NeuroEndocrine Cancer Australia

Anaesthesia Factsheet

Carcinoid Crisis

Sometimes people with NETs have a particularly bad episode of carcinoid syndrome triggered by stress, general anaesthetic or certain treatments. This is called 'carcinoid crisis'. Symptoms include intense flushing, diarrhoea, abdominal pain, wheezing, palpitations, low or high blood pressure, altered mental state and, in extreme cases, coma. Your NET specialist will ensure you are monitored during a procedures (including dental work and anaesthetics), in which you may be susceptible to these symptoms and may give you medication to prevent such a crisis occurring (e.g. an infusion of a somatostatin (octreotide) analogue).

A wallet sized card is available on Neuroendocrine Cancer Australia website for patients to carry to alert health professionals to Carcinoid Crisis and management of this.

Anaesthesia for patients with neuroendocrine tumours

Patients with neuroendocrine tumours (NETs) can safely tolerate procedures that require general anaesthesia (inhalational or intravenous), regional/local anaesthesia and sedation (medication to relax you) provided that the procedure is managed by anaesthetists that understand and can manage a carcinoid crisis.

A carcinoid crisis during an operation / procedure, major or minor, is a specific risk for NET patients and occurs in up to 20-30% of surgeries. This includes dental procedures. Therefore, NET patients need to be managed in centres with experience in the treatment and management of NETs patients.

Carcinoid crisis is characterised by one or more of the following signs:

- Hypotension (low blood pressure) or hypertension (high blood pressure) – "haemodynamic instability"
- Tachycardia (fast heart rate)
- Flushing
- Bronchospasm (asthma)
- Hyper-pyrexia (high body temperatures)

Risk factors for developing carcinoid crisis:

- Large tumour burden of disease (e.g. liver metastases)
  - High Chromogranin A (CgA) levels
  - High urinary 5-HIAA levels
- Presence of carcinoid heart disease

Potential triggers for developing carcinoid crisis:

- Minor or major surgery; PRRT; endoscopic procedures; chemoembolization of tumours
- Anxiety, stress
- Induction of anaesthesia; hypothermia during an operation; histamine releasing drugs

It is very difficult to accurately predict 'at risk' patients for a carcinoid crisis during an operation therefore the anaesthetic team must be prepared for its occurrence. Octreotide is used to both prevent and manage carcinoid crisis.

Octreotide (somatostatin analogue)

Octreotide is a somatostatin analogue that inhibits the release of growth hormone, glucagon, insulin and other gastrointestinal peptides and also binds to somatostatin receptors (type 2,3,5) on neuroendocrine tumours, inhibiting cell growth and proliferation.

Octreotide is poorly absorbed orally and is therefore administered parenterally (intravenous, intramuscular or subcutaneous (under the skin) injections).

Octreotide is rapidly absorbed from subcutaneous injection with a peak plasma concentration and onset of action at 20-30 minutes and plasma half-life of 60-90 minutes.

It is primarily metabolised by the liver (65%) and excreted by the kidneys. Elimination from the body is delayed in patients with impaired kidneys.

Octreotide can be safely be used in large amounts and has been used in high doses (1500µgm/hr) with minimal side effects whilst controlling symptoms and signs of carcinoid crisis.

During the operation octreotide is administered intravenously and is stable in normal saline, water, 5% dextrose for 24 hours. It can be given as a rapid single injection or constant infusion for best to effect.

There is no consensus as to exact dosages for the prevention against a carcinoid

crisis pre-induction bolus of 500µgm followed by constant infusion at 500µgm/hr diminishes the risk of intraoperative carcinoid crisis significantly (<4%).

Patients currently on long acting octreotide (Sandostatin LAR, Lanreotide) often require higher doses of intraoperative octreotide which may reflect a degree of tachyphylaxis (decrease response) to the drug.

Information for your surgery team:

Pre-operative
Full preoperative work-up including cardiac investigations for carcinoid heart disease Correct electrolyte abnormalities, dehydration and pre-existing protein abnormalities Appropriate monitoring (arterial pressures, central venous pressures).
Pre-medication
Octreotide 100-1000µgm as bolus then 100-1000µgm/hr infusion (titrated to effect) Antihistamines • H1 antagonist – diphenhydramine, loratidine, etc • H2 antagonist – ranitidine, famotidine Anxiolytic • Benzodiazepines – midazolam, diazepam etc
Intra-operative
Octreotide - continue infusion at 100-1000µgm/hr with boluses when indicated Avoid drugs that have a potential for histamine release Eg. Morphine, pethidine, codeine, atracurium, mivacurium
Effective blunting of the pressor response to intubation and maintenance of depth of anaesthesia Prepare for periods of potential carcinoid crisis during manipulation of tumour.

Management of carcinoid crisis haemodynamic instability
Bolus doses of octreotide 100-1000µgm
Use of crystalloids or colloids to expand intravascular space whilst avoiding right ventricular overload or strain.
Use of vasoconstrictors – phenylephrine, metaraminol, noradrenaline (low doses)
Adrenaline has the potential to cause more release of vasoactive peptides but this is inconsistently seen and has been used in resuscitation of NET patients.
Monitor fluid balance, temperature and blood sugar levels
Post-operative period
Continue octreotide infusion and wean over days
Monitor in a high dependency or intensive care setting
Ensure good pain control with regional techniques; neuraxial blockade; patient-controlled analgesia (PCA)

Reference

Kaltsas et al (2017) ***"ENETS Consensus Guidelines for the Standards of Care in Neuroendocrine Tumors: Pre- and Perioperative Therapy in Patients with Neuroendocrine Tumors"***

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5637287/

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