Original Article

DOI: 10.17354/ijss/2016/156

Comparison of Bolus Bupivacaine, Fentanyl, and Mixture of Bupivacaine with Fentanyl in Thoracic Epidural Analgesia for Upper Abdominal Surgery

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Abstract

Introduction: Thoracic segmental epidural analgesia despite its technical difficulty and time consumption provides better analgesia and has a beneficial effect on the post-operative pulmonary and metabolic function; immunological and stress response.

Aims and Objectives: To study the efficacy of fentanyl for pain relief of inpatients after upper abdominal procedures and compare with bupivacaine alone and with bupivacaine and fentanyl combination (1) To find out the synergistic effect of bupivacaine with fentanyl. (2) Assessment of severity of pain at rest and during function, intensity of post-operative pain relief, duration of post-operative pain relief, and the incidence of side effects.

Materials and Methods: After institutional approval, patients were allocated into three groups of 30 patients each. Group A patients receiving 10 ml of 0.25% bupivacaine epidurally; Group B patients receiving 10 ml of fentanyl 50 μg epidurally, and Group C patients receiving 10 ml of 0.25% bupivacaine with fentanyl 50 epidurally. Required parameters were assessed.

Result: Combination of bupivacaine with fentanyl in thoracic epidural analgesia after upper abdominal surgery, showed better analgesic efficacy, synergistic effect, short onset of action, and longer duration of action (ranges from 150 to 280 min) with minimal side effects.

Conclusion: The thoracic epidural is strongly recommended technique for post-operative pain relief after upper abdomen surgery.

Key words: Analgesia, Bupivacaine, Epidural, Fentanyl

INTRODUCTION

The pathophysiologic consequences of upper abdominal surgery are intimately associated with severe post-operative pain and resultant higher incidence of post-operative complication and increased morbidity. Conventional methods of narcotic analgesia not only provide inadequate pain relief but are also associated with deleterious systemic side effects.

Access this article online

www.ijss-sn.com

Month of Submission : 01-2016
Month of Peer Review : 02-2016
Month of Acceptance : 02-2016
Month of Publishing : 03-2016

Intermittent doses of bupivacaine (0.25-0.5%) provides adequate neural blockade for effective post-operative analgesia. It provides undesirable motor blockade in some patients in the post-operative period. Hence, a search was on to find a suitable drug, which would provide adequate sensory block without affecting motor neurons.

The discovery of opioid receptors in the brain and spinal cord[1] raised exciting new possibilities in the management of severe pain. Opioids are known for the production of profound analgesia without loss of other sensations, minimal or nil central nervous system depression, and devoid of unpleasant consequences of the autonomic blockade.

Epidural opioids have been widely used for facilitation of central neuraxial blockade and post-operative analgesia.

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Although they may be used alone in this regard, multiple studies have shown that analgesia is more effective when they are combined with local anesthetics.[2-4]

Extradural opioids are preferred to subarachnoid because of lower rate of infection, the lack of a post-spinal headache, and low incidence of side effects, further incremental doses can be given through an indwelling catheter to increase the duration of action and minimize the side effects.

Ideal opioids for extradural use should fulfill the following criteria;

- High lipid solubility including fast diffusion into neural tissues
- Lowest systemic absorption with minimal side effects
- Strong receptor binding protein producing prolonged effects
- High molecular weight
- Intense and prolonged intrinsic activity.

Fentanyl, a new synthetic opioid, fulfills almost all these criteria.

Given the unique pharmacologic properties of each opioid and studies that show different rates of accumulation in the cerebrospinal fluid, there is biologic plausibility for differences in the side effect profiles and analgesia among different opioids.[5-8]

Fentanyl also has a remarkable safety profile. The near absence of respiratory depression with fentanyl (with permissible doses) and better pulmonary spirometric function (forced vital capacity and forced expiratory volume in 1 s) as reported by Guinard *et al.* and shorter hospitalization makes it an ideal drug for extradural use.[9]

For optimal analgesia, the thoracic epidural route should be used for pain relief after upper abdominal surgery.[10]

In this study, an attempt was made to compare bolus bupivacaine, fentanyl, and mixture of bupivacaine with fentanyl in thoracic epidural analgesia for upper abdominal surgery.

