"From the Trough"

Perioperative Interest Group Notes

Based on Cases discussed at the Weekly PIG Clinical Meeting on 7th December 2017. Publication date 29th January 2017.
Website: www.perioptalk.org

The imperfect opinions in these reports are only meant to stimulate discussion:- they should not be considered a definitive statement of appropriate standards of care.

TOPIC 1: Patient with hypoxaemic respiratory disease

A 54 year old male is booked for a ureteric laser lithotripsy. He recently had a cystoscopy and stent insertion under a general anaesthetic. He is on home and portable oxygen – saturation in the clinic is 92% on 4 litres a minute. Breathless on minimal exertion. Also is on methadone. FEV1 0.47L (13% of predicted). **Question:-** How to manage?

Discussion: - Firstly clarify with the surgeons:- Is the surgery appropriate and necessary? Are there alternatives (such as ESWL)? Assessment should incorporate noting what his bicarbonate level is this may give an indication of CO2 retention. Blood gases will clarify this further. Spinal anaesthetic is not feasible for ureteric interventions. The spirometry 'measurement' must be treated with some scepticism. Pragmatically, the patient recently had a successful cystoscopy. Although this procedure requires general anaesthesia, there is no ongoing pain or muscle injury that will impair respiration so the real challenge is just to get the patient through the anaesthetic and initial recovery. Keeping things "as simple as possible" is a good idea. Ketamine and propofol would be a good option.

TOPIC 2: Resources to guide Perioperative Medication Management.

A recent authoritative reference text/manual to guide Perioperative Medication Management has been produced from within the NHS in Britain, and is available freely on line. The text is organised by drug class and uses generic names, but once familiarised it is reasonably easy to use, and most recommendations are consistent with Australian practice. It has been posted on www.perioptalk.org.

TOPIC 3: Mania as a Complication of Spinal Anaesthetic?

A woman in her 70's had a spinal anaesthetic for a total knee replacement which went well. Unfortunately two weeks post-operatively she contacted the orthopaedic surgeons complaining of tinnitus, urinary incontinence, and distressing agitation/confusion (verging on hypomania). The orthopaedic surgeons referred to anaesthetics, suggesting this may be a reaction to the spinal anaesthetic. The consultant anaesthetist considered the possibility of other adverse drug reactions (i.e. reviewed all the drug exposures in the perioperative episode) although there did not appear to be any drug that would be recognisably associated with this outcome(s). A neurologist was consulted, who recommended that an MRI should be performed in case there was co-incidental intracranial pathology. The tinnitus may be considered as associated with the spinal anaesthetic and CSF leak.

After careful discussion and review of medical history it was elicited that the lady had some preoperative symptoms of occasional urinary incontinence. It was considered that this may have been worsened by the spinal and just by the perioperative emotional/physiological stress. The latter may also have contributed to the 'mania'. Explanation was given and she was reassured, with expectant treatment advised sympathetically. After 1 week she was less confused, less manic and the tinnitus was improving. After 2 weeks it had improved further and no further treatment was given.

Persistent CSF leaks with classical symptoms after spinal anaesthetics, or after spinal puncture for diagnostic purposes, is well recognised. But Tinnitus? Two reports in the literature of patients with tinnitus and hearing loss after spinal anaesthetics treated by blood patches were found.

REFS

Surkilar et al Turkish Journal of Anaesthesiology and Reanimation 2015 Oct, 43(5): 371-372,
Narchi et al, Anesthesia and Analgesia 1996 June Vol 82(6): 1303).

TOPIC 4: **Awareness of atraumatic spinal needles among neurologists……..**

Of note from general medical literature (The Lancet!):- A paper authored by neurologists with an accompanying comment discusses the advantages of using atraumatic needles for diagnostic lumbar punctures. Most neurologists surveyed reported they use large 22 gauge needles for diagnostic lumbar punches. Awareness of atraumatic needles for lumbar punctures appears to be low amongst neurologists. (It could also be commented that there appears to be little awareness that many - if not most - lumbar punctures are performed for spinal anaesthetics.)

