Section: Anaesthesiology

Research

COMPARISON BETWEEN THE EFFICACY OF INTRATHECAL CLONIDINE AND FENTANYL AS AN ADJUVANT TO HYPERBARIC BUPIVACAINE FOR SPINAL ANAESTHESIA IN LOWER ABDOMINAL SURGERIES

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Abstract

Background: There are many adjuvants used along with bupivacaine for subarachnoid block, but fentanyl and clonidine are commonly used as adjuvant to intrathecal bupivacaine for prolonging both sensory and motor blockade as well as postoperative analgesia in patients undergoing lower abdominal surgeries. **Aim:** To compare the effects between the two adjuvant drugs – fentanyl and clonidine when used with hyperbaric bupivacaine in terms of sensorimotor blockade and postoperative analgesia in patients undergoing lower abdominal surgeries. **Materials and Methods:** Hundred ASA I & II patients posted for lower abdominal surgery were randomly divided into two groups of fifty each and were given 2.5ml of 0.5% hyperbaric bupivacaine with either 30µg of clonidine with 0.3ml normal saline (group BC) or 25µg of fentanyl (group BF) intrathecally, keeping the total volume of drug as 3 ml. The onset and duration of sensory and motor block, sedation score, hemodynamic parameters, total analgesia time and potential side effects were recorded and compared. **Result:** Addition of clonidine to hyperbaric bupivacaine prolongs the duration of sensory and motor blockade and two segment regression as compared to fentanyl. Intrathecal clonidine as an adjuvant also provides prolonged postoperative analgesia while onset of sensorimotor blockade and hemodynamic profiles remains comparable in both the groups, providing satisfactory anesthesia and analgesia. Sedation score is more in clonidine group. **Conclusion:** Addition of clonidine to intrathecal bupivacaine offers longer duration of postoperative analgesia than fentanyl but with higher sedation.

INTRODUCTION

Lower abdominal surgeries are one of the most common surgeries performed daily. These surgeries are preferably performed under regional anesthesia as it is the most convenient anesthetic technique that offers many advantages. Intrathecal anesthesia and epidural anesthesia, being the most popular regional anesthesia.

Hyperbaric Bupivacaine is the most commomly used intrathecal local anesthetics for spinal anesthesia.[1] Adjuvants drugs are usually added to improve the block characteristics of intrathecally administered local anesthetics. The primary aim of our study was to compare the effects between two adjuvant drugs – fentanyl and clonidine when used with hyperbaric bupivacaine in terms of sensorimotor blockade and postoperative analgesia in patients undergoing lower abdominal surgeries. The secondary aim was to compare the hemodynamic parameters and side effects, if any in the two study drugs.

MATERIALS AND METHODS

The proposed study was conducted after obtaining approval from Institutional Ethics committee and written informed consent from all the patients.100 patients belonging to American Society of Anesthesiologists (ASA) I or II between 18 and 65years of age planned for elective lower abdominal surgery were selected for the study. Patients belonging to ASA grade III &IV, patient on medications which interact with local anesthetics and opioids, patients with neurovascular diseases, spine abnormalities were excluded from the study.

The patients were then randomized by computer generated sequentially marked sealed enveloped into two groups of fifty each, and were given 2.5ml of 0.5% hyperbaric bupivacaine with either 30µg of clonidine with 0.3ml normal saline (group BC) or 25µg of fentanyl (group BF) intrathecally, keeping the total volume of drug as 3 ml.

After attaching the routine monitors such as ECG, blood pressure and oxygen saturation, preloading of 10ml/kg was done with ringer lactate.

Subarachnoid block was given under all aseptic precautions, using 25-gauge Quincke's needle in sitting position at the level of L3-4 interspace and depending upon the groups, either 25 µg fentanyl or 30 µg clonidine admixed with 2.5 ml of 0.5% hyperbaric bupivacaine to a total volume of 3ml was injected intrathecally.

