

# May we consider the use of nalbuphine as postoperative opioid in bariatric patients?

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## Opinion

Nalbuphine is a semi-synthetic lipophilic drug chemically related to Oxymorphone and Naloxone,<sup>1</sup> acting essentially as kappa-agonist (KOR) and as a mu-receptor antagonist (MOR) with a similar analgesic potency of Morphine, with equivalence of both 1mg to 1mg.<sup>2</sup> It is clinically indicated for mild to moderate pain and causes a low dependence rate and with few side effects, compared to morphine.<sup>3</sup> It produces its analgesic and sedative effect using the kappa-opioid receptor and, otherwise, the antagonism in mu-opioid receptor is related to fewer adverse effects.<sup>4-7</sup>

There are several studies demonstrating the equianalgesia between Nalbuphine and Morphine during and after certain surgeries<sup>1,8-11</sup> not including thoracotomy<sup>12,13</sup> and with some controversial results in hip surgery.<sup>1,14</sup> It was not reported any neurotoxicity associated with intrathecal administration of Nalbuphine.<sup>6</sup> A singular characteristic of kappa-agonists is the highly effectiveness in women.<sup>2,15</sup> This sexual dimorphism could be bypassed using naloxone, in a dose-dependent manner (ratio Nalbuphine: Naloxone 12,5: 1), strategy that also improve analgesia in women.<sup>15</sup>

The prescription of an opioid in postoperative period is almost mandatory and historically the most popular of them are morphine. The development of another mu-opioid agonists to improve postoperative analgesia with fewer adverse events does not produce significant advances. Pruritus, postoperative nausea and vomiting, urinary retention and, most dangerous, respiratory depression could be limiting factors to opioid use after a surgery, resulting in a sub-optimal treatment of the patients pain. The application of the kappa-opioid agonist/mu-opioid antagonist Nalbuphine was tested in a lot of studies,<sup>1,3,7-14,17-19</sup> including this author and colleagues,<sup>16</sup> but only after an elegant meta-analysis from Zeng Z et al.,<sup>17</sup> we can seriously review our postoperative opioid election.<sup>17</sup>

The popularity of Morphine comes from its great efficacy in postoperative pain control, so a possible alternative must be as effective as morphine. The meta-analysis of Zeng et al.,<sup>17</sup> shows a Relative Risk of 1.01; 95% confidence interval [CI], 0.91 to 1.11; P = 0.90. Considering the occurrence of heterogeneity, Bayesian meta-analysis was performed, showing similar results (RR 1.102(95% credible interval: 0.6697–1.627).

Besides the equianalgesic effect, Nalbuphine shows us better side-effects profile, increasing the reasons to consider it as an option. The incidence of pruritus with Nalbuphine and Morphine was 0,047 and 0,206, respectively, and the pooled RR was 0.17 (95%CI, 0.09–0.34; P < 0.000). The incidence of nausea/vomiting with Nalbuphine and Morphine was 0,199/0, 16 and 0,307/ 0,284, respectively, and the pooled RR was 0.78 (95%CI, 0.602–0.997; P = 0.048) for nausea, 0.65 (95%CI, 0.50–0.85; P = 0.001) for vomiting. The incidence of respiratory depression with Nalbuphine and Morphine was 0,075 and

0,197, respectively, and the pooled RR was 0.27 (95%CI, 0.12–0.57; P = 0.001). The most serious side effect of opioid use is respiratory depression. Nalbuphine has a plateau effect on respiratory depression, and it has been shown to reverse the respiratory depression from both intravenous<sup>18</sup> and epidural<sup>19</sup> mu-opioids.

Because of the growing number of indications and performance of bariatric surgeries, more obese patients are being admitted in the Intensive Care Unit (ICU).<sup>20</sup> Among factors predisposing to admission in the ICU are mentioned: male gender, age ≥50 years BMI ≥60 Kg/m<sup>2</sup>, diabetes mellitus, OSAS, cardiopathies, venous difficulty and complications in the intra or immediate postoperative<sup>20,21</sup> mainly due to respiratory complications such as pneumonia, thromboembolic disease, respiratory failure requiring mechanical ventilation and to a lesser extent, respiratory arrest.<sup>21-23</sup> Postoperative complications and stay in the ICU increase hospital costs.<sup>22</sup> The opposite is also true, fewer complications reduce hospital stay and therefore lessen hospital costs.<sup>24</sup>

At postoperative, obesities present difficulties in early mobilization. Immobility increases the risk of adverse thromboembolic events, especially in surgeries of the upper abdomen.<sup>24</sup> On the other hand, early walking reduces the risk of pulmonary thromboembolism and other respiratory problems at postoperative affording and improving lung expansion, minimizing and reverting atelectasias formed by the prolonged decubitus in the bed.<sup>20</sup>

The rationale for the use of Nalbuphine instead of Morphine in Bariatric patients is based on its profile of equal analgesia and fewer side effects, mainly concerning ventilation, that could favor early mobilization of these patients improving morbidity and mortality. There is none published material available comparing the use of Nalbuphine and Morphine in post-bariatric analgesia, although we are conducting the first one. We hope as soon as possible we will publish partial data in order to confirm the efficacy and safety of the use of Nalbuphine in post-bariatric analgesia.

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## Conflicts of interest

Author declare that there is no conflict of interest.

