



Comparative Study of Epidural Clonidine, Buprenorphine As Adjuvants With Plain 0.125% Bupivacaine For Postoperative Analgesia in Orthopedic Surgeries

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ABSTRACT

Background and objectives: We have conducted a Double blind study to evaluate and compare the efficiency of epidurally administered buprenorphine and clonidine as an adjuvant with bupivacaine and the onset of analgesia, duration of analgesia and side effects.

Methods: 60 patients aged 20-60 years, who were undergoing elective orthopedic surgeries, were randomly allocated to receive either 3µg/kg or 90 µg buprenorphine (group B) or 1.5µg/kg or 75 µg clonidine (group C) (whichever is lower), solution was made to 10 ml by adding normal saline and given epidurally. Patients were followed for 24 hours after the surgery. VAS for pain intensity, onset and duration of analgesia, vital signs and side effects was monitored at 0, 5,10, 15, 20, 30, 45minutes, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 and 24th hour of the postoperative period.

Results: Onset time of analgesia for groups B and C was almost same but duration of analgesia in group B was significantly longer than in group C (p<0.0001). Pain scores were lower with group B. All patients remained haemodynamically stable during the study period and no clinical respiratory depression was seen in group B.

Conclusion: The study revealed that the epidural buprenorphine provides adequate and prolonged postoperative analgesia than clonidine.

KEYWORDS Bupivacaine, buprenorphine, clonidine, orthopedic surgeries, epidural, postoperative analgesia.

INTRODUCTION

Epidural anaesthesia has been used for various purposes. It was performed accidentally by corning.Morphine was isolated from opium by Freidrich(1).

The term opioid has been introduced to group together all drugs ,both naturally occuring and synthetic ones.This was described by Martin(2).Buprenorphine is synthetic opioid with both agonist and antagonist properties. (3)Lanz E and Simko G also showed that buprenorphine prolongs the duration of analgesia(4).

Clonidine has been shown to be effective in relieving neuro-pathic pain,especially when administered epidurally.(5)

PATIENTS & METHODS:

The present study was conducted in the Department of Anaesthesiology, Kurnool medical college, Kurnool attached to Government General Hospital, Kurnool. The protocol was approved by the hospital ethical committee and informed consent was taken from each of the patients. Sixty ASA Grade 1 and 2 patients, aged 20 - 60 years undergoing elective orthopaedic surgeries were divided into two groups of 30 each . patients with poorly controlled hypertension, angina and congestive cardiac failure, Atrial fibrillation, arrhythmias, local infection at back , low platelet count were excluded .

In Group B, 2.5 ml 0.5% bupivacaine + buprenorphine 3µg/kg or 90 µg , and in Group C 2.5 ml 0.5% bupivacaine + clonidine 1.5µg/kg or 75µg were given .The solution was made to 10 ml by adding normal saline and was injected through epidural catheter after patient complained of pain in postoperative period (VAS scores > 3).

Pre Anaesthetic Evaluation

was done and the sensitivity to the local anaesthetics was tested in all the groups. Baseline vital parameters like PR, BP, RR, and Spo2 were recorded .An intravenous line was established with 18G IV cannula and preloading was done with Ringer lactate -.The patients were premedicated with injection Ranitidine 50mg and injection Ondansetron 4 mg was given IV slowly preoperatively 5 minutes before surgery.

Under aseptic precautions L2-L3 / L3-L4 intervertebral space was identified in sitting position.. Local infiltration of 2ml of 1% lignocaine was given ,then 18G tuohy needle was introduced and epidural space was identified by loss of resistance to normal saline. 18 G epidural catheter was inserted so that 2-3cm of catheter is inside the epidural space. Spinal anaesthesia was given in lower space. parameters like SBP, DBP, MAP, Spo2, PR, RR, and VAS were monitored.

Recovery from local anaesthetic was gauged by Bromage scale and at two segment recession of sensory blockade . The pain scores were evaluated at 0, 5, 10, 15, 30, 45, 60, 120, 180, 240, 300, 360, 420, 480, 540, 600, 660minutes and 12 and 24 hrs after surgery. In postoperative period all the vital parameters were monitored and onset of analgesia, duration of analgesia and side effects were noted. Pain was treated with intra muscular Diclofenac injections as rescue analgesic. Duration of analgesia was noted by using "Prince Henry" pain scale and visual analogue scale. All the patients were observed for side effects

OBSERVATIONS AND RESULTS

Demographic variables (Table 1) like Age,Sex,Body weight and vital data (Heart rate,Systolic blood pressure,Diastolic blood pressure,Respiratory rate,SPO2) were comparable.(table 2)

Table 1:

PARAMETERS OBSERVED	GROUPB (BUPRENORPHINE) n=30	GROUPC (CLONIDINE) n=30	P value
Age	20-59	20-60	0.30723878
Sex	M:F = 19:11	M:F = 25:5	0.144376523
Body weight	55.4+/-8.1	55.03+/-10.6	0.1244764

Table 2:

PARAMETERS OBSERVED	GROUPB (BUPRENORPHINE)n=30	GROUPC (CLONIDINE) n=30	P value
Heart rate T 300	84.1+/-14.2	87.9+/-15.1	0.31302265
SBP T 300	99.1+/-8.9	96.9+/-9.3	0.35556749
DBP T 300	66.6+/-8.3	62.4+/-8.5	0.058571552
Spo2 T 300	97.9+/-1.4	98.4+/-1.04	0.194605
Respiratory rate T 300	13.43+/-0.81	13.7+/-0.7	0.180485

The onset and duration of analgesia as well as the need for rescue analgesics were compared between the two groups.

