

Preliminary Study of Epidural Nalbuphine in Treatment of Post Operative Pain: A Comparison with Equipotent Dose of Epidural Morphine

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Epidural analgesia was used in 45 patients submitted to upper abdominal surgery. In 30 of them 0.15 mg/kg nalbuphine (EN group) was injected and in the remained, an equipotent dose of 0.1 mg/kg of preservative free morphine (EM group) was used. The patients were observed concerning the severity of pain before and after narcotic administration, duration of analgesia, occurrence and severity of side effects among them. The severity of pain was stated by the McGill pain score (from 0 to 5). Duration of analgesia was defined as the time interval from pain relief after narcotic administration until requirement of an additional epidural narcotic injection. The adequacy of ventilation was estimated by sequential measurements of arterial PCO_2 .

Pain relief was excellent in all patients after both narcotics administration. The analgesia time was significantly longer with epidural morphine than in the EN patients. Besides drowsiness, the other side effects incidence was lower with epidural nalbuphine than with epidural morphine. Two patients in the EM group presented clinical respiratory depression, showing a significant increase in arterial PCO_2 .

We believe that the lack of respiratory depression seen in EN group is a consequence of the rostral diffusion of the drug, which reaches high concentrations at the respiratory centers level and a direct antagonist action upon them.

Our results showed that epidurally administered nalbuphine provides a good analgesia, with minor side effects and favorably compares with epidural morphine. (Key words: epidural analgesia, narcotics, nalbuphine, morphine)

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Pleuropulmonary complications are frequently seen after upper abdominal surgery. Pain play a major role in their genesis, since it may be severe enough to impair patient's ability to cough, breath deeply and clean the tracheobronchial tree from secretions^{1,2}.

The use of epidural injections of local anesthetics for treatment of post opera-

tive pain and prophylaxis of pleuropulmonary complications was recommended by some authors^{3,4}. However, hypotension and tachyphylaxis after repeated doses occur frequently. In the late 70s, Behar and co workers⁵ used epidural morphine in treatment of pain. Nevertheless, despite a good and longlasting analgesia obtained, epidural morphine can produce several side effects ranging from pruritus to severe respiratory depression.

Nalbuphine, a newer narcotic with a dual agonist/antagonist activity produces good

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Table 1. McGill pair score

	EN	EM	
Before injection	4.37±0.7	4.41±0.6	$P > 0.05$
After injection	0.75±0.3	0.65±0.25	$P > 0.05$
	$P < 0.05$	$P < 0.05$	

Table 2. Time of analgesia

EN	6 h 30 min ± 2 h 15 min
EM	16 h 40 min ± 5 h 50 min
	$P < 0.05$

Table 3. Sequential P_{CO_2} measurements (mmHg)

	Precp	1h	2h	4h	6h	10h	16h	24h
EN	36.6±2	36.3±4	37.5±3.8	37.6±4.3	36.5±2.9	37.6±3	36.4±2.9	38.1±1.9
EM	36.8±1.8	37±3	38.1±5	38.5±2.8	45.7±5(a)	43±6(a)	38±5	38.5±2.6
	NS	NS	NS	NS	$P < 0.05$	$P < 0.05$	NS	NS

(a) $P < 0.05$ compared to preoperative values

Table 4. Complications

	EN	EM	
Nausea and vomiting	5/30	7/15	$P < 0.05$
Drowsiness	16/30	3/15	$P < 0.05$
Pruritis	0/30	8/15	$P < 0.05$

analgesia with a low degree of respiratory depression when parenterally administered and could provide an alternative to epidural morphine. We compare, herein, the efficacy and side effects of epidural nalbuphine (EN) with those of epidural morphine (EM) among patients submitted to upper abdominal surgery.

Methods

The study was approved by local ethics committee and informed consent was obtained from 45 patients undergoing upper abdominal surgery. At the end of surgery, an indwelling 18 G epidural catheter was inserted through a 16 G Tuohy needle in the second lumbar interspace. No narcotics were given during the anesthesia.