Aims and Objectives

The present study was undertaken with the following aims and objectives:

1. To study the efficacy of fentanyl for pain relief of in-patients after upper abdominal procedures and compare with bupivacaine alone and with bupivacaine and fentanyl combination
2. To find out the synergistic effect of bupivacaine with fentanyl
3. Assessment of severity of pain at rest and during function
4. Assessment of the intensity of post-operative pain relief
5. Assessment of the duration of post-operative pain relief
6. Assessment of the incidence of side effects.

MATERIALS AND METHODS

The present study was carried out in the Department of Anesthesiology, N.S.C.B. Medical College, Jabalpur, Madhya Pradesh.

After institutional approval, a total number of 90 patients of ASA Grades I, II, and III of either sex, aged 20-60 years were included in this study. Patients scheduled for elective and emergency upper abdominal surgeries. The name, age, sex, and body weight of the patients noted, and all the patients were assessed before the surgery and judged fitness for the study. A detailed history was taken and thorough physical examination was done. Routine investigation and essential evaluation according to the requirement of the case were done before the operation.

For the purpose of the study, the patients were randomly allocated into three groups of 30 patients each.

Group A: Patients receiving 10 ml of 0.25% bupivacaine epidurally

Group B: Patients receiving 10 ml of fentanyl 50 μg epidurally

Group C: Patients receiving 10 ml of 0.25% bupivacaine with fentanyl 50 μg epidurally.

In case of routine surgery, a thoracic epidural block was performed in sitting position before induction of general anesthesia, while in case of emergency surgery, the block was performed in lateral decubitus after the completion of surgical procedure under general anesthesia and patients were still under general anesthesia and intubated, at interspace between T7 and T10 depending on level of surgical incision with taking all aseptic precautions.

After recovery room where they kept and received post-operative analgesia as decided by the random numbers.

Preparation of the Drugs

Group A (n = 30): 0.25% bupivacaine 10 ml

Group B (n = 30): 50 μg of fentanyl (1 ml fentanyl ± 9 ml of normal saline).

Group C (n = 30): 50 μg of fentanyl ± 0.25% bupivacaine (10 ml) (1 ml fentanyl ± 9 ml of 0.25% bupivacaine).

When the score on visual analog scale (VAS) was ≥25, the solution of local anesthetic and/or opioid injected into the epidural space.

Time taken for pain relief, i.e. onset of analgesia. Time of reappearance of pain, i.e. duration of analgesia and side effects of the drugs were noted.

Following parameters - pulse rate, blood pressure, respiration, intensity, and duration of analgesia was monitored during the post-operative period every 15 min for first 30 min, and thereafter 1 h for 5 h.

The intensity of pain was assessed by VAS.

RESULTS

About 90 patients of ASA Grades I-III from both sexes who were to undergo upper abdominal surgeries under general anesthesia were chosen for this study. Patients who already received analgesics preoperatively were excluded from the study.

The patients were randomly allocated into three equal groups of thirty each.
Group A: 30 patients (only bupivacaine)
Group B: 30 patients (only fentanyl)
Group C: 30 patients (bupivacaine with fentanyl)

The onset and duration of analgesia, changes in blood pressure, pulse rate respiration, and side effects, if any, were noted for each group.

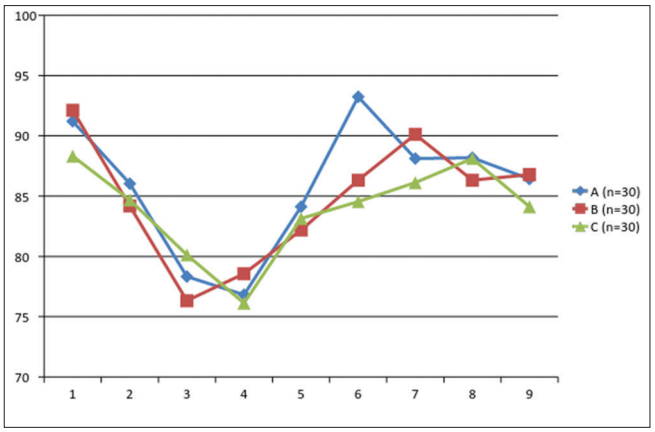
The study population was similar with respect to age, sex, and weight.

A fall in pulse rate was observed after 15 min in all the groups. However, the mean pulse rate returned to pre-operative values subsequently (Graph 1).

