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Advantages of Buprenorphine in Comparison to Morphine in Post-operative Pain Control.

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Abstract:

Introduction: Pre-emptive analgesia has been used widely and effectively for post operative pain relief. In this study Bupernorphine, a partial agonist of opioids has been compared to Morphine as preemptive analgesic with the aim to achieve better pain control and less post operative complications.

Methods and Material: In this randomized double blind clinical trial, 60 patients were assigned in two equal groups of study (each group=30). Bupernorphine group received 4mcg/kg IV of the drug and morphine group received 0.1mg/kgIV of the drug, 10 minutes before induction of anesthesia. The average time of the first demand for post operative analgesic, the frequencies of demands and the total amount of administered analgesics were recorded. The incidence of post operative complications such as respiratory depression and postoperative nausea and vomiting (PONV) were recorded.

Results: The average time of the first demand for analgesic in Bupernorphine group (410±20minutes) was significantly longer than morphine group (240±25minutes), p<0.0001. The number of patients demanded analgesic were lower in Bupernorphine group (46.7%) than morphine group (90%), p<0.0001. The average increase in arterial paco2 was higher in Morphine group. No significant differences were noted between two groups in the incidence of post operative shivering and Nausea and vomiting.

Conclusions: Intravenous Bupernorphine before induction of anesthesia was more effective and had fewer side effects than morphine in post operative pain management.

Keywords: Preemptive analgesia, Bupernorphine, Morphine PONV, Abdominal surgery.

Introduction

Postoperative pain is a complicated response to the vascular dilation and inflammation, due to tissue injury or underlying disease. With enough knowledge about pathophysiology of pain, the perioperative pain control has become one of the most important aspects of patients care and has resulted in lower level of post operative mortality and morbidity.[1]

Preemptive analgesia has been shown to be one of the effective ways for post operative pain control [2, 3]

Morphine, an opioid receptor agonist has been used traditionally for pain relief, but it has many side effects such as PONV and respiratory depression.[2]

Bupernorphine, a partial agonist of opioid receptors, is 33 times more potent than morphine, but has been shown to have very low level of respiratory depression.[2, 4] In animal models of studies Bupernorphine has been reported to be very effective in pain control.[5, 6]

In these studies Bupernorphine has been used in different routs, such as intramuscular (IM), intravenous (IV), sublingually, intrathecally .transdermally and even as a local anesthetic for peripheral nerve blocks.[7, 16]

In this study we compared this drug to morphine regarding their degree of pain relief and degree of postoperative side effects after abdominal surgery.

Materials and and Methods:

In this study 60 ASA class 1, II patients, with the age of 25-65 scheduled for abdominal surgery were elected. Informed consent and ettic committee approval were obtained. Patients with major systemic and psychiatric diseases and, those with recent narcotic usage were excluded from our study.

All patients received 5 mg of diazepam as premedication.

Patients were divided in two separate groups (30 in each group) based on computer generated randomization, received either 0.1mg/kg of morphine IV or 4mcg/kg Bupernorphine IV, 10 minutes before induction of anesthesia.

Results:

No significant statistical differences in age, sex, weight, and duration of operation were present between two groups of study (table 1).

The mean time for the first analgesic demand in Bupernorphine group (410±20 minutes) was longer than morphine group (240±25minutes), $p<0.0001$,(table2).

The number of the patients received analgesics in first 24 hours after operation in Bupernorphine group (46.7%) were significantly lower than morphine group (90%), $p<0.0001$.

10% of Bupernorphine group and 53.3% 0f morphine group needed more than two

injections for pain relief in first 24 hours, ($p<0.0001$).

The incidence of shivering, nausea and vomiting were low in both groups with no statistical differences. No respiratory depression in both groups were noticed, but the average amount of the arterial $Paco_2$ level was significantly lower in Bupernorphine group than Morphine group, $p=0.02$.

Table 1: demographic results in two groups of study (mean ± standard deviation)

Group / Variant	Morphine Group	Bupernorphine Group	p Value
Number	30	30	
AGE (yr)	46.70±12.62	44.22±10.80	0.65
Weight (kg)	64.30±16.2	62.50±12.42	0.92
Sex (F/M)	12/18	11/19	0.89
Duration of Surgery (minutes)	115±12.00	125±15.30	0.13

Table 2: Postoperative results in two groups (mean ± standard deviation)

Group	Morphine group	Buprenorphine group	P value
Time of the first narcotic request	240 ±20	410 ±20	< 0.0001
Number of patients requested postoperative narcotic	27(90%)	14(46.7%)	< 0.0001
Number of injections in first 24 hours (0/1/2)	5/9/16	16/11/3	< 0.0001
Shivering	8(26.7%)	5(16.7%)	0.34
PONV	6(20%)	4(13.3%)	0.48
Pco_2	45.11 ±5.02	42.44 ±4.27	0.02

Discussion:

Pain signals resulting from tissue inflammation and injury are responsible for over excitement of the peripheral and central neural pathways.

Blockage of these pathways before induction of anesthesia could prevent overreaction and hypersensitivity.

Clinical and experimental experiences have proved the effects of preemptive narcotics in post operative pain relief.[1, 3]

In contrast with multiple animal models of studies about the effects of Bupernorphine, there are few human beings studies.

In animal models it has been shown that the analgesic effects of bupernorphine is done at the supra spinal level while morphine affects spinal cord receptors.[4, 5] Recent human studies have shown less side effects of Bupernorphine compared to morphine. [6]Lacoste et al used sublingual Bupernorphine with good results in thyroid surgery.[7] In another study intramuscular Bupernorphine injection had a very good pain relief.[8] Takahashi et al also used intravenous Bupernorphine for post operative pain control with very good results.[9] Beltrutti et al also reported intravenous buprenorphine with intrathecally morphine as a good combination to pain relief.[10] In our study regarding the effects of Bupernorphine, we found that pre-emptive bupernorphine resulted less narcotic demands in PACU and during 24 hours post operative period than morphine.

Bupernorphine is very lipophilic drug and is 25-30 times more potent than morphine. Its duration of action is also longer than morphine (more than ten hours). Detachment of this drug from μ receptors (166 minutes approximately) is more slowly than morphine.[2, 11-14] In another study even longer pain relief, more than 12 hours with IM injection has been reported.[14] PONV is controversial regarding to Buprenorphine, and some investigations have showed its anti emetic actions due to deposition of morphine from supraspinal levels by this drug.[10] In contrast Khan et al has found higher levels of PONV with this drug.[15]

In our study the incidence of PONV and Shivering was very low in Bupernorphine group in comparing with Morphine Group.

There was no respiratory depression in both groups of study but the average increasing in the level of the arterial paco2 was significantly higher in Morphine group than Bupernorphine group. In conclusion administration of intravenous bupernorphine ten minutes before induction of anesthesia is more effective and has fewer side effects than morphine in post operative pain management

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