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RESEARCH ARTICLE

CLINICAL EVALUATION AND COMPARISON OF ANALGESIC EFFICACY OF INTRATHECAL FENTANYL AND BUPRENORPHINE USED ALONG WITH 0.5% BUPIVACAINE

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ABSTRACT

Background: One of the primary aims of anaesthesia is to alleviate the patients' pain and agony, there by permitting the performance of surgical procedures without any discomfort. Any expertise acquired in this field should be extended into the postoperative period, the period of severe, intolerable pain requiring attention. It is well known that when pain is treated pre-emptively, the amount of drug required is considerably less than which would be required, if treatment is delayed until the pain becomes apparent. **Objectives:** To evaluate the efficacy and safety of Buprenorphine (90 µg) and Fentanyl(25 µg) for intraoperative analgesia and postoperative pain relief, when administered intrathecally along with local anaesthetic agent 0.5% Bupivacaine (heavy). Study the characteristics of sensory and motor blockade, quality of block, and any side effects produced by combination of both drugs. **Methods:** Randomized, double blind, placebo controlled study of 120 pts; ASA I and II; aged between 15 - 60 years. Ethical committee approval, applied inclusion and exclusion criteria. Patients randomly divided in 3 groups of 40 each. Group A(control) Group B(Buprenorphine) and Group C(Fentanil). Postoperative pain evaluated by VAS. All figures in tables are expressed as mean ± SE. The results of data between the groups were analyzed statistically using unpaired t-test. A $p<0.05$ was considered significant and $p<0.001$ as highly significant. **Results:** All groups were comparable in relation to sex and age. The differences in mean pulse rate, mean respiratory rate, mean arterial pressure and oxygen saturation between the groups before and after administration of drugs were statistically insignificant ($p>0.05$). Onset of sensory and motor blockade was significantly rapid ($p<0.05$) in Fentanil group as compared to group A and B. None of the pts. had respiratory depression. Onset of sensory block was early in group C as compared to group A and B(1.26 ± 0.63, Vs 4.05±1.25 and 4.46±2.33 min) while time for two segment regression of sensory block was higher in group B(136.73±26.48 min) as compared to group A(115.5±11.62 min.) and group C(119.5±26.76 min.). The onset of motor block was early in group C(2.23± 1.47 min.) as compared to groups A(4.47 ± 2.23 min) and B(5.03± 2.58 min.). The mean duration of postoperative analgesia was higher in group B(10.34 ± 3.70 hrs) as compared to groups A(2.7 ± 0.78 hrs) and C(5.43 ± 1.31hrs). None of the patients in three groups had any statistically significant intra or postoperative side effects. **Conclusion:** From the observations of our study, it can be concluded that intrathecal administration of Buprenorphine and Fentanyl significantly enhances the onset of sensory analgesia. Doesn't alter the characteristics of motor block. Prolongs the duration of sensory blockade. Provides excellent surgical anaesthesia and postoperative analgesia without any significant increase in side effects.

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INTRODUCTION

The intensity of postoperative pain depends on the nature of surgery and the duration of surgical procedure. It is more severe in the first 10 hours after operation (Gjessing and Tomlin, 1979). The intrathecal administration of narcotics has been shown to produce intense and prolonged segmental analgesia (Wang, Nauss and Thomas, 1979). Intrathecal administration of opioid has the advantage of simplicity, reliability and low dose requirement when compared to epidural administration.

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The analgesia resulting from the administration of opioids is most likely a result of activation of opiate receptors located in substantia gelatinosa of spinal cord. Five types of opiate receptors have been demonstrated namely Mu, Kappa, Delta, Sigma and Epsilon (Rance, 1983).

The Mu receptor is probably the dominant site in mediating analgesia, although delta and kappa receptors are also believed to play the role. Narcotics with high lipid solubility are hypothesized to provide long lasting analgesia and lower incidence of potentially dangerous complications like early and late respiratory depression. SAB with opioid is more predictable, more intense and long lasting.

