by Hilfiker-Kleiner and Sliwa[5] is that most women with PPCM report no family history of cardiomyopathy. Mutations associated with dilated cardiomyopathy have been found in screening of relatives with PPCM and indeed the physiological stressors of pregnancy may reveal a dilated cardiomyopathy that is mistaken for PPCM.[4]

Prolactin and vasoinhibin

PPCM is a disease of late pregnancy and early postpartum and as such it is reasonable to assume that a factor specific to late pregnancy may be the cause. Prolactin is a hormone which is present in large quantities in late pregnancy and its role in the development of PPCM has gained traction in recent years.[4,9]

Prolactin is responsible not only for lactation but also has widespread effects on the cardiovascular system. It is associated with increased blood volume, decreased angiotensin responsiveness and a reduction in sodium and water retention. It also has effects on the endothelium and can exert various effects on angiogenesis depending on which form it is circulating in.[5,14]

Experimental evidence from Hilfiker-Kleiner et al.[14] demonstrated that in mice a deletion of STAT3 leads to enhanced expression of cardiac cathepsin-D, which promotes the cleavage of the normal 23kDa prolactin into a 16kDa fragment. This 16kDa prolactin, also called vasoinhibin, is potently antiangiogenic and proapoptotic.[5]

The formation of this 16kDa prolactin may be the central pathophysiological mechanism in PPCM. Unbalance oxidative stress from multiple sources leads to increased levels of cardiac cathepsin-D which leads to cleavage of the 23kDa prolactin. The subsequent increased levels of vasoinhibin cause damage to the cardiac microvasculature, reduce cardiac function and promote ventricular dilatation. It also inhibits the action of VEGF, induces apoptosis and impairs nitric oxide mediated vasodilatation.[4,6,14,15]

Further support for the prolactin model has come from the successful use of bromocriptine, which inhibits the actions of prolactin, in the treatment of PPCM.[3,15]

A pictorial summary of the pathophysiological mechanisms in PPCM is shown in Figure 1.

Presentation

Distinguishing true pathological symptoms from the normal symptoms of late pregnancy can be difficult. Mild oedema and shortness of breath are common in late pregnancy, as are mild ventricular dilatation and increased cardiac output, and as such

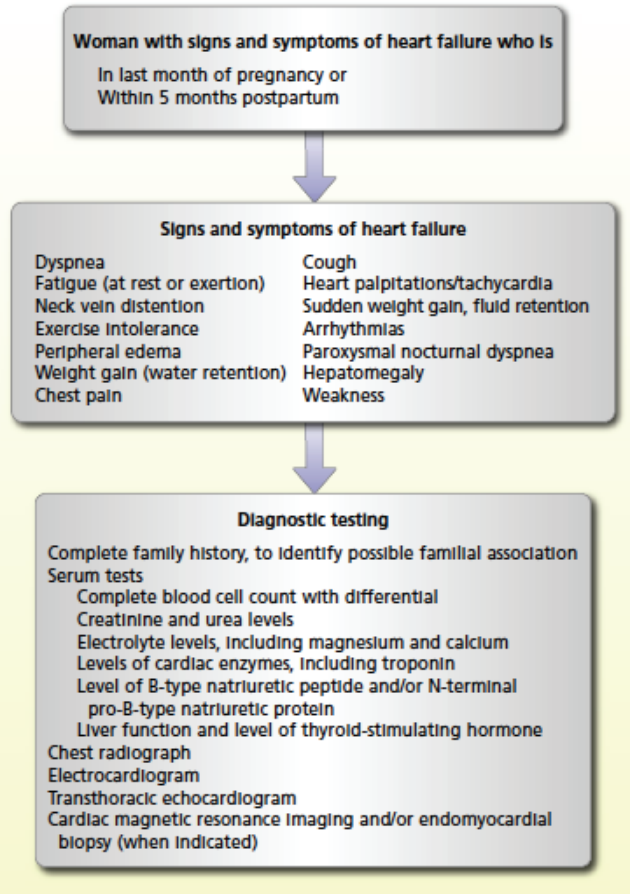

Figure 2. Evaluation of PPCM[9]

a high index of suspicion is required in the diagnosis of PPCM.[9] Particularly important is to ascertain the timing of symptoms and whether they are new onset.

Commonly reported symptoms that should warrant further investigation are dyspnoea (90%) which is typically New York Heart Association (NYHA) grade III or IV, fatigue (90%), palpitations (62%) and peripheral oedema (62%).[4] Persistent nocturnal cough, orthopnoea and paroxysmal nocturnal dyspnoea are also frequently reported.[16] Other symptoms such as dizziness, chest pain and abdominal discomfort have also been reported. Rarely, patients may present with acute cyanosis, thromboembolic events, liver failure and sudden cardiac arrest.[4]

In terms of signs, the presence of tachycardia is nearly universal, and it cannot be stressed enough how important accurately measuring the pulse rate is in these patients. Other signs are those consistent with heart failure: raised jugular venous pressure, third heart sound, displaced apex beat, new murmur of tricuspid or mitral regurgitation and evidence of pulmonary oedema.[16]

The blood pressure may be normal, increased or decreased. A patient presenting with low blood pressure and symptoms of heart failure may be in decompensated heart failure and should be treated as an emergency.[9] The presence of a high blood pressure does not rule out PPCM but should raise suspicion for another cause of cardiac dysfunction in pregnancy, namely preeclampsia.[6] Cardiac involvement in preeclampsia is common, with diastolic dysfunction and raised filling pressures but normal systolic function.[17] Echocardiography will allow the differentiation between PPCM and preeclampsia with cardiac dysfunction.

