

Comparative Study of Epidural Fentanyl and Buprenorphine for Post Operative Analgesia in Lower Abdominal and Lower Limb Surgeries

Arun Kumar Gupta¹, Narjeet Kaur Osahan², Valsamma Abraham²,
John Abraham³

1. Assistant professor, 2. Professor - Department of Anaesthesiology and critical care
Christian Medical College & Hospital, Ludhiana, Punjab, India.

3. Professor & Principal- Pondicherry institute of medical Sciences, Pondicherry.

Correspondence: - Dr Arun Kumar Gupta

Abstract: This study was conducted on 60 adult patients of either sex, 20-60 years of age group belonging to ASA I and II scheduled for lower abdomen and lower limbs surgeries were randomly divided into two groups of 30 each to receive 200 microgram of fentanyl dissolved in 10 ml of normal saline (Group I) or 600 microgram of buprenorphine dissolved in 10 ml of normal saline (Group II). When patient complaint of pain, they were given the drugs through the epidural cannula and then the cannula was removed. Patients Pulse rate, blood pressure, respiratory rate and oxygen saturation were recorded before injecting the drugs which were taken as control and at 10 minutes intervals for the first 30 minutes and thereafter hourly for 24 hours. Patients were assessed for pain relief, onset and duration of analgesia, side effects like headache, nausea, vomiting, pruritis, drowsiness and urinary retention, The onset of analgesia was earlier with group I. The duration of analgesia was 30 hours with group II and 6 hours with group I. Fentanyl causes pruritis, headache and drowsiness but other systemic side effects like nausea, vomiting, and urinary retention are more common with epidural buprenorphine.

Key words: Epidural anaesthesia, Post operative Analgesia, Fentanyl, Buprenorphine.

I. Introduction

Pain has a teleological function in warning the patient that something is amiss and is a protective phenomenon. But, it is also possible that some of the protective functions may exert deleterious effect on body functions and pain may hinder early mobilization and recovery. Hence, adequate pain relief in the post operative period is not only indicated on humanitarian grounds, but also to ameliorate some of the harmful side effects.

Cleland in 1949 was the first person to describe the technique of epidural analgesia for post operative pain relief. (1) Epidural opioids administration has been shown to provide high quality of analgesia in many situation including post operative pain (2). It has been seen that patients given epidural analgesia have significantly higher arterial oxygen tension during the first three post operative days with a lower incidence of pulmonary complications and chest infections (3) Epidural morphine was first used by Behar for pain relief in 1979 (4). Since then, a number of opiates have been used epidurally for post operative analgesia viz Pethidine, Pentazocine and Methadone. They often cause side effects like respiratory depression, nausea, vomiting, pruritis, urinary retention and drowsiness (2).

In view of these side effects, there has been a constant search for newer and safer drugs. Buprenorphine is a relatively new semi synthetic opioid analgesic of high potency and long duration of action. It was introduced as an analgesic in 1976 (5). It is 25-50 times more potent than morphine in producing analgesia. Epidural buprenorphine was first used for post operative analgesia in 1984 (6).

Fentanyl is a synthetic opioid related to phenylpiperidines. It is primarily a mu agonist and is estimated to be 100-200 times more potent than morphine as an analgesic. Fentanyl was introduced into clinical practice in 1961. It can be used via Intramuscular, intravenous, transdermal, intrathecal and epidural routes of administration. The action of fentanyl given epidurally is rapid, intense and of short duration (7, 8) Epidural Fentanyl and buprenorphine is being frequently used for operative analgesia and the procedure is gaining wide acceptance for post operative pain relief as well.

II. Aims of the study

This study is undertaken to

- a) Evaluate the onset, duration of analgesia and the incidence of side effects of epidural Fentanyl for post operative analgesia and
- b) To compare it with epidural buprenorphine.

III. Material and Methods

After approval from institutional ethics committee the present study was undertaken at Christian Medical College and Hospital, Ludhiana. It was conducted on 60 adult patients of both sexes between the age group of 20-60 years of ASA grade I and II(9) undergoing elective or emergency surgical procedure of the lower abdomen and lower limb.

