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Original Research Article

A Prospective Comparative Evaluation of Two Epidural Solutions Bupivacaine, Fentanyl and Adrenaline verses Bupivacaine and Fentanyl for Post Operative Analgesia in Upper and Lower Abdominal Surgeries

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Conflict of interest: Nil

Abstract:

Objective: To study efficacy of epidural infusion of two solutions (bupivacaine +fentanyl +adrenaline and bupivacaine +fentanyl) for post operative analgesia in upper and lower abdominal surgeries.

Methods: The study was conducted on adult patients of both sexes in age group of 18 - 60 years belonging to ASA I and II physical status undergoing elective abdominal surgery under epidural and general anesthesia. Two groups: Group BFA: 0.1% bupivacaine +2mcg/ml fentanyl + 2mcg/ml adrenaline Group BF: 0.1% bupivacaine + 2mcg/ml fentanyl

Results: The total dose requirement of local anesthetics and opioids in Group BFA was significantly lower than Group BF. Post operative analgesia in Group BFA was significantly greater than Group BF initially at 1, 3 & 6 Hrs. but similar quality of analgesia present in both the groups later. VAS score and quality of pain relief was better in Group BFA as compared to Group BF. The level of sensory blockade did not differ significantly between two study groups. The requirement of rescue analgesics was similar in both the groups and was not significant. The degree of motor block assessed using Modified Bromage score was similar and non-significant between two groups. Change in hemodynamic parameters like HR, SBP, DBP, MAP, Respiratory rate after surgery were not statistically significant in both the groups.

Conclusion: Adding adrenaline helps in improving quality of analgesia in first 6 hrs when pain is of high intensity. It is safe to add adrenaline as evident by minimal and equal side effects and no systemic effects of adrenaline were seen. Quality of pain relief improved on first 6 hrs of post operative period which can help reducing overall morbidity.

Keywords: VAS Score, Quality of Pain Relief, Modified Bromage Score, Hemodynamic Parameters.

Introduction

The advantages of effective postoperative pain management include patient comfort and therefore satisfaction, earlier mobilization, fewer pulmonary and cardiac complications, a reduced risk of deep vein thrombosis, faster recovery with less likelihood of the development of neuropathic pain, and reduced cost of care. The effective relief of pain is of the utmost importance to anyone treating patients undergoing surgery. Pain relief has significant physiological benefits; hence, monitoring of pain relief is increasingly becoming an important postoperative quality measure. The goal for postoperative pain management is to reduce or eliminate pain and discomfort with a minimum of side effects. [1]

All opioids have significant side effects that limit their use. The most important side effect is respiratory depression that could result in hypoxia and respiratory arrest. Hence, regular monitoring of respiration and oxygen saturation is essential in patients on opioids postoperatively. In addition, nausea, vomiting, pruritus, and reduction in bowel motility leading to ileus and constipation are also common side effects of these medications. Long term use of opioids can lead to dependence and addiction. [2]

Epidural analgesia is the main stay in multimodal post operative pain management. The use of epidural catheter for providing analgesia has increased dramatically. Improved equipment, methods and medications have broadened its application to include among others, surgical anesthesia, chronic pain relief and the management of post operative pain. Epidural analgesia with local anesthetics alone is effective in relieving postoperative pain for limited period. This problem

led to trials of additional adjunct like epidural narcotics along with local anesthesia for postoperative pain management. Opioids acts as an adjunct but are not free from side effects. The side effects of epidural opioids are dose dependent which restricts their liberal use. [3,4]

Beneficial properties of adrenaline have been exploited both in peripheral regional blockades and in central neuraxial blockade. Beneficial effects are presumed from an adrenaline-mediated vasoconstrictive effect that decreases local blood flow in epidural space, thereby resulting in slower local anesthetic clearance from the epidural space. [5] To support this pharmacokinetic mechanism, several studies have demonstrated a decrease in peak plasma concentrations of local anesthetics when adrenaline is added, both in peripheral and central blockade. Adrenaline improve the pain-relieving effect and reduce the consumption of the local anesthetics and opioids. Adrenaline increases sensory blockade by acting on spinal cord receptors and reduces the absorption of opioid and local anesthetic drug from the epidural space ,thereby increasing both the safety and efficacy of the mixture. Adrenaline is a mixed α/β adrenergic receptor agonist. Stimulation of α_2 receptors in the substantia gelatinosa in the dorsal horn of spinal cord provides analgesic effect. Stimulation of α_1 receptor predominantly causes vasoconstriction which decreases absorption thereby prolonging the duration of action. Safety of adrenaline when added as an adjunct: It is possible to reduce the total amount of bupivacaine and fentanyl needed for adequate pain relief. Thus decreasing plasma level and associated side effects of bupivacaine and fentanyl. As the side effects of epidural mixture are dose dependent, thus reducing the dose needed of each component. At the same time maintaining the analgesic effect. [6,7]

The aim and objectives of this study is to explore feasibility of reducing the dose of LA and opioids, thus reducing side effects with the use of adrenaline along with infusion mixture. [8,9]

Materials and Methods

Comparative evaluation of efficacy of bupivacaine + fentanyl + adrenaline with bupivacaine + fentanyl for epidural post operative analgesia in upper and lower abdominal surgeries after approval from institutional ethical and scientific committee.

