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A COMPARATIVE STUDY OF INTRATHECAL BUPIVACAINE WITH BUPIVACAINE-TRAMADOL AND BUPIVACAINE-FENTANYL FOR POST-OPERATIVE PAIN RELIEF IN LOWER ABDOMINAL AND LOWER LIMB SURGERIES

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ABSTRACT

This clinical study was undertaken to evaluate and compare the efficacy of intrathecal bupivacaine, intrathecal bupivacaine with tramadol and bupivacaine with fentanyl for post-operative pain relief in lower abdominal and lower limb surgeries. 90 patients were given either of the three sets of intrathecal drugs randomly so the each group comprised 30 patients. Group A – bupivacaine HCL 15 mg (3ml) 0.5% heavy Group B – bupivacaine HCL 15 mg (3ml) 0.5% heavy and tramadol HCL 25 mg (0.5ml) Group C – bupivacaine HCL 15 mg (3ml) 0.5% heavy and Fentanyl citrate 25 µg (0.5ml) The mean time of onset of sensory block seen in different groups was found to be 110.10+10.02 sec. in Group A, 110.8+11.17 sec in Group B and 112.87+9.65 sec in Group C. The mean duration of sensory block was 3.38+0.21, 4.58+0.46 and 6.86+0.75 hrs in Group A, B and C respectively In the present study mean time of onset of motor block was 254+49.22, 250+44.45, 267.3+42.88 sec in Group A, B and C respectively The mean pulse rate/min before intrathecal injection was 84.80+11.10, 85.56+13.05, 86.13+14.47 in Group A, Group B and Group respectively. The differences were statistically insignificant The mean respiratory rate/min before intrathecal injection in this study was 16.23+1.4, 15.91+3.02, 16.38+2.34 in Group A, Group B and Group C respectively.

KEYWORDS: **intrathecal bupivacaine, tramadol, fentanyl**

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INTRODUCTION

Presently bupivacaine is a commonly used local anesthetic agent, it has a longer duration of action and lesser side effects as compared to the earlier agents. As the local anesthetic agents have there set duration of action other drugs are supplemented with them to prolong sensory analgesia in the post-operative period. Tramadol a relatively new, centrally acting analgesic drug has preferatian activity at opioid receptors. The adverse effect profile of tramadol especially respiratory depression is that of weak opioid at effective analgesic doses with low abuse and addiction potential. Tramadol and fentanyl have also been used interathecally adjuvant to lacal spinal anesthetic drugs to provide post-operative analgesia and improve the quality of neuraxial blocks. This clinical study was undertaken to evaluate and compare the efficacy of intrathecal bupivacaine, intrathecal bupivacaine with tramadol and bupivacaine with fentanyl for post-operative pain relief in the lower abdominal and lower limb surgeis.

Aims and objective

1. To study the effect on onset, level and duration of sensory block of intrathecal bupivacaine and compare it when combined with tramadol and fentanyl respectively.
2. Comparision of tramadol and fentanyl given intrathecally with bupivacaine 0.5% heavy on onset, degree and duration of motor block.
3. To study the quality and duration of post operative pain relief in different groups.
4. To observe and compare the effects on hemodynamic parameters.
5. To study the incidence of side effects and complications of both the drugs, intra-operatively and post-operatively.

MATERIALS & METHODS

The present study has been carried out in department of anaesthesiology, S.S. Medical College and associated Sanjay Gandhi Memorial Hospital and Gandhi Memorial Hospital, Rewa. This study comprised of 90 cases of ASA grade I and II, of both sexes and age ranging between 18 to 60 years, posted for routine surgies of lower abdominal and lower limb surgeries. Detailed preoperative examination including history, physical examination and vertebral column checkup were done. Routine investigation including hemoglobin, blood sugar, blood urea, total leukocyte count, differential leukocyte count, urine analysis, chest x-ray and ECG were done preoperatively. Patient with absolute contraindication for sub arachnoid block like raised intracranial tension, infection at the site of injection, any neurological deficit, any bleeding disorders, spinal deformity, undergoing anticoagulant were not included in the study. Anesthetic procedure was explained in detail and written consent was obtained from all the patients. 90 patients were given either of the three sets of intrathecal drugs randomly so the each group comprised 30 patients.

