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THE ANALGESIC EFFICACY AND SAFETY OF EPIDURAL CLONIDINE FOR POST OPERATIVE ANALGESIA IN PATIENTS UNDERGOING LUMBOSACRAL SURGERY

Nahila Mahajan[1], Malik Zaffer Iqbal[1], Farooq Ahmad Ganie*[2], Vilayet Nabi Bucch[1], Imtiyaz A. Naqash[1]

Departments of Anaesthesiology and Critical Care and Cardio Vascular and Thoracic Surgery, Sher-I-Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir, India.

*** Corresponding Author Dr. Farooq Ahmad Ganie**
Departments of Anaesthesiology and Critical Care and Cardio vascular and Thoracic Surgery, Sher-I-Kashmir Institute of Medical Sciences, Srinagar, Jammu and Kashmir, India.

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ABSTRACT

Aims: The aim of the study was to evaluate the efficacy of epidural clonidine for postoperative analgesia after lumbosacral surgery and to assess its safety and morphine sparing effect in postoperative period. **Settings and Design**: Prospective, randomized, double-blind study. **Subjects and Methods:** Seventy patients of ASA physical status I and II of either sex, in the age group 18-60 years undergoing lumbosacral surgery, were allocated to two groups of 35 patients each to receive epidural clonidine hydrochloride 1.5µg/kg in 5ml saline or normal saline the on arrival to PACU, followed by infusion of clonidine or normal saline, which was continued in the next 24 hours postoperatively. Postoperative hemodynamic parameters (systolic and diastolic arterial blood pressure and heart rate), pain scores using VAS, total morphine consumption and side effects (nausea, vomiting, sedation) were recorded and analysed statistically. **Results:** VAS over 24 hours were generally low in both the groups throughout the study, with the mean VAS score of 1.68±0.387 and 2.35±0.371 ($p<0.001$). The mean morphine consumption over 24 hours postoperatively was higher in group I than group II (1.54±0.864 mg versus 2.62±0.693 mg; p-value of 0.039. There were statistically significant differences in the postoperative hemodynamic parameters over 24 hours ($p<0.001$).Only 3 patients (8.6%) in group I and 11 patients (31.4%) in group II had postoperative nausea and vomiting. There was no significant difference in sedation scores, demographic characteristics among the two groups. **Conclusion:** It can be concluded from our study that the epidural clonidine, as a sole analgesic agent, provides adequate analgesia in spine surgeries in terms of VAS score and overall patient satisfaction and it reduces the demand for intravenous morphine. It produces few side effects of its own.

KEYWORDS: clonidine, spine surgery.

INTRODUCTION

Relieving post-operative pain of spine surgeries has become an indispensable component in anesthesiology. Various methods have been tried for the management of post-operative pain in spine surgeries out of which epidural techniques are becoming most promising.[1] a2 adrenergic agonists have both analgesic and sedative properties when used as an adjuvant in regional anesthesia.[2] Clonidine is an alpha2 adrenoreceptor and imidazoline receptor agonist which has anaesthtic concentration-sparing effects. It has been used orally, IV,[3,4] and epidurally.[3,5-7] In spinal surgery, there is a reluctance to use local anesthetic based epidural analgesia postoperatively because of fears of masking important signs of nerve root or spinalcorrd injury.

SUBJECTS AND METHODS

After institutional ethical committee approval, 70 patients of either sex, belonging to ASA physical status I-II, in the age range of 18 to 60 years undergoing elective lumbosacral surgery were included in this study. Exclusion criteria were patient already on strong opioids for pain relief, known allergy to study drug, pregnant and lactating women and patients with complicated chronic pain history. During the preoperative visit, all patients were clinically evaluated, assessed and investigated as per the proforma. The study protocol was explained to all the patients and they were demonstrated the VAS pain scoring system, as the method of postoperative pain assessment and written informed consent taken from them.No patient was given any premedication. In the Operating room, the anesthesia technique was similar in all the patients. Anesthesia was induced with fentanyl 2 mcg/kg, propofol 2 mg/kg and vecuronium bromide 0.1 mg/kg body weight. Anesthesia was maintained with isoflurane (0.5-1.0 MAC) with oxygen - nitrous oxide mixture and incremental doses of vecuronium bromide as per train of four ratio. Analgesia was maintained with fentanyl 1µg/kg every hour. Just before closure an epidural catheter was placed under vision by the surgeon. On arrival to Post Anesthesia Care Unit (PACU), patients were randomly allocated to two groups of 35

