Effect of Low Dose Fentanyl, Dexmedetomidine and Clonidine in Spinal Anaesthesia

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ABSTRACT

BACKGROUND

This study was conducted to compare the effect of intrathecal hyperbaric bupivacaine with clonidine 30 µg, fentanyl 25 µg and dexmedetomidine 5 µg in lower abdominal surgeries.

METHODS

120 patients belonging to ASA 1 & II, aged between 20 and 50 years, posted for elective lower abdominal surgeries were randomly allocated into three groups with 40 subjects in each group. All patients received intrathecal hyperbaric bupivacaine 0.5%. Subjects in Group-C received clonidine 30 µg; subjects in Group-D received dexmedetomidine 5 µg, and subjects in Group-F received fentanyl 25 µg.

RESULTS

The patients studied across the groups did not vary much with respect to age, sex or height. The onset of motor blockade was earlier in dexmedetomidine group when compared to clonidine and fentanyl group. Duration of sensory blockade was prolonged in dexmedetomidine group when compared to clonidine and fentanyl group. Time duration of motor blockade was prolonged in dexmedetomidine group when compared to clonidine and fentanyl group. The difference of fall in systolic blood pressure, mean arterial pressure, and pulse rate between the groups at different time intervals studied was statistically insignificant and responded to treatment and hence these changes are clinically insignificant. The time of first request of analgesics by the patients was more in dexmedetomidine group when compared to clonidine and fentanyl group. Thus, prolonged duration of analgesia was observed in the dexmedetomidine group. The adverse effects observed in the study were minimal.

CONCLUSIONS

Use of intrathecal dexmedetomidine as an adjuvant to bupivacaine seems it to be a desirable alternative to fentanyl and clonidine for prolonged duration surgical procedures due to its profound intrathecal anaesthetic and analgesic properties combined with minimal side effects.

KEYWORDS

Intrathecal Dexmedetomidine, Bupivacaine, Fentanyl, Clonidine

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BACKGROUND

Spinal anaesthesia is popular and commonly used worldwide. The advantages of an awake patient, minimal drug cost, and rapid patient turnover, have made this a method of choice for many surgical procedures. Hyperbaric bupivacaine is the most commonly used intrathecal local anaesthetic. Various adjuvants have been added to bupivacaine to prolong the duration of block. The present study was performed to compare fentanyl, clonidine and dexmedetomidine in their efficacy as adjuvants to subarachnoid block.

It has been found that many drugs, such as opioids (morphine, fentanyl, and sufentanil), α_2 adrenergic agonists (dexmedetomidine and clonidine), magnesium sulfate, neostigmine, ketamine, and midazolam, can be used as adjuvants for intrathecal local anesthetics to improve the quality of spinal anaesthesia.[1] However, the opioids and α_2 adrenergic agonists are more commonly used as adjuvants in clinical practice. During the intrathecal or epidural administration, fentanyl has a more rapid onset and shorter duration of action than morphine, which has become one of the most commonly used neuraxial opioids. Dex, a selective α_2 adrenergic receptor agonist, has been shown to be a better adjuvant of local anesthetics for neuraxial blocks,[2,3] although clonidine is the first clinically used intrathecal α_2-adrenoreceptor agonist.[4] Our aim is to compare 0.5% hyperbaric bupivacaine 15 mg and fentanyl 25 µg, clonidine 30 µg and dexmedetomidine 5 µg when given intrathecally.

METHODS

It is Perspective randomized double blind 120 patients undergoing elective lower abdominal surgeries under spinal anesthesia at Government General Hospital, Vijayawada attached to Siddhartha Medical College, Vijayawada, were included in the study. The study was approved by the ethics committee

Inclusion Criteria

Patients of 20-50 years of either sex, ASA Grade-I and Grade-II.

Exclusion Criteria

Patients having abnormal spine, severe systemic diseases, metabolic disorders, neurological, congenital and cardiovascular diseases.

These patients were randomly assigned using sealed envelope technique to one of the three groups in a double-blind manner as follows-

1. **Group C:** 40 patients received 3 mL of 15 mg of hyperbaric bupivacaine 0.5% with 0.5 mL of 30 µg of clonidine.
2. **Group D:** 40 patients received 3 mL of 15 mg of hyperbaric bupivacaine 0.5% with 0.5 mL of 5 µg of dexmedetomidine.
3. **Group F:** 40 patients received 3 mL of 15 mg of hyperbaric bupivacaine 0.5% with 0.5 mL of 25 µg of fentanyl.

In all the groups, the total volume administered was made up to 3.5 mL to achieve subarachnoid block.