Group A – bupivacaine HCL 15 mg (3ml) 0.5% heavy
Group B – bupivacaine HCL 15 mg (3ml) 0.5% heavy and tramadol HCL 25 mg (0.5ml)
Group C – bupivacaine HCL 15 mg (3ml) 0.5% heavy and Fentanyl citrate 25 µg (0.5ml)

All patients were kept nil orally for 6 hours before the scheduled time of surgery. Xylocaine sensitivity was performed in all the patients. Patients were taken operation table and vital parameters were recorded. Monitor was set up for pulse rate, blood pressor and Spo_2. A wide bore intravenous line was established and preloading done with 15ml/kg bogy weight of ringer lactate solution about 15 min. prior to the intended time of intrathecal drug administration. Uniform premedication with i.v.Glycopyrolate 0.2 mg was done about 5min before subarachnoid block. The pulse rate, blood pressure, respiratory rate, Spo_2, reading were taken and recorded as basal parameters. Under all aseptic precautions, lumber puncture was performed at L_{2-3}/L_{3-4} intravertebral space using midline approach with 25 guage spinal needle. After ensuring a free flow of cerebrospinal fluid, the drugs according to the groups were injected. The patients were laid in supine position, to all the cases oxygen was given by polymask (3-4 lit/min). The vital parameters like pulse rate, blood pressor and Spo_2 were recorded every 2 minutes for initial 10 min, then every 5 minutes till 30 minutes, then every 10 minutes till completion of surgery. During surgery IV fluids (crystalloids, colloids) and blood were administered as required. A record was also made of blood loss, urine output and i.v. fluids given. Patients were observed for any discomfort, pain bradycardia, hypotension and any other side effect and the need for any other additional medication was also recorded.

Monitoring

During monitoring of patrameters, pulse rate of less than 60/min was graded as bradycardia and greater than 100/min as tachycardia. Atropine 0.6mg was administered in case of bradycardia. Whenever there was a fall of ≥20% of systolic blood pressure from the base line value or to less than 90mmhg, it was treated with IV fluids and/or by Mephentramine sulphate 3mg. A respiratory rate of less than 10/min or Spo_2 less than 90% was taken as respiratory distress. Onset of sensory analgesia was assessed by pin prick method. Time from intrathecal drug administration to loss of sensation to Pin-Prick was taken as time of onset of sensory analgesia. The highest level at which patient could not feel pin prick sensation was taken as level of sensory analgesia. After completion of surgery patients were shifted to post-operative wards and the time interval from onset of analgesia to first complain of pain by the patient was recorded as duration of analgesia. The time onset of motor block was taken as the time elapsing from an injection of drug to failure to raise the lower limb on command. Degree of motor block was assessed by the

ability to perform limb movements. This was classified in to four grades according to criteria described by Bromage P.R. et al in 1962[1]. Duration of motor block was recorded as time taken from the onset of the motor block to the time when the patient was able to perform limb movements.

Bromage Score

(A) Grade I – free movements of leg and feet
(B) Grade II – just able to flex knees with free movements of feet
(C) Grade III – unable to flex knee, but with free movement of feet
(D) Grade IV – unable to move legs or feet

Duration of surgery was taken as time period from skin incision to skin closure after completion of surgical procedure. Patients were closely monitored in the intra operative and post operative periods for any complication and/or side effects. The observed parameters recorded in all the three groups were tabulated and statistical analysis was carried out by using chi-square and student "t" test (paired for intragroup and unpaired for intergroup comparison). P value <0.05 was taken to be statistically significant and <0.001 highly significant.

