

COMPARATIVE STUDY BETWEEN EPIDURAL BUPIVACAINE WITH BUPRENORPHINE AND EPIDURAL BUPIVACAINE FOR POST-OPERATIVE ANALGESIA IN ABDOMINAL AND LOWER LIMB SURGERIES

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ABSTRACT: AIMS: This study was done to ascertain whether epidural bupivacaine with buprenorphine provides better quality of analgesia when compared to epidural bupivacaine. The onset of pain relief, Duration of action, Changes in haemodynamic parameters, Side effects due to drugs was monitored. **MATERIALS AND METHODS:** 60 patients of both sexes who were to undergo lower limb and abdominal surgeries were selected. They were randomly divided into 2 groups of 30 patients each. Group A received 0.25% bupivacaine with 0.15mg buprenorphine for post-operative analgesia and Group B received 0.25% bupivacaine. The parameters recorded were HR, RR, MAP, VAS and Wt of patient, onset of analgesia and duration of analgesia. **RESULTS:** The significance was calculated using T test. The results showed that 0.25% bupivacaine and buprenorphine was better than 0.25% Bupivacaine alone even though there was some amount of respiratory depression present. **CONCLUSION:** Addition of buprenorphine to bupivacaine by epidural injection for post-operative analgesia improves the onset, the duration and the quality of analgesia, albeit keeping the possibility of late respiratory depression. **KEYWORDS:** Epidural, Bupivacaine, Buprenorphine, post-operative analgesia, opioids.

INTRODUCTION: Among the remedies which has pleased Almighty God to give to man is to relieve his sufferings, none is so universal and so efficacious as opium"- Sydenham (1680). Epidural administration of various analgesics gained increasing popularity following the discovery of opioid receptors in the spinal cord. Analgesia provided by epidural and peripheral techniques (particularly when local anesthetics are used) is superior to that with systemic opioids.¹ Some studies have shown decreased morbidity and mortality with epidural analgesia as compared to systemically administered opioids.² Buprenorphine which is 30 times more potent than morphine and is agonist-antagonist with a lipid solubility about 5 times greater than that of morphine, has been used epidurally for post-operative analgesia which has lower incidence of delayed respiratory depression, because there is no rostral spread.³ A few clinical reports show that even though epidural Bupivacaine is short acting, it does not cause the side effects as seen in epidural opioids, like nausea, vomiting, respiratory depression and pruritis.⁴ The type of analgesia produced by epidural bupivacaine was equipotent when compared to epidural buprenorphine. This study was envisaged and designed to evaluate the effectiveness of relief of pain, onset of pain relief and side effects due to epidural administration of bupivacaine with buprenorphine mixture and bupivacaine alone in patient who had undergone abdominal and lower limb surgeries.

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METHODOLOGY: Sixty patients undergoing various lower abdominal and lower limb surgeries which included orthopaedic procedures were randomly selected for the study. They were posted to undergo surgery at S.V.R.R.G.G.H., S.V. Medical College, Tirupati, Chittoor District. The study was approved by the Hospital Ethics Committee, written informed consent was taken from the patients.

Inclusion Criteria: Patients of either sex, ASA grade I and II, Age between 20 to 60 years, Body weight between 45 to 80 kgs, Planned for elective general surgery, orthopaedic surgery and gynaecological surgeries.

Exclusion Criteria: Patients refusal for consent, Patients with spinal deformities, Patients with bleeding disorders, Patients with neurological deficit, Patients with local skin sepsis around the site of needle insertion.

Pre anaesthetic examination done (By reviewing history, general examination, investigations).

After obtaining written informed consent, initial pre-operative counseling and reassurance was done to gain the confidence and to reduce the emotional component of pain. The nature of the procedure was explained and the patients were taught to assess the intensity of pain using the visual analogue scale (VAS). All the patients received diazepam 0.1 to 0.2 mg/kg body weight at bed time on previous night of surgery.