A proposed evaluation algorithm for PPCM by Johnson-Coyle et al.[9] is illustrated in figure 2.

In summary, it is vital that clinicians, including obstetricians and anaesthetists, look out for features of heart failure in late pregnancy and early postpartum.

Investigations

Routine laboratory investigations should include a full blood count, urea and electrolytes, calcium, magnesium and phosphate, liver function test, thyroid function test and markers of cardiac function (troponin and brain natriuretic peptide). These tests are to ascertain the patient's level of organ dysfunction as well as to exclude other causes of heart failure.

A 12-lead electrocardiogram (ECG) should be obtained in all patients with suspected PPCM. While no single ECG abnormality has been found to be pathognomonic for PPCM, a study in South Africa by Tibazarwa et al.[18] found that 96% of patients with PPCM had at least one ECG abnormality. The most common abnormalities were: T-wave changes, p-wave abnormalities and QRS-axis deviation. Thus the ECG is an important negative prediction tool in the investigation of PPCM and may reveal another diagnosis, such as myocardial infarction or pulmonary embolism.[4]

Echocardiography remains the most reliable and easiest diagnostic modality for PPCM and should be obtained urgently in suspected cases. The echocardiogram will show reduced left ventricular function with an ejection fraction of less than 45% in nearly all cases.[2] Fractional shortening of less than 30% and an end-diastolic diameter of more than 2.7 cm/m^2 are also diagnostic.[11] Other echographic findings are left atrial enlargement, left atrial or ventricular thrombus, dilated right ventricle and mitral and tricuspid regurgitation. The presence of pulmonary hypertension should be noted, if present.[4]

Chest radiography should be obtained with foetal shielding and will be able to detect the presence of cardiomegaly and pulmonary oedema. However, it is not an essential investigation in the diagnosis of PPCM.[4]

Other investigations such as cardiac magnetic resonance imaging, cardiac catheterization and endomyocardial biopsy are not routinely indicated. These are reserved for cases where the diagnosis is in doubt, especially if viral myocarditis or coronary artery disease are suspected.[4,9]

Management

The management of PPCM is similar to that for other forms of systolic heart failure, but should also take into account whether there is a need for operative delivery as well as the potential foetal side effects of therapy. A multi-disciplinary team of obstetricians, cardiologists, neonatologists, intensivists and anaesthetists should be involved. A clear plan for labour and delivery should

be established in advance and distributed to all persons who are likely to be involved in the case.[19]

The principles of treatment are to improve haemodynamic status, reduce preload and afterload, improve contractility, reduce symptoms and prevent thromboembolism. It is important to distinguish between compensated and decompensated heart failure as these will require different treatment as well as necessitate differences in the urgency of delivery.[9]

Patients with compensated heart failure who are antepartum should be commenced on beta-blockers and thiazide diuretics. The addition of hydralazine, digoxin and loop diuretics should also be considered based on symptoms and response to treatment. Low molecular weight heparin should be started in patients with an ejection fraction of less than 35%. The pregnancy should be allowed to continue as long as the patient is stable and there is no obstetric indication for delivery. Once the patient has delivered, she should be started on an angiotensin converting enzyme inhibitor or angiotensin receptor blocker and spironolactone. Heparin can then be changed to warfarin.[9]

Table 1: Management of compensated heart failure in peripartum cardiomyopathy[9,20]

Non-pharmaceutical therapies
Low sodium diet: limit of 2 g sodium per day
Fluid restriction: 2 L/day
Light daily activity
Oral pharmaceutical therapies
Antepartum management of peripartum cardiomyopathy
Beta-blocker
Vasodilator
Digoxin
Thiazide diuretic
Low molecular weight heparin if ejection fraction < 35%
May consider loop diuretic with caution
Postpartum management of peripartum cardiomyopathy
Angiotensin converting enzyme (ACE) inhibitor
Angiotensin-receptor blocker (ARB)
Consider nitrates or hydralazine if woman is intolerant to ACE and ARB
Loop diuretic
Aldosterone antagonist
Beta-blocker
Warfarin if ejection fraction is less than 35%

Decompensated heart failure should be managed as a medical emergency with advanced cardiac life support principles. These patients should be managed in a high care or intensive care unit. The airway should be secured in patients who are severely distressed with the initiation of positive pressure ventilation. Supplemental oxygen should be provided to all other patients and non-invasive ventilation can be considered to reduce left ventricular afterload. Circulatory support is required in patients who are hypotensive, the agents of choice are milrinone and dobutamine. Levosimendan can also be considered. Invasive haemodynamic monitoring should be inserted, and foetal monitoring must be obtained. Preload reduction is obtained with the use of diuretics and vasodilators. Anticoagulation must also be commenced.[4,9] Delivery for these patients is urgent to reduce the myocardial strain caused by pregnancy.[19]

Table 2: Management of decompensated heart failure in peripartum cardiomyopathy[9,20]

Airway
Intubate promptly upon distress for increased work of breathing to prevent complications with difficult airway later in treatment
Breathing
Provide supplemental oxygen
Maintain continuous pulse oximetry
Measure arterial blood gases every 4-6 hours
Circulation
Start cardiac and blood pressure monitoring
Insert arterial catheter
Insert central venous catheter
In antepartum women, obtain foetal monitoring
Intravenous loop diuretic
Intravenous vasodilator
Positive inotropic agent
Avoid beta-blockers in the acute phase as they may decrease perfusion
Heparin, alone or with oral warfarin therapy
If no improvement clinically:
Consider cardiac magnetic resonance imaging
Perform endomyocardial biopsy
Assist devices:
Intra-aortic balloon pump
Left ventricular assist device
Extracorporeal membrane oxygenation
Transplantation
Consider bromocriptine therapy

Bromocriptine

Since the discovery of an inflammation induced increase in cathepsin D and the production of 16kDa prolactin as a pathophysiological process in PPCM, the use of bromocriptine to block the production of prolactin has gained interest. A pilot study by Sliwa et al.[21] in 2010 demonstrated an improvement in left ventricular ejection fraction, improvement in NYHA class and fewer deaths when bromocriptine was added to standard heart failure treatment.