Observation

Table 1
Distribution of patients according to the drug administered

S.N.	Groups	drug administered	No. of cases
1	A	bupivacaine HCL 15 mg (3ml) 0.5% heavy	30
2	B	bupivacaine HCL 15 mg (3ml) 0.5% heavy and tramadol HCL 25 mg (0.5ml)	30
3	C	bupivacaine HCL 15 mg (3ml) 0.5% heavy and Fentanyl citrate 25 µg (0.5ml)	30
Total			90

Table 2
Demographic profile in different groups

Variances	Group A (n=30)	Group B (n=30)	Group C (n=30)
AGE (yrs)	40.35±2.23	41.90±2.55	41.21±2.35
WEIGHT (Kg)	58.3±5.83	59.60±6.70	58.67±5.72
HIGHT (cm)	161.18±3.34	162.80±3.89	162.94±3.94

Table 3
Sex distribution in different groups

Sex	Group A (n=30)	Group B (n=30)	Group C (n=30)	Total
Male	15(50%)	12(40%)	14(46.67%)	41(45.55%)
Female	15(50%)	18(60%)	16(53.33%)	49(54.45%)
Total	30	30	30	90

Table 4
Distribution of patients according to the type of surgery

Department	Group A (n=30)	Group B (n=30)	Group C (n=30)	Total
General surgery	8	10	9	27
Gynaecological surgery	12	7	13	32
Orthopaedic surgery	10	13	8	31
Total	30	30	30	90

Table 5
Mean basal heart rate, systolic blood pressure, diastolic blood pressure & respiratory rate

Parameters	Group A (n=30)	Group B (n=30)	Group C (n=30)
heart rate (1/min)	**84.80**±11.10	**85.56**±13.06	**86.13**±14.47
SBP(mmhg)	**126.98**±13.5	**127.73**±13.2	**125.12**±10.83
DBP(mmhg)	**81.23**±6.51	**79.28**±8.69	**82.81**±9.54
RR(1/min)	**16.23**±1.4	**15.91**±3.02	**16.38**±2.34
Spo_2(%)	**98.22**±1.5	**98.38**±1.18	98.48±1.28

Table 6
Mean time of onset of sensory block

Parameters	Group A (n=30)	Group B (n=30)	Group C (n=30)
Time(sec)	**110.10**±10.02	**110.8**±11.17	**112.87**±9.65

Intergroup comparison

Group A Vs B p = 0.799
Group A Vs C p = 0.279
Group B Vs C p = 0.445

Table 7
Mean time of onset of motor block

Parameters	Group A (n=30)	Group B (n=30)	Group C (n=30)
Time(sec)	**254**±49.22	**250.4**±44.45	**267.3**±42.88

Intergroup comparison

Group A Vs B p = 0.767
Group A Vs C p = 0.269
Group B Vs C p = 0.139

Table 8
Mean duration of motor block

Parameters	Group A (n=30)	Group B (n=30)	Group C (n=30)
Time(hrs)	**3.15**±0.17	**3.20**±0.22	**3.19**±0.11

Intergroup comparison

Group A Vs B p = 0.328
Group A Vs C p = 0.283
Group B Vs C p = 0.787

Table 9
Mean duration of sensory block

Parameters	Group A (n=30)	Group B (n=30)	Group C (n=30)
Time(hrs)	**3.38**±0.21	**4.58**±0.46	**6.86**±0.73

Intergroup comparison

Group A Vs B p < 0.001
Group A Vs C p < 0.0001
Group B Vs C p < 0.0001

Table 10
Effect on pulse rate and mean arterial pressure (MAP)

Interval	Pulse rate			mean arterial pressure (MAP)		
	Group A (n=30)	Group B (n=30)	Group C (n=30)	Group A (n=30)	Group B (n=30)	Group C (n=30)
Baseline	84.80±11.10	85.56±13.05	86.13±14.47	84.05±5.53	84.94±4.08	84.28±5.07
5 min	83.16±8.39	84.56±9.21	83.39±7.16	82.78±4.61	80.30±4.84	80.21±5.665
15 min	88.40±7.67	86.08±9.07	83.07±11.74	82.65±5.41	79.80±3.94	79.68±4.22
30 min	88.76±12.07	88.56±7.03	82.01±11.42	82.25±4.48	79.59±4.38	79.94±4.84
60 min	87.36±11.59	86.40±6.52	82.28±8.49	83.75±4.69	81.23±5.6	81.54±4.96
90 min	86.44±9.74	82.40±6.42	80.76±9.08	83.64±3.58	81.73±4.12	81.86±5.14
120 min	84.96±11.01	79.28±5.94	80.98±7.30	84.12±5.63	82.21±7.4	83.31±4.8
150 min	80.12±10.73	79.12±5.94	81.04±6.76	83.51±5.53	82.93±6.97	83.11±3.71
180 min	80.60±9.99	78.0±5.57	81.58±7.94	83.25±5.22	82.71±7.24	83.19±4.39