These Patients were divided into two groups of 30 each on alternate basis.

Group I -consisted of 30 patients, who received 200 microgram of Fentanyl diluted in 10 ml of normal saline

Group II-consisted of 30 patients, who were given 600 microgram of buprenorphine diluted in 10 ml of normal saline.

Patient with history of addiction to narcotics, bleeding disorders, pulmonary, hepatic, neurological, psychiatric illness, spinal deformity and infection at lumbar region were excluded from the study. All patients were examined and investigated in pre operative visit, patient/guardians were explained about surgical procedure, anaesthesia technique and written informed consent was obtained from them. All patients were kept nil per orally for 6 hours before surgery. No pre medication was given to the patients. No analgesic, sedation or otherwise was administered either intraoperatively or post operatively during the period of study. A standard anaesthesia technique was followed for all patients.

In the operation theatre the base line pulse rate, blood pressure, respiratory rate and oxygen saturation were recorded. An intravenous cannula was inserted and preloaded with 500 ml of ringer solution. The patient was positioned on left lateral with flexion at head, neck, spine hips and knees. Under all aseptic precaution a16 gauge Tuohy's needle was advanced 1-2 cms at L3-L4 inter vertebral space.10 ml glass syringe filled with 5-6 ml air attached to the needle. The needle was advanced into the tissues about 1-2 cms at a time, while applying intermittent pressure on the plunger with rapid tremolo movement of the thumb alternately compressing and releasing the air in the syringe. Entry into epidural space was confirmed by "Loss of resistance" technique. Two ml of 0.5% bupivacaine was injected as a test dose .The epidural catheter was gently threaded through the needle till 12-14 cms marks, needle removed and catheter fixed with patients back. The Luer -lock connector was attached to the epidural catheter. The patient was then turned supine and anaesthesia was maintained with 0.5% bupivacaine. The patient pulse rate, blood pressure, respiratory rate and oxygen saturation was monitored every minute for first 10 minute then every 5-10 minute till termination of the surgery. At the termination of surgery, the patient was transferred to recovery room and the study began when the patient started complaining of pain and demanded pain relief. They were given either of the two drugs as on the alternate basis through the epidural cannula. The epidural cannula was removed. The patient pulse rate, blood pressure, respiratory rate and oxygen saturation were recorded before injecting the drugs which were taken as the control value and at10 minutes intervals for the first 30 minutes and there after hourly for 6 hours.

All the patients were evaluated for efficacy of post operative analgesia using Magill's classification for the degree of pain. Grade 0- No pain, Grade 1-Slight pain, Grade 2- Discomfort, Grade 3- Unbearable pain, Grade

4- Excruciating pain.

Grade 0 and 1 will be considered as satisfactory analgesia, Grade 2 will be mild pain and

Grade 3 and 4 will be considered as severe pain for statistical purposes.

The time of onset of analgesia was taken as the time interval between the injection of the drug and the onset of the pain relief (Grade 0 or 1).Duration of analgesia was considered as the time from onset of pain relief till the reappearance of pain (Grade2 or more).

Any complications like nausea, vomiting, pruritis, headache, urinary retention, drowsiness, hypotension, bradycardia and respiratory depression were noted at 30 minutes, one hour and then hourly interval for 6 hours post injection. At the end of study the data were compiled. For the purpose of analysis haemodynamic variables within group comparison were made by using either 'Student's' paired't' test or" Wilcoxon "signed rank test as was applicable. For the purpose of between group comparison student'S two sample 't' test on Mann Whitney 'U' statistics was used. All multiple group comparison within or between groups 'p' value were adjusted by using Bon Ferroni principle. All p values less than 0.05 were taken as significant.

IV. Results

The drug under study group were injected post operatively when the patient complained of pain and demanded pain relief. Various parameters were observed as per the protocol i.e. Types of surgery, Age, Sex, weight, Pulse rate, blood pressure, respiratory rate, oxygen saturation, pain relief, onset of analgesia, duration of analgesia and side effects like nausea, vomiting, pruritis, headache, drowsiness and urinary retention .