Aims and Objectives

- To evaluate the efficacy and safety of Buprenorphine (90 µg) and Fentanyl(25 µg) for intraoperative analgesia and postoperative pain relief, when administered intrathecally along with local anaesthetic agent 0.5% Bupivacaine (heavy) 3 ml.
- To find out characteristics of sensory and motor blockade produced by combination of Buprenorphine + Bupivacaine and Fentanyl + Bupivacaine when injected intrathecally.
- To find out any untoward effects of Buprenorphine and Fentanyl when given intrathecally along with Bupivacaine.
- To compare between two opioids for analgesic potency and side effects.

MATERIALS AND METHODS

After approval from hospital ethical committee and informed written consent of patients and relatives the Randomized, double blind, placebo controlled study was undertaken on 120 patients; ASA grade I and II; aged between 15 - 60 years.

INCLUSION CRITERIA

Those patients who gave the consent for study. Age between 15 – 60 years. ASA Gr. I and II and Surgical procedures lasting for 90 – 120 min.

EXCLUSION CRITERIA

Those patients on anticoagulants, MAO inhibitors, those taking drugs acting on central nervous systems as well as patients with compromised respiratory function, patients having any major systemic disease were excluded from the study. Each patient evaluated pre-an aesthetically and detail history about previous illness and drug treatment was elicited. All necessary investigations were done.

120 patients were randomly divided in 3 groups of 40 each.

- Group A – 3 cc of Bupivacaine 0.5% (heavy) + 0.5 cc of normal saline
- Group B – 3 cc of Bupivacaine 0.5% (heavy) + 0.3 cc of Buprenorphine (90 µg) + 0.2 cc normal saline.
- Group C – 3 cc of Bupivacaine 0.5% (heavy) + 0.5 cc of Fentanyl (25 µg)

After all monitors attached an intravenous access with 20 gauge cannula preloading with 20 cc/kg of Ringer lactate, lumbar puncture was done in L3-L4 interspace using 25 or 26 G spinal needle and drug injected as per groups. The characteristics of block, haemodynamic changes in pre, intra and postoperatively along with any side effects were noted in all three groups. Duration of adequate postoperative analgesia was recorded using a standard 10 cm linear visual analog scale (VAS).

(0= no pain, 10= worst pain imaginable)

A VAS <6 showed adequate analgesia. All figures in tables are expressed as mean ± SE. The results of data between the groups were analyzed statistically using unpaired t-test.

A $p<0.05$ was considered significant and $p<0.001$ as highly significant.

Monitoring: Non invasive arterial blood pressure, Heart rate, Electrocardiogram, Respiratory rate, Oxygen saturation (SpO2) with the help of multipara monitor for every 2 minutes for first 15 min; at 5 min intervals for first 2 hours and at 4 hourly intervals for the first 24 hours.

RESULTS

Three groups were comparable in respect to age, sex distribution of patients.

Demographic data of patients in both groups: All three groups were comparable in relation to sex ratio and the difference in sex ratio was statistically non significant (p>005). The mean age of the patients in group A was 38.13 ± 14.43 years, in group B was 38.56 ± 14.01years and in group C it was 32.8 ± 10.34 years. Thus the difference in mean age in all the three groups was statistically not significant (p>005). The differences in mean pulse rate, mean respiratory rate, mean arterial pressure and oxygen saturation between the groups before and after administration of drugs were statistically insignificant (p>0.05).

Onset of sensory block – time required to produce loss of pinprick sensation. Motor blockade assessed with Bromage scale, Bromage score 1 – time to onset of complete motor blockade. Onset of sensory and motor blockade was significantly rapid ($p<0.05$) in Fentanyl group as compared to groups control and Buprenorphine group. 2 patients in group A and group B and 4 patients in group C experienced mild hypotension and treated with inj. Mephentermine. None of the patients experienced respiratory depression (R.R. <10/min.) or hypoxaemia (SpO2 <90%) in any group. Characteristics of spinal blockade in all groups (Table No. 1). Sensory Block – onset of sensory block was 4.05±1.25 min in group A, 4.46±2.33 min in group B and 1.26 ± 0.63 min in group C. This shows that onset of sensory block was faster in Fentanil group as compared to groups A and B. The difference in onset of sensory block was highly significant when compared with three groups ($p<0.001$). Maximum level of analgesia was almost same in all the three groups (T8 – T6). Time for maximum cephalic spread was 12.3± 2.91min in group A, 12.06±3.77 min in group B and 11.36± 3.67 min in group C. when all the three groups were compared among themselves the difference between the groups was statistically not significant ($P>0.05$). When compared for time for two segment regression, group B patients had long lasting analgesia as compared to groups A and C (136.73±26.48 vs 98.87 ± 30.21 and 119.5±26.76). the difference is statistically highly significant ($p<0.001$).