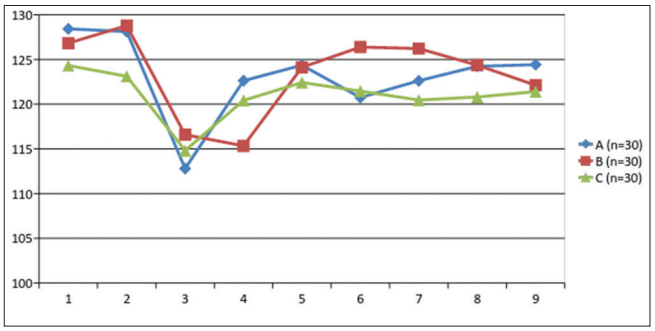
A change in mean systolic pressure was recorded at 15 min, 30 min, and 1 h thereafter. Mean of the values recorded has been shown in Graph 2.

A fall in blood pressure was observed to be more in Groups A and B, as compared to Group C (Graph 3).

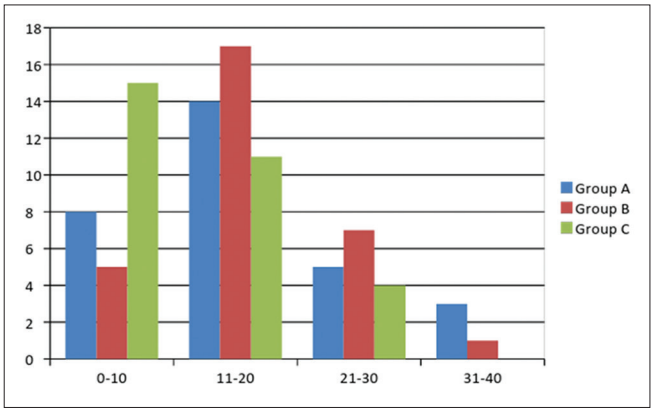
The change in mean respiratory rate among the three groups has been depicted in Graph 4. In the post-operative period 15 min after the drug administration, there was a transient but not significant decrease in respiratory rate. This may be due to the relief of pain by the drug administered. Later on, there was a gradual increase to pre-operative values.



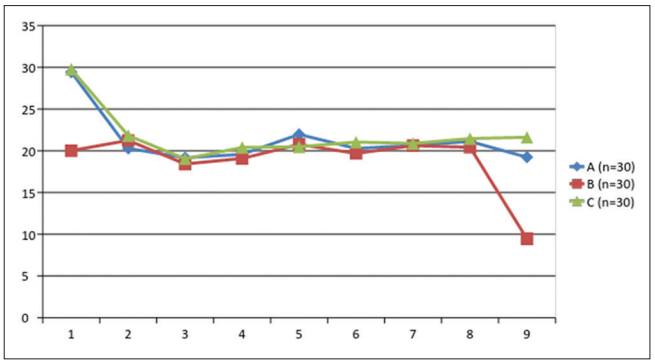
Graph 1: Change in mean pulse rate ± standard deviation



Graph 2: Change in mean systolic blood pressure (mmHg) ± standard deviation



Graph 3: Fall of blood pressure (systolic) (%)



Graph 4: Change in mean respiratory rate ± standard deviation

Mean time of onset of analgesia was 13.42 ± 4.60 min in Group A, 6.06 ± 2.43 min in Group B, and 4.46 ± 2.38 min in Group C (Table 1).

Mean duration of analgesia was 132.63 ± 34.78 min in Group A, 166.30 ± 24.64 min in Group B, and 192.84 ± 18.72 min in Group C (Table 2).

A comparison of mean pain score has been shown in Graph 5. While the maximum pain score (score-4) was seen in Groups A, B, and C at about 3 h, 4 h, and 5 h, respectively (Table 3).

Most of the patients of Groups A, B, and C needed supplementation in between 2 and 3 h (70%), 3-4 h (76.6%), and 4-5 h (70%), respectively. It is clear from these data that the subsequent repeat of drug administration is least in the case of fentanyl with bupivacaine group in comparison to only bupivacaine and fentanyl alone group (Table 4).

The incidence of side effects was minimal as depicted in Table 5.

DISCUSSION

An ideal analgesic should provide relief of pain without change of consciousness and should permit the early return of normal function. It should have its effect localized to where analgesia is required and should not produce a systemic side effect.

A safe and effective post-operative analgesia should induce a maximal analgesic response without any appreciable effects on the respiratory and cardiovascular systems or any tendency to produce post-operative complications.