PROCEDURE: Patient shifted to the OT, IV line secured, monitors (PR, NIBP, SPO₂, RR, and ECG) connected. All the patients were preloaded with 500 ml of Ringer lactate solution. All the patients were put on left lateral position, with aseptic precautions, epidural space was found with 18G Tuohy needle at L₂ - L₃ space by loss of resistance using air injection technique and an 20G epidural catheter was threaded through this needle for 3-4 cms in the cephalad direction and properly fixed. Intraoperative anaesthesia was achieved by intrathecal route with 3ml of 0.5% heavy bupivacaine given in L₃-L₄ subarachnoid space with 23G spinal needle. All the patients were continuously monitored for pulse rate, blood pressure, respiratory rate and oxygen saturation for every 5 min for first half an hour and every 15 min till the end of the surgery. Intraoperative hypotension was treated with IV fluids, oxygen supplementation and titrated doses of mephentermine 3-6 mg intravenous. Bradycardia was treated with injection atropine 0.6 mg. After completion of the surgery, the patients were observed in the postoperative recovery room till the level of anaesthesia wears off to the spinal segment T12 before shifting to the post-operative ward. When the patient complains of pain (VAS >3), Group A Patients received 12 ml of 0.25% bupivacaine +0.15 mg of buprenorphine, Group B: Patients received 12 ml of 0.25% of bupivacaine alone. Then onset of action and intensity and duration of pain relief were recorded at 10 minutes intervals for first half an hour and then at 60th min, thereafter every 2 hrs interval (3, 5, 7, 9, 11, 13, 15, 17, 19, 21 hrs) for 21 hrs period.

A total of 60 patients of either sex participated in the study. Statistical data was analyzed using Chi-square test, Student t-test (Paired and unpaired t-test), A P value of <0.05 significant <0.01 - Highly significant, <0.001 - Very highly significant, >0.05 not significant.

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Demographic Data Analysis:

No. of patients	Age (in years)	Weight (Kgs)	No. of Male Patients	No. of Female Patients
30	23-60	46-72	11	16
Mean	42.33	52.5	36.6	63.4

Table 1: Group -A: 0.25% Bupivacaine with 0.15 mg of buprenorphine

No. of patients	Age (in years)	Weight (Kgs)	No. of Male Patients	No. of Female Patients
30	23-60	45-74	9	21
Mean	41.67	48.17	30	70

Table 2: Group -B: 0.25% Bupivacaine

Age (Yrs)	Group – A	Group – B
20-30	8	4
31-40	6	12
41-50	9	8
51-60	8	6

Table 3: Age Distribution

Weight (kgs)	Group – A	Group – B
<50	13	16
> 50	17	14

Table 4: Weight Distribution

Groups	No. of patients	Mean onset of analgesia (in min)	SD	T	Significance
Group – A	30	7.52	2.71	2.36	P<0.05
Group – B	30	15.50	1.50		

Table 5: Onset of Analgesia

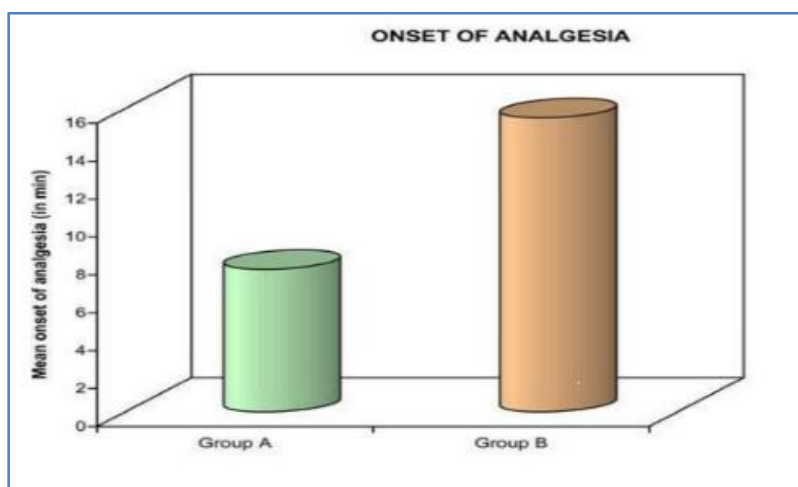


Fig. 1: Onset of analgesia

It is observed that onset of analgesia in Group – A (0.25% bupivacaine +0.15 mg buprenorphine) was 7.52 min. When compared to Group – B (0.25% bupivacaine) which was 15.50 min, which is statistically significant ($P < 0.05$). It shows bupivacaine with buprenorphine has faster onset of pain relief when compared to bupivacaine, given epidurally.