Table1-Type of surgery

	GROUP Fentanyl)		GROUP II (Buprenorphine)	
	NO ,CASES	PERCENTAGE	NO.CASES	PERCENTAGE
GENERAL SURGERY	11	36.60	07	23.30
UROLOGY	03	10.00	07	23.30
ORTHOPAEDICS	16	53.40	16	53.40
TOTAL	30		30	

In Group I (N=30) 11 patients underwent general surgical procedure, 3 patients Urological surgery and remaining 16 patients underwent orthopaedic procedure.

In Group II (N=30) 7 patients underwent general and urological surgical procedure, remaining 16 patients underwent orthopaedic procedures.

Table2-Sex Distribution

DRUG GROUP	MALE	FEMALE	TOTAL	p Value
FENTANYL (GroupI)	29 (96.6%)	01 (3.4%)	30	P>0.05
BUPRENORPHINE(GroupII)	28 (93.4%)	02 (6.6%)	30	

In the Fentanyl group there were 96.6% male and 3.4% female patients. In buprenorphine group 93.4% were male and 6.6% were female. The difference was statistically not significant (p >0.05).

Table3- Demographic data and duration of surgery

	Group 1(Fentanyl)		Group II (Buprenorphine)		p value
	MEAN	S.D	MEAN	S.D	
AGE (Yrs)	43.03	12.15	40.17	12.92	0.62
WEIGHT (Kg)	43.03	5.63	68.67	5.26	0.78
Onset of Analgesia(Minutes)	8.43	2.65	13.70	3.24	0.00002
Duration of Analgesia(Hrs)	211.0	57.62	964.0	346.63	0.0000

On statistical analysis there was no significant difference between the two groups in respect to age and weight of the patients (p>0.05).

We found that the time of onset of action for fentanyl was shorter than buprenorphine. This was statistically significant (p < 0.05).The mean duration of analgesia of fentanyl was shorter than buprenorphine. The difference was statistically significant (p < 0.05).

Table4 -Efficacy of Analgesia (Pain Score)

Group I -Fentanyl

SCORE	0 MIN	15 MIN	30 MIN	1 HOUR	2HOUR	3 HOUR	4 HOUR	5 HOUR	6 HOUR
0	-	7	28	30	27	15	3	3	-
1	-	23	2	-	3	8	7	1	2
2	5	-	-	-	-	6	17	16	10
3	19	-	-	-	-	1	1	8	16
4	6	-	-	-	-	-	2	2	2

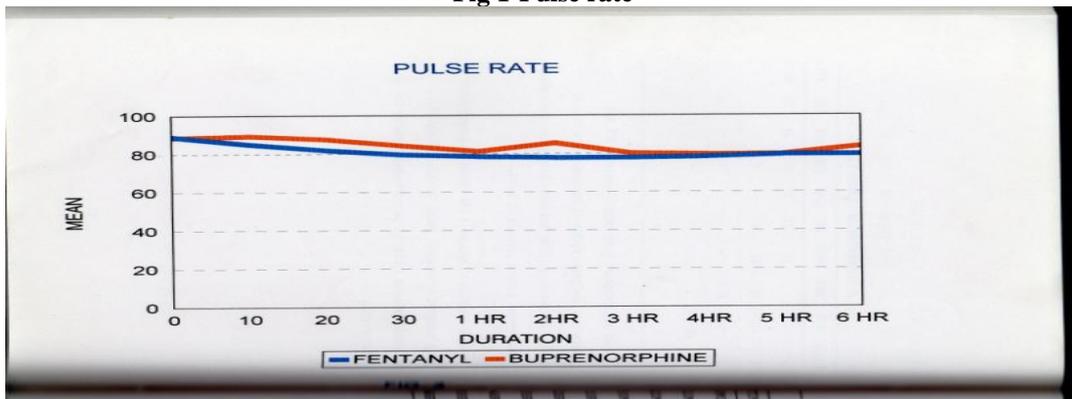
Within 15 minutes 100% of the patients in the fentanyl group had complete pain relief and it lasted till 2 hours. 76.6% patients had analgesia upto 3 hours, 33.3% patients had for 4 hours, 13.3% had analgesia for 5 hours and rest 6.7% required rescue analgesia after 5 hours.