In the post operative period, when the patients were complaining of pain, 0.15 mg/kg weight of nalbuphine (EN group - 30 patients) or 0.1 mg/kg weight of morphine (EM group - 15 patients) in 20 ml of normal saline was administered through the epidural catheter. Both groups were similar concerning age and site of surgery. The narcotics were chosen randomizedly and after

the first injection we continue to administer epidurally the same drug as necessary.

The severity of pain was evaluated by the patients before and after epidural narcotic injection, according to the McGill score (0 to 5, corresponding to no pain, mild, discomforting, distressing, horrible and excruciating). Duration of analgesia was recorded as the time interval from the relief of pain after the epidural injection until the next epidural administration for pain relief. The need for additional analgesia was assessed by the ward staff. The arterial pCO_2 was measured at 1, 2, 4, 6, 10, 16, 24 hours in order to estimate the ventilatory effects of both epidural narcotics. Patients were observed for nausea and vomiting, pruritis, excessive sedation and any sensory or motor dysfunction. Urinary retention could not be observed, since all patients had an urethral catheter in place.

Statistic analysis was performed using the student's T test for comparison of the McGill pain score and time of analgesia, the T test for pCO_2 measurements analysis and the Fisher exact test for comparison of complications incidence among both groups. In all cases $P < 0.05$ was considered statistically significant.

Results

Both drugs produced an excellent pain relief, as reflected in the McGill pain score changes (table 1). The time of analgesia was 6 hours 30 min ± 2 hours 15 min (range 4

to 16 hours) in the EN group compared to 16 hours 40 min \pm 5 hours 50 min (range 12 to 26 hours) in the EM group ($P < 0.05$) (table 2). The changes in arterial pCO₂ were summarized in table 3. In the EM group two patients presented clinical significant bradypnea (6 breaths/min in one patient and 8 breaths/min in the other). No patient in the EN group developed respiratory depression. Table 4 shows the incidence of side effects in both groups; about 50% among EM patients ($P < 0.05$). The most common side effect found in EN patients was drowsiness (16/30 versus 3/15 $P < 0.05$).

Discussion

Pain following upper abdominal surgery is one of the main etiologic factors of pulmonary complications. It causes a consistent decrease in pulmonary volumes¹, impairs cough and cleaning of the tracheobronchial tree from secretions³, leading to atelectasis and hypoxemia².

The use of epidural injections of local anesthetics was suggested by some authors for treatment of post operative pain and prophylaxis of pleuropulmonary complications^{3,4}. However, hypotension and tachyphylaxis are common, being a limiting factor for an wide use of this technique⁴.

The efficacy of intratechal morphine to provide a long lasting analgesia without changes in ECG and blood pressure was demonstrated in rats by Yaksh and Rudy⁶. Two years later, Behar and co workers⁵ reported long lasting analgesia with epidural morphine in treatment of acute and chronic pain in humans. However, epidural or intratechal morphine can cause several side effects, ranging from itching to severe respiratory depression^{7,8}.

Nalbuphine is a newer narcotic drug chemically related to oxymorphone and naloxone with a dual agonist/antagonist activity⁹. Its analgesic action is slightly less than that of morphine and 1.5 mg of nalbuphine are equipotent to 1 mg of morphine^{10,11}. In normal doses (10 mg/70 kg weight), nalbuphine causes similar respiratory depression as morphine. Nevertheless,

when higher doses are used, a ceiling effect for respiratory depression is noted¹².

In order to obtain good analgesia without significant respiratory depression we used epidural nalbuphine. Indeed, our results proved that despite a shorter analgesia obtained with epidural nalbuphine compared to epidural morphine, the lack of side effects commonly seen with the latter (as itching, severe vomiting and principally respiratory depression) favorably compares EN to EM.

Although one can criticize the use of sequential measurements of arterial pCO₂ for determination of ventilatory suitability, the two isolated cases of important slowing of respiratory rate were among EM patient and in both arterial pCO₂ reflected the hypoventilation (57 mmHg and 60 mmHg).

We speculate that the complete lack of respiratory depression in the EN group is a consequence of the rostral diffusion of the drug¹³, which promotes high drug levels on the respiratory centers and a direct antagonist action upon them. Our results clearly demonstrate that epidurally administered nalbuphine is adequate for post operative analgesia, causes few side effects and provide an excellent alternative for epidural morphine analgesia.

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