Onset of Analgesia was 14.1133 ± 1.13948 minutes in Group B, and 14.26 ± 1.2218 minutes in Group C, and was comparable in both these groups but statistically not significant with a p-value 0.6324. Duration of Analgesia was 540.333 ± 51.2252 minutes in Group B and 466.6667 ±30.8872 minutes in Group C which was statistically highly significant with P value< 0.00001. Rescue analgesics were given before 450 minutes in 1 patient Group B and where as 7 patients in group C. Between 450-500 minutes interval the rescue analgesia was given to 10 patients in Group B and 20 patients in group C. In group B 19 patients were received res-

cue analgesics where as 3 patients in group C after 500 minutes interval. There was a statistically highly significant difference in both the groups with P value < 0.00001.

TABLE 3:

PARAMETERS OBSERVED	GROUPB (BUPRENORPHINE) n=30	GROUPC (CLONIDINE) n=30	P value
Onset of analgesia(min)	14.1+/-1.1	14.2+/-1.2	0.632446
Duration of analgesia(min)	540.3+/-51	466.6+/-30.8	<0.00001
Rescue analgesics 400-500min	10	20	<0.00001

Table 4 : Side effects

	Nausea	Vomitin-g	Itching	Respiratory Depression	Retention of Urine	Sedate-on	Hy-pote-nision	Brady-car-dia	Dryness of Mouth
Group B (n=30) bu-prenor-phine	8	4	3	0	0	7	0	0	0
Group C (n=30) Clonidine	4	2	0	0	0	2	1	1	0

In Group-B the side effects reported were nausea in 8patients (26.6%), vomiting in 4 patients (13.3%), Itching in 3patients (10%) and mild sedation, drowsiness was observed in seven patients (23.3%). In Group-C the side effects reported were nausea in 4 patients (13.3%), vomiting in 2 patients (6.6%), mild sedation in 2 patients (6.6%) and hypotension and bradycardia(3.3%) ,which was treated with inj. atropine 0.6 mg i.v . The difference observed between the two groups is not significant.

VAS score:

Table -5 : VAS score

VAS	T 480		T 540		T 600		T 660		T 720	
	GroupB	Group C	Group B	Group C	GroupB	Group C	GroupB	GroupC	GroupB	Group C
0	27	7	15	1	4	0				
1	2	16	4	2	5	0	1	0		
2	1	5	9	7	6	1	3	0		
3	0	2	1	14	10	2	6	0	1	0
4			1	4	3	11	5	1	4	0
5			0	2	1	10	10	3	5	0
6					1	6	5	26	20	30
Chi square value	25.64409305		26.55741039		28.84341991		25.14641322		6.338181818	
P value	< 0.00001		< 0.00001		< 0.00001		0.000005		0.096267	

In above table-5 except T-720 the VAS scores at time intervals T-480, T-540, T-600 and T-660 were significantly lower (P <0.05) in group B when compared with group C. VAS scores at all remaining intervals were homogenously similar in both the groups.

DISCUSSION

The present study was done with an aim to compare the duration of post operative analgesia produced by fixed dose of epidural buprenorphine, with fixed dose of epidural clonidine and for any incidence of side effects. we used clonidine as a bolus of 75 µg because smaller doses (30 µg) have been shown not to improve analgesia significantly, whereas larger doses (150 or 300 µg as bolus or in repeated doses) have

resulted in bradycardia, sedation. In our study we used buprenorphine as a bolus of 90 µg because smaller doses (<60 µg) have been shown not to improve analgesia significantly, where as larger doses (300 µg as bolus or in repeated doses) have resulted in more side effects. In our study 0.125% bupivacaine was added to either Buprenorphine or Clonidine.

In our study, the mean time of **onset of analgesia** in Group-B was 14.1133 ± 1.13948 minutes and in Group-C was 14.26 ± 1.2218 minutes (Table-5). The Statistical analysis by Student's unpaired t-test showed that time of onset of analgesia in Group B, Group C was nil significant. Our results matched with the study done by Bonnet Boica ET al⁶ who compared epidural clonidine 150ug with epidural saline injec-

tion. In their study onset of analgesia was within 15 minutes.