patients each, by computer generated numbers, to receive either epidural clonidine or epidural placebo as follows: Group I (Clonidine group): Received a bolus dose of clonidine hydrochloride 1.5µg/kg in 5ml saline via the epidural catheter, followed by infusion of clonidine (5ml/h of a solution containing 5µg/ml of clonidine). Group II (Placebo group): Received an equivalent volume of normal saline via the epidural catheter, followed by an equivalent infusion of normal saline. All patients received injection paracetamol 1gm intravenous 6hrly postoperatively. All the patients received injection morphine 3mg intravenously in PACU. If VAS score of the patients was >3 at any time postoperatively, injection morphine 1mg intravenous followed by repeated doses,with an interval of 10 minutes between the subsequent doses, was given titrating to VAS score of ≤3.The anesthetic, surgical and ward team were blinded to the identity of the epidural infusion. Following parameters were monitored and recorded up to 24 hours: Hemodynamic parameters (heart rate, Systolic blood pressure, Diastolic blood pressure) were recorded every 15 min in the first hour, followed by every hour for 4 hours and then 4 hourly up to 24 hours postoperatively, Pain scores were recorded every 15 min in the first hour, followed by every hour for 6 hours and then 2 hourly up to 24 hours, Pain scores were measured on standard Visual Analogue Scale (Flacke J, Bloor B, Flacke W, 1987), where VAS 0 = no pain, VAS 10 = worst pain. The degree of sedation was measured and recorded 4 hourly using a 4 point scale (Jeffs SA, Hall JE, Morris S, 2002) as follows: 0: Awake and alert. 1: Drowsy. 2: Mostly sleepy 3: Difficult or impossible to awaken. The total amount of morphine consumed during the study period was recorded. Side effects like Bradycardia (heart rate <50 bpm), hypotension (SBP <90 mmHg), postoperative nausea and vomiting were recorded and treated accordingly.

Data thus obtained was analyzed statistically using analysis of variance and Student's t-test for hemodynamic variables, Chi-square test for demographic variables. Data were presented as mean ± standard deviation $P < 0.05$ was considered as statistically significant.

RESULTS

The difference in age, weight, and sex between two groups was comparable [Table 1]. Figure 1 and 2 shows heart rate and systolic blood pressure for two groups. There were statistically significant differences in the postoperative hemodynamic parameters over 24 hours. The mean heart rate in group I was 70.15±4.102 beats/min and that in group II was 74.43±3.638 beats/min, with p-value of 0.009. The mean systolic blood pressure in clonidine and placebo group was 115.71±3.253 mmHg and 121.829±2.069 mmHg respectively (p‹0.001). None of the patients in any of the groups had bradycardia or hypotension, at any time in the postoperative period. The pain scores according to VAS over 24 hours were generally low in both the groups throughout the study, although less in Group I (clonidine) when compared to Group II (placebo), with the mean VAS score of 1.68±0.387 and 2.35±0.371 in group I and group II respectively. All these differences were statistically significant (p<0.001).

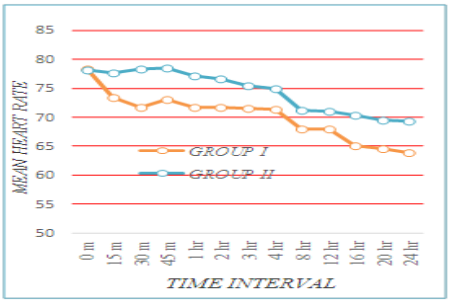
The mean morphine consumption over 24 hours postoperatively in group I was 1.54±0.864 mg and that in group II was 2.62±0.693 mg. This difference was statistically significant with p-value of 0.039. The cumulative dose in group I was significantly lower than that in group II (9mg vs 16mg), with p-value of ‹0.001. The percentage reduction in morphine consumption in group I was 40% in comparison to group II.

