Opioid Free Anesthesia and Analgesia in the Bariatric Patient

Dr. Adrian Sultana, MD FRCP (Glasg) FANZCA^{a,b,c,d}

Definitions

Opioid Free Anesthesia (OFA) is a technique where no intra-operative systemic, neuraxial, or intracavitary opioid is administered during the anesthetic. OFA similarly avoids opioids in the perioperative period.

Background

There are many compelling reasons to avoid opioids in the surgical population including the avoidance of:

- Respiratory depression
- Central muscle rigidity
- Pharyngeal muscle weakness
- Obstructed breathing
- Negative inotropism
- Nausea, vomiting, ileus and constipation
- Urinary retention
- Tolerance and addiction
- Dizziness
- Excessive somnolence

It is logical, indeed mandatory, to avoid respiratory depressants in patients who are either known or suspected to be suffering from obstructive sleep apnea.

More recently, concerns have arisen about impaired healing,¹ immunosuppression,² and worsening of oncologic outcomes³ with systemic opioids. In addition to these, perioperative cognitive dysfunction and opioid induced hyperalgesia remain concerns with any opioid-based technique.^{4,5} Conversely, since most bariatric procedures are laparoscopic and control of the hemodynamic responses to intubation, pneumoperitoneum, and surgery is mandatory, remifentanil-based techniques in combination with propofol or inhalational agents have become increasingly popular.

Opioid Free Anesthesia (OFA)

Mulier has popularized OFA in Europe,^{6,7} and a number of case reports and small prospective studies from all over the world support its benefits especially in the morbidly obese population.⁸⁻¹¹

The cornerstones of this technique are enumerated below (1-3 are mixed together in an infusion known as the "Mulimix"):

1. Sympatholysis, analgesia, and anesthesia (MAC reduction) with **dexmedetomidine**^{12,13}

^aFoundation Anaesthetist, Sydney Institute for Obesity Surgery

^bUniversity of New South Wales; Sydney, Australia

^cAustralian School of Advanced Medicine, Macquarie University; Sydney, Australia

^dMember, Board of Directors, International Society for the Perioperative Care of the Obese Patient

- 2. Analgesia with low-dose **ketamine**¹⁴
- 3. Co-anesthesia and sympatholysis with intravenous lignocaine¹⁵
- 4. Profound **neuromuscular blockade** maintained up to the end of surgery and appropriately reversed
- 5. **0.7 -1.0 MAC desflurane** in oxygen/air titrated to entropy or BIS EEG monitoring
- 6. **Magnesium** infusion as a further co-analgesic 16

Inadequate sympatholysis may be corrected with titrated boluses of clonidine. Excessive sympatholysis may be corrected with pressors, preferably ephedrine because of its chronotropic effect.

In addition dexamethasone, high dose paracetamol, NSAIDS, and gabapentin may be used as adjuncts to the multi-modal pain regimen. Intraperitoneal/wound infiltration with local anesthetic is routinely performed.

We have adopted a protocol based on Mulier's technique for laparoscopic bariatric procedures including revision banding surgery, sleeve gastrectomy, and gastric bypass coming through our multidisciplinary bariatric unit.

Anesthesia Technique

A loading infusion of 20 ml/hr of "Modified Mulimix" is started equivalent to 2ug/kg/hr of dexmedetomidine (for a 100 kg patient; Fig. 1). Patients are then induced with 2 mg/kg IBW of propofol and intubated with the aid of 1 mg/kg IBW rocuronium, after which maintenance of 0.7-1.0 MAC desflurane in air is commenced and neuromuscular blockade is maintained with 0.5 mg/kg/hr IBW of rocuronium for the duration of pneumoperitoneum. Neuromuscular blockade will then be reversed "as appropriate".

Routine antiemetic prophylaxis is administered with ondansetron, and dexamethasone is given in high dose both as an antiemetic and an adjunctive analgesic. Currently, we do not routinely employ the magnesium limb of the technique.