Motor block: When all three groups were compared for time for onset of motor block (Bromage 3), it was shortest in group C (2.23± 1.47 min) as compared to group A (4.47 ± 2.23 min) and group B(5.03± 2.58 min). The difference of time for onset of motor block in all the three groups was statistically highly significant ($p<0.001$). All the three groups were compared for duration of motor block (Bromage 3-0) and found that when both study groups were compared with control group, in group A, total duration of motor block was 98.87 ± 30.21 as compared to 138.87 ± 23.84 minutes in group B and 132.12 ± 23.46 min. in group C. there was statistically significant difference in duration of motor block ($p<0.01$).

Table no. 1. Showing characteristics of spinal blockade in all groups

Observations	Group A	Group B	Group C
Sensory block			
a) Onset of sensory analgesia (min.)	4.05±1.25	4.46±2.33	1.26 ± 0.63
b) Maximum level of analgesia (segment)	T6 (T4 – T8)	T4 (T4 – T8)	T4 (T4 – T8)
c) Time for maximum cephalic spread (min.)	12 3± 2.91	12 06±3.77	11 36± 3.67
d) Time for two segment regression (min.)	115.5±11.62	136.73±26.48	119.5±26.76
Motor block			
a) Time for onset of motor block (Bromage 3)	4.47 ± 2.23	5.03 ± 2.58	2.23± 1.47
b) Duration of motor block (Bromage 3-0) in min.	98 87 ± 30 21	138.87 ± 23.84	132.12 ± 23.46

Table no 2. Showing quality of surgical analgesia in all groups.

Groups	Excellent		Fair		Poor	
	No.	%	No.	%	No.	%
Group A	24	60	16	40	0	
Group B	35	87.5	05	12.5	0	
Group C	36	90	04	10	0	

Excellent – no complaints of pain intraoperatively; Fair – minimal pain, requiring supplement analgesia;
Poor – general anaesthetic has to be administered

Table no. 3. Showing duration of adequate postoperative analgesia in all groups

Groups	Duration of analgesia (hrs)	p-value
Group A	2.7 ± 0.78	P<0.001
Group B	10.34 ± 3.70	P<0.001
Group C	5.43 ± 1.31	P<0.001

P< 0.001 – highly significant

Table no. 4. showing Intraoperative side effects in all groups

Side effects	Group A		Group B		Group C	
	No.	%	No.	%	No.	%
Level of consciousness						
1	38	95.0	24	60	26	65
2	02	5.0	14	35.0	14	35.0
3	0		02	65.0	0	
4	0		0		0	
Pruritus	0		2	5.0	6	15.0
Nausea	3	7.5	4	10.0	3	7.5
Vomiting	2	5.0	3	7.5	3	7.5
Hypotension	1	2.5	1	2.5	2	5.0
Respiratory depression	0		0		0	

Level of consciousness
1- Awake & alert
2 -Drowsy, responding to verbal command
3 -Drowsy, responding to physical stimulus
4 -Un arousable

Table no. 5. Incidence and comparison of intraoperative complications in Fentanyl group with other studies

Authors	Dose	Intraoperative Side effects	Pruritus	nausea	vomiting	hypo	brady	drowsi	resp depr
Buvanendran	25 µg	36.4%	-	-	4.5%	7.5%	0	0	
D. Shende	15 µg	15%	30%	-	0	20%	0	0	
Sergio D.	25 µg	40%	6.6%	6.6%	0	8%	0	0	
Montserrat R	25 µg	21%	5.33%	5.3%	58%	16%	0	31.6%0	
H. Usmani	25 µg	10%	10%	6.6%	10%	12%	6.6%	0	
Present study	25 µg	12.5%	2.5%	5%	10%	10%	0	0	