Period of Study: October 2022 to May 2024

Study group

1. **Group BFA** :0.1 % bupivacaine +2mcg/ml fentanyl + 2mcg/ml adrenaline
2. **Group BF:** 0.1% bupivacaine + 2mcg/ml fentanyl

Inclusion Criteria:

1. Patients of either sex
2. Patients with age between 18-60 years
3. Patients with ASA physical status I and II
4. Patients posted for elective upper and lower abdominal surgery under epidural and general anaesthesia.

Exclusion Criteria:

1. Patient refusal
2. Pregnant female
3. Patients with known allergy to study drugs
4. Those with contraindication for regional anaesthesia like local infection , coagulopathy
5. Laparoscopic surgery

Types of surgery:

Types of Surgery	Surgery
Upper Abdominal Surgery	Hepatectomy Cholecystectomy Gastrectomy Gastric Bypass Whipples Surgery Pancreatic Surgery Hepaticojejunostomy Spleenectomy Oesophagectomy Nephrectomy Sdrenalectomy Pcnl
Lower Abdominal Surgery	Ovarian Debulking Total Abdominal Hysterectoy Apr Proctocolectomy Inguinal Hernia Repair Cystectomy Vvf Repair

Study population: The study was conducted on adult patients of both sexes in age group of 18 - 60 years belonging to ASA I and II physical status undergoing elective abdominal surgery under epidural and general anesthesia.

Methodology:

1. **Method of randomization:** Preoperatively a computerized randomization was done to allocate the patient to either of the groups (Group BFA and Group BF ,30 patients in each group)
2. The stock solution of Group BFA drug was prepared with 100 ml of 0.5 % bupivacaine with 20 ml fentanyl citrate and 1 ml adrenaline in 379 ml of 0.9% sodium chloride solution (Total 500 ml)
3. The stock solution of Group BF drug was prepared with 100 ml of 0.5 % bupivacaine with 20 ml fentanyl citrate in 380 ml of 0.9% sodium chloride solution (Total 500 ml)

Conduct of Anesthesia: Pre anesthetic evaluation including detailed history and clinical examination was done on the evening before surgery and informed consent was obtained. Patients were explained about the study protocol and the use of a Visual analog scale (VAS – a horizontal line where in 0 = no pain, 10 = worst pain ever)

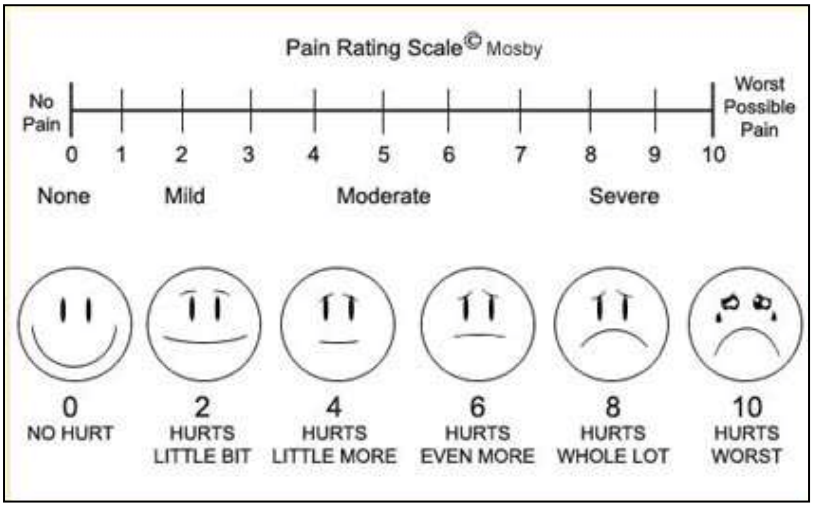


Figure : Visual analog scale (VAS)

After patient is taken into the operating room ECG, oxygen saturation, heart rate and NIBP will be monitored throughout the surgery.

Site of epidural: For upper abdominal surgery – T11-T12.

For lower abdominal surgery – L2-L3.

Under all aseptic precaution epidural catheterization was performed in the sitting position with 18 G tuohy needle by loss of resistance technique (after local infiltration of 2 ml of 2% inj. Lignocaine) 3-4 cm of epidural catheter will be kept in the epidural space.

General anesthesia was induced with oxygen, nitrous oxide (50:50), sevoflurane, intravenous fentanyl 2mcg/kg, propofol 2-3mg/kg and atracurium 0.5 mg/kg. The trachea was intubated with appropriate size of ETT at 0.7 MAC and anesthesia will be maintained with oxygen and nitrous oxide (50:50) and sevoflurane titrated to maintain the MAC of 0.9.

In the intra operative period, a bolus of 0.2ml/kg of 0.25% bupivacaine with 2mcg/ml fentanyl was given epidurally before incision. A bolus of 0.2 ml/kg of 0.25% bupivacaine with 2mcg/ml fentanyl was given as and when required depending on the hemodynamics of the patient till the end of surgery in both the groups.

30 min before extubation a 0.2ml/kg bolus of epidural stock solution was given either from Group BFA or Group BF (blinded to the researcher) followed by 3 ml/hour infusion through syringe pump.

Post Operative Monitoring: After arrival in recovery room VAS score was assessed at 0, 1,2,3,6,12,18,24 hours. If pain control is inadequate (VAS >3), then epidural infusion rate was changed. A bolus of 0.1 ml/kg of stock solution followed by increase in epidural infusion rate by 2ml/hour each time with a maximum of 8 ml/hour. If pain relief is still not achieved within 20 min of maximum infusion rate of 8 ml/hour, then rescue analgesic of tramadol 50 mg IV will be given along with ondansetron 4 mg and infusion was continued at that rate.

