S Afr Fam Pract 2015;57(2)(Suppl 1):S25

S Afr Fam Pract
ISSN 2078-6190 EISSN 2078-6204

REFRESHER COURSE

New Diabetic Drugs: A Summary

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Keywords:

Drugs administered subcutaneously

Insulin

Insulin is used in both type 1 and brittle type 2 diabetics. Traditionally insulin has been administered with multiple daily injections (MDI) and patients had to *self monitor* their blood glucose (SMBG) by needlestick.

Improved technology has enabled a closed loop artificial pancreas (AP).[3] A small needle inserted in the buttock and abdomen is attached to a pump worn by the patient which delivers subcutaneous insulin infusions (CSII). A separate sensor is able to continuously monitor glucose (CGM) and is able to relay the information via Bluetooth to a device such as a cell phone to give accurate blood sugar estimations. Therefore continuous real time glucose monitoring is now feasible (CGM-rt). Five hundred thousand patients in the USA now have insulin pumps.

Anaesthetic concerns: Pumps and disposables are very expensive and some devices are destroyed with radiation and electro- cautery. The subcutaneous needle if placed in the surgical field must be removed at least 24 hours prior to an operation.

Incretin analogues *Exenatide (Byetta®); Liraglutide (Victoza®)*[1]

Glucagon-like peptide (GLP-1) is found in entero-endocrine cells in the distal ileum and large intestine. One of the main physiological effects of incretins is to rapidly increase insulin and decrease glucagon secretion in response to an ***oral*** glucose load. This is known as the *incretin effect*. Other effects are: appetite suppression, as a feeling of satiety is experienced due to delayed stomach emptying.

Dipeptidyl peptidase (DPP-IV) rapidly breaks down GLP-1. A DPP-IV inhibitor increases incretin levels and is used to control type II diabetics.

These drugs have been proven to decrease the cardiovascular risk and also allow for significant weight loss in 1/3 of patients which obviously has an enormous impact on type 2 diabetics.

As these drugs are costly, they have not yet been introduced into state hospitals.

Anaesthetic concerns: Unlikely to give peri-operative hypoglycaemia. Nausea may occur in some patients and renal and hepatic pharmacokinetics may be altered. Weight loss is due to anorexia due to gastroparesis. Therefore PONV and an aspiration risk may be of concern to the anaesthetist.

New drugs administered orally

- ***DPP-4 antagonists*** (sitagliptin (Januvia®), saxagliptin (onglyza®) and vildagliptin (Galvus®)
  These drugs are used in combination with insulin.
  They do not cause hypoglycaemia and have few side effects
- ***Sodium-glucose co-transporter 2 (SGLT2)*** Dapagliflozin[3]
  Block reabsorption of glucose in the kidney (~50% of normal glucose load is reabsorbed at the level of the proximal tubule). The action is independent of the glucose load.
  Not available in South Africa, but is in the pipeline.
  Does not cause hypoglycaemia.

Older oral hypoglycaemics[4]

- ***Metformin***
  Concern maybe intra-operative lactic acidosis
- ***Sulphonylureas***[4]
  As these drugs act by blocking potassium channels, they may prevent intra-operative pre-conditioning.

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