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POSTOPERATIVE ANALGESIA;

A COMPARISON OF SUBLINGUAL BUPRENORPHINE AND INTRAMUSCULAR MORPHINE FOR PAIN RELIEF AFTER ABDOMINAL HYSTERECTOMY

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ABSTRACT... iubk@hotmail.com **Objective:** To determine the effectiveness of sublingual buprenorphine in terms of duration of action, quality of analgesia, convenience of administration and safety, as compared to intramuscular morphine for postoperative analgesia after abdominal hysterectomy. **Design:** Prospective, randomized and comparative study. **Place and duration of study:** Combined Military Hospital Jhelum, from January, 2001 to October, 2003. **Subjects and methods:** Women undergoing abdominal hysterectomy were randomly assigned to receive postoperative analgesia with sublingual buprenorphine 0.007 mg/kg body weight or intramuscular morphine 0.2 mg/kg body weight. No analgesic was used before or during anaesthesia. First dose of analgesic was given when patients complained of pain after recovery and doses repeated on required basis. Main outcome measures was effectiveness of analgesia as measured by modified VAS and four point verbal rating scale. Secondary outcome measures were degree of sedation, respiratory rate and blood pressure. **Results:** Both drugs provided effective postoperative analgesia but buprenorphine provided slightly better pain relief for a much longer duration and thus required fewer doses (p=.ooo as determined by Pearson chi-square test). Onset of action was slower for buprenorphine (36.8±5.7 mins) as compared to morphine (12.2±2.7 mins). Mean arterial blood pressure remained stable in buprenorphine group but slightly decreased in morphine group. Respiratory rate slightly reduced in both groups. The incidence of adverse reactions like nausea, vomiting and drowsiness were slightly more common in buprenorphine as compared to morphine group. **Conclusion:** Both drugs provide equally effective postoperative analgesia. Ease of administration and longer duration of action of sublingual buprenorphine make it a more acceptable option.

Key words: Postoperative pain; Morphine; Buprenorphine.

INTRODUCTION

It has long been acknowledged that doctors treat post-operative pain poorly. Post-operative pain is under-treated for a number of reasons. There include lack of knowledge regarding the dose range and duration of action of opioids; an exaggerated fear of

respiratory depression and addiction in hospitalized patients; and inherent inconvenience of techniques used (intermittent injection of opioids such as morphine). Although new concepts of the prophylaxis of post-operative pain started much earlier, during recent years has been a tremendous increase in our understanding of the pathophysiology of acute pain and in development of new techniques for the administration of analgesics.

Buprenorphine is an opioid, partial agonist that has emerged as an option for post operative analegesia[2].It is available in tablet form which is given to the patient sub-lingually. It can solve the problems of those patients, who would suffer pain rather than receive an injection. In this article sublingual buprenorphine has been compared with intramuscular morphine for post-operative pain relief.

SUBJECTS & METHODS

A total of 60, ASA I and II patients of middle age(between 40-60 years), were studied for pain relief after abdominal hysterectomy. The patients selected were randomly divided into two groups. Group I(n=30) received sublingual buprenorphine 0.007 mg/kg body weight and Group II (n=30) received intramuscular morphine 0.2 mg/kg body weight. All patients underwent surgery under anaesthesia. They were pre-medicated with oral diazepam 5mg on the eve of surgery.

Anaesthesia was induced with 2.5% thiopentone sodium 4-6 mg/kg body weight. Endotracheal intubation was done with the aid of suxamethonium 1mg/kg body weight. Anaesthesia was maintained with O_2, N_2O and halothane (1-2%). Pancuronium bromide 0.06 mg/kg body weight was given as a bolus dose with increments as required. None of the patients received any narcotic analgesia before or intra-operatively.

At the end of surgical procedure all patients were shifted to recovery room where first dose of analgesia was administered as soon as the patient complained of pain (0 hour). They were instructed to ask for further analgesia as soon as pain at rest returned. The parameters noted during the study were effectiveness of analgesia using modified Visual Analogue Scale[3] and four-point verbal rating scale, blood pressure, respiratory rate, and degree of sedation. They were measured immediately before starting analgesic therapy and then 4 hourly for 48 hours. Pain was assessed according to modified visual analogue vertical scale (Figure 1).

Intensity of pain was assessed immediately before the administration of the drug. Time of onset of analgesia was noted after first dose and then assessment of pain score was made 4 hourly. The duration of analgesia-time between administration of the analgesic drug and request for additional pain medication-was recorded. Pain was also assessed subjectively on the morning of first postoperative day.

The patients were asked to give an estimate of pain relief on a four-point verbal rating scale (no pain, mild pain, moderate pain, and severe pain). Degree of sedation was assessed by a scale of 0-3. The presence or absence of nausea and vomiting were recorded. All the results were computed and analyzed by chi-square test.

RESULTS

Both groups were matched for age, weight and analgesic regimen (Table 1). Onset of analgesia was delayed for group I (36.8$\pm$5.7 mins) as compared to group II (12.2 $\pm$2.7 mins). Duration of analgesia was significantly greater in group I so that number of doses required in 48 hours in this group were less compared to group II (Table II).