Analysis of the German PPCM registry from 2013 demonstrated a beneficial effect of bromocriptine therapy.[3] Significantly higher numbers of patients treated with bromocriptine were classified as improvers. Subsequent to this a multicentre randomized study was conducted by Hilfiker-Kleiner et al.[15] in Germany comparing 1 week of bromocriptine therapy with 8 weeks of bromocriptine therapy, in addition to standard heart failure therapy. It was considered unethical to have a control group. Bromocriptine therapy was associated with an improvement in left ventricular function and low morbidity and mortality. There was no significant difference in treatment outcome between 1 week and 8 weeks of therapy, however there was a trend toward better recovery in patients with a very low ejection fraction (< 30%) in the 8-week group. The proposed scheme of the actions of bromocriptine is depicted in Figure 3. The authors recommend large prospective registries be developed in countries to allow

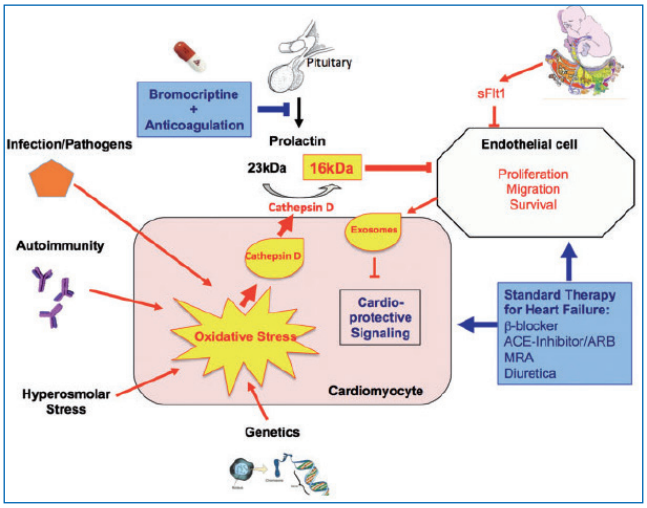

Figure 3. Disease specific therapy with bromocriptine[15]

for greater knowledge on the effects of bromocriptine therapy in large numbers of patients.[15]

Based on the above evidence the Hannover Medical School recommends the use of bromocriptine in patients with PPCM whose ejection fraction is less than 35%.[3]

Anaesthetic management of PPCM

Hilfiker-Kleiner and Sliwa report that 43% of patients with PPCM in South Africa will present in the antepartum period.[5] Many of these patients will require anaesthetic intervention for both normal vaginal delivery and caesarean section. It is important for anaesthetists to be involved in the multi-disciplinary management of such patients.[19,22] It is also vital that the decision for the method of delivery be a multi-disciplinary one. In general, patients who are stable may be allowed progress to spontaneous labour provided there is no deterioration, while patients in decompensated heart failure should have urgent operative delivery.[4,22]

Preoperative assessment

The preoperative, or pre-anaesthetic assessment of patients with PPCM should focus on determining the severity of the patient's condition and whether heart failure is compensated or decompensated. Specific warning symptoms are: NYHAIII/IV and an inability to lie flat. Careful attention should be paid to the respiratory and pulse rate, blood pressure, the presence of a third heart sound and clinical features of pulmonary hypertension.[19,23] The ECG and echocardiogram should be reviewed with specific emphasis on the ejection fraction and left ventricular end-diastolic volume.[22]

Labour analgesia

The provision of adequate labour analgesia is beneficial in achieving the haemodynamic goals required in PPCM. These are specifically a reduction in afterload and maintenance of contractility. The functional sympathectomy from a carefully titrated labour epidural can achieve these goals. The patient's anticoagulation status should be checked prior to the insertion of any neuraxial blockade. It is prudent to institute invasive blood pressure monitoring before any intervention and the patient should be in a high care environment. The epidural should be inserted early in labour with very slow, careful titration so as not to drop the preload or afterload too drastically. These patients will be unable to compensate for hypotension with an increase in cardiac output.[19,22,23]

A controlled second stage of labour with forceps or vacuum delivery is advised to reduce the straining and pushing efforts of the mother.[22] Careful attention should be paid to the fluid management during labour as the patients tolerate hypovolaemia poorly, but are also at risk for fluid overload. The use of oxytocin in the active management of the third stage of labour should be carefully considered and boluses should be avoided, with the use of an infusion if required.[19]

Intraoperative management

While spontaneous vaginal delivery is preferred for patients with stable PPCM, some of these patients will require operative delivery for an obstetric indication. Unstable patients will require urgent caesarean section to reduce maternal cardiovascular strain and possibly prevent foetal loss. An experienced anaesthetist and surgeon should be present.[4,9]

Stable patients presenting for caesarean section are ideally managed with regional anaesthesia with invasive blood pressure monitoring as for those receiving labour analgesia. The theatre should be fully prepared for any complication that may arise intraoperatively. This includes the availability of inotropic agents dobutamine, milrinone and levosimendan and dilator drugs such as nitrocine or nitroprusside.

