ORIGINAL RESEARCH

A study of instillation of buprenorphine in epidural space for postoperative analgesia in postlaminectomy patients

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Abstract

Background: Instillation of buprenorphine in the epidural space during laminectomies for mitigating postoperative pain has been attempted in this study.

Material and Methods: In the present study, forty patients of either sex scheduled to undergo lumbar or thoracic laminectomy were selected and divided into 20 in each group. The anaesthetic technique was standardized in both groups. At the end of the operation, before final closure, 0.3 mg diluted buprenorphine (study group) or saline (control group) (volume - 10 ml), was instilled in the epidural space under vision by the surgeon. All patients received diclofenac sodium 75 mg IV whenever they reported pain in the postoperative period. Pulse rate, mean arterial pressure (MAP), SpO_2, respiratory rate, pain score and adverse effects (if any) were recorded before the operation and at 1, 2, 3, 4, 5, 6, 12, 18, and 24 hours postoperatively. The results were compared statistically between the study and the control group.

Results: The pulse rate was consistently lower compared to the control group, indicating adequate analgesia in the study group. There was a significant difference in pain score in the buprenorphine group at 2, 3, 4, 5, 6, 12, 18^{th} hours postoperatively when compared with placebo ($p \leq 0.01$). In the control group, the use of analgesics was more than in the study group.

Keywords: Laminectomy, buprenorphine, postoperative analgesia, epidural

Introduction

Laminectomy and discectomy is one of the common surgical procedures performed to relieve the pain caused due to intervertebral disc prolapse [(1)]. Immediate pain relief post-operatively will significantly affect the outcome of the procedure performed and operative morbidity [(2)]. Parenteral administration of opioids has been the mainstay of treatment for postoperative pain after laminectomy. The main drawback of parenteral opioids is that these are usually given with large time lapses and hence there are wide fluctuations in clinical effect [(3)]. Furthermore, high doses of opioids used to decrease pain may be associated with adverse effects like nausea, vomiting, respiratory depression, urinary retention, drowsiness, pruritus or postoperative ileus [(4, 5)].

An alternative to standard pain management is epidural administration of opioids, which are proven to be effective and have a longer duration of action. It is administered as a single dose during the surgery or via an epidural catheter postoperatively [(6)]. Epidural catheters are difficult to maintain after spine surgery and there is a concern of infection, restricting its widespread application [(7)].

Buprenorphine is a semisynthetic opioid that binds to mu, kappa and delta opioid receptors [(8)]. It is an opioid with an analgesic activity 25-40 times more than morphine. The drug does not have a ceiling effect for analgesic effects [(9)]. Because it is more potent and lipid-soluble and has a longer duration of action, it is said to have advantages over morphine for epidural use in postoperative pain relief [(10)].In this innovative study, we have attempted to evaluate the effect of direct instillation of buprenorphine in epidural space

in patients undergoing laminectomy surgeries for postoperative pain relief.

Materials and Methods

After obtaining clearance and approval from the ethical committee, this comparative study was conducted in a randomized double-blinded manner. 40 patients of either sex between the ages 20-60 years falling under ASA grade I or II scheduled to undergo lumbar or thoracic laminectomy were included in the study. Patients undergoing cervical laminectomies, spine-fixation surgery, those with herniated sequestered discs, previous history of spine surgery, patients having neuromuscular disease or psychological disease, and history of substance abuse were excluded from the study. Patients who had accidental dural tear while undergoing laminectomy were also excluded from the study.

All patients were instructed to keep fasting for 8 hours preoperatively and were prescribed 0.25mg alprazolam tablet at night. In the preoperative area, inj. pantoprazole 40mg was given 30 minutes before induction. After shifting to the operation theatre standard non-invasive monitors (ECG, pulse oximetry, NIBP, and end-tidal CO_2) were connected and baseline parameters were noted. The pain score (VAS) was also recorded.

100% pre-oxygenation from Bain's circuit was done for 3-5 mins. Inj. glycopyrrolate 0.005 mg/kg IV, Inj. ondansetron 0.10mg/kg IV, Inj. midazolam 0.05 mg/kg IV, Inj. fentanyl 2 µg/kg IV was injected followed by an induction dose of propofol (2 mg/kg). An appropriate-sized endotracheal tube was used to intubate approximately 3 minutes after a 2ED95 intravenous dose of vecuronium. General anaesthesia with ETT intubation with controlled ventilation was followed for all the patients. Anaesthesia was maintained with volatile anaesthetic agents with a 33:66 ratio of oxygen and nitrous oxide and intermittently half ED95 dose of inj. vecuronium (IV) was given throughout the surgery as required. Both the groups received paracetamol 1g IV 30 mins before extubation.