The loading "Mulimix" infusion is generally continued until intubation, head up position, peritoneal insufflation, and placement of abdominal ports are complete. The infusion is then progressively stepped down to 10 and 5 ml/hr equivalent to 1 ug/kg/hr and 0.5 ug/kg/hr of dexmedetomidine, respectively, and stopped briefly at the completion of surgery. 1-2 grams of intravenous paracetamol and 40 mg of parecoxib, together with intraperitoneal local anesthetic and wound infiltration, provide additional analgesia. The "Mulimix" is reintroduced in the PACU at the lower rate where it is frequently the only analgesia required, or it is used as a bridge to fentanyl PCA prior to ward transfer. We are awaiting the evolution of nursing protocols prior to continuing the Mulimix for extended analgesia on the ward or HDU.

Disadvantages of Opioid Free Anesthesia and Analgesia

- 1. Ketamine perturbs the EEG monitoring of awareness.
- 2. Some patients will require vasopressor support.
- 3. OFA may have to be breached to achieve ideal intubating conditions with small doses of short acting opioid.
- 4. Cutaneous vasoconstriction an expected alpha 2 effect may alarm clinicians.

- 5. There is clearly a learning curve for the individual and institution.
- 6. Awareness is a possibility if the technique is incorrectly applied or misused.

Advantages of Opioid Free Anesthesia and Analgesia

- 1. Avoidance of remifentanil and opioid induced hyperalgesia⁴
- 2. OSA and other opioid mediated problems eliminated
- 3. Easily "protocol-driven"
- 4. Aids optimization of "laparoscopic working space".2
- 5. Guarantees analgesia and sympathetic blockade/moderate amnesia 12
- 6. Awareness unlikely if BIS (entropy) is kept below 60 (Fig. 2)

Can OFA Be Employed as Part of TIVA?

A TIVA version of OFA has not been perfected. Although dexmedetomidine decreases anesthetic requirements for desflurane by up to 90%, the effect on propofol requirements is only a decrement of about 30%. Also, most propofol-based techniques have relied on the pharmacodynamic interaction between the short acting opioids and propofol for their success. ¹⁷

Conclusions

Thousands of bariatric procedures have been completed in Europe with an opioid free anesthesia technique, and opioid free analgesia seems feasible in the perioperative period after laparoscopic bariatric surgery. Case reports and small clinical trials from varied locations support the safety and efficacy of this technique worldwide. Of recent interest is a volunteer study that validates an allometric TCI model for dexmedetomidine. This may prove promising once clinical application evolves and may be incorporated into a TCI-based version of OFA. There is an urgent need for a prospective double blind trial of this technique versus a "standard" or opioid-based technique to improve the evidence base on a promising method of providing optimum anesthesia care for our bariatric patients.