Heart rate and blood pressure were recorded initially at baseline and 1minute after drug administration and then at every 5minutes till 20 mins, then at 30 minutes, 1hr, 2hrs, 6^{th} and 12^{th} hour. Any hypotension, MAP<60mmHg and bradycardia (HR<50bpm) was treated with intravenous fluids and if needed injection mephentermine 6 mg iv given in alliquotes and atropine 0.6 mg iv respectively.

Block characteristics were assessed by testing for sensory and motor block. Sensory blockade was monitored with the pin-prick test at 1minute (min) intervals for the first 5 mins, then every 5 mins for 20 mins, until the end of surgery. Observations were recorded as T0 = time of subarachnoid block administration, Ts =onset of sensory block time, Tm = onset of motor block time, Tpsb = peak sensory block time (at the level of T6), Ttsr = time of two segment regression of sensory block, Twmb = time of wearing off of motor block and Tpra = time of first dose of postoperative rescue analgesia, given at VAS Score ≥4.

Residual sensory blockade was monitored and its wearing-off time was noted using two segment sensory regression (sensation to pin-prick gets two dermatomal segments regression). Residual motor blockade was monitored and its wearing off time was noted when patient starts to lift legs against gravity

Modified Bromage scale was used to assess the degree of motor block, at 1min interval for the first 5 mins, then every 2mins for 20 mins until the end of surgery.[2]Bromage score at the beginning and end of surgery was noted.

Any side effects such as nausea, vomiting, shivering, pruritis and sedation were also recorded. Campbell Sedation Score was used to assess the degree of sedation and scoring as 1- wide awake, 2- awake and comfortable, 3-drowsy and difficult to arouse, 4- not arousable.[3] Rescue analgesia in the form of injection paracetamol 1g iv infusion was given and the time of injection of rescue analgesic drug was noted as Tpra.

Statistical Analysis

Parameters were recorded and data collected were analysed using student's t test and Chi square test.The p value was finally determined to evaluate the level of significance. The statistical test was taken as significant at $p < 0.05$ at 5% level of significance; $p < 0.01$ considered significant at 1% significance level and $p < 0.001$ as highly significant.

RESULTS

The demographic profile of patients in the both our study groups was similar with respect to mean age and gender. [Table 1]

In our study, we found that the values obtained at Tpsb, Ttsr, Twmb, and Tpra were statistically significant in between the groups. The mean value of Tpsb of Group BC was 7.19±0.87 minutes and Group BF was 8.23±1.27minutes respectively ($P<0.0001$), the mean value of Ttsr of Group BC was 283.7±34.65 minutes and Group BF was 208.7±25.33 mins respectively. The mean value of Twmb of Group BC was 312.4±30.94 mins and Group BF was 240.6±24.94 mins respectively. The mean value of Tpra of Group BC was336.4±35.44 mins and Group BF was 284.2± 26.43 minutes ($P<0.0001$), recorded at a VAS score ≥4. [Table2].

While in the hemodynamic parameters, Heart rate, there was statistically significant differences in values obtained at 2,6 and12 hrs in between the two groups The readings of Systolic and diastolic BP were significant at 6hrs, while in mean BP , it was significant at 6 and 12 hrs. [Table 3,4,5,6].

The incidence of side effects in both groups are shown in [Table 7]. The side effects that occurred were sedation, nausea, vomiting and shivering.

More sedation was observed in Group BC as compared to Group BF. According to Campbell sedation score, 13 patients were sedated in Group BC in which 5 patients had sedation score of 2 and 8 patients had sedation score of 3.[Table 8]

Only 3 patients were sedated in Group BF with sedation score of 2.

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Table 1: Age distribution (Mean±SD) and Gender (Number and percentage of patients)

VARIABLES	GROUP BC	GROUP BF	p-value
Age(yrs)	46.22±9.67	46.90±10.76	0.7403
Sex(M/F),n(%)	14/36 (28.0/72.0)	20/30 (40.0/60.0)	0.2052

Table 2: Comparison of blockade (onset and regression of sensory and motor block) and analgesic duration (Mean±SD)

Time (minutes)	GROUP BC	GROUP BF	p Value
Ts	1.93±0.55	2.09±0.48	0.1244
Tm	3.58±1.03	4.00±1.23	0.0672
Tpsb	7.19±0.87	8.23±1.27	<0.0001*
Ttsr	283.7±34.65	208.7±25.33	<0.0001*
Twmb	312.4±30.94	240.6±24.94	<0.0001*
Tpra	336.4±35.44	284.2±26.43	<0.0001*

Ts=onset of sensory block time, Tm=onset of motor block time, Tpbs=peak sensory block time at T6 level, Ttsr=two segment regression time, Twmb=wearing of motor block time, Tpra=first dose of postoperative rescue analgesia time.