Buprenorphine provided slightly better analgesia but difference was not significant (p=.146). At each assessment, the mean pain score was recorded. Both drugs used in the study produced significant decrease in pain scores. The mean pain score in buprenorphine group was less than morphine group (Figure 2). Subjective pain assessment was done on first post-operative morning. 13 patients in group I had no pain, 12 had mild pain and only 5 had moderate pain as compared to group II in which 6

had no pain, 16 had mild pain and 8 had moderate pain. So during visit on first post-operative morning, although majority of patients in both groups were satisfied with their pain control but in group I most of the patients were more comfortable. None of the patients, in any group complained of unbearable pain (Table III).

Table I: Demographic Data

Description	Group I	Group II
Number	30	30
Age (year)	50.7 ± 7.0	50.2 ± 5.7
Weight (kg)	57.5 ± 7.8	56.2 ± 7.4
Analgesic Regimen	Buprenorphine 0.007 mg/kg body weight (Sublingual)	Morphine 0.2 mg/kg body weight (Intramuscular)

Table II: Comparison of post-operative buprenorphine and morphine. (Pearson chi-square test used)

Description	Group I (n=30)	Group II (n=30)	df	p-value
Duration of analgesia (hours) (Mean values)	8.0025 (s.d = 1.4969)	5.2002 (s.d = 0.9019)	2	.000
Number of doses required in 48 hours	3.7417 (s.d = 0.6400)	5.2123 (s.d = 0.7324)	2	.000

Table III: Subjective pain assessment assessed by four-point verbal rating scale on 1st post-operative morning.

Description	Group I (n=30)	Group II (n=30)
No pain	13	6
Mild pain	12	16
Moderate pain	5	8
Unbearable pain	-	-

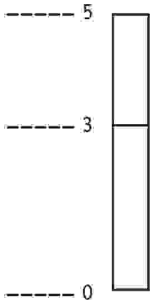
Table IV: Frequency of side effects. (No of patients (%)

Side effects	Group I(n=30)	Group II(n=30)
Respiratory depression (Resp. rate< 10)	0	0
Hypotension (>30% decrease in systolic blood pressure)	0	0
Nausea/Vomiting	8 (26.6%)	5 (16.6%)

Table V: Degree of sedation (Number of patients)

Degree of Sedation	Group I(n=30)	Group II(n=30)
0 = Awake and alert	8	10
1 = Awake but drowsy	9	14
2 = Drowsy but rousable	13	6
3 = Unrousable	0	0

Figure I: Modified Visual Analogue Scale (VAS) for objective pain assessment. (Score 5: frequent need for analgesis. Score 3: pain on movement, reluctant to get out of bed. Score 0: sits in the bed walks around easily, found to be asleep.)[3]



Respiratory rate decreased in both groups but reduction was not significant. Reduction of respiratory rate was slightly more in group I as compared to group II, but the difference was not statistically significant (Figure 3). The effects of both drugs on arterial blood pressure are shown in (Figure 4).

There was slight reduction in blood pressure in both groups but these changes were not statistically significant. The incidence of side effects are listed in Table IV & V. Drowsiness was more common in

group I as compared to group II. Frequency of nausea and vomiting was more in group I as compared to group II.

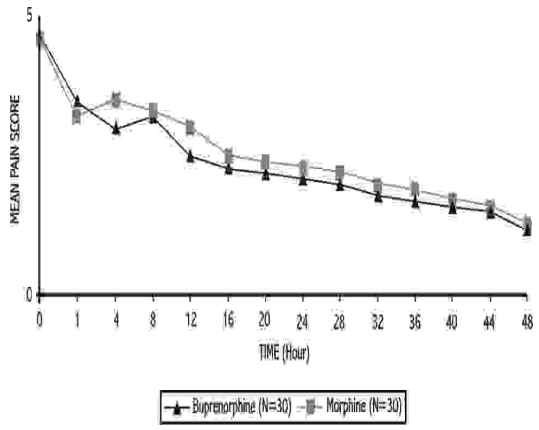


Figure II: Buprenorphine provided slightly better (pain relief as compared to morphine).

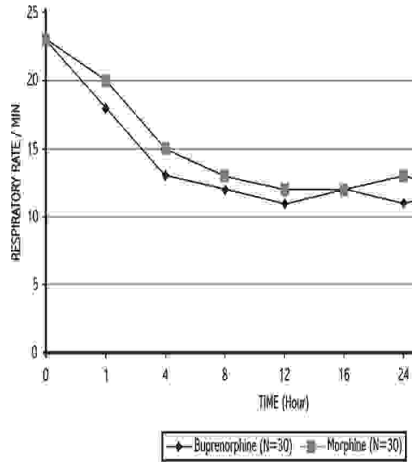


Figure III: Comparison of respiratory rate after administering buprenorphine and morphine.