Hypo – hypotension, brady – bradycardia; drowsi – drowsiness; resp depr – respiratory depression

Table no.6. Incidence and comparison of intraoperative complications in Buprenorphine group with other studies

Author/year	Dose	Intraoperative Side effects Pruritus	nausea	vomiting	hypoten	bradycar	drowsi	resp depr
Mittal, 1988	300µg	0	10%	10%	8%	7.5%	5%	0
Nalini, 1990	300 µg	4%	4%	4%	6%	10%	0	0
Badwaik, 1991	300µg	4%	8%	8%	7.5%	13%	20%	0
Mamta,1991	200µg	0	13.3%	15%	4%	6%	26.6%	0
Thomas1997	50 µg	5%	4%	7.5%	0	12.5%	14%	0
Present study 2006	90 µg	5%	5%	7.5%	10%	15%	5%	0

Hypo – hypotension, brady – bradycardia; drowsi – drowsiness; resp depr – respiratory depression

When groups were compared for quality of intraoperative surgical analgesia we found that 60% of patients in group A, 87.5% patients in group B and 90% patients in group C had excellent surgical analgesia and 40% of patients in group A, 12.5% patients in group B and 10% of patients in group C had fair surgical analgesia while no patients from all the three groups were having poor analgesia. That means most of the patients from group C were having excellent surgical analgesia.

Mean change in pulse rate in group A was 2.5 and that in group B was 2.7 and in group C it was 5.25. This difference was statistically not significant (P>0.05). No change in systolic blood pressure was observed in 17.5%, 12.5% and 12.5.5% of patients in groups A, B and C respectively While 7.5% of patients in group A, 10% of patients in group B, 10% of patients in group C had hypotension (fall in systolic blood pressure by > 30 mm of Hg), which was treated with injection Mephenteramine. Duration of adequate postoperative analgesia (table no. 3). The duration of postoperative pain relief was calculated from the difference between duration of analgesia and duration of surgery. When all the three groups were compared, the duration of postoperative analgesia was longer duration in group B (10.34 ± 3.70 hrs), followed by group C (5.43 ± 1.31hrs.) as compared to group A(2.7 ± 0.78 hrs). The difference in the mean duration of postoperative analgesia between all the groups is statistically highly significant ($p < 0.001$) Quality of surgical analgesia (Table no. 2). We assessed quality of surgical analgesia in intraoperative period, it was excellent in 60% of patients in group A while 87.5% and 90% of patients in group B and C. Quality of analgesia was fair in 40% of patients in group A while 12.5% and 10% of patients in groups B and C. while there was no patients having poor quality surgical analgesia in all three groups. Excellent – no complaints of pain intraoperatively, Fair – minimal pain, requiring supplement analgesia, Poor – general anaesthetic has to be administered.

Intraoperative changes in pulse rate in all groups

Mean change in pulse rate in group A was 2.5 and that in group B was 2.7. This difference was statistically not significant ((P > 0.05). 15% patients in group A, 7.5% of patients in group B and 10% of patients in group C had mild bradycardia which was treated with inj. Atropine. Intraoperative changes in blood pressure in all groups. No change in systolic blood pressure was observed in 17.5%, 12.5% and 12.5.5% of patients in groups A, B and C respectively. While 7.5% of patients in group A, 10% of patients in group B, 10% of patients in group C had hypotension (fall in systolic blood pressure by > 30 mm of Hg), which was treated with injection Mephenteramine. Mean respiratory rate in pre/intra/postoperative period in all groups
All patients in the three groups were compared for mean respiratory rates in pre, intra and postoperative period.