	No. of patients	Mean onset of analgesia (in min)	SD	T	Significance
Group – A	30	7.52	2.71	2.36	$P < 0.05$
Group – B	30	15.50	1.50		

Table 6: Duration of Analgesia

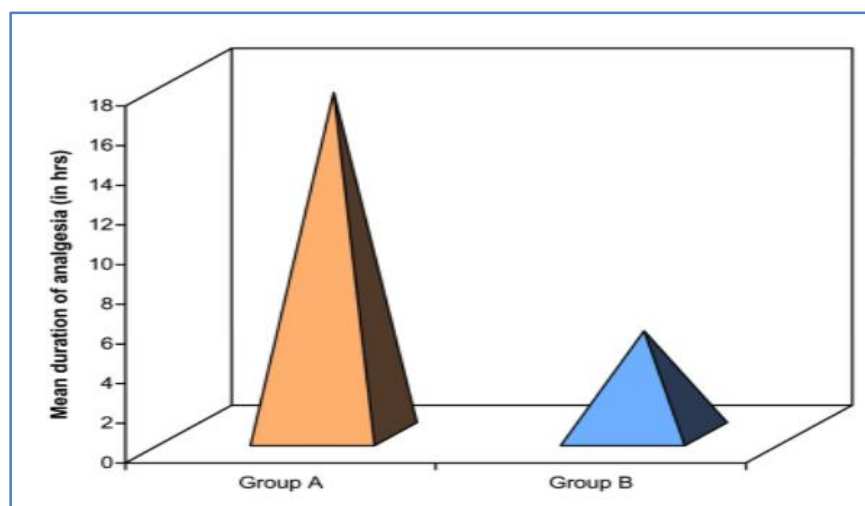


Fig. 2: Duration of Analgesia

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Duration of analgesia in Group – A is 17.23 hrs compared to Group – B, which is 5.20 hrs. This is statistically significant ($P < 0.05$).

Effect on Cardiovascular System- Variation in pulse rate within each group was studied and compared.

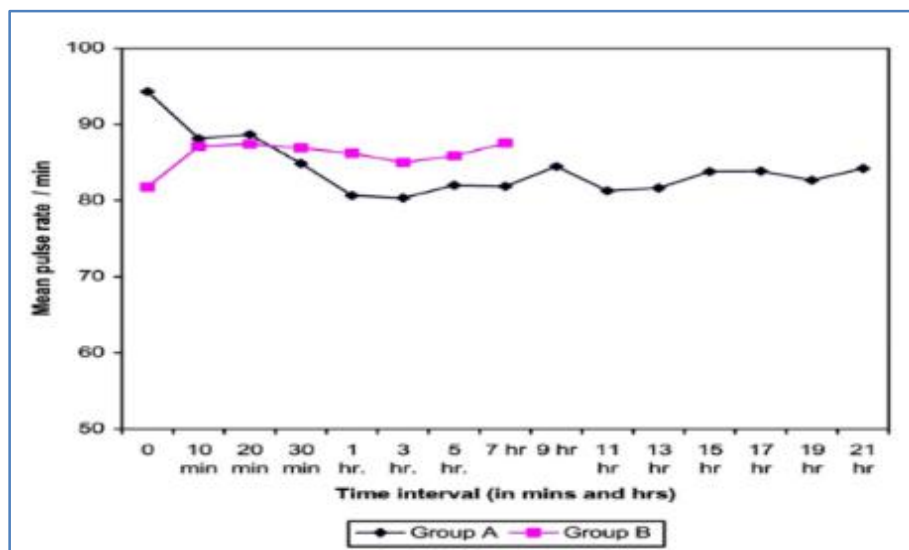


Fig. 3: Mean Pulse Rate

Mean of mean arterial pressure in between group-A and Group – B at different time intervals