Table 1: Demographic data of the groups

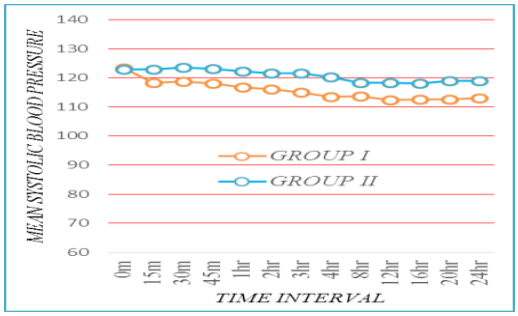
	Group I (CLONIDINE)	Group II (PLACEBO)	P VALUE
Age (years)	37.69±10.023	41.57±11.526	0.137
Male/female	20/15	20/15	1.00
Weight (Kg)	62.51±6.012	64.26±0.133	0.312

The sedation scores among the two groups were compared at various time intervals and the differences were statistically insignificant (p<0.05). No patient had sedation score of more than 2, in any of the groups at any time.

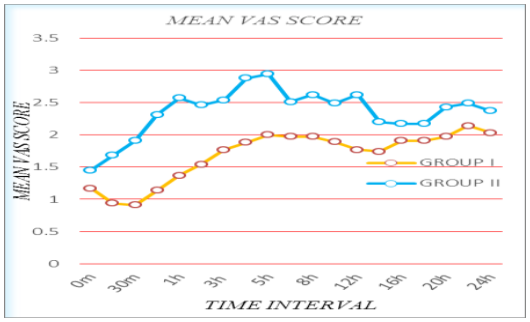
Only 3 patients (8.6%) in group I and 11 patients (31.4%) in group II had postoperative nausea and vomiting. This difference was statistically significant with p=0.017.



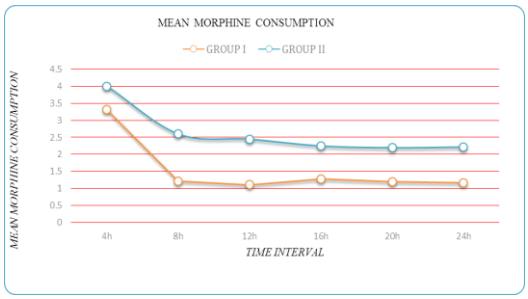
GRAPH 1: Line graph representing mean heart rate (beats/min) in the two groups at different time intervals over 24 hours postoperatively.



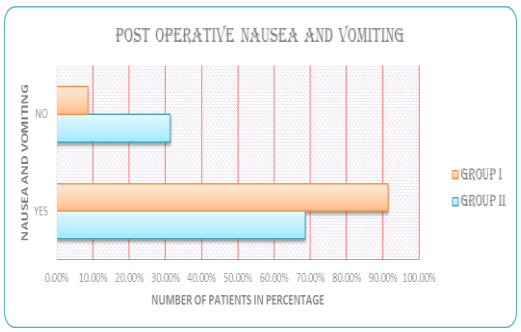
GRAPH 2: Line graph representing mean systolic blood pressure (mmHg) in the two groups at different time intervals over 24 hours postoperatively



GRAPH 3: Line graph representing mean VAS score in the two groups at different time intervals over 24 hours postoperatively.



GRAPH 4: Line graph representing mean morphine consumption (mg) in the two groups at different time intervals over 24 hours postoperatively



GRAPH 5: Bar graph representing number of patients with postoperative nausea and vomiting in the two groups over 24 hours postoperatively

DISCUSSION

The main aim of post-operative pain relief is to provide subjective comfort, in addition to inhibiting nociceptive impulses caused by trauma and to blunt autonomic as well as somatic reflexes to pain. Subsequently, this might enhance restoration of function by allowing the patient to breathe, cough and to be easily ambulant. Giving epidural analgesia for post-operative spine surgeries is a newer technique and challenging one for pain relief because inserting an epidural catheter in the surgical site has lot of controversies and drawbacks; however, we overcame these issues and got good results.[1,2,8,9] The surgical incision for the spine surgeries involved the nerve supply area of not more than nine spinal segments and less than six spinal segments. The instrumentation of the epidural space soon after surgery requires a larger amount of drug than the usual.