REFS

Nath S, Koziarz A, Badhiwala JH, et al. Atraumatic versus conventional lumbar puncture needles: a systematic review and meta-analysis. Lancet 2017; published online Dec 6. http://dx.doi.org/10.1016/S0140-6736(17)32451-0.
Comment:-
van de Beek D, Brouwer MC Atraumatic lumbar puncture needles: practice needs to change Lancet 2017; Published Online December 6, 2017 http://dx.doi.org/10.1016/S0140-6736(17)32480-7

TOPIC 5: **Euglycaemic Diabetic Ketoacidosis - A Danger of Gliflozins (SGLT2 inhibitors)**

In the last few months there have been a number of local patients (at JHH and nearby hospitals) diagnosed with this condition, in some cases critically ill. It appears to have been precipitated by a perioperative stress (or in other cases, non-operative stress) in patients being treated with SGLT2 inhibitors. These drugs of the "gliflozin" group relatively new therapies for diabetes, which act by reducing glucose reabsorption by the proximal tubule of the kidney.

Prescriptions of gliflozins (dapagliflozin *Forxiga* and empagliflozin *Jardiance*) have risen dramatically since licensing in 2014. This is expected to continue due to increasing evidence of multiple benefits in patients with Type 2 diabetes. They are described as 'blockbuster drugs' in financial/investment media.

In the face of physiological stress, normal physiological response is to increase glycogenolysis and mobilisation of energy stores, accompanied by an increase in insulin release which drives cellular glucose uptake. If there is inadequate insulin release, glucose remains extracellular, and cells switch to ketogenic metabolism, as seen in classical hyperglycaemic diabetic ketoacidosis. The resulting hyperglycaemia is the usual marker for increased insulin release, or for medical intervention (e.g. insulin infusion is adjusted to match the increased physiological requirements in the face of physiological stress). In the presence of Gliflozins, the 'normal' hyperglycaemic response may not be seen, and the patient develops Euglycaemic Diabetic Ketoacidosis (euDKA). This may not be recognised, particularly as the patient's glucose may not be abnormally raised.

Diagnosis requires awareness of the possibility in patients recently on gliflozins, or in patients recommencing the drug postoperatively. Diagnosis is based on clinical signs typical of ketoacidosis including altered mental state and tachypnoea; by testing for ketosis or ketonaemia, and by blood gas acid-base estimation to identify acidosis. Treatment is based on insulin infusion/glucose infusion.

NOTE Normal point of care (fingerprick) blood testing devices can also be used for testing for ketones.

Case reports and editorials have appeared in Canadian and USA anaesthesiology journals. It is expected that an authoritative editorial discussing the problem in more detail will be appearing in Anaesthesia & Intensive

Care in March 2018. In the interim, recommendations for perioperative management of patients using gliflozins are attached.

REFS

Rosenstock J, Ferrannini E. Euglycemic diabetic ketoacidosis: a predictable, detectable, and preventable safety concern with SGLT2 inhibitors. Diabetes Care. 2015 Sep 1;38(9):1638-42.

Hoffman C, Green M, Megafu O. Sodium-glucose linked transporter 2 inhibitor-associated perioperative euglycaemic diabetic ketoacidosis: a case for a perioperative guideline. Anaesthesia and intensive care. 2017 Nov;45(6):758.

Peacock SC, Lovshin JA, Cherney DZ. Perioperative considerations for the use of sodium-glucose cotransporter-2 inhibitors in patients with type 2 diabetes. Anesth Analg 2018 (Published Ahead of Print)

Peacock SC, Lovshin JA. Sodium-glucose cotransporter-2 inhibitors (SGLT-2i) in the perioperative setting. Canadian Journal of Anesthesia/Journal canadien d'anesthésie. 2017 Nov 20:1-5.

Recommendations for perioperative management of patients using Gliflozin (SGLT2-i) therapies.