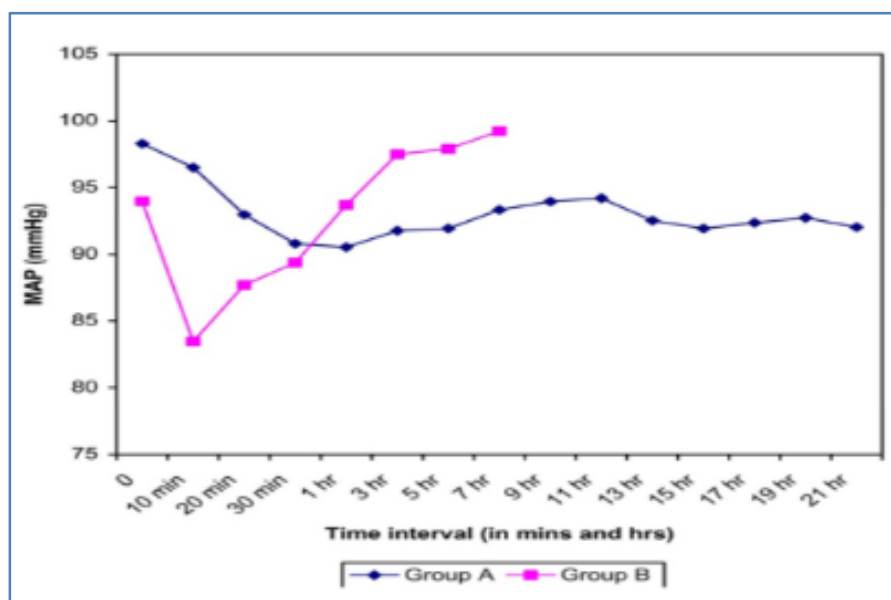


Fig. 4: MAP

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Effect on respiratory system:

Time Interval (in hrs)	Respiratory rate per min				t	Significance
	Group A		Group B			
	Mean	SD	Mean	SD		
Basal value	17.7	1.29	15.2	1.374	-	-
10 min.	16.96	1.35	15.133	1.136	6.46	P<0.05S
20 min	16.2	1.09	14.766	1.351	6.11	P<0.05S
30 min.	15.9	1.15	15.33	1.268	0.08	P<0.05S
1 hr.	16.3	1.54	15.6	1.28	0.15	P>0.05NS
3 hr.	14.73	1.98	14.83	1.80	0.84	P>0.05NS
5 hr.	13.03	2.00	14.87	1.33	0.0001	P>0.05NS
7 hr.	12.56	1.79	14.67	1.86	3.99	P<0.05S

Table 7: Mean respiratory rate between Group – A and Group-B at different time intervals

SD: Standard Deviation, NS: Not Significant.