Preoperative mean respiratory in group A was 16.53 ± 0.89 breaths/min, in group B was 16.73±1.11breaths/min and in group C was 16.73±1.11breaths/min. Intraoperative mean respiratory rate in groups A,B and C was 16.29± 0.17, 16.67± 0.05 and 16.43 ± 0.10 breaths/min respectively. While postoperative mean respiratory rate in groups A,B and C was 16.40 ± 0.1, 16.58 ± 0.03 and 16.75 ± 0.03 breaths/min respectively. There were no changes in respiratory rate. The mean respiratory rate in all the groups was comparable and found to be non significant (P > 0.05). Duration of adequate postoperative analgesia (Table no. 3): The duration of postoperative pain relief was calculated from the difference between duration of analgesia and duration of surgery. The difference in the mean duration of postoperative analgesia between all the groups is statistically highly significant ($p < 0.001$). Incidence of intraoperative side effects (Table no. 4). The data in table no.4 shows that incidence of the side effects in the intraoperative period was not high in group A, B and group C except that of emetic sequelae. The incidence of urinary retention was found in groups A, B, and C and was 2.5% in all the three groups. The incidence of postoperative headache was found in groups A, B and C and it was 5%, 2.5% and 2.5% respectively. Backache was found in groups A and C only and the incidence was 2.5% in both the groups.

DISCUSSION

One of the primary aims of anaesthesia is to alleviate the patient's pain and agony, there by permitting the performance of surgical procedures without any discomfort. But any expertise acquired in this field should be extended into the postoperative period, which is the period of severe, intolerable pain requiring attention. The intensity of postoperative pain depends on the nature of surgery and the duration of surgical procedure. It is more severe in the first 10 hours after operation (Gjessing and Tomlin, 1979). It is also well known that when pain is treated prophylactically (pre emptive), the amount of drug required is considerably less than that which would be required, if treatment is delayed until the pain becomes apparent. Mean age in group A was, 38.13 ± 14.43; in group B was, 38.56 ± 14.01; in group C, was 32.8 ± 10.34. Thus, all three groups were comparable in age. All the groups were comparable in the sex and type of surgery.

Time of onset of sensory analgesia: When groups A and C and groups B and C were compared for time of onset of sensory block, the difference was statistically significance ($p<0.001$). We observed that intrathecal Fentanyl – Bupivacaine combination leads to rapid onset of sensory and motor blockade, as could be explained by highly lipophilic nature of drug and synergism between opioids and local anaesthetics. Similar results were observed by Monstserrat Rue et al (1996), 13.5 ± 4.2 min in control group and 10.1 ± 0.8 min in Fentanyl group, Hammad Usmani et al (2003), 3.19 ± 0.8 minutes in control group as compared to 2.10 ± .12 in

Fentanyl group. In all studies the difference was statistically highly significant ($p<0.001$) W. Thomas, V. Abraham, B. Kaus in 1997, observed onset of analgesia with 50 µg Buprenorphine and 3 cc Bupivacaine. The mean time of onset of analgesia was 2.37 ± 0.56 minutes in study group and 6.37 ± 2.05 minutes in control group. They concluded that there is statistically highly significant difference in the onset of analgesia and that the addition of Buprenorphine hastens the onset of action of Bupivacaine. When both the study groups were compared to each other for time of onset of sensory analgesia, the difference was statistically highly significant. ($p< 0.001$). It was attributed to high lipid solubility of Buprenorphine that will enhance the penetration of drug in neuronal tissue and hastens the onset of analgesia. Time for maximum cephalic spread depends on baricity of solution, dose of drug, tilt of table etc. In our study the highest level of cephalic spread was in between T4 – T8.

Mean time for maximum cephalic spread in-group A was 12.3 ± 2.91 minutes as compared to mean time of 12.06 ± 3.77 minutes in group B and 11.36 ± 3.67 minutes in group C. There was no statistically significant difference between three groups in time taken for maximum cephalic spread. ($p>0.05$) We compared our study with D. Shende et al (1998), (6.5 minutes in Fentanyl group as compared to 8.0 minutes in control group) and D. Celleno et al (1988), (6.82 ± 90 minutes in Buprenorphine group as compared to 7.8 ± 1.2 minutes in control group). The difference was not statistically significant in both the studies ($p>0.05$).