Group II -Buprenorphine

SCORE	0 MIN	15 MIN	30 MIN	1 HOUR	2HOUR	3 HOUR	4 HOUR	5 HOUR	6 HOUR
0	-	-	19	30	30	30	30	30	30
1	-	18	11	-	-	-	-	-	-
2	4	11	-	==			=		
3	22	1	----	-----	-----	-----	-----	-----	-----
4	4	----	-----	-----	-----	-----	-----	-----	-----

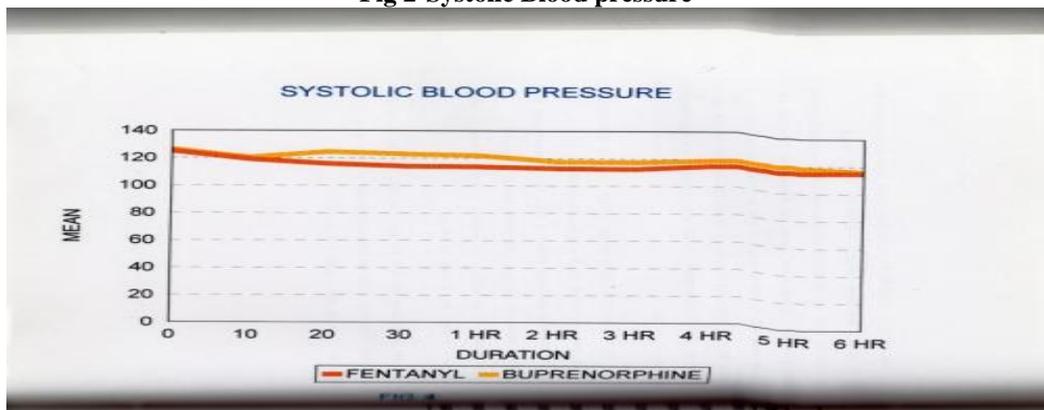
In Buprenorphine group within 15 minutes 60% patients had satisfactory analgesia, but within 30 minutes all patients (100%) had satisfactory analgesia which lasted beyond 6 hours (upto 24-30 hours).

Fig 1-Pulse rate



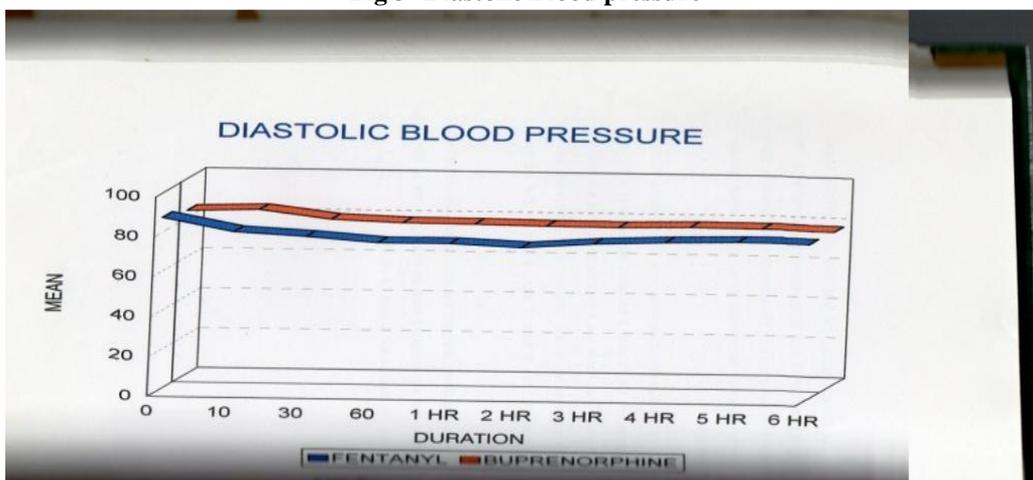
The pulse rate showed a tendency to decrease in the Fentanyl group at all the observed timings. These changes were statistically significant when compared to the base line value ($p < 0.05$). In the buprenorphine group also the mean pulse rate showed a tendency to decrease at all the recorded timings, but this was statistically significant only from 20 minutes to 6 hours ($p < 0.05$). Between the two groups there was a statistically significant decrease in the pulse rate at 20 minutes, 30 minutes, 1 hour and 2 hours ($p < 0.05$).

