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

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Opinion

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Nalbuphine is a semi-synthetic lipophilic drug chemically related to Oxymorphine 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 equianalgesia 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 náusea and vomiting, urinary retention and, most dangerous, respiratory depression could be limitating 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 colleages [16], but only after an elegant meta-analisys 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-analisys 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-analisys 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 thromboembolitic 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].

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, manly 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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