The demographic characteristics (age, weight, male-female ratio) were comparable in both the two groups ($p>0.05$).

Although epidural route of analgesia increases the possibility of hemodynamic instability, the cardiorespiratory parameters remained stable throughout the study period, which reaffirms the established effects of α-2 agonists in providing hemodynamically stable postoperative analgesia.[10] There was no significant difference of heart rate and systolic and diastolic blood pressure ($P>0.05$) in both the groups at the time of administration of drug, but it started to decrease in group I (clonidine group) as evident at 15 min interval after clonidine administration. There was a decreasing trend of heart rate in group I (Clonidine group) but none of the patient had bradycardia (HR ‹50b/min) or hypotension (SBP <90mmHg) at any time postoperatively.

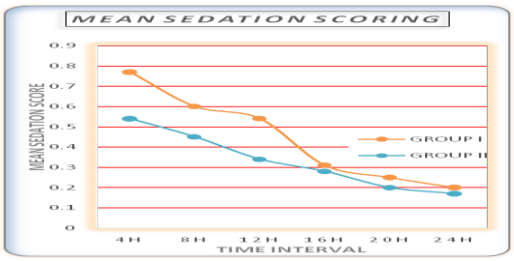
In our study, VAS score was used to evaluate the efficacy of epidural route for postoperative pain. Pain scores were generally low in both groups throughout the study. On comparing the VAS scores between the two groups at various intervals, a statistically significant difference was found between clonidine and placebo group. The pain scores according to VAS over 24 hours were generally low in both the groups throughout the study, although less in Group I (clonidine) when compared to Group II (placebo), with the mean VAS score of 1.68±0.387 and 2.35±0.371 in group I and group II respectively. All these differences were statistically significant ($p<0.001$).

Other studies have also evaluated the efficacy of epidural in spine surgeries. **Jellish, et al.**[11] found that a single epidural bolus dose of 150µg after laminectomy surgery performed with bupivacaine spinal block significantly reduced postoperative pain scores, although the effect was short lived being most marked in the first 60 min. We have shown that this benefit can be extended by following this initial bolus with a low-dose infusion for up to 24 h.

The fact that little effect on sedation could be demonstrated is in keeping with **Hall JE et al.**[12] Dose ranging study of systemic clonidine on sedation and cognitive function, for which the lowest dose producing minimal sedation was three times larger than the dose used here. In our study percentage reduction in morphine consumption in group I was 40% in comparison to group II. **Farmery AD et al.**[13] observed that mean morphine consumption at 36h in Clonidine group was about 43% less than that in Placebo group.

Sedative-hypnotic effects of α-2 adrenergic agonists are related to the inhibition of neural firing in the locus coeruleus[14], a brainstem nucleus located in the dorsal part of the medulla. This supraspinal effect is logical after systemic administration of clonidine, but has also been documented after intrathecal injection[15], probably because of a rostral cerebrospinal fluid spread.[16]

The marked and significant reduction in postoperative nausea and vomiting (PONV) seen in Group I (clonidine group) is also notable in study done by **Farmery AD et al.**[13] They attributed the effect on PONV, to some extent to the fact that patients who received clonidine also received less morphine. However, they found the PONV reduction disproportionately large with respect to the morphine sparing and argued that at least some of the effect is directly due to α-2 adrenergic effects in the brainstem and clonidine may deserve further study as an antiemetic in its own right.



GRAPH 6: Line graph representing mean sedation score in the two groups at different time intervals over 24 hours postoperatively

CONCLUSION

It can be concluded from the study the epidural route provided adequate analgesia in spine surgeries in terms of VAS score and overall patient satisfaction and reduces demand for morphine by aprosimateiy by 40% over 24 hr. epidural clonidine is effective at low doses, probably lower than IV administration found by others[1]. It produces few side effects of its own, and, by reducing consumption of morphine, may reduce side effect of later.

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