Motor block was assessed with modified Bromage score at 0, 1,2,3,6,12,18,24 hours after surgery. Upper and lower sensory levels were determined 0, 1,2,3,6,12,18,24 hours after surgery with an ice

cube inside a sterile glove. The area of cold hypoesthesia was mapped on both sides. Any hypotension, respiratory depression was noted at 0, 1,2,3,6,12,18,24 hours after surgery. Hypotension was defined as a decrease in systolic arterial blood pressure by 30% from baseline (preoperative value) or to a value ≤ 90 mm Hg. Respiratory depression was defined as a respiratory rate less than 10 breaths/min.

The side effects like nausea and vomiting, numbness of lower limbs, urinary retention of all the study drugs were assessed at 0,1,2,3,6,12,18,24 hours after surgery. Nausea and vomiting were treated with injection ondansetron (4 mg), and in urinary retention foleys catheter were inserted.

Observation Chart

Table 1: Inter-group comparison of mean rate of infusion.

Rate of infusion (ml/Hr)	Group BFA (n=30)		Group BF (n=30)		P-value
	Mean	SD	Mean	SD	
0-Hrs	3.00	0.00	3.00	0.00	0.999^{NS}
1-Hrs	3.13	0.51	3.40	0.81	0.133^{NS}
2-Hrs	3.40	0.81	3.73	0.98	0.157^{NS}
3-Hrs	3.40	0.81	4.07	1.01	0.007^{**}
6-Hrs	3.40	0.81	4.07	1.01	0.007^{**}
12-Hrs	3.40	0.81	4.13	1.00	0.003^{**}
18-Hrs	3.40	0.81	4.20	0.99	0.001^{***}
24-Hrs	3.40	0.81	4.20	0.99	0.001^{***}
Values are mean and SD, P-values by independent sample t test. P-value<0.05 is statistically significant. **P-value<0.01, ***P-value<0.001, NS-Statistically non-significant.					

The distribution of mean rate of infusion at 0-Hrs, 1-Hrs and 2-Hrs did not differ significantly between two study groups (P-value>0.05 for all). The distribution of mean rate of infusion at 3-Hrs, 6-Hrs, 12-Hrs, 18-Hrs and 24-Hrs is significantly higher in Group BF compared to Group BFA (P-value<0.01 for all).

Table 2: Inter-group comparison of mean dose of bupivacine and fentanyl given in 24-Hrs.

Dose	Group BFA (n=30)		Group BF (n=30)		P-value
	Mean	SD	Mean	SD	
Bupivacine (mg)	26.53	5.17	30.80	6.05	0.005^{**}
Fentanyl (mcg)	53.07	10.34	61.60	12.09	0.005^{**}
Values are mean and SD, P-values by independent sample t test. P-value<0.05 is statistically significant. **P-value<0.001.					

The distribution of mean ± SD of bupivacine dose given in Group BFA and Group BF is 26.53 ± 5.17 mg and 30.80 ± 6.05 mg respectively. The dose of bupivacaine was significantly higher in Group BF compared to Group BFA (P-value<0.05). The distribution of mean ± SD of fentanyl dose given in Group BFA and Group BF is 53.07 ± 10.34 mcg and 61.60 ± 12.09 mcg respectively. The dose of fentanyl was significantly higher in Group BF compared to Group BFA (P-value<0.05).

Table 3: Inter-group comparison of mean pain score (VAS).

Pain Score (VAS)	Group BFA (n=30)		Group BF (n=30)		P-value
	Mean	SD	Mean	SD	
0-Hrs	2.37	0.99	2.77	0.68	0.075^{NS}
1-Hrs	2.37	0.89	2.87	0.73	0.021^{*}
2-Hrs	2.43	1.04	2.77	0.77	0.164^{NS}
3-Hrs	2.00	0.83	2.57	1.00	0.021^{*}
6-Hrs	1.73	0.94	2.27	0.78	0.021^{*}
12-Hrs	1.77	0.82	2.03	0.81	0.209^{NS}
18-Hrs	1.77	0.86	1.70	0.75	0.750^{NS}
24-Hrs	1.27	0.74	1.43	0.57	0.332^{NS}
Values are mean and SD, P-values by independent sample t test. P-value<0.05 is considered to be statistically significant. *P-value<0.05, NS-Statistically non-significant.					

The distribution of mean pain score (VAS) at 0-Hrs, 2-Hrs, 12-Hrs, 18-Hrs and 24-Hrs did not differ significantly between two study groups (P-value>0.05 for all). The distribution of mean pain score (VAS) at 1-Hrs, 3-Hrs and 6-Hrs is significantly higher in Group BF compared to Group BFA (P-value<0.05 for all).

Table 4: Inter-group comparison of level of sensory blockade.