Time for two segment regression of sensory block: In group A, time taken for two segment regression of sensory block was 115.5 ± 11.62 minutes as compared to 136.73 ± 26.48 minutes in group B and 119.5 ± 26.76 minutes in group C. When both study groups were compared with control group, there was statistically significant difference between the time taken for two segment regression of sensory block. ($p < 0.01$). We compared our results with Bruce Ben David et al (1997), who observed sensory block regression significantly slower with the addition of intrathecal Fentanyl 10 µg with 1ml of bupivacaine which was 67.0 ± 19 minutes and 11.0 ± 3 minutes in control group. The difference was highly significant ($p< 0.001$).

Time taken for onset of motor block: In group A, time taken for onset of motor block (Bromage score 3) was 4.93 ± 1.31 minutes while in group B, time taken for onset of motor block was 5.06 ± 2.58 minutes, in group C, time taken for complete motor block was 2.23 ± 1.47 minutes. When compared with control group, there was statistically significant difference between the all groups in time taken for onset motor block ($p < 0.01$). Addition of Buprenorphine and fentanyl to local anaesthetic agents enhances the motor block due to rapid penetration through lipid layers of neurons.

Total duration of motor block: When both study groups were compared with control groups, in group A, total duration of motor block (Bromage 3 – 0) was 98.87 ± 30.21 as compared to 138.87 ± 23.84 minutes in group B and 132.12 ± 23.46 min. in group C. there was statistically significant difference in duration of motor block ($p<0.01$). Nalini Damle et al, 1990, observed prolonged duration of sensory and motor block when 300 µg of Buprenorphine added to 1 ml of 5% Lignocaine. As Buprenorphine is lipophilic and dissociates slowly from the opiate receptors, the rate of removal of the drug from the site of action is slow, hence, the prolonged duration of block. (Bullingham, 1981). Akerman et al (1988), Karpal S. et al (1996), demonstrated that opioids when added to local anaesthetic solutions had potentiating effects on local anaesthetics. Harbhej Singh et al (1995) and Montserrat Rue et al (1996), observed similar results when they used Fentanyl with Bupivacaine for intrathecal analgesia.

Pulse rate changes: 15% patients in group A, 7.5% of patients in group B, 10% of patients in group C had bradycardia. As compared to study group, incidence of bradycardia is more in group A. Thus, Buprenorphine and Fentanyl does not cause statistically significant alteration in pulse rate but instead saves patients from traction pain and bradycardia ($p>0.05$). W. Thomas et al, 1997; Nalini et al, 1990; K.P. Chansoria et al, 1987,observed the similar findings in their studies.

Blood pressure changes

When both study groups were compared there was no statistically significant difference in blood pressure when Buprenorphine or fentanyl was added to Bupivacaine ($p>0.05$). W. Thomas et al, 1997; Nalini damle et al, 1990; K.P. Chansoria et al, 1987, was observed similar results in their studies. Main concern after spinal opiate is respiratory depression. Early respiratory depression is more common with lipid soluble opioids while late depression is related to the rostral diffusion and mixing of opioids in CSF (Bullingham et al, 1982). The incidence of respiratory depression is less with intrathecal Buprenorphine as compared to Morphine due to high lipid solubility and high affinity for opiate receptors, diffusion from spinal cord into the blood stream is slow and does not cause significantly higher plasma concentration to cause respiratory depression when administered intrathecally. Also, Buprenorphine does not reach the bulbar centres with the bulk flow of CSF. Thus, late respiratory depression is not seen. Although, systemic use of Buprenorphine is known to depress the respiratory centres to about the same extent as Morphine. (Budd, 1981; Gunderse et al, 1986)

Incidence of intraoperative side effects: (Table no. 4). Nausea, vomiting, itching, respiratory depression, dryness of mouth were looked for in all the patients intraoperatively. Since, they are known for complications of intrathecally administered opioids. The number of patients with significant fall in systolic blood pressure (> 30 mm Hg) was similar in groups A and C which was statistically significant ($p<0.05$). Hypotension was treated with injection Mephentermine 15 mg intravenously. Incidence and comparison of intraoperative complications in Buprenorphine group with other studies (Table no.5). We found that the incidence of intraoperative complications was very minimal and treatable in control group as well as both study groups. From our observations, it is evident that higher the dose of buprenorphine used, more are the side effects. So in present study, the incidence of intraoperative side effects is reduced by reducing the dose to 90 µg.

