# Regional anaesthesia: the A, B and Cs

#### Peer reviewed © Medpharm

Quan C Correspondence to: Celeste Quan, e-mail: barrowceleste@gmail.com

#### S Afr Fam Pract 2013;55(3)(Suppl 1):S32-S35

## Introduction

I will be addressing concepts related to regional anaesthesia which are pertinent to practice in South Africa.

- Awake or not: Should regional anaesthesia be performed in awake or anaesthetised patients?
- **B** mode ultrasound: Should regional anaesthesia be carried out under ultrasound or not?
- **C**ancer surgery: Should anaesthesia for cancer surgery involve regional anaesthesia?

The oversimplified answers to each question are:

- Awake: Yes.
- **B** mode ultrasound: Yes.
- Cancer surgery: Yes.

## Awake patients

There are no prospective randomised controlled studies which compare the relative risks of regional anaesthesia performed on awake or anaesthetised patients. Available data are derived from retrospective qualitative studies (critical incident reporting, closed claim analysis and case reports) where there has been a negative outcome.<sup>1</sup> These studies have inherent weaknesses: reporting bias, incomplete voluntary reporting and an increasing frequency of medico-legal claims, which means that the numerator is unknown. In addition, the denominator is also unidentified as the total population at risk and the frequency of different techniques is also unspecified. To add to the complexity, there may also be a time lag between the actual procedure and the reporting and analysis of the complication. In addition, the incidence of serious morbidity relating to regional anaesthesia is extremely rare.<sup>2</sup>

The benefits of performing regional anaesthesia in anaesthetised patients include:

 Greater patient acceptance, especially where the cultural experience has been to expect a general anaesthetic.

- Easier performance.
- Better conditions for teaching.

The disadvantage is:

 Removal of verbal contact results in a loss of warning against intraneural injection, as well as local anaesthetic toxicity. Pain and paraesthesia are insensitive indicators of needle-nerve contact, but their positive predictive value is close to 100%.<sup>3</sup>

Some would argue that there is no potential benefit to the patient that is worth any risk of serious morbidity.

It is generally deemed acceptable to perform blocks in anaesthetised children. Children cannot always be reasoned with to lie still. Sudden movement can be potentially hazardous. The risk of peripheral regional anaesthesia in paediatrics is low. However, there does seem to be a higher risk of complications in the central block group. An incidence of 1.5 per 1 000 has been quoted by Sang et al.<sup>4</sup>

The issue is not so clear in adults. Auroy performed a prospective study of > 100 000 regional anaesthetics and found that 62% of serious neurological complications pertaining to subarachnoid blocks were associated with paraesthesiae.<sup>2</sup> Generally, it is accepted that subarachnoid blocks are now carried out when the patient is awake.

Feely conducted a survey in 2006 in the Oxford region. He examined the views and practice of the performance of regional anaesthesia, when combined with general anaesthesia for adults. Eighty-five per cent performed epidurals awake, 77% conducted combined spinal epidurals awake, and 86% completed subarachnoids awake. However, the figures were lower for upper limb blocks, and even lower for lower limb blocks. Fifty-two per cent believed it was safer to perform interscalene blocks before induction, but only 36% felt this to be the case for axillary blocks. The numbers for the lower limbs included lumbar plexus 25%, sciatic 16%, femoral 15% and ankle 7%. Importantly, when this study was performed, peripheral nerve stimulators were regarded as the gold standard and ultrasound was not commonly used. In summary, the decision as to whether or not to carry out a block awake or asleep should be individualised according to the patient profile, the skill of the practitioner, the availability of ultrasound and the site of the block. The more central the block, the stronger the case for performing the block while the patient is awake.

## **B** mode ultrasound

It is now almost 20 years since ultrasound was first described as a tool for nerve localisation. The first decade established the feasibility of ultrasound-guided regional anaesthesia and approaches to common peripheral nerve blocks were described. The second decade featured investigators experimenting with deeper blocks and placement of perineural catheters. Now, anaesthesiologists are appreciating the advantages and limitations of the ultrasound.

The American Society of Regional Anesthesia and Pain Medicine appointed a group of ultrasound-guided regional anaesthesia experts to review the scientific underpinnings of ultrasound as a tool for nerve localisation. Their findings were published in 2010.<sup>5</sup>

The panel considered three areas:

- Block-related outcomes, e.g. onset, duration and patient satisfaction.
- Process-related outcomes, e.g. block performance time.
- Safety-related outcomes.