The benign side effect profile of fentanyl despite good analgesic activity is thought to be due to its lipophilicity which restricts its fast rostral spread, thus limiting its ill effects such as respiratory depression, and pruritus. Its lipophilic nature also contributes to its shorter duration of action but used for continuous epidural analgesia. It is preferred over other hydrophilic compounds because of its rapid onset; it becomes much easier to observe the desired effects and thus titrate the dosage, to an optimal analgesic level.[11] There are a few studies regarding its effect in continuous epidural analgesia.[12]

In this clinical study, patients aged more than 60 years and <20 years of age were excluded to circumvent the variables at the extremes of age. Patients belonging to ASA I-III subjected to routine and emergency surgical procedures were taken for the study. Patients who received analgesics before surgery were excluded from the study. In this study, fentanyl was given in two different forms; 50 μg s only in Group B and 50 μg s in Group C with 0.25% bupivacaine. A study by Torda *et al.*[13] have shown that fentanyl 50 μg administered epidurally is effective for post-operative pain relief. As the intravenous dose of fentanyl for analgesia is 1-2 μg/kg, a dose of 50 μg was considered safe for epidural use.

Table 1: Mean onset of analgesia (minutes±SD)

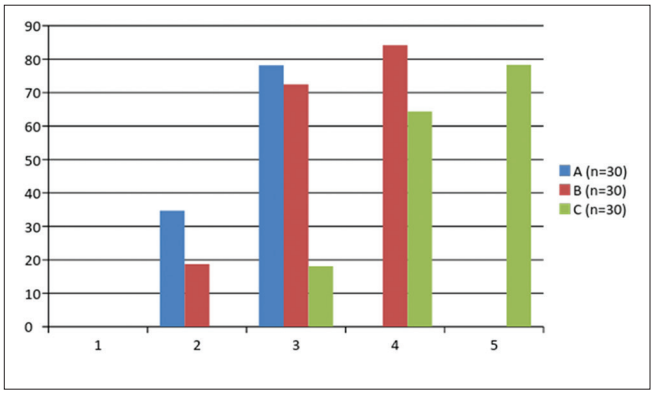
Groups (*n*=30)	Onset in minutes	Range in minutes
A	13.42±4.60	8.4-18.2
B	6.06±2.43	4.2-10.2
C	4.46±2.38	3.6-8.4

SD: Standard deviation

Table 2: Mean duration of analgesia (minutes±SD)

Groups (*n*=30)	Duration in minutes	Range in minutes
A	132.63±34.78	96-170
B	166.30±24.64	124-210
C	192.84±18.72	150-280

SD: Standard deviation



Graph 5: Comparison of mean pain score (± standard deviation)

Table 3: Five level paint score

Group (*n*=30)	0-1		1-2		2-3		3-4		4-5	
	Paint (%)	Score	Paint (%)	Score	Paint (%)	Score	Paint (%)	Score	Paint (%)	Score
A	53	0	68	2	46	3	100	4	-	-
B	100	0	85	1	80	2	80	3	100	4
C	100	0	93	0	84	2	86	3	63	4

Table 4: Number of patients requiring supplementation (post-operative)

Groups (*n*=30)	Hours after operation (%)			
	1-2	2-3	3-4	4-5
A	6 (20)	21 (70)	3 (10)	-
B	0	4 (13.3)	23 (76.6)	3 (10)
C	0	3 (10.3)	6 (19.6)	21 (70)

Table 5: Incidence of side effects

Side effects	Group A (%)	Group B (%)	Group C (%)
Hypotension	5 (16.67)	5 (16.67)	6 (23.3)
Nausea and vomiting	2 (6.67)	4 (13.3)	4 (13.3)
Sedation	2 (6.67)	3 (10)	3 (10)
Pruritus	0	4 (13.3)	5 (16.67)
Respiratory depression	0	1 (3.33)	0
Motor weakness	1 (3.33)	0	0

In our study, it was observed that there was an initial decrease in the pulse rate in all the three groups 15 min after drug administration and, later on, rise back to pre-operative value. This is more marked in Groups A and B and less in Group C. This observation is similar to the observation of Torda *et al.*[13] that the effects on heart rate are not significantly different between the studies.

It was also seen that there was an initial fall in mean systolic blood pressure, 15 min after the epidural drug administration. The fall in systolic blood pressure was more in Group A and Group B as compared Group C. This observation also corroborates with the observations of Torda *et al.*[13] This fall of systolic blood pressure was followed by a gradual rise in all the three groups to pre-operative values at about 1 h.

We also recorded a fall in systolic blood pressure in this study. For most of the patients in any group, the fall was within 20 mmHg. However, in Group C, the fall was within 10 mmHg in 50% patients.