Table 3: MEAN HEART (Mean ±SD)

Time	GROUP BC	GROUP BF	p Value
0 min	83.88±11.53	83.02±10.66	0.6699
1 min	83.86±11.60	82.48±10.25	0.5299
5min	82.98±11.67	82.02±10.39	0.6639
10min	80.80±11.22	80.14±10.06	0.7575
15min	78.38±10.96	77.92±10.14	0.8280
20min	77.02±11.61	75.28±9.53	0.4147
30min	72.34±10.97	70.60±9.16	0.3914
1hr	70.42±10.41	66.90±9.12	0.0752
2 hrs	71.20±8.22	65.80±9.41	0.0029 *
6 hrs	75.62±10.28	70.26±9.44	0.0078 *
12hrs	77.40±12.11	73.26±9.19	0.0013 *

Table 4: SYSTOLIC BP ((Mean ±SD)

Time	GROUP BC	GROUP BF	p Value
0 min	132.6±21.61	136.56±12.99	0.2695
1 min	134.08±12.15	136.36±13.10	0.3288
5min	125.58±12.86	129.14±13.05	0.1726
10min	113.34±13.00	116.20±12.32	0.2616
15min	103.82±12.76	105.36±10.23	0.5071
20min	98.34±12.40	98.74±11.71	0.8686
30min	98.26±9.80	95.78±11.48	0.2481
1hr	103.42±15.86	102.36±10.01	0.6903
2 hrs	109.92±8.26	107.80±11.87	0.3025
6 hrs	125.3±12.49	119.56±11.51	0.0188 *
12hrs	127.04±15.43	121.6±12.68	0.0570 *

Table 5: DIASTOLIC BP ((Mean ±SD)

Time	GROUP BC	GROUP BF	p Value
0 min	79.08±9.91	81.56±8.86	0.1902
1 min	78.46±9.96	81.24±8.61	0.1386
5min	73.3±10.21	76.50±9.06	0.1006
10min	65.34±9.72	67.40±8.95	0.2730
15min	59.12±9.71	60.1±±7.46	0.5727
20min	56.00±7.97	55.84±7.52	0.9180
30min	55.84±6.84	55.50±7.56	0.8141
1hr	59.88±5.86	58.94±7.37	0.4819
2 hrs	61.84±6.93	60.80±7.62	0.2298
6 hrs	76.74±12.49	70.58±13.44	0.0195*
12hrs	77.12±9.86	72.60±10.01	0.1539

Table 6: MEAN BP ((Mean ±SD)

Time	GROUP BC	GROUP BF	p Value
0 min	97.34±9.54	99.56±8.36	2.220
1 min	96.44±9.49	99.16±8.28	0.720
5min	90.48±9.49	93.7±8.96	0.0871
10min	80.9±9.34	83.26±9.09	0.1293
15min	73.68±9.71	74.6±6.64	0.5815
20min	69.78±8.51	69.88±8.43	0.9530
30min	69.54±6.69	68.56±8.13	0.5120

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1hr	74.72±5.96	73.14±7.44	0.2440
2 hrs	77.6±6.29	75.98±7.48	0.2440
6 hrs	90.82±12.78	85.1±10.30	0.0153*
12hrs	93.54±10.84	88.78±10.06	0.0250 *

Table 7: Side effects

	GROUP BC	GROUP BF
Nausea	4	10
Vomiting	0	2
Shivering	2	7

Table 8: Campbell Sedation score

Sedation Score	GROUP BC (n=50)(%)	GROUP BF (n=50)(%)
2	5 (10)	3 (6)
3	8 (16)	0 (0)