The choice of anaesthetic technique is varied, and many approaches have been used successfully and include epidural anaesthesia, combined spinal epidural and continuous spinal anaesthesia. George et al.[24] describe the use of epidural anaesthesia over 6 hours to achieve adequate anaesthesia. This may not be practical in many instances. Schnaider et al.[25] prefer the use of a combined spinal epidural due to a lower failure rate, better patient satisfaction and superior haemodynamic profile. The key principles of all these techniques is the avoidance of large single boluses and the maintenance of cardiovascular stability. A single shot spinal is not advised due to the sudden reduction in preload and afterload associated with the rapid sympathectomy.[22]

A novel technique described by Tiwari et al.[26] is the "epidural volume extension" technique. They describe a case series of five patients with PPCM presenting for caesarean section. These patients had a lumbar epidural catheter placed preoperatively that was not activated. After the institution of invasive monitoring the patients underwent a single shot spinal of 1 ml of 0.5% bupivacaine. They were then laid supine and had 8 ml of normal saline injected into the epidural. The theory of this technique is that the epidural expansion will allow surgical anaesthesia with a smaller volume of local anaesthetic. All patients achieved a dermatome level of anaesthesia of T4 with haemodynamic stability and uneventful intraoperative course.

Unstable patients with decompensated heart failure are best managed under general anaesthesia due to the ability to titrate anaesthesia to haemodynamic stability as well as the benefits of positive pressure ventilation in reducing left ventricular afterload. The insertion of an arterial and central venous line should be done prior to the induction of anaesthesia and inotropic and vasodilator infusions should be prepared. Cardiac output monitoring is ideal, and the availability of a transoesophageal echo can provide invaluable information.[23]

The actual choice of anaesthetic technique is depended on the patient's haemodynamic status and anaesthetic experience. A modified rapid sequence technique must be employed balancing the risk of maternal aspiration against haemodynamic stability. A high dose opioid technique will provide maximum haemodynamic stability, but must be weighed against the possible need for maternal postoperative ventilation and foetal respiratory depression. Other techniques include the use of etomidate, remifentanil and volatile anaesthetics. Total intravenous anaesthesia with propofol and remifentanil has been described in one case report, but this should be viewed with extreme caution due to the risk of vasodilation with propofol and the reduction in heart rate from remifentanil that may significantly impair cardiac output.[19,22,23]

Acidosis, hypercarbia and anaemia should be avoided. Careful titration of fluids to maintain preload but not over distend the myocardium is essential. A single dose of furosemide may assist in countering the autotransfusion following delivery of the foetus. Meticulous attention must be paid to blood loss as these patients tolerate hypovolaemia poorly. Syntocinon should be administered via small boluses titrated slowly to response and ergometrine should be avoided.[22]

Postoperative

These patients should be monitored in a high care or intensive care unit postdelivery with continuous invasive monitoring as there are ongoing haemodynamic changes in the postpartum period.[9] Positive pressure ventilation may be required for patients with decompensated heart failure or those who have received a high dose opioid anaesthetic. Heart failure treatment should be continued with the introduction of drugs that were contraindicated in the antepartum period, particularly ACE inhibitors.[4,25]

Prognosis and outcome

Left ventricular recovery is common in PPCM with reported rates of 45 to 78% at 6 months postpartum. Mortality rates vary between 0 and 19%. Overall predictors of mortality are left ventricular ejection fraction of less than 30%, higher maternal age, black race and multiparity.[4] Blauwet et al.[27] analysed predictors of outcome in 176 South African patients and identified increased left ventricular end-systolic diameter, lower body mass index, and lower serum cholesterol as independent predictors of poor outcome.

Patients should be monitored for at least 12 months postpartum and be counselled on the risk of relapse in subsequent pregnancy. They should be provided with effective contraception.[4]

Conclusion

PPCM remains a significant cause of maternal morbidity and mortality as well as a diagnostic challenge. All clinicians involved in the management of pregnant women should maintain a high index of suspicion for PPCM. Management is as for other forms of systolic heart failure with cognizance of the physiological changes and demands of pregnancy and the puerperium. The use of bromocriptine has been shown to improve outcome.

Anaesthetists should be part of the multi-disciplinary team when PPCM is diagnosed antepartum and may be called upon to provide labour analgesia and administer anaesthesia for operative delivery. Anaesthetic goals are to provide cardiovascular stability, reduce preload and afterload and maintain contractility. Where possible, anaesthetists experienced in cardiac and obstetric anaesthesia should be called upon to manage patients with PPCM.

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NW REFRESHER COURSE

Smoking and Vaping: is there a difference?

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Introduction

Tobacco smoking is a major contributing factor in the development of most diseases and it poses major challenges in the perioperative period.[1] In 2015, the World Health Organisation (WHO) published the "global report on trends in prevalence of tobacco smoking". It was reported that smoking is responsible for about six million deaths across the world. The report estimated that about 19% of the South African population smoked in 2010.[2]

Due to the adverse health effects attributable to traditional tobacco smoking, vaping or electronic cigarette (e-cigarette) use is becoming a popular nicotine alternative. The popularity of e-cigarette use is further promoted by the perception that they are healthier than tobacco cigarettes. It is also believed that they help smokers to quit.[3]

This review aims to describe the differences between cigarette smoking and vaping. For the purpose of this review, tobacco cigarette smoking will be referred to as cigarette smoking, whereas vaping will refer to the use of e-cigarettes. The two types of smoking will be described in terms of constituents and effects on the different organ systems.