Table.11
Effect on respiratory rate and Spo_2

Interval	respiratory rate			Spo_2		
	Group A (n=30)	Group B (n=30)	Group C (n=30)	Group A (n=30)	Group B (n=30)	Group C (n=30)
Baseline	16.23±1.4	15.91±3.02	16.39±2.34	98.22±1.5	98.38±1.18	98.48±1.28
5 min	16.28±1.5	16.12±2.8	16.32±2.23	98.20±1.19	98.54±1.07	98.38±1.19
15 min	16.26±1.4	16.24±3.01	16.61±2.81	98.54±1.07	98.38±1.19	98.20±1.12
30 min	17.01±1.05	16.14±2.9	16.48±2.62	98.36±1.12	98.10±1.09	98.38±1.18
60 min	16.98±1.4	16.28±2.7	16.22±2.01	98.40±1.16	98.42±0.97	97.22±1.15
90 min	16.29±1.6	16.29±2.8	16.00±1.86	97.44±1.28	98.20±1.19	98.01±1.28
120 min	16.59±1.6	16.21±2.6	16.09±1.96	98.21±1.6	98.00±1.94	98.08±1.48
150 min	16.71±1.6	16.16±2.9	16.81±2.46	97.64±1.02	98.86±0.99	98.61±1.89
180 min	16.90±1.4	16.12±2.8	16.97±2.32	98.18±0.90	98.54±1.07	98.38±1.19

DISCUSSION

The present study entitled “A Comparative study of Intrathecal Bupivacaine with Bupivacaine with Bupivacaine-Tramadol and Bupivacaine-Fentanyl for Post-operative Pain Relief in Lower Abdominal and Lower Limb Surgeries” has been carried out in the Department of Anesthesiology, S.S. Medical College and Associated Sanjay Gandhi Memorial Hospital and Gandhi Memorial Hospital, Rewa . This study comprised of 90 cases of ASA grade I and II, of both sexes and age ranging between 18 to 60 years, posted for routine surgeries of lower abdomen and lower limb. These 90 patients were given either of the three sets of intrathecal drugs randomly so that each group comprised 30 patients.

Group A -Bupivacaine HCL 15mg (3ml) 0.5% heavy
Group B -Bupivacaine HCL 15mg (3ml) 0.5% heavy and Tramadol HCL 25mg (0.5ml)
Group C -Bupivacaine HCL 15mg (3ml) 0.5% heavy and Fentanyl citrate 25µg (0.5ml)

J.A. Alhashemi et al (2003)[2] used Bupivacaine 0.5% heavy 3ml with 25mg Tramadol for postoperative pain relief in patients undergoing transurethral resection of prostate (TURP). Harbhej Singh et al (1995)[3] used 25µg Fentanyl with hyperbaric Bupivacaine to study the effect of Fentanyl on sensory Bupivacaine spinal block.

Demographic Date

In the present study mean age was40.35+2.23yrs in Group A, 41.90±2.55 yrs in Group B and 41.21±2.35 yrs in Group C. The mean weight of patients in this study was 58.83±5.83 kg in Group A, 57.60±6.70 kg in Group B and 58.70±5.72kg in Group C. The mean height of patients was 161.94=3.94 cm in group A. 162.80±3.89 cm in group B and 162.94±3.94 cm in group C. All three groups were similar in terms of weight and height (Table No. 2). Similar age, weight and height distribution was also seen in the study of Torres et al (1993)[4], Harbhej Singh et al (1995)[3]. Khusniemi K.S. et al (2000)[5], Susmita Chakraborty et al (2008)[6], S. Goel et al (2003)[7] and B.N. Biswas et al (2002)[8].