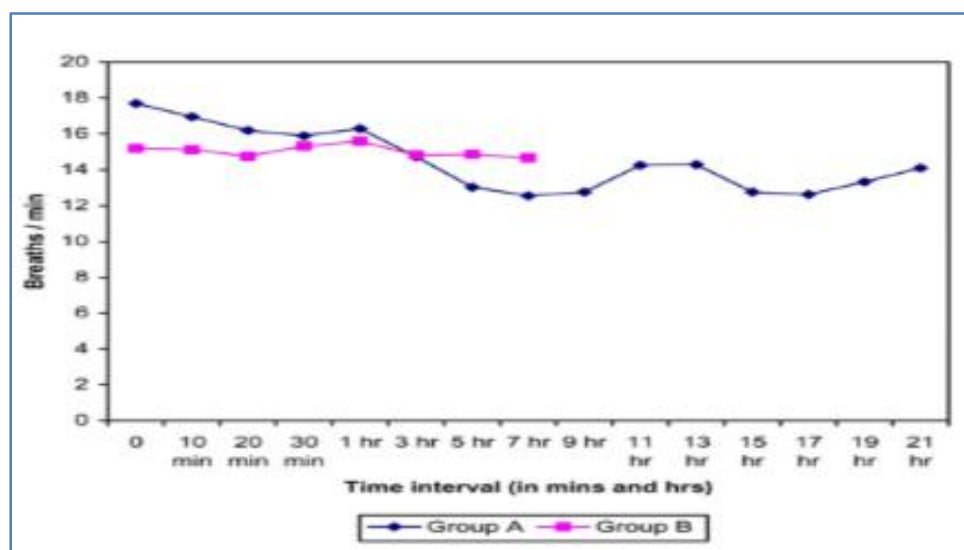


Fig. 5: Mean respiratory rates

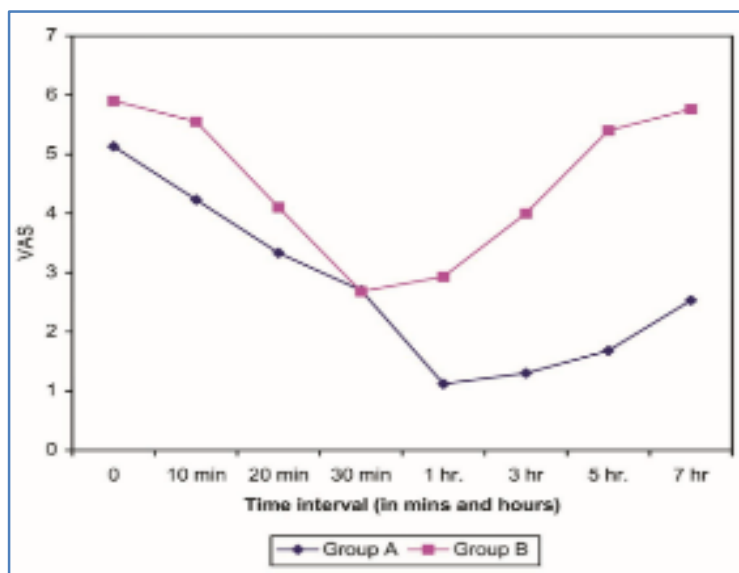


Fig. 6: Comparison of analgesia by VAS in between group A and Group B

Time Interval (in hrs)	VAS				t	Significance
	Group A		Group B			
	Mean	SD	Mean	SD		
Basal value	5.13	0.63	5.9	0.88	-	-
10 min.	4.23	0.72	5.55	0.65	4.78	P<0.05S
20 min	3.33	0.63	4.10	0.92	0.0006	P>0.05NS
30 min.	2.7	0.89	2.68	0.855	0.941	P>0.05NS
1 hr.	1.12	0.715	2.93	0.45	5.17	P<0.05S
3 hr.	1.3	0.59	4.0	0.91	1.09	P>0.05NS
5 hr.	1.68	0.61	5.4	0.56	2.49	P>0.05NS
7 hr.	2.53	0.75	5.76	0.50	3.45	P>0.05NS

Table 8: Comparison of VAS in between Group – A and Group-B at different time intervals

SD: Standard Deviation, NS: Not Significant, S. Significant.

Side effects	Group A		Group B	
	No.	%	No.	%
Nausea and vomiting	5	16.5	1	3.3
Urinary retention	2	6.61	0	0
Pruritus	-	-	-	-
Hypotension	-	-	-	-

Table 9: Incidence of side effects

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DISCUSSION: Surgical trauma and subsequent postoperative pain result in a broad range of endocrinologic, immunologic and inflammatory responses. In recent times many opioids have been used for postoperative analgesia as these drugs increase the duration of analgesia with minimum side effects. Studies have shown that buprenorphine increases the duration of analgesia when compared to bupivacaine, we wanted to study whether the onset of analgesia, cardiovascular effects, respiratory effects and side effects were significant when compared to that of epidural bupivacaine. In our study, 0.25% of bupivacaine with 0.15 mg of buprenorphine in group A and 0.25% bupivacaine in group B were given epidurally. The patients were chosen between 20 to 60 years of age, either sex, belonging to ASA grade I or grade II, undergoing various abdominal, lower limb, orthopaedic and gynaecological surgeries. Results were compared within the groups by applying statistical paired 't' test and between the groups compared by unpaired 't' test.

Onset of analgesia-Onset of analgesia is taken as time interval between drug administration and time when patient started getting pain relief. Mean time of onset of analgesia is Group-A-7.53 min, Group-B-15.50 min. The onset of analgesia was significantly faster in group A compared to group B.

Zenz M, Pipenbrock S⁵ did a double blind comparison of epidural Buprenorphine and epidural morphine for postoperative pain relief. Morphine 4 mg and buprenorphine 0.15 mg were given through epidural route. Both substances produced analgesia with short latency 6.8 min, which is close to our observation of 7.53 min.