Their goal was to directly compare ultrasound-guided regional anaesthesia to other nerve localisation tools with regard to block- and performance-related outcomes and patient safety issues;<sup>2</sup> global issues such as postoperative neurological symptoms and local anaesthetic systemic toxicity; and two block-specific issues, namely hemidiaphragmatic paresis and pneumothorax. The panel also assessed the role of ultrasound in paediatrics and interventional pain medicine.

## Upper extremity blocks

Ultrasound-guided regional anaesthesia has a faster performance time, as well as faster sensory block onset time, than peripheral nerve stimulation. There are also less needle passes with ultrasound-guided regional anaesthesia. However, this did not consistently translate to improved patient satisfaction or blockrelated complications. Block success, when defined by anaesthetised nerves, was higher with ultrasoundguided regional anaesthesia. However, there was less of a difference when block success was defined by more clinically relevant measures: readiness for surgery, need for block supplementation, or the addition of general anaesthesia. There is also a lower complication rate [Horner's syndrome and hemidiaphragmatic paresis].

#### Lower extremity blocks

Ultrasound-guided regional anaesthesia had a faster onset time. There was no difference in the need for supplemental analgesia or rescue anaesthesia, but there was a more complete block of studied nerves. Two studies demonstrated the ability of ultrasound-guided regional anaesthesia to reduce the amount of local anaesthetic necessary to achieve an adequate block (absolute mean reductions of 9 ml for femoral blocks and 20 ml for sciatic blocks). Catheter placement popliteal sciatic blocks were performed faster under ultrasound guidance.

#### **Truncal blocks**

Truncal blocks include paravertebral, intercostal, transversus abdominis plane (TAP), rectus sheath, and ilioingional or iliohypogastric blocks. At present, there are insufficient data to draw conclusions on paravertebral, intercostal and TAP blocks. Ultrasound-guided rectus sheath blocks resulted in a higher success rate, as opposed to a blind technique, in the hands of trainees.

## **Neuraxial blocks**

Ultrasound is used in neuraxial techniques to determine the midline, targeted interspace or depth of skin to epidural or subarachnoid space, before performing the procedure using traditional methods. Practically, it is almost impossible to perform a neuraxial technique under real-time ultrasound imaging.

Ultrasound is superior to physical examination, but inferior to radiological imaging. Ultrasound guidance is likely to be the most useful in patients with a challenging anatomy. Ironically, obtaining adequate images in this group of patients will be more difficult. At this stage, there are inadequate data to draw any conclusions.

#### Paediatrics

This population group is often anaesthetised prior to block placement. However, existing studies are too small to assess the usefulness of ultrasound-guided regional anaesthesia. Similar to adults, studies show that sensory block onset is often faster, but ultrasound equipment setup time is typically not reported. Studies demonstrate the ability of ultrasound to identify the duramater and ligamentum flavum. However, there are little data to translate this to improved block success or safety. The ability to use smaller volumes of local anaesthetic in children is particularly appealing.

#### Chronic pain

The benefits of ultrasonagraphy in interventional chronic pain procedures include decreased radiation exposure to both the patient and the operator. Preliminary feasibility studies support the use of ultrasound guidance for cervical selective nerve root and stellate ganglion block. However, no data exist to compare the efficiency of ultrasound to fluoroscopic guidance for lumbar facet injection, lumbar nerve root injection, or cervical selective nerve root injection.

## Patient safety

Ultrasound-guided regional anaesthesia has the advantage of directly visualising the target nerve, surrounding tissues and injectate spread. It would seem almost intuitive that this advantage might reduce complications such as nerve injury, local anaesthetic systemic toxicity, pneumothorax or hemidiaphragmatic paresis. Unfortunately, the most serious of these complications (permanent nerve injury and local anaesthetic systemic toxicity) are so rare that they defy statistical proof. With regard to nerve injury, there are many other variables other than the use of ultrasound or not. These include patient factors, and surgical and positioning factors. Ultrasound limits the frequency of vascular puncture, but there is conflicting evidence whether this results in a reduction in local anaesthetic systemic toxicity. Although the use of ultrasound and low local anaesthetic volume reduces the frequency and intensity of hemidiaphragmatic paresis, it does so unpredictably. Finally, pneumothorax has been reported despite the use of ultrasound guidance.