Level of Sensory blocked		Group BFA (n=30)		Group BF (n=30)		P-value
		n	%	n	%	
0-Hrs	T5 – T8	23	76.7	20	66.7	0.390^{NS}
	T9 – T11	7	23.3	10	33.3	
1-Hrs	T5 – T8	23	76.7	20	66.7	0.390^{NS}
	T9 – T11	7	23.3	10	33.3	
2-Hrs	T5 – T8	23	76.7	22	73.3	0.766^{NS}
	T9 – T11	7	23.3	8	26.7	
3-Hrs	T5 – T8	23	76.7	21	70.0	0.559^{NS}
	T9 – T11	7	23.3	9	30.0	
6-Hrs	T5 – T8	23	76.7	21	70.0	0.559^{NS}
	T9 – T11	7	23.3	9	30.0	
12-Hrs	T5 – T8	23	76.7	21	70.0	0.559^{NS}
	T9 – T11	7	23.3	9	30.0	
18-Hrs	T5 – T8	23	76.7	22	73.3	0.766^{NS}
	T9 – T11	7	23.3	8	26.7	
24-Hrs	T5 – T8	23	76.7	22	73.3	0.766^{NS}
	T9 – T11	7	23.3	8	26.7	
Values are n (% of cases). P-values by Chi-Square test. P-value<0.05 is considered to be statistically significant. NS-Statistically non-significant.						

The distribution of level of sensory blockade at 0-Hrs, 1-Hrs, 2-Hrs, 3-Hrs, 6-Hrs, 12-Hrs, 18-Hrs and 24-Hrs did not differ significantly between two study groups (P-value>0.05 for all).

Table 5: Inter-group comparison of motor blockade (modified Bromage score).

Motor blockade		Group BFA (n=30)		Group BF (n=30)		P-value
		n	%	n	%	
0-Hrs	4 – 5	22	73.3	17	56.7	0.176^{NS}
	6	8	26.7	13	43.3	
1-Hrs	4 – 5	12	40.0	8	26.7	0.273^{NS}
	6	18	60.0	22	73.3	
2-Hrs	4 – 5	6	20.0	3	10.0	0.278^{NS}
	6	24	80.0	27	90.0	
3-Hrs	4 – 5	2	6.7	2	6.7	0.999^{NS}
	6	28	93.3	28	93.3	
6-Hrs	4 – 5	1	3.3	1	3.3	0.999^{NS}
	6	29	96.7	29	96.7	
12-Hrs	4 – 5	1	3.3	1	3.3	0.999^{NS}
	6	29	96.7	29	96.7	
18-Hrs	4 – 5	0	0.0	0	0.0	0.999^{NS}
	6	30	100.0	30	100.0	
24-Hrs	4 – 5	0	0.0	0	0.0	0.999^{NS}
	6	30	100.0	30	100.0	
Values are n (% of cases). P-values by Chi-Square test. P-value<0.05 is considered to be statistically significant. NS-Statistically non-significant.						

The distribution of level of motor blockade at 0-Hrs, 1-Hrs, 2-Hrs, 3-Hrs, 6-Hrs, 12-Hrs, 18-Hrs and 24-Hrs did not differ significantly between two study groups (P-value>0.05 for all).

Table 13: Inter-group comparison of requirement of rescue analgesia.

Rescue Analgesia Used		Group BFA (n=30)		Group BF (n=30)		P-value
		n	%	N	%	
0-Hrs	No	29	96.7	28	93.3	0.999^{NS}
	Yes	1	3.3	2	6.7	
1-Hrs	No	25	83.3	23	76.7	0.519^{NS}
	Yes	5	16.7	7	23.3	
2-Hrs	No	27	90.0	24	80.0	0.472^{NS}
	Yes	3	10.0	6	20.0	

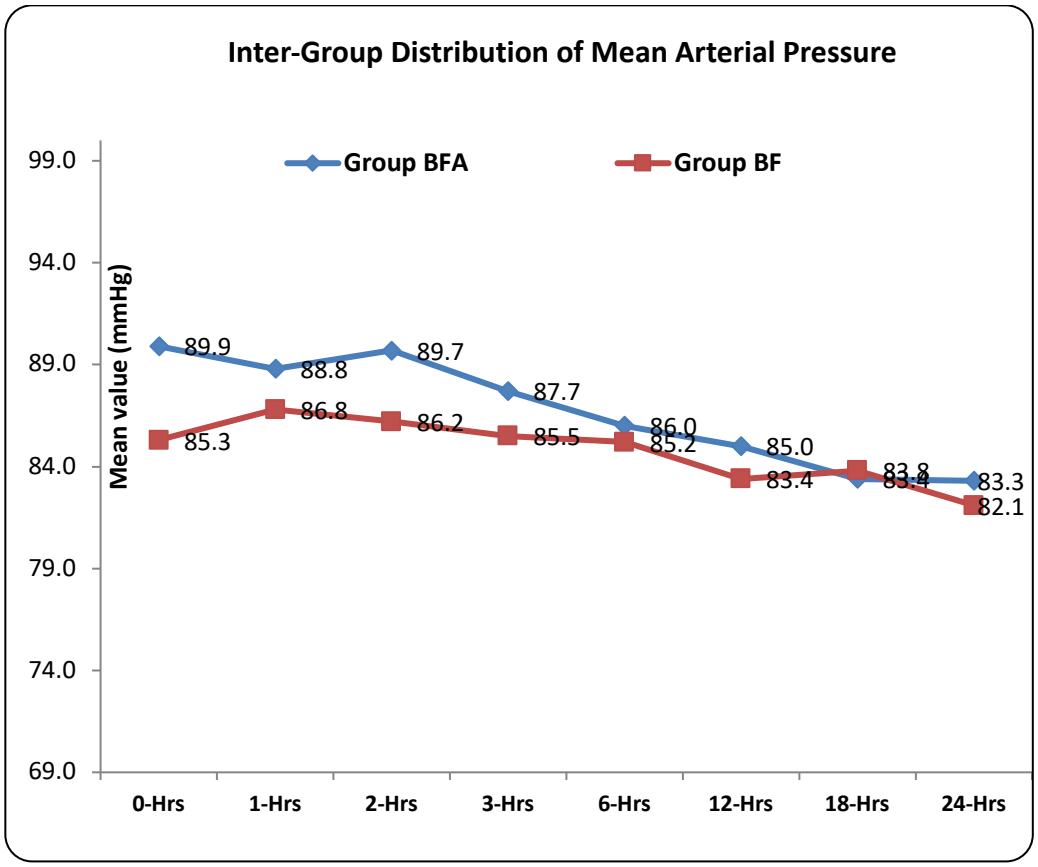
3-Hrs	No	27	90.0	24	80.0	0.472^{NS}
	Yes	3	10.0	6	20.0	
6-Hrs	No	26	86.7	30	100.0	0.112^{NS}
	Yes	4	13.3	0	0.0	
12-Hrs	No	29	96.7	29	96.7	0.999^{NS}
	Yes	1	3.3	1	3.3	
18-Hrs	No	30	100.0	30	100.0	0.999^{NS}
	Yes	0	0.0	0	0.0	
24-Hrs	No	30	100.0	30	100.0	0.999^{NS}
	Yes	0	0.0	0	0.0	
Values are n (% of cases). P-values by Chi-Square test. P-value<0.05 is considered to be statistically significant. NS-Statistically non-significant.						