Sensory Block

a. Onset of sensory block

In the present study the onset of sensory block was tested by pin-prick method, this has been the commonest method of testing the onset of sensory block. The mean time of onset of sensory block seen in different groups was found to be 110.10±10.02 sec. in Group A, 110.8±11.17 sec in Group B and 112.87±9.65 sec in Group C (Table-6). On intergroup comparison p>0.05 for all the groups which is statistically not significant. This

shows that there is no effect of Tramadol or Fentanyl on onset of sensory block.

Duration of sensory block

In the present study duration of analgesia was estimated from the time of completion of intrathecal injection to the time of first complain of pain by the patient. The mean duration of sensory block was 3.38+0.21, 4.58+0.46 and 6.86+0.75 hrs in Group A, B and C respectively (Table-9). On intergroup comparison the difference were statistically significant for Group A with Group B ($p<0.001$) and highly significant for Group C and Group B with Group C ($P<0.0001$). Though duration of sensory block is prolonged with both Tramadol and Fentanyl, but is more prolonged with Fentanyl. Torres et al (1993)[4] compared the analgesic efficacy of intrathecal Tramadol and Bupivacaine with Fentanyl and Bupivacaine in moderate to severe postoperative pain. They concluded that intrathecal administration of Bupivacaine with Tramadol or Fentanyl prolongs the duration of sensory block was more prolonged in Fentanyl group as compared to the Tramadol group. Harbhej Singh et al (1995)[3] studied the effect of intrathecal Fentanyl on the onset and duration of hyperbaric Bupivacaine induced spinal block. They concluded that Fentanyl 25µg intrathecally prolonged the duration of Bupivacaine induced sensory block. Roussel J.R. and Hindel L (1999)[9] in their study concluded that Fentanyl prolongs post operative analgesia. B.N. Biswas et al (2002)[8] studied the effect of addition of Fentanyl to Bupivacaine to improve the quality of spinal anaesthesia. They conclude that the duration of effective analgesia (time from intrathecal injection to first parenteral analgesic) was increased with addition of Fentanyl. M. Ravishankar et al (2002)[10], A.M. Kaki et al (2003)[11] and Susmita Chakraborty et al (2008)[6], in their respective studies concluded that when Tramadol was added to Bupivacaine it increases the analgesic effect of the spinal block.

Motor Block

In the present study mean time of onset of motor block was 254+49.22, 250+44.45, 267.3+42.88 sec in Group A, B and C respectively (Table-7). On intergroup comparison $p>0.05$ for all groups which is statistically not significant. The mean duration of motor block in the present study was found to be 3.15+0.17, 3.20+0.22 and 3.19+0.11 hrs in Group A, B and C respectively (Table-8). On intergroup comparison it statistically not significant (Group A with Group B, $p>0.05$, Group A with Group C, $P>0.05$, Group B with Group C, $p>0.05$). The results we got were comparable with the result obtained by Torres et al (1993)[4]. They compared the analgesic efficacy of intrathecal Tramadol and Bupivacaine with Fentanyl and Bupivacaine in moderate to severe post operative pain. There was no effect on the time of onset and duration of motor block in any of the group. Harbhej Singh et al (1995)[3] found that there was no significant effect on the onset and duration of motor block by the addition of Fentanyl to hyperbaric Bupivacaine. J.A.Alhashemi et al (2003)[2] and Susmita Chakraborty et al (2008)[6] found no significant change in the onset and duration of motor block by addition of Tramadol to hyperbaric Bupivacaine. Roussel JR and Heindel L (1999)[12] studied the effect of intrathecal Fentanyl on duration of Bupivacaine spinal block. They concluded that Fentanyl does not enhance the onset & duration of motor block. Thus it is quite clear that addition of Tramadol or Fentanyl to Bupivacaine 05.% heavy does not cause any significant change in time of onset and duration of motor block.