Graph 4 shows the changes in mean respiratory rate in the post-operative period compared before and after drug administration. Hence, it can be inferred from these finding that epidural fentanyl and bupivacaine combination can provide post-operative analgesia without early or delayed clinical respiratory depression. This corroborates with the findings of Torda *et al.*[13]

The mean onset of analgesia in Groups A, B, and C, were 13.42 ± 4.60, 6.06 ± 2.43, and 4.46 ± 2.38 min, respectively. The difference between Groups A and Group C was found to be highly significant. This confirms with the findings of George *et al.*[10] that fentanyl had an onset of action within 4-10 min and was superior compared to bupivacaine.

The mean duration of analgesia (minutes) in Groups A, B, and C was 132.63 ± 34.78, 166.30 ± 24.64, and 192.84 ± 18.72, respectively. The difference between the three groups in different combinations was found to be statistically significant. It is observed that Group C (bupivacaine and fentanyl) produced prolonged analgesia in comparison to Group A and Group B. This is similar to the findings reported by Cooper and Turner.[14] They have found that combination of fentanyl with bupivacaine is more effective for post-operative pain relief.

In our study, the mean pain score during the post-operative period was highest for Group A at 2-3 h. In the Group B, it peaked at 3-4 h while in Group C it was highest during 4-5 h. From these findings, it is clear that combination of fentanyl and bupivacaine provided longer duration of analgesia than only fentanyl (50 μg) and bupivacaine alone. This corroborates with the findings of George *et al.*[10]

Most of the patients of Groups A, B, and C needed supplementation in between 2 and 3 h (70%), 3-4 h (76.6%), and 4-5 h (70%), respectively. It is clear from these data that the subsequent repeat of drug administration is least in the case of fentanyl with bupivacaine group in comparison to only bupivacaine and fentanyl alone group.

There were no significant changes in the vital parameters. Mild hypotension was found in 5 patients of Group A, 5 patients of Group B, and 6 patients of Group C, easily corrected with crystalloid infusion (Table 5).

The incidence of side effects was remarkably minimal. The most common side effects found in this study were hypotension, nausea and vomiting, pruritus, sedation, respiratory depression, and motor weakness.

Nausea and vomiting have been observed following epidural administration of all currently employed opioids and also local anesthetics. The incidence of nausea is dependent on many factors such as age, sex, and type of operation. In the present study, the incidence was 2 patients in Group A and 4 patients in Groups B and C, each. In this study, the incidence is almost equal in all the three groups, i.e. 13.3%. This corroborates with the findings of Torda *et al.*[13]

Pruritus was seen in 13.3% patients in Group B and 16.6% of patients of Group C. Respiratory depression was seen in only one patient of group B, easily managed by oxygen supplementation using the face mask.

Motor weakness was seen in 1 patient in Group A that is thought to be due to some motor blocking action of

bupivacaine. Opioid lack this effect and hence the choice for post-operative pain relief.

Remarkably no complication was noted in our study regarding the technique of epidural puncture or catheter insertion or removal. Only in three patients epidural failure (lack of post-operative analgesia) were seen and they were excluded from the study.

In our study, we also found that the post-operative epidural analgesia was satisfactory.

SUMMARY AND CONCLUSION

It is concluded from observations and results that combination of bupivacaine with fentanyl in thoracic epidural analgesia after upper abdominal surgery, comparatively showed the:

1. Better analgesic efficacy
2. Synergistic effect, short onset of action, longer duration of action (ranges from 150 to 280 min) with minimal side effects
3. Intensity of pain was least, associated with low pain scores and severity was also minimal at rest and during function (five level pain score)
4. The incidence of side effect which occurred was remarkably minimal.

The thoracic epidural is strongly recommended the technique for post-operative pain relief after upper abdomen surgery as it is highly beneficial for the patient, highly accepted by the surgeon also, and epidural fentanyl with bupivacaine provides effective, prolonged analgesia in comparison to either fentanyl or bupivacaine alone.

However, the present study invites positive criticism and hopes for further studies.

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How to cite this article: Gajbhiye S, Narang N, Mahendra R, Singh R, Godwin RB, Ilyas M. Comparison of Bolus Bupivacaine, Fentanyl, and Mixture of Bupivacaine with Fentanyl in Thoracic Epidural Analgesia for Upper Abdominal Surgery. Int J Sci Stud 2016;3(12):238-243.

Source of Support: Nil, **Conflict of Interest:** None declared.