The distribution of requirement of rescue analgesia at 0-Hrs, 1-Hrs, 2-Hrs, 3-Hrs, 6-Hrs, 12-Hrs, 18-Hrs and 24-Hrs did not differ significantly between two study groups (P-value>0.05 for all).

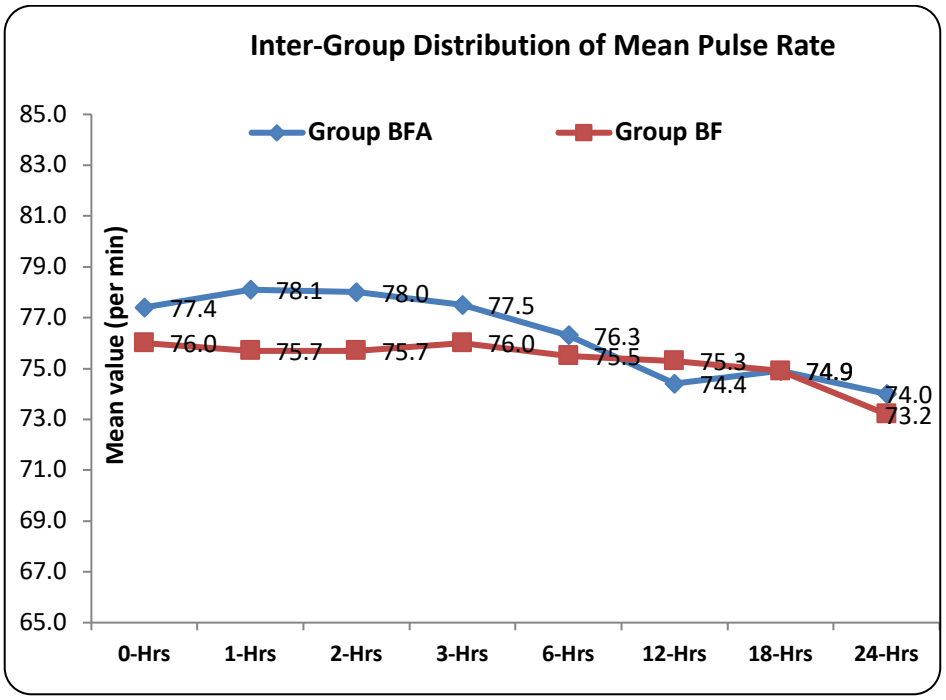
But we have found that in Group BFA required less no. of rescue analgesics in 24 hrs. than Group BF (17 & 22 respectively). Total number of rescue analgesics requirement in 24 hrs. is not significant in both the groups

Table 6 Intergroup comparison of total number of patients requiring rescue analgesia

Required Rescue Analgesia	Group BFA		Group BF		P-Value
	n	%	n	%	
Yes	10	33.3	21	70.0	0.009**
No	20	66.7	9	30.0	
Total	30	100.0	30	100.0	
Values are n (% of cases), P-values by Chi-Square test. P-value<0.05 is statistically significant. **P-value<0.01.					