Mean duration of post operative analgesia: In Buprenorphine group, the mean duration of analgesia was highest (620.4 ± 2.25 minutes) as compared to Fentanil group (325.8 ± 78.6 minutes) and control group (162 ± 46.8 minutes). The difference in the mean duration of analgesia between all the groups was statistically highly significant ($p < 0.001$).

Following studies were compared with our study when Buprenorphine – Bupivacaine combination was used N. K. Mittal(1988) - 300 µg – 48 hrs, Chansoria(1987) - 30 µg – 20 hrs, D. Celleno(1989) - 30 µg – 7-8 hrs, H. Usmani(2003) - 60 µg – 11 hrs, r.K. Lalla(1997) - 40 µg and80 µg – 11 and 22 hrs, W. Thomas(1997 - 50 µg- 15 – 18 hrs, Jagtap(1991 - 300 µg – 19 hrs. and in present study we used 90 µg and we got 8 – 12 hrs postoperative analgesia with minimal side effects. From above studies, it was observed that Buprenorphine given intrathecally produces longer duration of analgesia with much smaller doses as compared to other routes. So, intrathecal route is excellent for prolonged duration of pain relief with single administration. Buprenorphine is lipophillic and hence, undergoes tissue uptake, low plasma concentrations are achieved quickly, the liver will eliminate most of the drug passing through it but the absolute amount destroyed is small relative to the total quantity in the body. These extensive body stores maintain the plasma concentration over a long time period producing prolonged effect (Cook et al, 1982).

Following studies were compared with our study when Fentanyl – Bupivacaine combination was used

D. Shende(1998) - 15 µg - 184 ± 42 min; Buvendran(1998) - 25 µg – 94.5 ± 24.6 min;
H. Usmani(2003) - 25 µg - 450 ± 29 min; Montserret(1996) - 25 µg - 222.1 ± 13.8 min;
H. Singh(1995) - 25 µg - 93 ± 22 min; Roxane F(2000) - 40 µg - 214.0 ± 120 min.

In our study we used 25 µg dose of Fentanil and found that 5.43 ± 1.31 hours postoperative analgesia. Higher the dose used, more are the side effects observed in above studies. Opioids and local anaesthetics exerts their antinociceptive effect in the spinal cord by different mechanics. The µ - agonist Fentanyl exerts its action by opening K^+ channels and reducing Ca+ influx, resulting in inhibition of transmitter release. The µ - agonists also have a direct postsynaptic effect, causing hyperpolarization and reduction in neuronal activity. Local anaesthetic, Bupivacaine acts mainly by blockade of voltage gated Na+ channels in the axonal membrane. Local anaesthetics may also interfere with synaptic transmission by a pre synaptic inhibition of Ca+ channels in addition to their effects on nerve conduction. A combination of these effects may explain the observed synergism between bupivacaine and fentanyl.

Number of rescue analgesics required in first 24 hours: The number of mean rescue analgesics required in group A was 3.46 ± 0.62, in group B it was 1.22 ± 0.42 and in group C it was 2.73 ± 0.58. Group A required highest number of rescue analgesics than group B and C and group B required less number of rescue analgesics as compared to group A and C. As Buprenorphine is lipophilic and dissociates slowly from opiate receptors, the rate of removal of the drug from the site of action is slow and hence, the prolonged duration of action of analgesia (Bullingham, 1981) and so patients required less number of rescue analgesics. The difference between control and study groups was statistically highly significant when groups were compared to each other for the number of rescue analgesics required in first 24 hours. ($p < 0.001$; A vs B, B vs C and A vs C).

Conclusions

From the observations of our study, it can be concluded that- Intrathecal administration of 90 µg Buprenorphine and 25 µg Fentanyl significantly –

- Enhances the onset and duration of sensory analgesia.
- Doesn't alter the characteristics of motor block
- Provides excellent surgical anaesthesia and postoperative analgesia without any significant increase in side effects.
- Allows complete avoidance of conventional parenteral analgesia postoperatively.
- Provides ease of administration and convenience for patient as well as anaesthesiologists.
- Though Buprenorphine provides longer lasting analgesia, Fentanyl had profound analgesic potency with minimal side effects.

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