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## References

1. Fournier R, Van Gessel E, Macksay M, et al. Onset and offset of intrathecal morphine versus nalbuphine for postoperative pain relief after total hip replacement. *Acta Anaesthesiol Scand*. 2000;44(8):940–945.
2. Brunton LL, Chabner BA, Knollmann BC. Goodman, Gilman's pharmacological basis of therapeutics. 12th ed. The McGraw-Hill Companies, Inc., New York, New York, USA; 2011. p. 481–525
3. Zacny JP, Conley K, Marks S. Comparing the subjective, psychomotor and physiological effects of intravenous nalbuphine and morphine in healthy volunteers. *J Pharmacol Exp Ther*. 1997;280:1159–1169.
4. Chen JC, Smith ER, Cahill M, et al. The opioid receptor binding of dezocine, morphine, fentanyl, butorphanol and nalbuphine. *Life Sci*. 1993;52(4):389–396.
5. De Souza EB, Schmidt WK, Kuhar MJ. Nalbuphine: an autoradiographic opioid receptor binding profile in the central nervous system of an agonist/antagonist analgesic. *J Pharmacol Exp Ther*. 1988;244(1):391–402.
6. Gunion MW, Marchionne AM, Anderson CTM. Use of the mixed agonist–antagonist nalbuphine in opioid based analgesia. *Acute Pain*. 2004;6(1):29–39.
7. Yu–Chang Y, Tzu–Fu Lina, Hung–Chi, et al. Combination of Low–dose Nalbuphine and Morphine in Patient–controlled Analgesia Decreases Incidence of Opioid–related Side Effects. *J Formos Med Assoc*. 2009;108(7):548–553.
8. Pinnock CA, Bell A, Smith G. A comparison of nalbuphine and morphine as premedication agents for minor gynaecological surgery. *Anaesthesia*. 1985;40(11):1078–1081.
9. Beaver WT, Feise GA. A comparison of the analgesic effect of intramuscular Nalbuphine and Morphine in patients with postoperative pain. *J Pharmacol Exp Ther*. 1978;204(2):487–496.
10. Minai FN, Khan FA. A comparison of morphine and nalbuphine for intraoperative and postoperative analgesia. *J Pak Med Assoc*. 2003;53(9):391–396.
11. Van den Berg AA, Honjol NM, Prabhu NV, et al. Analgesics and ENT surgery. A clinical comparison of the intraoperative, recovery and postoperative effects of buprenorphine, diclofenac, fentanyl, morphine, nalbuphine, pethidine and placebo given intravenously with induction of anaesthesia. *Br J Clin Pharmacol*. 1994;38(6):533–543.
12. Baxter AD, Langanieri S, Samson B, et al. A dose–response study of nalbuphine for post–thoracotomy epidural analgesia. *Can J Anaesth*. 1991;38(2):175–182.
13. Etches RC, Sandler AN, Lawson SL. A comparison of the analgesic and respiratory effects of epidural nalbuphine or morphine in postthoracotomy patients. *Anesthesiology*. 1991;75(1):9–14.
14. Fee JP, Brady MM, Furness G, et al. Analgesia after hip replacement surgery: comparison of nalbuphine with morphine. *Br J Anaesth*. 1989;63(6):756–758.
15. Hurley RW, Murphy JD, Wu CL. Chapter 98 – Acute Postoperative Pain. In: Miller RD, et al. Miller's Anesthesia. (8th edn), Elsevier Saunders, 1600 John F, Kennedy Blvd, Philadelphia, USA; 2015. p. 2974–2998.
16. Mende FF. Is Nalbuphine a better option than morphine in post ambulatory videolaparoscopic colectomy? Random double blind study. *Rev DOR*. 2004;5(4):389–394.
17. Zeng Z, Lu J, Shu C, et al. A Comparison of Nalbuphine with Morphine for Analgesic Effects and Safety :Meta–Analysis of Randomized Controlled Trials. *Sci Rep*. 2015;5:10927.
18. Moldenhauer CC, Roach GW, Finlayson DC, et al. Nalbuphine antagonism of ventilatory depression following high–dose fentanyl anesthesia. *Anesthesiology*. 1985;62:646–650.
19. Penning JP, Samson B, Baxter AD. Reversal of epidural morphine–induced respiratory depression and pruritus with Nalbuphine. *Can J Anaesth*. 1988;35(6):599–604.
20. Pieracci FM, Barie PS, Pomp A. Critical care of the bariatric patient. *Crit Care Med*. 2006;34(6):1796–1804.
21. Helling, TS, Willoughby TL, Maxfield DM, et al. Determinants of the need for intensive care and prolonged mechanical ventilation in patients undergoing bariatric surgery. *Obes Surg*. 2004;14(8):1036–1041.
22. Cend JC, Abu–aouf D, Gabrielli A, et al. Utilization of intensive care resources in bariatric surgery. *Obes Surg*. 2005;15(9):1247–1251.
23. Poulouse BK, Griffin MR, Zhu Y, et al. National analysis of adverse patient safety events in bariatric surgery. *Am Surg*. 2005;71(5):406–413.
24. Juvin P, Marmuse JP, Delorme S, et al. Post–operative course after conventional or laparoscopic gastroplasty in morbidly obese patients. *Eur J Anaesthesiol*. 1999;16(6):400–403.
25. Gear RW, Gordon NC, Miaskowski C, et al. Dose ratio is important in maximizing naloxone enhancement of nalbuphine analgesia in humans. *Neurosci Lett*. 2003;351(1):5–8.