Before final closure, Group R received 0.3mg buprenorphine (diluted to 10 ml) and Group P received saline (volume - 10 ml) which was instilled in the epidural space under vision directly by the surgeon. All patients received diclofenac sodium 75 mg IV whenever they reported pain in the postoperative period.

Pulse rate, mean arterial pressure (MAP), respiratory rate, pain score by VAS, and SpO_2 were recorded preoperatively and at 1st, 2nd, 3rd, 4th, 5th, 6th, 12th, 18th and 24 hours postoperatively. The duration of pain relief was defined as the time from the end of the operation until the patient required any supplementation of analgesia. Patients were also observed for postoperative complications such as respiratory depression, nausea, vomiting, and bradycardia. For the study, bradycardia was defined as a heart rate less than 50 bpm, respiratory depression was defined as a respiratory rate less than 10 per minute, the need for oxygen supplementation was recorded if patients had an oxygen saturation of less than 92% and urinary retention was labelled as an absence of spontaneous voiding more than 7 hours after removal of the catheter.

The Statistical software namely SPSS 22.0, and R environment ver. 3.2.2 were used for the analysis of the data. Student t-test was used to study the significance of continuous data and Leven's test to assess the homogeneity of variance. The Chi-square/ Fisher Exact test was used to find the significance of study parameters on a categorical scale between two or more groups in a non-parametric setting for Qualitative data analysis. The Fisher Exact test is used when cell samples are very small.

Results

Out of 40 patients, 20% belonged to 30-40 years, 35% to 41-50 years and 45% to the 51-60 years of age group. 45% of Group R is females and 55% is males, while 40% of Group is females and 60% is males and is not statistically significant.

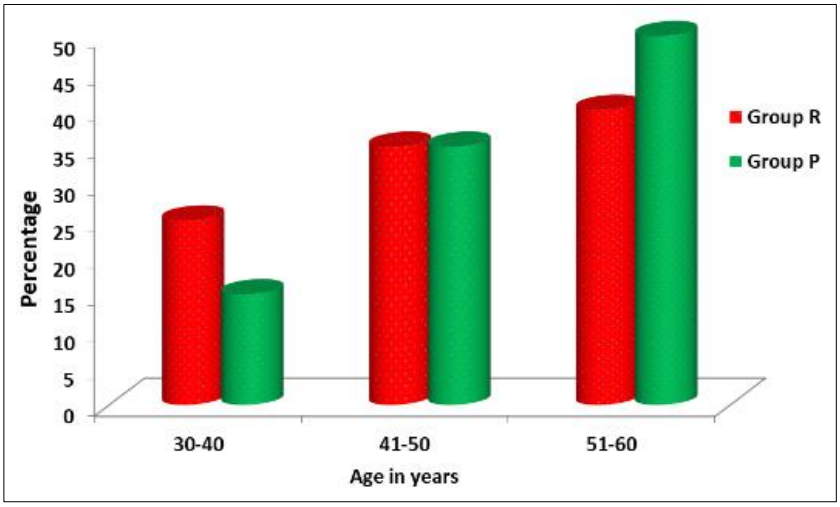

Fig 1: Age

The mean pulse rates of the study and control groups were statistically insignificant in the preoperative period. However, the mean pulse rate of the study group was strongly significant and statistically lower compared with the control group at all-time intervals until 24 hours ($p \leq 0.01$)

Table 1: Pulse rate

Pulse Rate (bpm)	Group R	Group P	P Value
Baseline	85.2±4.56	86±6.32	0.649
1st hour	76.6±4.55	88.35±4.94	<0.001**
2nd hour	79.25±3.92	89.2±3.58	<0.001**
3rd hour	80.2±4.16	89.35±3.44	<0.001**
4th hour	77.45±3.93	85.7±4.39	<0.001**
5th hour	81.05±2.54	85.55±5.53	0.002**
6th hour	81.4±4.13	87.5±4.81	<0.001**
12th hour	83.1±3.58	87.45±5.67	0.006**
18th hour	79.85±2.48	87.35±5.34	<0.001**
24th hour	77.45±2.98	87.2±4.16	<0.001**