Duration of Analgesia by comparing the pain scores at different intervals of time, pain scores were comparable in the two groups. Measured using VAS at every 10 mins in first half an hour, then at 60 min and thereafter every 2 hours for 21 hours. There was no difference in base line VAS between the group A (5.13 cm) and group B (5.9 cm). In study conducted by Mohammed Naguib et al,⁶ the duration of analgesia with epidural 0.25% bupivacaine was 5±0.65 hours.

The VAS reading started falling at 10 min itself in group A (4.2 cm) and then till further gradually to 2.7 cm at 30 min and maximum analgesia achieved at first hour (1.62 cm) remaining below 2 cms up to 5 hours. Thereafter gradually increased to 4.23 cms at 9 hr, still remaining below 5 cms up to 21 hrs in most of the patients.

In group B, there was no significant analgesia at 10 min, VAS 5.5 cms but VAS started falling 20 min onwards (4.1 cms), peaked at 30 min to 2.5 cms. There was no significant analgesia between 2 groups; at 30 min. Analgesia was maximum only up to 2 hrs in group B and VAS started rising thereafter. Reading 5.4 cms in 5th hour and 5.76 by 7th hour, all these patients needed first top up of epidural injection by 7th hour, hence study stopped. In our study, mean duration of analgesia in group A was 17.23 hours which was significantly higher compared to group B of mean duration of analgesia 5.20 hrs.

On Cardiovascular system The objective parameters of analgesia like mean arterial pressure and heart rate were compared, before giving the drug and after giving the drug at intervals of 10, 20, 30 min and then at 60th min thereafter wards at regular interval of 2 hours for 21 hours in group A and at 10, 20, 30 min and then thereafter wards at regular intervals of 2 hours for 7 hours in group B. The reductions in MAP were statistically significant in group A

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compared to group B. In group A MAP from base line 98.3 mmHg fell to 90.8 mmHg at 30 min, then picked up to 94.92 at 11th hour, remained same throughout the study. In group B MAP from baseline 93.97 mmHg fell to 83.43 mmHg at 10 min and then picking up slowly to 93.7 mmHg at 1st hour thereafter remained significantly high throughout the study. The mean HR reduction indicating analgesia was also significant in group A compared to group B. The mean base line heart rate in group A which was 94.3 min⁻¹, reduced gradually to 80.66 at 1 hr and remained low throughout the study. The mean base line heart rate which was in group B 81.76 min⁻¹, went up to 87.3 at 10 min, then significantly remained higher throughout the study.

Study done by D. Kumar and coworkers,⁷ J Cahill, Zenz M and coworkers,⁵ Wilde and coworkers, Simpson K.H.⁸ showed epidural buprenorphine had no serious haemodynamic derangement.

On respiratory rate: Variation of respiratory rate was studied at different intervals of time along with the pain scores in both the groups. In group A, mean base line respiratory rate from 17.7min⁻¹ fell to around 15.9 in 30min, gradually reducing to 12.56 by 7th hour, picking up slightly by 11th hour, again falling to 12.76 by 15th hour and then gradually raising to 14.26 by 21st hour. In group B, base line respiratory rate which was 15.2 fell to 14.76 at 20th min, remaining stationary throughout the study.

Zenz M, and coworkers⁵ while comparing epidural buprenorphine with epidural morphine for postoperative analgesia, reported no respiratory depression. Similar results were produced by J. Cahill and coworkers.

Side effects: Nausea and vomiting- In our study, the incidence of nausea and vomiting in group-A was 16.5% and the group-B was 3.3%. Observations of study done by D. Kumar and co-workers⁷ and K. H. Simpson and co-workers⁹ correlates with our study on Buprenorphine.

Urinary Retention: In our study, one patient (6.6%) had urinary retention in group - A for which patient had to be catheterised. Rajiv Lakhota and co-workers¹⁰ reported 27.27% of cases in their study. Group-B had no urinary retention.

Limitations of the study: Since pain is a subjective phenomenon associated with a wide variability of responses among the individuals, it is difficult to standardize the variable. What may be tolerable for one person may be intolerable for another person. Under these circumstances, it is difficult to assess and grade the pain the same manner leading to a lot of unwanted bias in this study.

CONCLUSION: Addition of buprenorphine to bupivacaine by epidural injection for post-operative analgesia improves the onset, the duration and the quality of analgesia, albeit keeping the possibility of late respiratory depression.

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