DISCUSSION

Post-operative pain relief is an under-treated entity. Members of public[4] and even eminent members of medical professional[5,6] have commented on the severity of pain after surgery and lack of efforts to relieve it. After being neglected for a long time, post-operative analgesia is developing considerably at present. New techniques such as sublingual tablets, patient controlled anagesia and spinal opioids are becoming popular among anaesthesiologists.

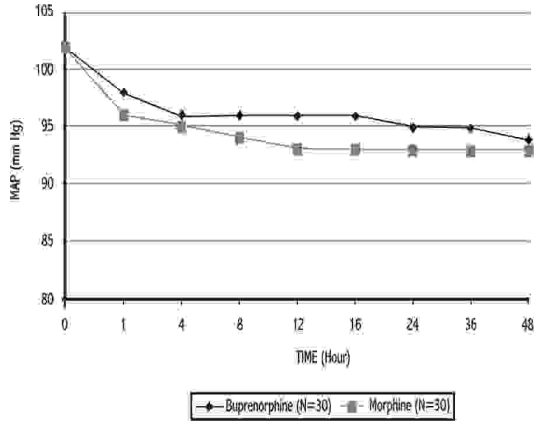


Figure IV: Comparison of blood pressure after administering buprenorphine and morphine.

Buprenorphine, an opioid partial-agonist that is readily absorbed from sublingual mucosal tissue, has emerged as an option for post-operative analgesia. It binds to u, g and k receptors but its activity at latter two sites is relatively insignificant[7].

In our study, sublingual buprenorphine has been compared with intramuscular morphine for post-operative pain relief after abdominal hysterectomy. Both drugs used in the study produced significant decrease in pain scores. However, the onset of action was delayed with buprenorphine group as compared to morphine group. The mean time of onset was 36.86 minutes with buprenorphine and 12.23 minutes with intramuscular morphine. The mean time of onset with buprenorphine was quite different from a previous study carried out by Risbo et al in 1985 which was 3 hour[8].

Duration of action was prolonged in buprenorphine group as compared to morphine group (Table II). The prolonged effect was similar to what has been reported previously by Cart et al in 1978[9].The quality of analgesia was better in buoprenorphine group as

evidenced by pain score (Figure II). On the first post-operative morning, majority of the patients in buprenorphine group were satisfied with the analgesia (no pain or mild pain) compared to morphine group in which 16 had a mild pain and 8 patients had a moderate pain (Table III).

In previous studies sublingual buprenorphine 0.4 mg was compared with conventional intramuscular morphine and found to provide comparable, satisfactory and prolonged post-operative analgesia[10,11]. In a recent study by Staway et al, buprenorphine appeared to be providing better analgesia than morphine and had longer duration of action[12]. Even in the treatment of acute renal colic, sublingual buprenorphine provides safe, effective and better analgesia than other narcotics[13]. Chronic and severe pain is also treated effectively with new formulation of buprenorphine[14].

The effect of buprenorphine on ventilation is controversial. Hovel had reported in 1977, that burprenorphine has only minimal effects on ventilation[15]. In our study buprenorphine depressed the ventilation more than morphine (Figure III). However this effect was not significant. Respiratory depression (defined in breathing rate less than 10 per minute) was not seen in any of our patients. Probably decrease in respiratory rate was due to better pain control. In a study by Pederson et al in 1985, higher doses of buprenorphine were used which did not produce further respiratory depression and actually resulted in increased ventilation (predominance of antagonist effect). It produced respiratory depression with a ceiling effect after 1.2 mg in adults[16].

There was no effect of clinical importance on blood pressure in both groups. Hypotension (defined as 30% fall in systolic arterial blood pressure) was not seen in any of the patients. However there was slight fall in blood pressure in both groups. These effects were more evident in morphine group (Figure IV). This is similar to a study in which the haemodynamic effects of buprenorphine were found similar to those of morphine[17].

All clinically useful opioids produce some degree of nausea and vomiting [18]. In our study nausea and vomiting were seen in both groups but the frequency was more in buprenorphine group (Table IV). This was similar to previous study in which nausea and vomiting were found more common with buprenorphine[19].

Lastly, the side effects were drowsiness and sedation, which were more evident in group I as compared to group II (Table V). In anxious patients and pediatric surgery, sedation may be required. so this effect may be beneficial. Sub-lingual buprenorphine is as safe and effective as sublingual midazolam in providing sedation and anxiolysis for pediatric premedication[20].

CONCLUSION

Both drugs used in this study are effective in relieving post-operative pain. Among the two opioids, buprenorphine provides better pain relief for a longer duration but its onset of action is slow. Both the drugs when used in clinical doses are almost free from cardiovascular side effects. Morphine results in mild reduction in mean arterial blood pressure as compared to buprenorphine. Both drugs do not result in respiratory depression with the doses used in the study. Side effects like nausea, vomiting and drowsiness are slightly more common with buprenorphine than morphine. keeping in view the ease of administration and longer duration of action of buprenorphine, it can be used for effective post-operative pain control.

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