May We Consider the Use of Nalbuphine as Postoperative Opioid in Bariatric Patients?

Keywords: Nalbuphine; Morphine; Bariatric; Pain Postoperative

Opinion

Nalbuphine is a semi-synthetic lipophilic drug chemically related to Oxymorphone and Naloxone [1], 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 [2]. It is clinically indicated for mild to moderate pain and causes a low dependence rate and with few side effects, compared to morphine [3]. 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 [4-7].

There are several studies demonstrating the equianalgusia between Nalbuphine and Morphine during and after certain surgeries [1,8-11] not including thoracotomy [12,13] and with some controversial results in hip surgery [1,14]. It was not reported any neurotoxicity associated with intrathecal administration of Nalbuphine [6]. A singular characteristic of kappa-agonists is the highly effectiveness in women [2,15]. 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 [15].

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 naúsea 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 [1,3,7-14,17-19], including this author and colleagues [16], but only after an elegant meta-analyses from Zeng Z et al. [17] we can seriously review our postoperative opioid election [17].

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-analyses of Zeng et al. [17] 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 [18] and epidural [19] 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) [20]. Among factors predisposing to admission in the ICU are mentioned: male gender, age ≥ 50 years BMI ≥ 60 Kg/m2, diabetes mellitus, OSAS, cardiopathies, venous difficulty and complications in the intra or immediate postoperative [20,21] mainly due to respiratory complications such as pneumonia, thromboembolic disease, respiratory failure requiring mechanical ventilation and to a lesser extent, respiratory arrest [21-23]. Postoperative complications and stay in the ICU increase hospital costs [22]. The opposite is also true, fewer complications reduce hospital stay and therefore lessen hospital costs [24].

At postoperative, obeses present difficulties in early mobilization. Immobility increases the risk of adverse thromboembolic events, especially in surgeries of the upper abdomen [24]. 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 [20].
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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.

References

1. Fournier R, Van Gessel F, Mackay M, Gamulin Z (2000) Onset and offset of intrathecal morphine versus nalbuphine for postoperative pain relief after total hip replacement. Acta Anaesthesiol Scand 44(8): 940-945.
2. Brunton LL, Chabner BA, Knollmann BC (2011) Goodman, Gilman’s pharmacological basis of therapeutics. (12th edn). The McGraw-Hill Companies, New York, New York, USA, pp. 481-525.
3. Zacny JP, Conley K, Marks S (1997) Comparing the subjective, psychomotor and physiological effects of intravenous nalbuphine and morphine in healthy volunteers. J Pharmacol Exp Ther 280: 1159-1169.
4. Chen JC, Smith ER, Cahill M, Cohen R, Fishman JB (1993) The opioid receptor binding of dezocine, morphine, fentanyl, butorphanol and nalbuphine. Life Sci 52(4): 389-396.
5. De Souza EB, Schmidt WK, Kuchar MJ (1988) Nalbuphine: an autoradiographic opioid receptor binding profile in the central nervous system of an agonist/antagonist analgesic. J Pharmacol Exp Ther 244(1): 391-402.
6. Gunion MW, Marchionne AM, Anderson CTM (2004) Use of the mixed agonist-antagonist nalbuphine in opioid based analgesia. Acute Pain 6(1): 29-39.
7. Yu-Chang Y, Tsu-Fu Lina, Hung-Chi, Wing-Sum Chanb, Yong-Ping Wang, et al. (2009) Combination of low-dose Nalbuphine and Morphine in Patient-controlled Analgesia Decreases Incidence of Opioid-related Side Effects. J Formos Med Assoc 108(7): 548-553.
8. Pinnock CA, Bell A, Smith G (1985) A comparison of nalbuphine and morphine as premedication agents for minor gynaecological surgery. Anaesthesia 40(11): 1078-1081.
9. Beaver WT, Feise GA (1978) A comparison of the analgesic efficacy of intramuscular Nalbuphine and Morphine in patients with postoperative pain. J Pharmacol Exp Ther 204(2): 487-496.
10. Minai FN, Khan FA (2003) A comparison of morphine and nalbuphine for intraoperative and postoperative analgesia. J Pak Med Assoc 53(9): 391-396.
11. Van den Berg AA, Honjol NM, Pmbhu NV, Datta S, Rosario CJ, et al. (1994) 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 38(6): 533-543.
12. Baxter AD, Langaniere S, Samson B, McGilvery JJ, Hull K (1991) A dose-response study of nalbuphine for post-thoracotomy epidural analgesia. Can J Anaesth 38(2): 175-182.
13. Eitches RC, Sandler AN, Lawson SL (1991) A comparison of the analgesic and respiratory effects of epidural nalbuphine or morphine in postthoracotomy patients. Anesthesiology 75(1): 9-14.
14. Fee JP, Brady MM, Furness G, Chambers M, Clarke RS (1989) Analgesia after hip replacement surgery: comparison of nalbuphine with morphine. Br J Anaesth 63(6): 756-758.
15. Hurley RW, Murphy JD, Wu CL (2015) Chapter 98 - Acute Postoperative Pain. In: Miller RD, et al. Miller’s Anesthesia. (8th edn), Elsevier Saunders, 1600 John F, Kennedy Blvd, Philadelphia, USA, pp 2974-2998.
16. Mende FF (2004) Is Nalbuphine a better option than morphine in post ambulatory video-laparoscopic colecistectomy? Random double blind study. Rev DOR 5(4): 389-394.
17. Zeng Z, Lu J, Shu C, Chen Y, Guo T, et al. (2015) A Comparison of Nalbuphine with Morphine for Analgesic Effects and Safety : Meta-analysis of Randomized Controlled Trials. Sci Rep 5: 10927.
18. Moldenhauer CC, Roach GW, Finlayson DC, Hug CC, Kopel ME, et al. (1985) Nalbuphine antagonism of ventilatory depression following high-dose fentanyl anesthesia. Anesthesiology 62: 646-650.
19. Penning JP, Samson B, Baxter AD (1988) Reversal of epidural morphine-induced respiratory depression and pruritus with Nalbuphine. Can J Anaeath 35(6): 599-604.
20. Pieracci FM, Barie PS, Pop M (2006) Critical care of the bariatric patient. Crit Care Med 34(6): 1796-1804.
21. Helling, TS, Willoughby TL, Maxfield DM, Ryan P (2004) Determinants of the need for intensive care and prolonged mechanical ventilation in patients undergoing bariatric surgery. Obes Surg 14(8): 1036-1041.
22. Gend JC, Abu-ouf D, Gabrielli A, Caruso LJ, Rout WR, et al. (2005) Utilization of intensive care resources in bariatric surgery. Obes Surg 15(9): 1247-1251.
23. Poulose BK, Griffin MR, Zhu Y, Smalley W, Richards WD, et al. (2005) National analysis of adverse patient safety events in bariatric surgery. Am Surg 71(5): 406-413.
24. Juvin P, Marmuse JP, Delerme S, Leconte P, Mantz J, et al. (1999) Postoperative course after conventional or laparoscopic gastrectomy in morbidly obese patients. Eur J Anaesthesiol 16(6): 400-403.
25. Gear RW, Gordon NC, Miaskowski C, Paul SM, Heller PH, et al. (2003) Dose ratio is important in maximizing naloxone enhancement of nalbuphine analgesia in humans. Neurosci Lett 351(1): 5-8.