Vital Parameters

a. Hemodynamic

The mean pulse rate/min before intrathecal injection was 84.80+11.10, 85.56+13.05, 86.13+14.47 in Group A, Group B and Group respectively. The differences were statistically insignificant ($p>0.05$)(Table-10). The mean arterial pressure (MAP) before intrathecal injection in the present study was 84.05+5.53, 84.94+4.08, 84.28+5.07 mmHg in Group A, Group B and Group C respectively. The differences were statistically insignificant ($p>0.05$), slight fall in the MAP in all the groups were observed when the difference between the baseline value and after giving intrathecal injection at 5th, 15th and 30th minute was compared. This difference was statistically not significant (>0.05). After that there was no significant change in Mean arterial pressure in any of the group. Hypotension is anticipated sequelae after neuraxial block block but the addition of either Tramadol or Fentanyl to bupivacaine has not produced significant difference from the control group. As all the patients in the present study were of ASA grade I and II and were properly preloaded with 15ml/kg of Ringer's Lactate, no episode of moderate or severe hypotension was encountered. Majority of workers who evaluated the hemodynamic effects of intrathecal/epidural Tramadol or Fentanyl have found them safe. Torres et al (1993)[4]. Harbhej Singh et al (1995)[3], M. Ravishankar et al (2002)[10], Sushmita Chakraborty et al (2008)[6] found no significant change in pulse rate and blood pressure in there respective studies. S.Goel et al (2003)[7] studied the effect of Fentanyl with Bupivacaine when given intrathecally for day care surgery found that Fentanyl increased reliability of block with hemodynamic stability. Arora N. et al (2005)[12] reported there was no episodes of bradycardia or hypotension in patients given intrathecal Fentanyl. A.M. Kaki et al (2003)[11] in their study found that there was good hemodynamic stability with intrathecal Tramadol added to Bupivacaine. These observations were similar to the present study.

b. Respiratory Rate

The mean respiratory rate/min before intrathecal injection in this study was 16.23+1.4, 15.91+3.02, 16.38+2.34 in Group A, Group B and Group C respectively (Table-12). The difference between baseline value and after giving intrathecal injection at different time intervals in all the three groups were statistically insignificant ($p>0.005$).These observations were supported by various studies. Torres et al (1993)[4] in there study compared the analgesic efficacy of intrathecal Tramadol with Bupivacaine and Fentanyl with Bupivacaine in moderate

to severe postoperative pain. They found that respiratory rate was lower in Fentanyl group, but there was no respiratory depression (RR<10) intra-operatively as well as post-operatively. B.N.Biswas et al (2002)[8] in their study reported that none of the patient in either group experienced respiratory depression (RR<10/MIN OR SpO2<90%). HiralChavda and Purvi J Mehta (2009)[13]in there study concluded the Fentanyl (25µg) does not cause respiratory depression when administered intrathecally. M.Ravishankar et al (2002)[10], A.M. Kaki et al (2003)[11] and Susmita Chakraborty et al (2008)[6] found that intrathecal Tramadol with hyperbaric Bupivacaine does not cause respiratory depression.

Side Effects

In present study incidence and frequency of side effects and complications were closely monitored in intra-operative as well as post-operative period (Table 13). There was I patient in control Group A, 2 patients each in Group B and C; who had suffered bradycardia, which was effectively treated by i.e. Atropine 0.6mg. There were 2, 3, 3 patients in Group A, B & C respectively, who had hypotension, it was transient and treated by i.v. fluids and i.v.MephentermineSulphate 3mg. Although incidence of hypotension was more with Tramadol and Fentanyl group, none of the patient had moderate to severe hypotension. Nausea and Vomiting was most common in Group B (5 patients), followed by Group C (2 patients) & Group A (1 patient). It was treated with i.v.Pantoprazol 40mg and i.v. Metoclopramide 10mg. Shivering was found in 3 patients in Group A, there were no incidences of Shivering in Group B and Group C. They may be due to the anti shivering effect of Tramadol and Fentanyl. Incidence of sedation was equal in all three groups; 3 patients in every group. There were no incidences of headache, respiratory depression, pruritus or constipation intra-operatively and post-operatively. No incidence of urinary retention could be identified as all patients were catheterized intra-operatively till post-operative period.

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