References

- 1. Martin JL, Koodie L, Krishnan AG, Charboneau R, Barke RA, and Roy S. Chronic morphine administration delays wound healing by inhibiting immune cell recruitment to the wound site. *Am J Pathol*. 2010; 176(2):786-799.
- 2. Sacerdote P. Opioids and the immune system. Palliat Med. 2006; 20 Suppl 1:s9-15.
- 3. Fodale V, D'Arrigo MG, Triolo S, Mondello S, and La Torre D. Anesthetic techniques and cancer recurrence after surgery. *The Scientific World Journal*. 2014; 2014:Article ID 328513.
- 4. Patil SK and Anitescu M. Opioid-free perioperative analgesia for hemicolectomy in a patient with opioid-induced delirium: a case report and review of the analgesic efficacy of the alpha-2 agonist agents. *Pain Pract.* 2012; 12(8):656-662.
- 5. Fletcher D and Martinez V. Opioid-induced hyperalgesia in patients after surgery: a systematic review and a meta-analysis. *Br J Anaesth*. 2014; 112(6):991-1004.
- 6. Mulier JP, Wouters R, and Dekock M (2014). Pourquoi et comment éviter les opioïdes en anesthésie ambulatoire ? Non-opioid surgical anaesthesia, presented at JEPU Conference, Paris, 2014.
- 7. Mulier JP (2015). Opioid free anaesthesia (OFA) a Paradigm shift?. Retrieved from http://www.researchgate.net/publication/278307444.
- 8. Bakan M, Umutoglua T, Topuza U, et al. Opioid-free total intravenous anesthesia with propofol, dexmedetomidine and lidocaine infusions for laparoscopic cholecystectomy: a prospective, randomized, double-blinded study. *Rev Bras Anestesiol*. 2015; 65(3):191-199.
- 9. Mansour MA, Mahmoud AAA, Geddawy M. Nonopioid versus opioid-based general anesthesia technique for bariatric surgery: A randomized double-blind study. *Saudi J Anaesth*. 2013; 7(4):387-391.
- 10. Hofer RE, Sprung J, Sarr MG, and Wedel DJ. Anesthesia for a patient with morbid obesity using dexmedetomidine without narcotics. *Can J Anesth*. 2005; 52(2):176-180.
- 11. Ziemann-Gimmel P, Goldfarb AA, Koppman J, and Marema RT. Opioid-free total intravenous anesthesia reduces postoperative nausea and vomiting in bariatric surgery beyond triple prophylaxis. *Br J Anaesth*. 2014; 112(5): 906-911.
- 12. Sanders RD and Maze M (2013). Alpha2-agonists and other sedatives and amnestics. In AS Evers, M Maze, and ED Kharasch (Ed.), *Anesthetic Pharmacology* (pp. 478-492). 2nd ed. Cambridge: Cambridge University Press.
- 13. Grewal A. Dexmedetomidine: New avenues. *J Anaesthesiol Clin Pharmacol*. 2011; 27(3): 297-302.
- 14. Kurdi MS, Theerth KA, and Deva RS. Ketamine: Current applications in anesthesia, pain, and critical care. *Anesth Essays Res.* 2014; 8(3):283-290.
- 15. McCarthy GC, Megalla SA, and Habib AS. Impact of intravenous lidocaine infusion on postoperative analysis and recovery from surgery: a systematic review of randomized controlled trials. *Drugs*. 2010; 70(9): 1149-1163.
- 16. Albrecht E, Kirkham KR, Liu SS, and Brull R. Peri-operative intravenous administration of magnesium sulphate and postoperative pain: a meta-analysis. *Anaesthesia*. 2013; 68(1):79-90.
- 17. Egan TD and Minto CF (2013). Pharmacodynamic drug interactions in anesthesia. In AS Evers, M Maze, and ED Kharasch (Ed.), *Anesthetic Pharmacology* (pp. 147-165). 2nd ed. Cambridge: Cambridge University Press.
- 18. Hannivoort LN, Eleveld DJ, Proost JH, et al. Development of an Optimized Pharmacokinetic Model of Dexmedetomidine Using Target-controlled Infusion in Healthy Volunteers.

Anesthesiology. 2015; 123(2):357-367.

Fig. 1: Modified Mulimix Dexmedetomidine: 10 ug/ml

Ketamine: 2.5 mg/ml Lignocaine: 20 mg/ml

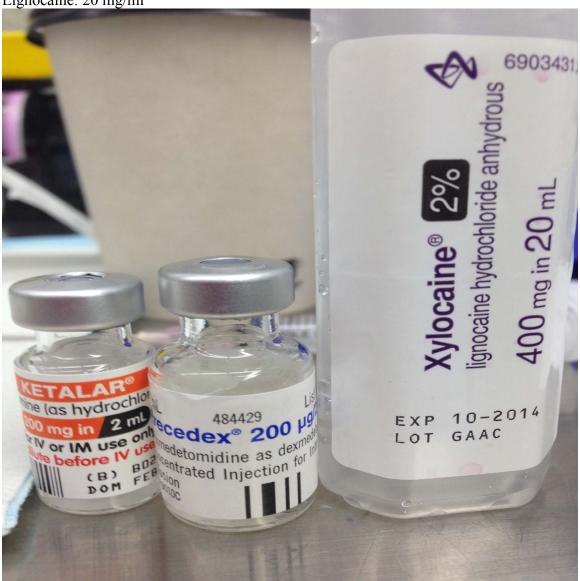


Fig. 2: Sympatholysed Hemodynamics while Entropy Runs "High" in a 166 kg Male Undergoing Sleeve Gastrectomy