DISCUSSION

Bupivacaine is considered the gold standard long-acting local anesthesia for most regional procedures,[4] especially for intrathecal administration, is well tolerated and provides effective anesthesia for lower abdominal surgeries.[5] Adverse effects associated with the use of high volume of drugs are reduced by using low doses of local anesthetics with the addition of an adjuvant drugs.[6]Intrathecal opioids like fentanyl and tramadol enhance sensory block without prolonging motor and sympathetic block. Among them, fentanyl has rapid onset of action, binds strongly to plasma proteins and potentiates the afferent sensory blockade and facilitates reduction in the dose of local anesthetics.[7]

Intrathecal opioids also produce a well documented synergistic effect, thus intensifying motor and sympathetic blockades, and enable successful anesthesia with the use of a low dose local anesthetic resulting in more stable hemodynamics.[8] However, central neuraxial opioids are known for their side effects such as pruritus, urinary retention and potentially catastrophic delayed respiratory depression, which has led us to compare fentanyl with an otheradjuvant, which would be equally efficacious and devoid of these side effects.[9]

Clonidine is a centrally acting selective partial α2 adrenergic agonist (220:1 α2 to α1) and provides dose-dependent analgesia. Clonidine is known for its synergism with local anesthetics but has side effects such as hypotension, bradycardia and sedation when given at higher dose.

Intrathecal clonidine is demonstrated to potentiate the effect of subarachnoid block as well as reduce the local anesthetic agent requirement. Intrathecal clonidine also offers prolonged postoperative analgesia, reduces shivering associated with subarachnoid block and is devoid of side effects associated with intrathecal opioids.[10]

In our study, we found that both the drugs are effective as an adjuvant to
intrathecal bupivacaine in prolonging the time of first rescue analgesia(Tpra) although it was significantly higher in Group BC (336.4 ± 35.44 minutes) than in Group BF (284.2 ± 26.43 minutes), (p <0.0001). Similar study was conducted by Bajwaetal using 50 µg of clonidine and 25µg of fentanyl with hyperbaric bupivacaine intrathecally and found that duration of analgesia was significantly longer with clonidine than fentanyl.[11]However, the drug concentration used in our study was 30µg clonidine.

Gecaj-Gashi et al,[12]also compared low dose 25µg clonidine in co-administration with 0.5% isobaric bupivacaine 7.5mg intrathecally, with increased regression of motor and sensory block, duration of postoperative analgesia in patient scheduled for transurethral surgical procedures. In our study, duration of peak sensory and weaning of motor blockade and two segment regression was significantly prolonged in Group BC compared to Group BF with statistical significant difference. The duration of postoperative analgesia was also prolonged in Group BC compared to Group BF and was statistically significant [Table2].

Gurpreet Singh et al compared the onset, degree and recovery time of sensory and motor block, the hemodynamic effects and postoperative analgesia using intrathecal bupivacaine alone (group A), bupivacaine along with fentanyl 25µg (group B) and clonidine30µg (group C) undergoing transurethral resection of prostate (TURP) surgeries.[13] Time of the first request of analgesia in Groups A, B and C in postoperative period were 132.50 ± 21.53 mins, 296.00 ± 50.07 mins, and 311.83 ± 65.34 mins respectively. Time of rescue analgesia was later in Groups B and C and was statistically significant as compared to Group A. Group C had mean time of analgesia required even later than in Group B, which was statistically significant**.** These results were comparable and correlated with our study, where Tpra of BF-Group was 284.2 ± 26.43 minutes and BC-Group was
336.4 ± 35.44 minutes which was statistically significant and similar hemodynamic characteristics were noted, but the total volume in our study was of 3ml, while Gurpreet et al had taken total volume of 2.5ml.