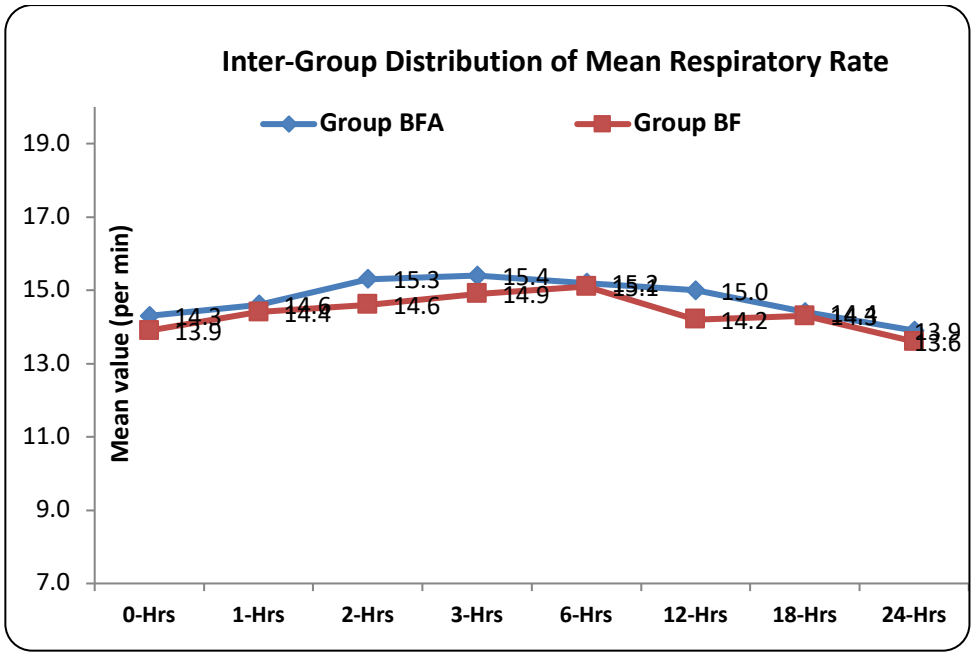


Graph 1: Inter-group comparison of mean arterial pressure (MAP).



Graph 2: Inter-group comparison of mean pulse rate.

The distribution of mean respiratory rate at 0-Hrs, 1-Hrs, 2-Hrs, 3-Hrs, 6-Hrs, 12-Hrs, 18-Hrs and 24-Hrs did not differ significantly between two study groups (P-value>0.05 for all).



Graph 3: Inter-group comparison of mean respiratory rate.

Table 7: Inter-group distribution of incidence of complications.

Complications	Group BFA (n=30)		Group BF (n=30)		P-value
	n	%	n	%	
Nausea	2	6.7	10	33.3	0.021*
Numbness	3	10.0	4	13.3	0.999NS
Urinary retention	3	10.0	8	26.7	0.181NS
Values are n (% of cases), P-values by Chi-Square test. P-value<0.05 is statistically significant. *P-value<0.05, NS-Statistically non-significant.					

Results

1. The mean rate of infusion between Group BFA and B differed significantly across most of the times at 3, 6, 12, 18 & 24 Hrs. However they were comparable at 0, 1 & 2 Hrs.
2. The total dose requirement of local anesthetics and opioids in Group BFA was significantly lower than Group BF.
3. Post operative analgesia in Group BFA was significantly greater than Group BF initially at 1, 3 & 6 Hrs but similar quality of analgesia present in both the groups later on.
4. VAS score and quality of pain relief was better in Group BFA as compared to Group BF. The mean VAS score in Group BF was significantly higher than Group BFA at 1Hrs, 3Hrs and 6Hrs.
5. The level of sensory blockade did not differ significantly between two study groups. The requirement of rescue analgesics was similar in both the groups and was not significant.
6. The degree of motor block assessed using Modified Bromage score was similar and non-significant between two groups.
7. Change in hemodynamic parameters like HR, SBP, DBP, MAP, Respiratory rate after surgery were not statistically significant in both the groups.
8. The incidence of nausea is significantly higher in Group BF compared to Group BFA. The distribution of incidence of numbness and urinary retention did not differ significantly between two study groups. No incidence of bradycardia and pruritus was noted in any patient of both groups.

Statistical Analysis: The collected data was summarized by using frequency, percentage, mean & S.D. To compare the qualitative outcome measures Chi-square test or Fisher's exact test was used. To compare the quantitative outcome measures independent t test was used. If data was not following normal distribution, Mann Whitney U test was used. SPSS version 22 software was used to analyze the collected data. p value of <0.05 was statistically significant.

Discussion

We carried out prospective, double blind study to evaluate efficacy and side effects of epidural infusion of bupivacaine + fentanyl +adrenaline and compare it with epidural infusion of bupivacaine + fentanyl in abdominal surgeries to provide analgesia. [10] The goal of our study was to determine the effectiveness of epidural bupivacaine when combined with epidural fentanyl and epinephrine during prolonged epidural infusion following abdominal surgeries. We felt that, by adding adrenaline with infusion, minimum concentration of bupivacaine and fentanyl also can provide effective analgesia and minimise side effects. [11]

The present study was undertaken to perform a comparative evaluation of epidural bupivacaine +fentanyl and bupivacaine +fentanyl +adrenaline for post operative analgesia in abdominal surgeries in relation to characteristics of sensory block, motor block and analgesic effect. [12] The changes in hemodynamic parameters and side effects were also observed. This double blind, prospective, randomised controlled study was conducted on 60 adult patients of ASA physical status I-II of either sex, in the age group of 18-60 years. Patients were allocated to either of the two groups according to computer generated random numbers. 30 patients in each group received 0.1% bupivacaine + 2mcg/ml fentanyl +2mcg/ml adrenaline in Group BFA and 0.1% bupivacaine + 2mcg/ml fentanyl in Group BF. [13,14]

The demographic data was comparable between the two groups. No statistically significant differences were found between the groups with respect to age, BMI, sex distribution, ASA physical status and type of surgery.[15]