Cigarette smoking

Cigarette is defined in the English Oxford Dictionary as "a thin cylinder of finely cut tobacco rolled in paper for smoking".[4] There are different ways of smoking tobacco, however this review will only focus on cigarette smoking.

Constituents of cigarette smoke

More than 4000 substances are found in the cigarette smoke. These substances have various effects, ranging from being antigenic, cytotoxic, mutagenic and carcinogenic. The cigarette smoke constituents are found in two phases, namely, the gaseous and particulate. The gaseous phase represent 80–90% of the smoke and it consists of mainly of nitrogen, oxygen and carbon dioxide. Other gaseous constituents include carbon monoxide, which impairs oxygen transport, as well as hydrocyanic acid and hydrazine, which are carcinogenic.[5]

Formaldehyde, acrolein and certain nitrosamines represent chemicals that are contained in the liquid-vapour portion of the smoke,[5,6] and they are found to be ciliotoxins and irritants.[5] The particulate phase is composed of nicotine, as the main toxic ingredient.[5] Nicotine is also the psychoactive drug in a cigarette smoke, which makes it addictive. Any attempts to quit smoking are then met with withdrawal symptoms, cravings and increased chances of relapse.[6] A traditional tobacco cigarette yields approximately 0.5 to 1.5 mg/cigarette.[7] Other particulate constituents are carcinogens, such as tar and hydrocarbons.[5]

Effects of cigarette smoking on the organ systems

Cigarette smoking results in adverse health effects and those effects will be described according to the systems affected.

Cardiovascular system

Most cardiovascular effects of smoking are due to the effects of nicotine. Cigarette smokers have plasma nicotine levels reaching 15–50 ng/ml. Nicotine results in an increase in heart rate, peripheral vascular resistance and blood pressure. This is due to the stimulant effect of nicotine on the adrenal medulla resulting in adrenaline release, as well as the effect on the carotid and aortic receptors. There is also stimulation of the autonomic ganglia by nicotine, which results in an increase in sympathetic tone.[5,8]

Cigarette smoking accelerates atherosclerosis in the coronary arteries, the aorta, cerebral arteries and large peripheral arteries. Smoking therefore increases the risk of acute cardiovascular events, namely, acute myocardial infarction and stroke. The acute cardiovascular events are as a result of smoking-induced hypercoagulable state, increased myocardial work, carbon monoxide-mediated reduction in oxygen carrying capacity of the blood, coronary vasoconstriction and catecholamine release.[9]

Carbon monoxide is the other constituent of smoke that affects the cardiovascular system. The amount of carbon monoxide contained in the cigarette smoke is 400 parts per million. Carbon monoxide binds to haemoglobin (Hb) 200 times more than oxygen to form carboxyhaemoglobin (COHb). The amount of COHb in the blood ranges from 5–5% in smokers, as compared to 0.3–1.6% in non-smokers.

The formation of COHb reduces the amount of Hb available to bind oxygen, shifting the oxygen-haemoglobin curve to the left and this results in a decrease in the amount of oxygen available to the tissues.[5]

Carbon monoxide also affects intracellular oxygen transport. This is as a result of binding with cytochrome oxidase and myoglobin,

therefore inactivating mitochondrial enzymes in the cardiac muscle. These effects result in chronic tissue hypoxia. Carbon monoxide also results cardiac arrhythmias.[5]

Respiratory system

Smoking results in increased mucous secretions as a result of the irritants present in cigarette smoke. This results in hyperviscous mucous and reduced elasticity.[5,10] The ciliotoxins present in smoke result in inactive cilia and impaired tracheobronchial clearance, therefore resulting in increased recurrent chest infections.[1,5] Smoking also leads to increased laryngeal and bronchial reactivity.[1,5,11] This increases the risk of laryngospasm. The epithelial lining of the lung is disrupted by cigarette smoke resulting in increased pulmonary epithelial permeability. The epithelial lining disruption leads easy penetration of irritants and stimulation of subepithelial irritant receptors, thus increasing pulmonary reactivity.[1,5,8]

Cigarette smoking leads to narrowing of the small airways, resulting in increased closing volume.[1,5] Smoking decreases pulmonary surfactant and causes an increase in proteolytic enzymes resulting in loss of lung elasticity.[5] This results in the development of chronic pulmonary disease[1] and emphysema.[5,8] Compared to non-smokers, chronic bronchitis occurs five times more often in smokers, with the incidence of 25%.[5]

Haematological system

Smoking leads to increased hypercoagulability,[1] due to increased platelet activation and circulating fibronectin.[3]

Renal system

Smoking results in an increase in antidiuretic hormone release, which leads to dilutional hyponatraemia.[5,8,10]

Gastrointestinal system

Cigarette smoking results in gastro-oesophageal sphincter incompetence, which develops four minutes after the start of smoking but returns to normal within eight minutes of ending the smoking session. There is no effect on gastric volume and gastric secretions pH.[5,10]

Immune system and wound healing

Smoking impairs both humoral activity and immune mediated immunity,[1,10] leading to increased risk of infection[1,5,10] and delayed wound healing.[1,3]

Cancer associations

Smoking is associated with cancers of most organs: lung, gastrointestinal, head and neck, and genitourinary system.[1,6] Studies looking at condensates collected from cigarette smoke found that they cause mutations and damage to deoxyribonucleic acid. Smoking condensates also showed the ability to induce malignant changes in mammalian cells.[6]

Drug interactions

Cigarette smoking increases the metabolism of some drugs by inducing liver microsomal enzymes. Chronic smokers require more analgesic drugs. Fentanyl and pentazocine undergo quicker metabolism in smokers.[5]