Fig 2-Systolic Blood pressure



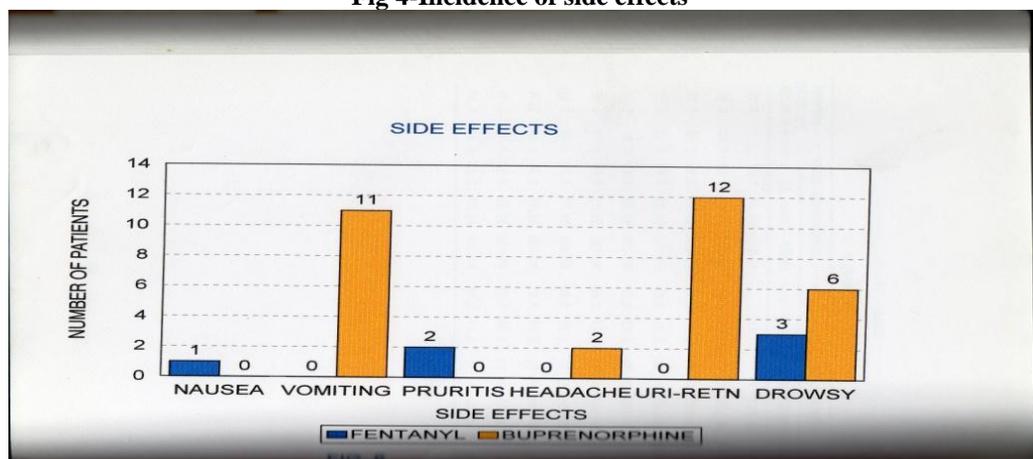
Between the two groups, a significant fall in systolic blood pressure was observed at 20 minutes, 30 minutes and 1 hour ($p < 0.05$).

Fig 3- Diastolic Blood pressure



The diastolic blood pressure showed a tendency to fall in the Fentanyl group at all the observed timings. This was statistically significant when compared to the base line value ($p < 0.05$). In the buprenorphine group, the diastolic blood pressure showed a fall at all observed timings from 20 minutes to 6 hours ($p < 0.05$). Between the two groups, no significant differences were observed at any time ($p > 0.05$). The respiratory rate did not show any significant changes in any group, statistically not significant ($p > 0.05$). The oxygen saturation was maintained above 98% in all the patients in both the groups.

Fig 4-Incidence of side effects



The incidence of nausea and vomiting was very common with epidural buprenorphine as compared to fentanyl. Pruritis was seen in 6.6% of patients in the fentanyl groups but none had in buprenorphine group. In our study 10% of patients in the fentanyl group were drowsy post injection. 6.6% patients experienced headache in buprenorphine group but none in fentanyl group. None of the patients in either group had respiratory depression. 40% patients in the buprenorphine group complained of urinary retention, out of which 10% needed catheterization but not seen in fentanyl group.

Summary

In summary our observations and results show that:

1. The onset of analgesia is earlier with the use of epidural fentanyl than buprenorphine.
2. The duration of analgesia with epidural fentanyl is significantly shorter than buprenorphine.
3. Though fentanyl causes pruritis and drowsiness, other systemic side effects like nausea, vomiting, headache and urinary retention are more common with epidural buprenorphine.

V. Discussion

There are different modalities of therapy available for the management of post operative pain, each with its own unique features. When comparing two or more of the various forms of therapy for post operative pain, two features are to be considered:

- A. The efficacy of a particular form of therapy in providing adequate analgesia for post operative pain
- B. And the incidence of side effects and their significance in the clinical setting.

Cleland in 1945 was the first to use the technique of epidural analgesia for post operative pain relief. (1) Touhy (1945) designed a needle with a curved Huber tip for continuous subarchnoid anaesthesia and Curbelo (1949) adapted this needle for continuous lumbar epidural blockade for surgical anaesthesia.