On the day prior to surgery all the patients were visited and detailed preanesthetic examination including history, clinical examination, systemic examination of cardiovascular, respiratory and central nervous systems and examination of spine for deformity and infection was carried out. The anaesthetic procedure was briefly explained to the patient. An informed written consent was obtained. Patients were kept nil per oral for 6 hours before surgery.

Routine investigations like Haemoglobin, Total Leucocyte Count, Differential Leucocyte Count, ESR, Complete Urine Examination, Random Blood Sugar, Electrocardiogram, Chest X-Ray, Blood Grouping/Typing, Blood Urea, Serum Creatinine were done.

All the patients were premedicated with IM promethazine 25 mg plus pentazocine 30 mg, 1 hr. prior to surgery. Patient's weight and height were also recorded. Once shifted to the operating room, the patient was connected to the routine monitors which included NIBP, SpO_2 and ECG. All emergency resuscitation equipment's like intubation trolley with airways, laryngoscopes, endotracheal tubes along with drugs like atropine, mephentermine and other emergency drugs were kept ready. The anaesthesia machine was also checked along with the oxygen delivery system.

Baseline Pulse Rate, Blood Pressure, Respiratory Rate, SpO_2 were recorded. A wide bore IV access was obtained and secured. All patients were preloaded with 500 mL of Ringer's lactate prior to spinal anaesthesia, and there after 10 mL/min of fluid was administered till the completion of surgery. Additional volume of fluids and vasopressor were given as per need and recorded.

The patients were then put in right lateral position. Under strict aseptic precautions, lumbar puncture was performed by midline approach by using disposable 25G Quincke spinal needle in L_3- L_4 intervertebral space. Assessment of Sensory blockade tested by pin-prick method. The time of onset taken from time of injection of drug into subarachnoid space to loss of pin-prick sensation at T_6 dermatomal level. The duration of sensory blockade was recorded from time of onset to time of return of pin prick sensation to S_1 dermatomal area, testing every 15 mins, postoperatively. After spinal anaesthesia, haemodynamic status was monitored by recording the patient's pulse rate and blood pressure at 0, 5 and every 5 mins up to 30 mins, every 15 mins up to 60 mins and then every 30 mins. Up to 120 mins.

Assessment of Motor Blockade by Bromage scale. The time interval between injections of drug into subarachnoid space, to the patient's inability to lift the straight extended

leg was taken as onset time. The time to achieve maximum motor blockade was noted from time of injection of the drug to maximum degree of motor block.

The duration of motor block was recorded from onset time to time when the patient was able to lift the extended leg, noted every 15 minutes, postoperatively.

Bromage Scale

0 - Free movement of legs and feet, with ability to raise extended leg.
1 - Inability to raise extended leg and knee flexion is decreased but full flexion of feet and ankle is present.
2 - Unable to flex knees, but some flexion of feet and ankle is possible.
3 - Unable to move feet, legs or toes.

The adverse effects like nausea and vomiting, hypotension, respiratory depression, shivering, pruritus, motor weakness and seizures are noted in both groups.

Statistical Analysis

The data was analyzed using one-way analysis of variance (ANOVA). All values were expressed as mean ± standard deviation. P < 0.05 was considered statistically significant. The results were presented in the tables and graphs.

RESULTS

Sex	Group C Clonidine		Group D Dexmedetomidine		Group F Fentanyl		Total	
	No.	%	No.	%	No.	%	No.	%
Male	16	40	15	37.5	17	42.5	48	40
Female	24	60	25	62.5	23	57.5	72	60
Total	40	100	40	100	40	100	120	100
P-Value	> 0.05							
Inference	Not Significant							
Age distribution								
20-29	10	25	4	10	3	7.5	17	14.2
30-39	6	15	10	25	13	32.5	29	24.1
40-50	24	60	26	65	24	60	74	61.7
Total	40	100	40	100	40	100	120	100
Mean +/- SD	40.99 +/- 8.77		41.77 +/- 6.9		41.1 +/-6.1			
P-Value	> 0.05							
Inference	Not Significant							
Height								
150-154	15	37.5	14	35	14	35	43	51.6
155-159	9	22.5	10	25	9	22.5	28	33.6
160-164	2	5	7	17.5	3	7.5	12	14.4
165-170	14	35	9	22.5	14	35	37	44.4
Mean +/- SD	159.1 +/- 6.2						159+/- 6.64	
P-Value	> 0.05							
Inference	Not Significant							
Height								
41-50	7	17.5	10	25	5	12.5	22	26.4
51-60	15	37.5	14	35	10	25	39	46.8
61-70	16	40	14	35	19	47.5	49	58.8
71-80	2	5	2	5	6	15	10	12
Mean +/- SD	60.83 +/- 6.95						58.43 +/- 8.75	
P-Value	> 0.05							
Inference	Not Significant							

Table 1. Demographic Distribution in the Three Groups

The Gender distribution of the patients in Group C, Group D and Group F were comparable. The mean age of the patient in Group C was 40.99 +/- 8.77**,** Group D was 41.77 +/- 7.4 and Group F was 40.8 +/- 5.8. The age distribution in all three groups were comparable.