In smokers, nicotine stimulates acetylcholine receptors. This is because nicotine concentration of smokers does not increase beyond 75 ng/ml and nicotine in smaller doses of < 100 ng/mL stimulates the acetylcholine receptors, as opposed to the blocking effect in larger doses. The stimulation of receptors results in the requirement of higher doses of muscle relaxants needed to block the receptors.[5]

Vaping

Electronic cigarettes (e-cigarettes) are defined as "products that deliver a nicotine-containing aerosol to users by heating a solution". This solution is made up of propylene glycol or glycerol, nicotine and flavouring agents.[12] E-cigarettes or electronic nicotine delivery systems (ENDS) simulate the cigarette smoking experience, and it has been portrayed as an alternative to reduce the amount of tobacco cigarette consumption. Heating of the solution leads to generation of a vapour, which is inhaled by the user, hence the term "vaping".[13]

Chemical constituents

The ingredients in the e-cigarette cartridges and solutions are relatively fewer than those found in traditional tobacco cigarettes. They are for the most part non-toxic and non-carcinogenic as compared to burned tobacco products, which contains thousands of compounds, many of which have been proven to promote carcinogenesis.[14] The major constituents of e-cigarettes include nicotine, propylene glycol, glycerine and flavouring.[3,14] Other constituents that may be emitted from e-cigarettes include aldehydes, such as formaldehyde, acetaldehyde and acrolein, which result from thermal degradation of propylene glycol and glycerol.[15] While there have been investigations showing the presence of some of the hazardous compounds normally found in tobacco smoke, in e-cigarettes cartridges, solution or mist, only a few reports detected high enough levels to pose a significant risk to humans.[14]

Manufacturers have claimed that e-cigarettes contain less or no nicotine as compared to combustible tobacco cigarettes. It is also claimed that e-cigarettes contain no tar or carcinogens found in tobacco cigarettes. However, these claims cannot be substantiated because of inadequate regulations regarding these products.[13] The amount of nicotine in most commonly available e-cigarettes ranges from 0–36 mg/mL.[16] Studies looking at the nicotine yield in different e-cigarette brands indicate that e-cigarettes deliver less nicotine than traditional cigarettes.[7] A study by Farsalinos et al.[17] showed that the nicotine delivery after using an e-cigarette with a nicotine content of 9 mg nicotine/mL for five minutes, was 0.46 mg. This was shown to be 54% lower than a traditional cigarette which yields about 1mg.[7]

Effects of vaping on the organ systems

Vaping or e-cigarette use has been considered by many to be a healthier alternative to the traditional combustible tobacco cigarette. However, the health consequences and health benefits associated with e-cigarette use are still controversial.[16] The next

section of this article will review the effects of vaping on different organ systems.

Cardiovascular system

Several studies showed that E-cigarette use increases heart rate acutely. Both diastolic blood pressure and heart rate were elevated after e-cigarette use, however to a lesser extend compared to tobacco cigarettes. The use of e-cigarettes has been associated with endothelial cell dysfunction and oxidative stress, but the effect was less pronounced in comparison with cigarette smoking. Acute exposure to e-cigarettes has been shown by some studies to have no immediate effects on coronary circulation, myocardial function and arterial stiffness.[15]

Studies relating to traditional tobacco cigarettes have shown that nicotine increased the risk of cardiovascular disease in smokers. E-cigarettes contain nicotine although the amount delivered is considerably less than conventional cigarettes. Studies showing the nicotine effects related to e-cigarettes are limited and controversial. Some studies have shown an increase in heart rate after e-cigarette use, whereas some found no changes in heart rate.[15]

In addition to nicotine, there are other potentially harmful components of e-cigarettes like carbonyls, including aldehydes, which may alter heart rate, blood pressure and cardiac contractility.[15]

Respiratory system

The use of e-cigarettes results in upper and lower respiratory tract irritation, bronchitis, cough and emphysema.[15] The upper respiratory infection-like symptoms caused by e-cigarettes have been associated with propylene glycol, which is a constituent of e-cigarettes.[16]

Haematological system

E-cigarette vapour extracts were shown to enhance platelet activation (aggregation and adhesion).[15]

Gastrointestinal system

E-cigarettes may cause throat and mouth irritation as well as induce nausea and vomiting.[15]

Immune system and wound healing

E-cigarettes may lead to inflammatory induction,[15] upregulation of certain inflammatory markers and acute phase reactants.[3] E-cigarettes also reduce immune efficiency.[15]

Smoking cessation

A study looking e-cigarettes versus nicotine patches for perioperative smoking cessation, found that e-cigarettes are a feasible tool and acceptable aid for perioperative smoking cessation. The study showed that quit rates were comparable to those of nicotine replacement patches.[18]

Conclusion

Cigarette smoke contains over 4000 substances, some of which are cytotoxic and carcinogenic,[5] while there have been investigations showing the presence of some of the hazardous compounds normally found in tobacco smoke in e-cigarettes, only a few reports detected high enough levels to pose a significant risk to humans.[14]

The nicotine delivered by e-cigarettes has also been shown to be considerably less than that of tobacco cigarettes, as a result e-cigarettes were shown to produce fewer effects as compared to conventional cigarettes.

E-cigarettes have become very popular worldwide, but despite that, research regarding the effects of these devices on human health is limited.[14] Although there is limited data, e-cigarettes are not entirely harmless as promoted by their manufacturers.[12] When looking at the harmful effects of conventional tobacco smoking, vaping is considered by some studies as a possible harm reduction tool.[14] More studies focusing on the comparison of conventional tobacco smoking and vaping regarding their effects on the health of patients should be done in order to reach a comprehensive conclusion.