Initially, local anaesthetic solutions were used through the epidural route for segmental pain relief. The patients were able to ambulate earlier, thereby decreasing chances of deep vein thrombosis and subsequent pulmonary emboli. Good analgesia in post operative periods after thoracic and abdominal surgeries resulted in improvement of pulmonary function, allowing the patients to breathe adequately which is very important in preventing postoperative atelectasis as well as allowing unrestrained coughing to bring up any secretion. (10, 11). There were several disadvantages of using local anaesthetic solutions for post operative analgesia like motor blockade of lower limbs, hypotension, tachyphylaxis and toxicity due to high plasma concentration. These disadvantages fueled the search for more selective analgesic agents for epidural use for post operative pain relief. Opiates when given by the epidural route diffuse through the dura to reach their respective receptors leading to selective, long lasting and profound analgesia. However, early and late respiratory depression is

major concerns with epidural opioids. Other side effects of epidural opioids which may cause discomfort are nausea, vomiting, urinary retention and pruritis.

A number of opioids have been studied viz. morphine, pethidine, diamorphine, methadone and buprenorphine to name a few. Study in tissue compatibility indicates that buprenorphine may safely be administered epidurally, its high lipid solubility, high affinity for opioid receptors (approximately twice of morphine) and prolonged duration of analgesia makes it a suitable choice for epidural analgesia (12). However buprenorphine too is plagued by the side effects of other opioids as mentioned above, its respiratory depression is not so readily reversed by naloxone and it may occur upto 24-36 hours after epidural administration, necessitating constant observation for upto 36 hours after administration.

Search for "better" epidural analgesics led to the discovery of fentanyl, a mu receptor agonist synthetic opioid analgesic. Following epidural administration, fentanyl had been shown to provide satisfactory analgesia in postoperative period, is well documented (13). This comparative study was conducted on sixty adult patients and various parameters, as per the protocol were noted.

Fentanyl is a highly lipid soluble narcotic agonist with a relatively short duration of action when used IV in small doses, and in vitro penetrates dura matter more rapidly than any other narcotic (14). The time taken for a drug to diffuse across the dura is one of the determinants of the rapidity of onset of analgesia. In various studies with epidural fentanyl the mean time for onset of analgesia has been less than 15 minutes (15, 16). The onset of analgesia in case of epidural buprenorphine is less than 20 minutes which has been reported by various investigators (17, 18).

In our study, we found that mean time of onset of analgesia was 8.43 in the fentanyl group as compared to 13.70 minutes in case of buprenorphine. The difference in mean onset time of analgesia between the two groups were statistically significant ($p=0.00002$). This conforms to the studies of Stephen Naulty and Blanco J et al (15, 19).

The duration of analgesia of epidural fentanyl is dose-dependent. In a study by Stephen Naulty et al (15), the duration of analgesia varied from 3- 7 hours (mean 1.5 hours) when 100 microgram of epidural fentanyl was administered for postoperative analgesia following post cesarean pain relief. Alfred Lomessy et al (20) used 200 microgram of epidural fentanyl following abdominal surgery which provided optimum analgesia for 2 hours.

The duration of analgesia with epidural buprenorphine lasts upto 48 hours depending upon the dose used. Ronomanska et al (18) and Shakuntala et al (21) reported high lipid solubility and high affinity for opioid receptors makes buprenorphine useful drug for rapid and prolonged analgesia.

In the present study the mean duration of analgesia in fentanyl group was 211.0 minute and 964.0 minutes in buprenorphine group. The duration of analgesia of buprenorphine was longer than that of fentanyl group. ($p < 0.000$). Thus the results here are in agreement with the result obtained in previous studies.

In patients receiving buprenorphine, the time taken for complete pain relief was longer (15 minutes) and it was seen in only 60% of patients. All the patients had complete analgesia only by 30 minutes; however the duration of satisfactory analgesia was more than 6 hours. Such results have been reported by other workers who also used buprenorphine (22). Hence fentanyl provides effective analgesia in a shorter time (2 hours) than buprenorphine (more than 6 hours).

In our study, there was a continuous decrease in the pulse rate with epidural fentanyl upto 3 hours, there after there was a marginal increase in pulse rate but it never reached the baseline. The decrease in pulse rate was statistically significant at all the observed timings. This correlates with work of Stephen Naulty et al (15) and Alfred Lomessy et al (20).