#### **Cancer surgery**

Surgical excision is the mainstay of treatment for potentially curable solid tumours. Metastatic disease is the most important cause of cancer-related deaths in these patients. The risk of metastases depends on the balance between the metastatic potential of the tumour and the antimetastatic host defenses, of which cell-mediated immunity and natural killer cell function are important. Surgery can inhibit important host defenses and increase the risk of metastases. Anaesthetic technique and drug choice can interact with the cellular immune system and affect long-term outcome.<sup>6</sup>

An analogy has been made between developing postoperative wound infection and postoperative metastasis. In both instances, the principle is that the postoperative time is a critical time and that the suppression of host defenses at this time can have a longterm outcome.<sup>7</sup> The chances of tumour metastasising depend on the balance between the metastatic potential of the tumour and the antimetastatic host defenses.<sup>8</sup> One hypothesis of how a tumour metastasises is referred to as the "seed and soil" theory.<sup>9</sup> Initially, a tumour's nutrient supply is met by diffusion. As the tumour grows, neovascularisation occurs as anajogenic factors are secreted, and a capillary network arises from the adjacent tissue. Tumour cells then enter the host circulation, embolise, extravasate, proliferate and ultimately develop their own blood supply.

Initially, tumour cells are weakly antigenic and do not elicit an immune response. As they mutate further, they become more antigenic. Ultimately, the tumour cells develop escape mechanisms in order to evade the immune response.

An intact cellular immune system is the critical host defense against the development of metastases. Natural killer cells are the primary defense. Animal studies have shown that stress-induced reduction in natural killer cell activity can cause increased tumour development.<sup>10</sup> Interleukin 2 and interferon gamma are important activators of natural killer cells. Cytotoxic T-cell function is also important, as are mononuclear cells and dendritic cells.

The potential ability of regional anaesthesia to improve long-term outcome after cancer surgery can be attributed to three different outcomes:

- Regional anaesthesia attenuates the immunosuppressive effect of surgery.
- Patients who have regional anaesthesia have lower opioid requirements. Opioids may inhibit cellular and humoral immune function.<sup>11</sup> Morphine inhibits natural killer cell cytotoxicity.<sup>12</sup> Opioids also promote and stimulate angiogenesis.<sup>13</sup>
- When regional anaesthesia is used in addition to general anaesthesia, the amount of required general anaesthesia is reduced. Anaesthetic induction agents and volatile anaesthetics suppress natural killer cells activity.<sup>14</sup>

To date, there are only retrospective analyses of the effect of regional anaesthesia on cancer metastases. Exadaktylos et al showed a fourfold reduction in recurrence or metastasis in patients who received a paravertebral block combined with general anaesthesia, as opposed to general anaesthesia and morphine analgesia, for primary breast cancer. The mean duration of follow-up was 32 months.<sup>7</sup>

Biki et al showed a 57% reduction in the incidence of biochemical cancer recurrence when epidural analgesia was used for open prostatectomy, when compared with postoperative opioid analgesia. (The follow-up interval was 2.8-12.8 years).<sup>15</sup>

Gildasio et al examined the use of intraoperative neuraxial anaesthesia for primary cytoreductive surgery in patients with ovarian cancer. The intraoperative epidural group had a mean time to recurrence of 73 (56-91) months, as opposed to the postoperative epidural group 33 (21-45), or the no epidural group 38 (30-47).<sup>16</sup>

Gottschalk et al explored the role of regional anaesthesia for lymph node dissection in malignant melanoma. They considered spinal versus general anaesthesia, and found a better mean survival rate (95.9 vs. 68.5).<sup>17</sup> Gottschalk et al also performed a study that examined the association between epidural anaesthesia and recurrence after colorectal cancer surgery. They did not find a decrease in recurrence in the epidural group. However, a potential benefit was observed in older patients. They concluded that the benefit of regional anaesthesia with regard to cancer recurrence might depend on the specific tumour type.<sup>18</sup>

All the abovementioned studies have serious limitations. They were all retrospective. Patients were not randomised and clinical care was not standardised. Consequently, selection bias and the effects of unmeasured confounding variables cannot be excluded. However, as pointed out by Ochroch and Fleisher, it is necessary to "look backward to point the way forward".<sup>19</sup> There is no doubt that prospective human trials are needed. The Outcomes Research Consortium (Cleveland Clinic, USA) has initiated multicentre randomised controlled trials that consider paravertebral anaesthesia and analgesia for breast cancer surgery and epidural anaesthesia and analgesia for laparoscopic colorectal cancer surgery. The primary end-point for these trials is cancer recurrence.