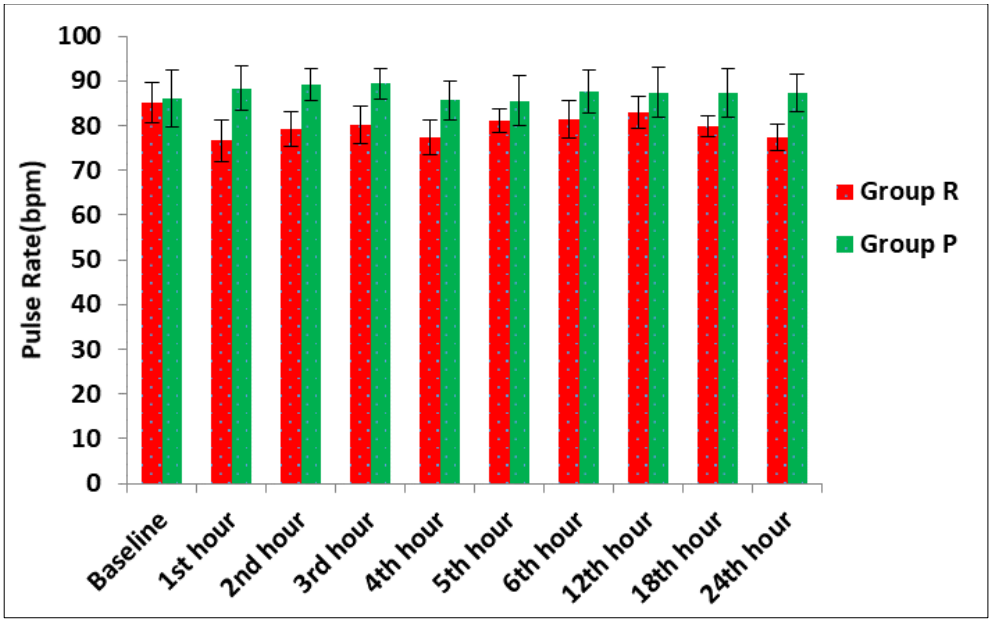

Fig 2: Pulse rate

There was no significant difference between the MAP, RR or SpO_2 of the two groups in the preoperative period and at 1, 2, 3, 4, 5, 6, 12, 18, or 24 hours after the operation ($p > 0.05$).

Table 2: Visual analogue score

Visual Analogue Score to assess pain	Group R	Group P	P Value
Baseline	9.2±0.7	9.25±0.64	0.814
1st hour	0.1±0.31	0.3±0.47	0.120
2nd hour	0.2±0.41	1.65±0.67	<0.001**
3rd hour	1.05±0.69	3.2±1.01	<0.001**
4th hour	1.8±0.7	3.7±0.73	<0.001**
5th hour	2±0.65	4.65±0.81	<0.001**
6th hour	3.3±0.8	6.25±0.64	<0.001**
12th hour	4.4±0.68	7.25±0.72	<0.001**
18th hour	6.55±0.89	7.85±0.67	<0.001**
24th hour	8.7±0.73	9.1±0.64	0.074+