Conflict of interest

There was no potential conflict of interest relevant to this article.

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CPR: ABC or CAB

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Cardiopulmonary resuscitation (CPR) has over the past 60 years become an ubiquitous skill amongst medical professionals and laypeople alike. Over the past several decades, a number of different research findings have led to fundamental changes in the methods used in attempts to reverse cardiac arrest. In order to understand our current practice, it is important to have a firm grip on the history of modern resuscitation.

CPR is comprised of 3 individual components; rescue breathing, compressions, and defibrillation. Each of these developed separately, in some cases over hundreds or even thousands of years.[1] Following a spate of drownings across Europe in the 18th century, the Paris Academy of Sciences (Académie des Sciences) in 1740 issued a recommendation for the use of mouth-to-mouth resuscitation in drowned victims.[2] In 1744, the first successful use of this method in a human was documented by Tossach.[1] Thereafter a number of different ventilation approaches were attempted, and it took more than 200 years before mouth-to-mouth and mouth-to-airway were shown to be the most efficient methods of artificial respiration.[3]

At around the same time, several investigations into the effect of electric shock applied to the myocardium brought forth the next leap forward in resuscitation science – defibrillation. In 1956, Zoll published his seminal paper detailing four patients in ventricular fibrillation who had been defibrillated, one of whom survived to discharge.[4] Despite this discovery it wasn't until the 60s that the various components of CPR began to be utilised together.

During defibrillation experiments on dogs, Kouwenhoven had noted that the pressure of the heavy paddles increased blood pressure, and that rhythmic pressure to the sternum maintained cerebral blood flow.[5] In 1960, he published his now famous article describing 'closed-chest cardiac massage' – so named because prior to this direct cardiac massage through an open chest had been the mainstay of cardiac arrest management.[6] A flurry of investigations and publications followed, which suggested a compression rate of 60 to 80 per minute, and a compression depth of 4 to 5 centimetres paired together with artificial respiration, as well as defibrillation and administration of vasopressors as the optimal approach to resuscitation.[7]

A few years later, in 1966, the first CPR guidelines were published and quickly spread worldwide.[8] Of note is that even at this early stage of modern CPR the danger of delay in initiation of resuscitation was clearly recognised as a poor prognosticating factor.[9]

In 1957, Safar published the 'ABC of Resuscitation' which subsequently informed the stepwise approach of 'Airway-Breathing-Circulation' by which CPR would be performed into the 21st century.[10] Up until 2005, this approach emphasised opening of the airway followed by assessment of breathing, rescue breaths as required, and then a circulatory assessment usually in the form of a pulse check, followed by chest compressions as required. In 1982, the Netherlands, noting experimental data which showed no significant drop in PO2 and O2 saturation in the first 5 minutes after arrest, changed their CPR algorithm from an ABC approach to a compressions-airway-breathing (CAB) approach. They found that starting chest compressions first resulted in quicker restoration of coronary perfusion pressure and more chance of successful defibrillation.[11] At the time, the Netherlands was the only country following this approach, briefly adopting the ABC approach to fall in line with European Resuscitation Council (ERC) guidelines before reverting to CAB with the 2005 ERC guidelines.

The Dutch decision has since been supported by evidence which shows that in animal models and human studies defibrillation performed from 3 to 5 minutes after arrest is more likely to result in return of spontaneous circulation (ROSC) if at least 90 seconds of CPR is completed immediately prior to shock. This finding is best described by a 3-phase time based physiological model of CPR divided into the electrical phase, the circulatory phase, and the metabolic phase. The electrical phase extends from the time of arrest to approximately 4 minutes thereafter and refers to a period during which the heart is exceptionally responsive to defibrillation. This explains the success of early external defibrillation as well as various devices including implantable cardioverter defibrillators (ICD). The circulatory phase, which runs from 4 to 10 minutes, is the time during which chest compressions are crucial to provide much needed oxygen amongst other substrates to the myocardium. In addition, the forward flow created by quality CPR allows for washout of various metabolic toxins which accumulate during ischaemia. The period after roughly 10 minutes following arrest is called the metabolic phase, during which it becomes increasingly difficult to adequately overcome the systemic metabolic derangement,

resulting in a massive inflammatory response, translocation of gut flora and irreversible tissue damage.[12]

Given this background, the importance of compressions as the single greatest intervention in cardiac arrest, along with defibrillation, has become clearer and more evidence-based in the past 20 years. The University of Arizona Sarver Heart Center Resuscitation Group pioneered the concept of cardiocerebral resuscitation (CCR). This method focuses on continuous compressions stopping only for rhythm checks and defibrillation as required so as to minimize the time spent off the chest.[13] This is because continuous uninterrupted chest compressions have been shown to result in physiologically appropriate perfusion pressures which can and do lead to ROSC.[14] In fact, multiple studies have repeatedly shown that CPR with a focus on chest compressions, whilst keeping interruptions to an absolute minimum, increase the chances of ROSC and improve neurological outcomes as well as patient survival.[15,16] During CPR, it takes about 45 seconds of continuous chest compressions to reach an optimal perfusion pressure. Therefore, any time taken before the initiation of chest compressions, including the first 45 seconds of those compressions, are periods of non-perfusion.[17]