Our study is also comparable to study conducted by M B Khezri et al who compared the analgesic

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efficacy of intrathecal clonidine and fentanyl added to bupivacaine for cesarean section in 90 patients who received bupivacaine 10mg combined with 75 µg clonidine (group C), bupivacaine 10 mg combined with 25µg fentanyl (group F) and bupivacaine 10 mg combined with 0.5 ml distilled water (group P), intrathecally.[14] The parameters were noted for the time to first analgesic request, sensory and motor blockade onset time, duration of sensory and motor blockade. The duration of anesthesia in clonidine group (275.10 ± 96.09mins) was longer compared to the placebo (211.73 ±74.80mins) and fentanyl (192.33 ± 30.36mins) groups. This difference between group C versus F (p= 0.006) and P groups (p< 0.001) was significant. Similarly, the mean time to first analgesic request was also longer in group C (519.44 ± 86.25mins) than in groups F (277.88 ± 94.25mins) and P (235.43 ± 22.35 mins). This difference between group C versus F (P < 0.001) and P groups (P < 0.001) was significant. In our study also, clonidine proved to be more effective although the dose of clonidine was lesser (30µg) but with more volume (3ml).

In our study, both the groups had similar results regarding onset of sensoryand motor block, but the duration of analgesia was significantly higher inclonidine group than in fentanyl group. Sedation scores also was more in clonidine group than in fentanyl group [Table 8].This can be compared with study by Shidhaya et al,[15] where duration of analgesia was also significantly higher in clonidine group (497.20 ± 139.78min) than in fentanyl group (416.87 ± 105.67mins), (*P* < 0.05). They reported that intrathecal addition of 25µg fentanyl to bupivacaine provides good analgesia with lesser sedation and concluded that fentanyl is a better option when sedation is not desirable. However intrathecal addition of 60µg clonidine to bupivacaine provided longer duration of postoperative analgesia and more sedation than 25µg of fentanyl and preferred option when sedation is acceptable or required. Our study which used 30µg clonidine has proved to be providing longer duration of analgesia and with similar hemodynamic characteristics with lesser dose compared to the study by Shidhaya et al.

In a study analyzed by Benyamin et al, it was noted that the use of opioid was commonly associated with side effects such as nausea and vomiting, even with low dose fentanyl added to Bupivacaine in spinal anesthesia.[16] Similarly in our study, Group BF exhibited more side effect such as nausea, vomiting as compared with Group BC [Table 7].

Intrathecal fentanyl frequently produces pruritus which is unfortunately difficult to prevent even by prophylactic medication.[17]The incidence of pruritis has been reported to be as high as 52% when 50 mcg fentanylwas used as adjuvant to 0.125% bupivacaine.[18]Few studies had reported high incidence of pruritus in fentanyl group compared to clonidine group.[19]However, in our study, 25µg fentanyl added to 0.5% hyperbaric bupivacaine reported no pruritus.

Bajwa et al,[11]did not observe bradycardia by addition of clonidine

even up to 45µg in 9mg of bupivacaine. Similar hemodynamic stability wasobserved by Agrawal et al while using 12.5 µg and 25 µg of intrathecal fentanyl.[20]

Gurpreet Singh et al,[13] and Sidharth Sabran Routrayet al,[21] in their studies also observed no significant differences in hemodynamic characteristics in the study groups. We also found similar results regarding hemodynamic characterstics[Table 3-6]. Initial fall in mean arterial pressure after spinal anaesthesia can be explained by the sympathetic blockade and vasodilatation. Adequate preloading prevented significant hypotension and bradycardia. Hemodynamic findings have been supported by study conducted by Agarwal et al,[20] who reported that there was no significant difference in fall of systolic blood pressure using clonidine as an adjuvant with bupivacaine. In our study also, no statistically significant differences was found as far as mean blood pressure was concerned.

CONCLUSION

Our study concludes that the addition of clonidine to hyperbaric bupivacaine prolongs the duration of sensory and motor blockade and two-segment regression as compared to fentanyl. Intrathecal clonidine as an adjuvant also provides prolonged postoperative analgesia while onset of sensorimotor blockade and hemodynamic profiles remains comparable in both the groups, providing satisfactory anesthesia and analgesia. Side effects like nausea, vomiting and pruritis were seen more with the addition of fentanyl while sedation was more with clonidine.

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