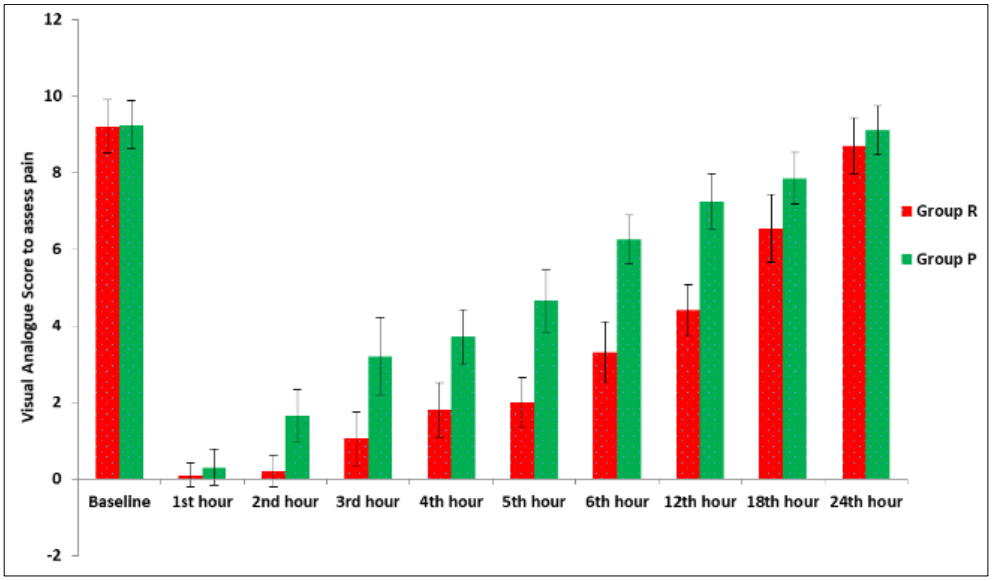

Fig 3: Visual analogue score

In 1st postoperative hour, the mean VAS score in groups A and B was not statistically significant. From the 2nd postoperative hour till the 18th hour, the mean VAS scores in groups A and B were statistically significant (p<0.001). 24 h after the surgery, the VAS score in group R was 8.7±0.73 and in group P was 9.1±0.64 and was not significantly different (p = 0.074).

Patients in group P received rescue analgesia much earlier than group R and this difference was statistically significant.

Overall, 15.6% of patients in the study group reported nausea. In the control group, the incidence of nausea was 14.4% and was not statistically significant. The vomiting was higher in the control group patients (14.3%) compared with the study group patients (7.6%).

Discussion

Acute postoperative pain is a complex, multimodal, and emotional perception and anesthesiologists have always sought new avenues to alleviate it [10]. Buprenorphine is a partial agonist type of opioid with a long duration of action. The high lipid solubility; high affinity for opioid receptors and prolonged duration of action make buprenorphine a suitable choice to alleviate postoperative pain [9].

Several reports have been published on the use of narcotics administered through the intact epidural space. In situations such as laminectomies, where the epidural space is exposed as part of the surgical procedure, the use of gel foam as an extended-release drug delivery system has been studied previously [11]. There is a report of direct epidural morphine injection during lumbar discectomy for postoperative analgesia, but using buprenorphine in this study is a novel attempt.

In a previous study by Mishra *et al*., where they used 300mcg buprenorphine-soaked in an absorbable gelatin sponge the duration of pain relief in the study group ranged from 12 to 18 hours (mean 14.8 ± 0.77 hours), longer than the control group.

We observed in our study that there was a decrease in pulse rate in both groups postoperatively. This may generally be attributed to the adequate analgesia obtained in both groups. However, the decrease in pulse rate at all-time intervals up to 24 hours postoperatively was statistically significant in the study group patients compared with the control (P value: δ0.01). This probably implies that analgesia was lesser in the control group patients than in the study group patients at all intervals.

An excessive decrease in pulse rate (below 50/min) was not observed in any patient. We did not notice any sharp fluctuations in MAP or any incidence of hypotension (a drop of >20% of MAP from the preoperative value).

The mean VAS score in the study group remained less as compared to the control group at all the time intervals studied and was statistically significant except at 1st hour. This implies that till 1st hour post-surgery, analgesia was adequate which may be attributed to the intraoperative analgesics used. Later from the 2nd to 18th hour patients in the study group had less pain as compared to the control group, which was statistically significant.

At 24th hour postoperatively, the pain score was high in both groups, suggesting buprenorphine-induced analgesia was present till 24 hours postoperatively. In the control group, supplemental analgesia was required for almost 20 hours earlier as compared to the study group.

In a study conducted by F.H. Kiabi *et al*., in patients undergoing lumbar discectomy, the VAS score was significantly lower for 24 hours in the group where sublingual buprenorphine was given when compared with the placebo group. The nausea was more in the study group patients, probably as a side effect of the direct instillation but there was less incidence of

vomiting. However, no patient developed a respiratory rate of less than 10/min, bradycardia, pruritus or urinary retention.

Our study is based on a small sample size and future studies with different dosages, more variables and a bigger sample size are therefore required to validate these outcomes.

Conclusion

The instillation of buprenorphine into epidural space after laminectomy is an easy, safe and economical means of achieving analgesia in the early postoperative period, devoid of any side effects.

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