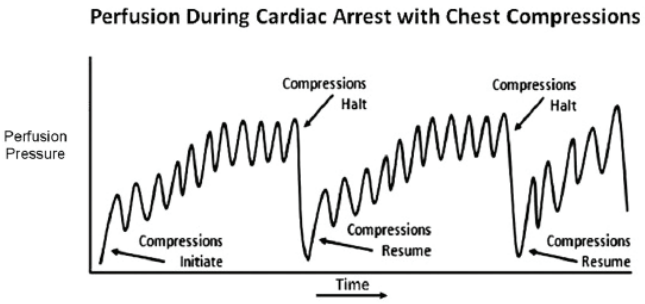

Figure 1: Perfusion pressure gradually increases with the initiation of chest compressions. Interruptions in chest compressions cause a sudden loss of this pressure[17]

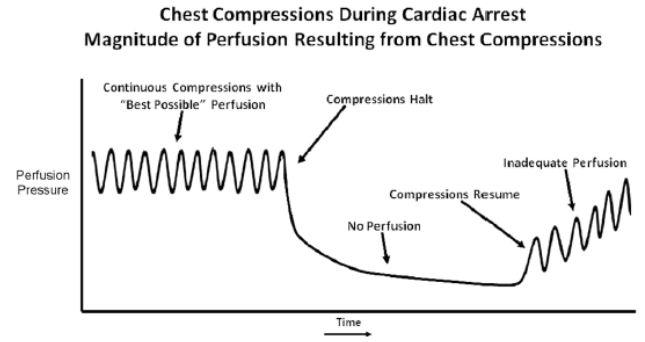

Figure 2: Prolonged interruptions in chest compressions lead to even greater periods of inadequate perfusion[17]

This information has greatly influenced the 2 major changes to CPR which took place in 2005 and 2010 respectively. The first of these was a move from a compression to ventilation ratio of 15:2 to that of 30:2 for single rescuers of victims of all age groups except neonates.[18] This change was justified by low CPR survival rates and the aforementioned evidence which highlighted improved coronary perfusion pressure and cardiac output with an increasing number of consecutive high quality chest compressions.[19] The second and arguably more controversial change was the move away from the ABC approach which had remained in place globally until 2010. The International Liaison Committee on Resuscitation (ILCOR) changed this recommendation to that of a CAB approach, emphasising that compressions should be of adequate rate and depth, allow for full chest recoil and minimize interruptions. This was done with the simultaneous removal of a step providing for initial rescue breaths prior to any chest compression.[20] The overriding justification for the implementation of CAB is the significantly shortened delay in starting compressions[21] and a reduced time to complete a cycle of compressions and ventilations.[22]

In 2015, ILCOR again released updated guidelines in which they continued to suggest CAB over ABC but noted the need for more evidence to improve the strength of the recommendation. Of note is that the approach to paediatric patients is left up to individual resuscitation councils, meaning that ABC may be recommended in this age since a greater number of arrests are hypoxia related.[23] It has however been shown that even in paediatric resuscitation rescuers identify the condition quicker, make fewer mistakes using the CAB sequence, and that this approach does not delay ventilatory support as compared to ABC.[24] Further additions to the 2015 guidelines with regards to compressions are the inclusion of a range for compression rate from 100 to 120 per minute, a maximum compression depth of 6 cm in adults, and the introduction of a compression fraction whereby chest compressions during CPR should comprise at least 60% of the total time in a resuscitation.[25] Following a CAB approach makes it somewhat easier to achieve a higher compression fraction.

The CAB mnemonic has had the effect of de-emphasising the role of airway management during CPR. Under the ABC approach, and until 2005, opening of the airway and assessing the patient for breathing, independent from any signs of circulation, was a standard of care. The 2005, 2010, 2015, and the latest 2017 guidelines all downplay the role of airway interventions in lieu of adequate chest compressions.[26] The belief that advanced airway techniques such as endotracheal intubation (ETI) or insertion of a supraglottic airway (SGA) is superior to bag-mask ventilation (BMV) is inconsistent with the available evidence, which currently indicates that advanced airway management during CPR is associated with lower survival rates.[27] In a large cohort study of more than 86 000 patients, intubation within the first 15 minutes of CPR was associated with a significant reduction in survival to hospital discharge.[28] This is most likely because intubation interrupts chest compressions by as much as 110 seconds in the average patient,[29] even though current guidelines recommend that ETI should never interrupt compressions for more than 5 seconds.[30] More recently, the use of video laryngoscopy (VL) in resuscitation has been compared to that of traditional direct laryngoscopy (DL). The literature is conflictory with some evidence suggesting greater first attempt success rates, most especially in less experienced clinicians,[31] while another study showed no difference between VL and DL in ETI success, although VL did cause fewer interruptions of chest compressions.[32]

At best when compared to BMV, the use of ETI shows no benefit over the more basic technique in a good example of clinical equipoise.[33] A related issue is that poor ventilation technique in cardiac arrest, which commonly includes hyperventilation, has poor survival outcomes.[34] This is due to various physiological derangements, most notably increased intrathoracic pressure leading to decreased cardiac output, coronary and cerebral perfusion.[35] The best approach to airway management remains unclear and there is a paucity of data with regards to CPR in the operating theatre when this process is performed by anaesthesiologists. Much of the data available for airway management during cardiac arrest is derived from out of hospital studies and then extrapolated for in-hospital practice.[36] Further investigation is thus required, but it is clear that instrumentation of the airway should not detract from time spent on the chest.

Since the invention and popularisation of CPR in the 1960s much has changed, and steady strides have been made in understanding the best approach to the patient in cardiac arrest. The CAB approach is part of this evolution, which now places emphasis on chest compressions, crucial in the initial phases of an arrest. Whilst ABC in this context serves a similar purpose, it likely delays the initiation of CPR thereby worsening outcomes, making CAB a more pragmatic and evidence-based approach to resuscitation.

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