In conclusion, interesting animal data suggest that regional anaesthesia is beneficial in cancer surgery. It has not been confirmed if this can be extrapolated to medical practice in humans. There have been limited, retrospective human clinical studies.<sup>2</sup> Prospective studies are underway, but we will have to wait a few years before the outcome is established.

## References

- Fischer H. Regional anaesthesia: before or after general anaesthesia. Anaesthesia. 1998;53:727-7279.
- Auroy Y, Narchi P, Messiah A, et al. Serious complications related to regional anesthesia. Anesthesiology. 1997;87(3):479-486.
- Perlas A, Niazi A, McCartney C, et al. The sensitivity of motor tonerve stimulation and paraesthesia for nerve localization as evaluated by ultrasound. Reg Anesth Pain Med. 2006;31(5):445-450.

- Sang C, Berde C. Safety on regional anesthesia study group. A multicentre study of safety and risk factors in paediatric regional anesthesia. Anesthesiology. 1994;81:A1386.
- Neal J, Brull R, Chan V, et al. The ASRA evidence-based medicine assessmentof ultrasound-guided regional anesthesia and pain medicine. Reg Anesth Pain Med. 2010;35(2):S1-S9.
- Snyder G. Effect of anaesthetic technique and other perioperative factors on cancer recurrence. Br J Anaesth. 2010;105(2):106-115.
- Exadaktylos A, Buggy D, Moriarty D, et al. Can anaesthetic technique for primary breast cancer surgery affect recurrence or metastasis. Anesthesiology. 2006;105(4):660-664.
- Shakhar A. Potential prophylactic measures against postoperative immunosupression: could they reduce recurrence rates in oncological patients. Annal Surg Oncol. 2003;10:972-992.
- Fidler I. The pathogenesis of cancer metastasis: thee "seed and soil" hypothesis revisited. Nat Rev Cancer. 2003;3(6):453-458.
- Ben-Eliyahu S, Page G, Yimiya R, Shakhar G. Evidence that stress and surgical interventions promote tumour development by supressing natural killer cell activity. Int J Cancer. 1999;80(6):880-888.
- Sacerdote P, Bianchi M, Gaspani L, et al. The effects of tramadol and morphine on immune responses and pain after surgery in cancer patients. Anesth Analg. 2000;90(6):1411-1414.
- Yeager M, Colacchio T, Yu C, et al. Morphine inhibits spontaneous and cytokine-enhanced natural killer cell cytoxicity in volunteers. Anesthesiol. 1995;83(3):500-508.
- Gupta K, Kshirsagar S, Chang L, Set al. Morphine stimulates angiogenesis byactivating proangiogenic and survival-promoting signaling and promotes breast tumour growth. Cancer Res. 2002;62(15):4491-4498.
- 14. Melamed R, Bar-Yosef S, Shakhar G, et al. Suppression of natural killer cell activity and promotion of tumor metastasis by ketamine, thiopental, and halothane, but not by propofol: mediating mechanisms and prophylactic measure. Anesth Analg. 2003;97(5):1331-1339.
- Biki B, Mascha E, Moriarty D, et al. Anesthetic technique for radical prostatectomy surgery affects cancer recurrence. Anesthesiology. 2008;109(2):180-187.
- 16. De Oliviera G, Ahmad S, Schink J, et al. Intraoperative neuraxial anesthesia but not postoperative neuraxial analgesia is associated with increased relapse-free survival in ovarian cancer patients after primary cytoreductive surgery. Reg Anesth Pain Med. 2011;36(3):271-277.
- Gottschalk A, Brodner G, Van Aken H, et al. Can regional anaesthesia for lymph-node dissection improve the prognosis in malignant melanoma. Br JAnaesth. 2012;109(2):253-259.
- Gottschalk A, Ford J, Regilin CC, et al. Association between epidural analgesia and cancer recurrence after colorectal cancer surgery. Anesthesiol. 2010;113(1):27-34.
- Ochroch E, Fleisher L. Retrospective analysis. Looking backward to point the way forward. Anesthesiology. 2006;105(4):643-634.