(n.b. Does not include management of diagnosed euDKA)

Gliflozins used in Australia are dapagliflozin (Forxiga), empagliflozin (Jardiance), or in combination with metformin (Xigduo, Jardiamet)

1) Awareness of euDKA is the most important change.
2) SGLT2-i therapies are used to optimise long-term diabetes care and reduce cardiovascular complications. There is no significant danger from temporarily ceasing these drugs, nor any apparent withdrawal syndrome. The recent reports suggest that current recommendations to cease SGLT2 inhibitors on the day of surgery, or the day before surgery, may be inadequate. The drugs should, ideally, be ceased four to five half-lives before surgery. The half-life for both empagliflozin and dapagliflozin is approximately 12 hours. We therefore recommend cessation 48 hours or more before surgery.
3) Pragmatically, patients may arrive for planned surgery without having ceased SGLT2 inhibitor therapy as early as we recommend. Whether to cancel planned surgery is controversial and will need to be based on individual patient circumstances including complexity and duration of surgery. At this time it is not clear how often euDKA occurs, however, we presume that the lower the perioperative physiologic stress the lower the risk of euDKA. The risk of euDKA can generally be managed with adequate awareness and monitoring, but ongoing SGLT2 inhibitor therapy may be regarded as a relative contraindication to surgery, particularly cardiac surgery and major non-cardiac surgery.
4) Patients having unscheduled and emergency surgery (and who therefore have not ceased these medications), may be at greater risk due to both ongoing SGLT2 inhibitor effects and increased stress from their surgical condition. Furthermore, the exact type of oral diabetes therapy may be unclear when assessing a patient before urgent surgery. Hence there should be increased awareness of the risk of the condition for non-elective patients.
5) Equipment for point of care (finger prick) blood testing for blood glucose and ketonaemia should be used for assessment and monitoring of patients perioperatively.
6) Patients on SGLT2 inhibitor drugs may be mildly volume depleted (like patients on ACE and AT_2 inhibitors). This may lead to increased blood pressure variability, particularly on induction, and may respond to a modest volume load.
7) SGLT2 inhibitor therapy is associated with increased risk of urinary tract and genital infections due to glycosuria. This should be considered, particularly in patients having urogenital procedures.
8) Where a decision is made to proceed with surgery in a patient who has had continuing SGLT2i therapy, we recommend the following:-
    a. As with all perioperative medicine, management should be in collaboration with surgeons, experts in diabetes care and intensive care colleagues.
    b. A plan of care should be documented in the general medical notes preoperatively. The preoperative 'Time-Out' check may be an appropriate time to review this.

c. The increased need for postoperative surveillance should be considered. For surgery with higher physiological stress, and patients with other risk factors, postoperative critical care admission should be considered.
d. Perioperative insulin and glucose therapy may reduce the risk of euDKA.
e. Regular monitoring for ketosis could commence at the time of surgery and significant ketonuria or ketonaemia (>0.6mMol/L preoperatively, or >1.5mMol/L postoperatively) should prompt a patient review, including blood gas acid-base estimation.
f. Continue monitoring until the physiological stress is resolved or for about 72 hours after cessation of SGLT2 inhibitor therapy.

9) There no need to be hasty in recommencing SGLT2 inhibitor therapy after surgery. Advice to recommence SGLT2 inhibitor therapy 'when eating normally', or that "Treatment may be restarted once the patient's condition has stabilised" may lack caution, particularly when enhanced recovery after surgery (ERAS) protocols emphasise early feeding postoperatively. For moderate or major surgery, the drugs should be withheld until the acute phase response and physiological stress has resolved, the patient is eating and drinking normally and the anabolic phase of physiological recovery is established. As a suggested guide for joint arthroplasty, a week or longer may be appropriate; for major body cavity surgery up to two weeks or longer.
10) When SLGT2 inhibitors are restarted, they should be ceased again if the patient deteriorates. Assessment for metabolic acidosis should be an early step in managing any deterioration.