Mean rate of infusion In our study we started infusion at the rate of 3 ml/hr in both Group BFA as well as Group BF. The distribution of mean rate of infusion at 0-Hrs, 1-Hrs and 2-Hrs did not differ significantly between two study groups (P-value>0.05 for all). The distribution of mean rate of infusion at 3-Hrs, 6-Hrs, 12-Hrs, 18-Hrs and 24-Hrs is significantly higher in Group BF compared to Group BFA (P-value<0.01 for all). [16] Signifies that more quantity of drugs infusion required in Group BF for keeping VAS score ≤ 3 in abdominal surgeries after 3-Hrs.The side effects ascribed to fentanyl and bupivacaine would have been reduced because of a delayed systemic absorption resulting in reduced serum concentrations of the two drugs . This result is expected because epidural vasoconstriction from adrenaline may be the main cause of the observed beneficial effect of adrenaline on the low rate of infusion required for analgesia and decreasing the side effects of epidural bupivacaine and fentanyl. [17,18]

Mean dose of bupivacaine and fentanyl In our study the total mean ± SD of bupivacine dose was 26.53 ± 5.17 mg in Group BFA and 30.80 ± 6.05 mg in Group BF. The total mean bupivacaine dose is significantly higher in Group BF compared to Group BFA (P-value<0.05). The total mean ± SD of Fentanyl dose was 53.07 ± 10.34 mcg in Group BFA and 61.60 ± 12.09 mcg in Group BF. The total mean Fentanyl dose is significantly higher in Group BF compared to Group BFA (P-value<0.05). [19] These observations are in similar nature with the results found in study conducted by

Baron et al, where they found a significant fentanyl sparing effect with reduced serum concentration of fentanyl when adrenaline 3.3mcg/ml to a thoracic epidural infusion of fentanyl. Adrenaline significantly reduced fentanyl dose requirements (1.19±0.11 mcg/kg/h group without adrenaline vs 0.82±0.07 mcg/kg/h adrenaline group). Adrenaline also reduced the number of fentanyl boluses required for equivalent and adequate analgesia. The reduced dose requirements significantly decreased plasma fentanyl concentrations. The plasma fentanyl concentrations reached relatively stable levels by 24 h postoperatively. Mean plasma concentrations at steady-state (24-72 h) were 0.91±0.13 ng/ml in the adrenaline Group and 1.65±0.23 ng/ml in the without adrenaline group. The systemic plasma fentanyl concentration required for analgesia after intravenous injection is 1.6-1.8 ng/ml. Therefore, the plasma fentanyl concentrations in the adrenaline group were too small to provide effective analgesia. This suggests that, when adrenaline is added to epidural fentanyl, the reduced dose requirements are caused by the effects of fentanyl, adrenaline, or both on the spinal cord. This may be caused by adrenaline reducing vascular uptake, resulting in higher and prolonged cerebral spinal fluid fentanyl concentrations. [20]

Similar trend was seen in the study of G. Niemi and H. Breivik, where they shown that adrenaline markedly improve the analgesic effect of a thoracic epidural infusion of bupivacaine and fentanyl. After major thoracic or upper abdominal surgery causing strong postoperative pain, epidural fentanyl 23 mcg/h with bupivacaine 11.5 mg/h clearly was sub analgesic, whereas a (12.5%) smaller dose of fentanyl and bupivacaine with adrenaline 20 mcg/h resulted in excellent analgesia even during coughing. These observations are in similar nature with the results found in study conducted by Soetens FM, Soetens MA, Vercauteren MP, where the hourly drug consumption was significantly larger in the without adrenaline group. Connelly NR et al, has observed similar results in his study where the administration of 0.625 mg/ml bupivacaine with epinephrine 5 mcg/ml at 10 ml/hr, compared with plain 0.625 mg/ml bupivacaine at 10 ml/hr. [21] In labouring patients, adrenaline increases the duration of analgesia and decreases dose of the local anaesthetic requirement. In study conducted by Darshan MS et al, where the addition of adrenaline 5 mcg/ml to an optimally titrated thoracic epidural analgesic infusion of bupivacaine 5 mg/ml and fentanyl 1 mcg/ml hastened the onset of anaesthesia and intensified the motor block. In a recent multicentric study with local anaesthetic and lipophilic opioid it was found that the addition of adrenaline decreased the dosage of the local anaesthetic and increased the rapidity of discharge from hospital with no significant side effects.

In our study we observed that the addition of adrenaline significantly reduces the consumption of bupivacaine and fentanyl because of the reduction of epidural blood flow by adrenaline impedes systemic absorption of fentanyl and bupivacaine. Epidural vasoconstriction from adrenaline may be the main cause of the observed beneficial effect of adrenaline on the analgesia and side effects of epidural bupivacaine and fentanyl. By delaying their removal from the epidural space, epinephrine may increase the amount of fentanyl and local anaesthetic drugs reaching the spinal cord and spinal nerve roots, resulting in a more intense and prolonged analgesic effect covering more spinal segments.