With buprenorphine also there was a significant decrease in the pulse rate from 20 minutes upto 6 hours. Similar findings have been reported by Marcus et al (23) and Cahill et al (24). The decrease in the pulse rate was significantly more with fentanyl at 20 minutes, 30 minutes, 1 hour and 2 hour when compared to buprenorphine.

In our study we recorded a consistent fall in the systolic blood pressure at all the recorded timings, and this was statistically significant. Similar findings have been reported by Marites et al (25). Buprenorphine group also showed a consistent fall in the systolic blood pressure but it was statistically significant only from 30 minutes to 6 hours. Orowin et al (26) have been reported similar findings in their study. On comparing the two groups the fall in the systolic blood pressure was significantly more with fentanyl at 20 minutes, 30 minutes and 1 hour. In our study we found that there was a fall in diastolic blood pressure with fentanyl at various observed timings and the fall was statistically significant. In buprenorphine group also fall in diastolic blood pressure was noted but it was statistically significant only from 20 minutes to 6 hours. The difference between the two groups was not statistically significant.

Gaffud et al (1986) in their study found that there was no respiratory depression seen with the use of epidural fentanyl. But Marcus et al (23) reported that respiratory depression is a common problem with use of

buprenorphine. In our study also no respiratory depression was seen in any patient who received epidural fentanyl or buprenorphine.

The oxygen saturation was maintained above 98% in both the groups. This correlates with studies of Lanz (17) and Cahil et al (24).

Nausea and vomiting are known side effects of opioid administration and have been observed in various studies with varying frequency. Grass et al (27) and Blanco et al (19) reported that nausea and vomiting were very minimal or not seen in their patients, when fentanyl was used epidurally. Similar results have been published by various other workers (Alferd Lomessy et al, (20) and Van Lersberghe et al, (28).

On the other hand Marcus et al (23) have reported nausea and vomiting is a very common problem with epidural buprenorphine. Lanz et al (17), Gunderson et al (22) also found that nausea and vomiting are common after epidural buprenorphine.

In our study only one patient (3.3 %) had nausea in fentanyl group where as 36.5 % of patients vomited after epidural buprenorphine, this conforms with the above studies.

Pruritis has also been noted as a side effect while using fentanyl epidurally by Van Lersbergh et al (28) and others. In the presented study only two patients (6.6%) complained of pruritis in fentanyl group but this was not troublesome. Whereas this was not seen in any patients receiving buprenorphine. Lanz et al (17) also reported that there was no incidence of pruritis after using epidural buprenorphine.

Drowsiness with fentanyl has been reported in many studies. Stephen Naulty et al (15), reported drowsiness as one of the common side effects in a study of extradural fentanyl. Other workers namely Scott et al (29) and Sylvie Rostening et al (1991) have given similar report. We found that there were 3 patients (10 %) in fentanyl group who experienced drowsiness, In comparison to 6 patients (20%) in buprenorphine group. High incidents of drowsiness with buprenorphine have already been reported by Kamel et al (30) and Cahill et al (24).

Headache was not seen in the present study with the use of epidural fentanyl, this findings correlates with that of the previous workers like Stephen Naulty et al (15) and Alfred Lomessy et al (20). On the other hand headache as a side effect was seen in 2 patients after using buprenorphine in the present study. Lanz et al (17) also reported the incidence of headache in patients in their study.

Urinary retention was not a problem in our patients with the use of epidural fentanyl. This finding correlates with that of Joshi et al (31) and Blanco et al (19). With the use of buprenorphine urinary retention is a common problem. It has also been reported by Kamal et al (30) and Lanz et al (17). In the present study 12 patients complained of urinary retention out of which 3 needed catheterization. This findings correlates with the previous studied,

From our point of view, fentanyl is a better analgesia as compared to buprenorphine because it provides shorter time of onset of action, quick pain relief and fewer side effects. Hence, we recommended that fentanyl can be safely used for post operative pain relief.

Declarations

The authors declared no conflict of interest.

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