In our study, **duration of analgesia** in Group-B was 540.333 ± 51.2252 minutes and range of analgesic duration was 440-610 minutes. Duration of analgesia in Group-C was 466.6667 ± 30.8872 minutes and the duration of range was 400-540 minutes. The time of duration of analgesia in Group-B was highly significant more when compared to Group-C ($t=6.745415215$, $P < 0.00001$). Our study results were comparable with the study done by Kiran Agarwal⁷, Navneet Agarwal who compared analgesic efficacy of buprenorphine or clonidine with bupivacaine in caesarean section. They found mean duration of the analgesia was significantly longer in the Group one patients receiving buprenorphine (0.075 mg) plus bupivacaine (690 ± 35 minutes) and bupivacaine plus clonidine (37.5 microgram) 590 ± 42 minutes, when compared with bupivacaine group alone. Shaloo IPE, Sara Korula ET al⁸ in their study compared epidural buprenorphine and intrathecal buprenorphine and proved that in both the Groups buprenorphine prolonged the sensory analgesia in all their patients by 6 hours. Bonnet⁹, Boico et al in their double blind study of 20 ASA1/2 patients undergoing orthopedic surgeries, evaluated the efficacy of 150ug of epidural clonidine in normal saline (15ug/ml) with that of normal saline. They found that mean duration of analgesia in epidural clonidine was significantly longer (210min vs. 45min).

Side effects:

In group-B (buprenorphine) we observed the side effects like nausea, vomiting, itching, mild sedation and drowsiness. In group-C (clonidine) side effects reported were nausea, vomiting, mild sedation, hypotension and bradycardia. The dif-

ferences observed between the two Groups were not significant. Kiran Agarwal⁷ et al in their study had 75 micrograms of epidural buprenorphine given to their patients had no sedation or drowsiness. Ochi and Arai¹⁰ showed that the incidence of emetic complications after, extradural buprenorphine for postoperative analgesia was related to the incidence of postoperative pain.

Koshi T ET al¹⁰ in 1994 compared epidural morphine with epidural buprenorphine for postoperative analgesia and side effects. They found side effects like pruritus occurred in 3 (13.3%) patients and urinary retention occurred in 8 (26.7%) patients.

Sedation:

In our study Group B patients had moderate drowsiness. Sedation was a common side effect of epidural buprenorphine administration. Its action on Kappa and Mu receptors causes sedation. Patients with an epidural buprenorphine administration of 3micrograms/kg had no respiratory depression, as described by findings of Lanz E and Simko G; Theiss D⁴ also showed that buprenorphine did not lead to prolonged respiratory depression. Mendez ET al¹¹ conducted a double blind, placebo controlled study to assess the appropriate dose of epidural clonidine for post cesarean section analgesia. 60 women were randomly assigned to three Groups and received either bolus saline, 400ug (5ug/kg) clonidine bolus or 800(10ug/kg) bolus clonidine. They concluded that there was no difference in respiratory rate at any time, and no patient had a respiratory rate of <12 breaths per minute.

CONCLUSION

Epidural Buprenorphine has an advantage of longer duration of action with minimal side effects when compared with epidural clonidine.

REFERENCES

1. Millers anaesthesia 7th edition; the term opium derived from opus greek word it is derived from papaver somniferous | 2. Martin W.R: Pharmacology of opioids. vpharmacol, Rev., 35:283,1983. | 3. Downing JW, Leary WP, White ES Buprenorphine: A new potent long acting synthetic analgesic. Comparison with morphine, Br J Anaesth, 49, 251 | 4. Lanz E, Simko G, Theiss D, Glocke MH. Epidural buprenorphine—a double-blind study of postoperative analgesia and side effects. Anesth Analg. 1984; 63(6):593. | 5. Eisenach JC, DuPen S, Dubois M, Miguel R, Allin D: Pain [1995, 61(3):391-9] Epidural clonidine analgesia for intractable cancer pain, The Epidural Clonidine Study Group | 6. Boico, O.; Bonnet, F.; Rostaing, S.; Loriferne, J. F.; Quintin, L.; Ghignone, M. Epidural Clonidine Produces Postoperative Analgesia. Anaesthesiology. 69(3A):A388, September 1988. | 7. Agarwal K, Agarwal N, Agrawal V, Agarwal A, Sharma M, Agarwal K. Comparative analgesic efficacy of buprenorphine or clonidine with bupivacaine in the caesarean section. Indian J Anaesth 2010; 54:453-7. | 8. Shaloo Ipe, Sara Korula, Sreelatha Varma A comparative study of intrathecal and epidural buprenorphine using combined spinal-epidural technique for caesarean section 2010; 205-209 | 9. Epidural clonidine combined with bupivacaine for analgesia in labor. Effects on mother and neonate. Cigarini I, Kaba A, Bonnet F, Brohon E, Dutz F, Damas F, Hans P.Reg Anesth. 1995 Mar-Apr; 20(2):113-20. | 10. Ochi G, Arai T. Incidence of nausea and vomiting associated with epidural buprenorphine for postoperative analgesia. An analysis in relation to its analgesic effect. J Anesth 1991; 5: 412-5. | 11. Mendez R, Eisenach JC, Kashtan K Epidural clonidine analgesia after cesarean section. Anaesthesiology. 1990 Nov; 73(5):848-52. |