Mean pain score (VAS) In our study the mean pain score (VAS) at 0-Hrs, 2-Hrs, 12-Hrs, 18-Hrs and 24-Hrs did not differ significantly between two study groups (P-value>0.05 for all). The mean pain score (VAS) at 1-Hrs, 3-Hrs and 6-Hrs are significantly higher in Group BF compared to Group BFA (P-value<0.05 for all). Baron et al, had similar observation where they found that there was good pain control in both groups, with no difference in VAS pain scores at rest or with mobilization at any time. Our findings were also similar to the work done by G. Niemi* and H. Breivik, where they shown that adrenaline markedly improve the analgesic effect of a thoracic epidural infusion of bupivacaine and fentanyl. They demonstrated that adrenaline markedly improved the pain-relieving effect and increased the sensory blockade of bupivacaine and fentanyl. Nausea was reduced, and mobilization of the patients was facilitated . Soetens FM, Soetens MA, Vercauteren MP, reached a similar conclusion where they shown that the VAS pain scores were similar for both groups before initiating epidural analgesia. At 15 min and 20 min after the initial loading dose the VAS pain scores were significantly lower in the adrenaline group. Connelly NR et al, observed similar results in their study which showed that the adrenaline group provide a longer time to re-dose, decreased pain scores at two time intervals, and had no significant difference in duration of labour or side effects. The addition of adrenaline improves analgesia associated with epidural bupivacaine in labouring patients. Adrenaline also decreases anaesthetic requirements for pain control. This finding may be explained by the theory that the local vasoconstriction decreases the “washout” (and, hence, increases the effectiveness) of epidurally administered drugs. Darshan MS et al, observed similar results with the addition of adrenaline to an optimally titrated thoracic epidural analgesic infusion of bupivacaine and Fentanyl hastened the onset of anaesthesia and intensified the motor block. Adrenaline increases their concentration locally to reaches the spinal cord and spinal nerve roots, resulting in a more intense and

prolonged analgesic effect covering more spinal segments. In our study we found that the adrenaline may increase the amount of fentanyl and local anaesthetic drugs reaching the spinal cord and spinal nerve roots, resulting in a more intense and prolonged analgesic effect covering more spinal segments. These results reflect that early mobilisation and faster recovery is possible with the use of adrenaline in epidural infusion. In our study we did not found any significant difference in motor blockade because of starting with very low rate of infusion in both the groups and also a small sample size of both groups.

Post operative hemodynamics We observed in our study ,that mean baseline pulse rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were comparable between both the groups (p value >0.05). There was no significant change in hemodynamic parameters in both the groups and the difference in mean pulse rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure between both the groups were statistically insignificant postoperatively (p value >0.05). Baron et al, observed similar results in their study, there was no difference in hemodynamics, with MBP and HR within 20% of baseline at 24, 48, and 72 h. Soetens FM, Soetens MA, Vercauteren MP, had similar observation that, they did not find a difference in maternal arterial blood pressure, maternal and fetal heart rate .These results show that the fall in blood pressure and its recovery as a physiological effect of epidural block is similar in both Group BFA and Group BF. It indicates similar sympathetic blocking effects in both groups.

Adverse events Out of 30 cases studied in Group BFA, 2 (6.7%) had nausea, 3 (10.0%) had numbness and 3 (10.0%) had urinary retention. Of 30 cases studied in Group BF, 10 (33.3%) had nausea, 4 (13.3%) had numbness and 8 (26.7%) had urinary retention. The incidence of nausea is significantly higher in Group BF compared to Group BFA (P-value<0.05). The distribution of incidence of numbness and urinary retention did not differ significantly between two study groups (P-value>0.05 for both). In our study the incidence of complications did not differ significantly between two study groups except nausea. These results were like Baron et al, they found that, the incidence of adverse effects was similar in the two groups. Most adverse effects were mild, requiring no treatment. Urinary retention occurred frequently (62%). A high incidence of urinary retention was observed early in the study, and, thereafter, Foley catheters were inserted during the operative procedure.

Similar findings have been reported by G. Niemi* and H. Breivik, shown that, the observed increase in nausea when epinephrine was removed may well have been caused by an increased systemic absorption of fentanyl from the epidural space, resulting in more supraspinal opioid side effects. These results were similar to Soetens FM, Soetens MA, Vercauteren MP, concluded that, there was no significant difference in maternal and fetal heart rate, the incidence or severity of maternal hypotension requiring ephedrine, and in the occurrence of other side effects between the two groups. They were unable to detect differences in the incidences of pruritus, nausea and vomiting.

The above results show that the epidural vasoconstriction from adrenaline may be the main cause of the observed beneficial effect. It may be due to the reduction of epidural blood flow by adrenaline impedes systemic absorption of fentanyl and local anaesthetics therefore reduces their serum concentration and adverse effect.

Conclusion

We conclude that by adding adrenaline helps in improving quality of analgesia in first 6 hrs when pain is of high intensity. It is safe to add adrenaline as evident by minimal and equal side effects and no systemic effects of adrenaline were seen. Quality of pain relief improved on first 6 hrs of post operative period which can help reducing overall morbidity.

Declarations:

Funding: None **Conflicts of interest/Competing interests**: None **Availability of data and material**: Department of Anaesthesiology LN Medical college JK Hospital and GMC & Hamidia Hospital Bhopal **Code availability**: Not applicable **Consent to participate**: Consent taken **Ethical Consideration**: There are no ethical conflicts related to this study. **Consent for publication**: Consent taken

Limitation:

1. Further studies need to be evaluation of use of adrenaline in high-risk patients.
2. We did not study plasma adrenaline and fentanyl concentration.
3. The study needs to be performed on larger sample size.

Recommendation:

1. Low dose of adrenaline (2mcg/ml) when used along with bupivacine and fentanyl provide better quality of analgesia in patient undergoing for elective abdominal surgeries
2. Adrenaline can be used as an adjuvant in epidural analgesia with bupivacaine and fentanyl.
3. Adrenaline when used as an adjuvant in epidural analgesia is safer and having minimal side effects.
4. Epidural adrenaline decreases the absorption of LA and opioid systemically hence reduces their dose.

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