The Height and Weight of the patients in Group B, Group C and Group D were comparable. Demographic profiles of the patients scheduled for study are comparable.

Onset of Sensory Block (Minutes)	Group C Clonidine		Group D Dexmed-etomidine		Group F Fentanyl		Total	
	No.	%	No.	%	No.	%	No.	%
3	12	30	11	27.5	12	30	35	29.6
4	13	32.5	21	52.5	13	32.5	47	39.7
5 & above	15	37.5	8	20	15	37.5	38	31.7
Mean +/- SD	4.2 +/- 1.2		4.1 +/- 1.1		4.3 +/- 1.1			
P-Value	> 0.05							
Inference	Not Significant							
Onset of motor blockade (minutes)								
3	12	30	24	60	12	30	48	40
4	15	37.5	12	30	17	42.5	44	36.7
5 and above	13	32.5	4	10	11	27.5	28	23.3
Mean +/- SD	6.61 +/- 1.51		5.42 +/- 1.33		6.66 +/- 1.41			
P-Value	< 0.001							
Inference	Highly Significant							

Table 2. Onset of Sensory and Motor Blockade (in Minutes)

The onset of sensory blockade was 4.2 +/- 1.2 minutes in Group C, 4.1 +/- 1.1 in Group D and in Group F was 4.3 +/- 1.1 minutes. The difference between the groups was statistically not significant. The onset of motor blockade was 6.61 +/- 1.51 minutes in Group C, 5.42 +/- 1.33 in group D and in Group F was 6.66 +/- 1.41 minutes. The difference between groups was statistically highly significant and earlier in Group D.

Duration of Sensory Block (Minutes)	Group C Clonidine		Group D Dexmedetomidine		Group F Fentanyl		Total	
	No.	%	No.	%	No.	%	No.	%
230-289	13	32.5	4	10	11	27.5	28	23.3
290-349	25	62.5	18	45	26	65	69	57.5
350-409	2	5	13	32.5	3	7.5	18	15
410-469	0	0	5	12.5	0	0	5	4.2
Mean +/- SD	301 +/- 34.6		342 +/- 44.2		303 +/- 33.34			
P-Value	< 0.001							
Inference	Highly Significant							
Duration of motor blockade (minutes).								
121-180	7	17.5	2	5	7	17.5	16	13.3
181-240	16	40	6	15	13	32.5	35	29.2
241-300	13	32.5	25	62.5	16	40	54	45
301-360	4	10	7	17.5	4	10	15	12.5
361-420	7	17.5	2	5	7	17.5	16	13.3
Mean +/- SD	224 +/- 44.37		270 +/- 44.1		221 +/- 42.1			
P-Value	< 0.001							
Inference	Highly Significant							

Table 3. Duration of Sensory Blockade (in Minutes)

Onset of Pain (Minutes)	Group C Clonidine		Group D Dexmedetomidine		Group F Fentanyl		Total	
	No.	%	No.	%	No.	%	No.	%
141-200	31	77.5	8	20	33	82.5	72	60
201-260	9	22.5	18	45	7	17.5	34	28.33
261-320	0	0	11	27.5	0	0	11	9.2
321-380	0	0	2	5	0	0	2	1.7
381-440	0	0	1	2.5	0	0	1	0.8
Mean +/- SD	191 +/- 23.7		255 +/- 52.2		185 +/- 22.3			
P-Value	< 0.001							
Inference	Highly Significant							

Table 4. Time of First Request Analgesic by Patients in the Three Groups in Minutes.

The time for complete sensory recovery was 301 +/- 34.6 in group C, 342 +/- 44.2 minutes in Group D and in Group F was 303 +/- 33.34 minutes. The duration of sensory blockade was longer in Group D. The difference was statistically highly significant. The time for complete motor recovery was 224 +/- 44.37 in group C, 270 +/- 44.1 minutes in Group D and in Group F was 221 +/- 42.1 minutes. The duration of motor blockade was longer in Group D. The difference was statistically highly significant. The time for first request analgesic by the patient was 191 +/- 23.7 in group C, 255 +/- 52.2 minutes in Group D and in Group F was 185 +/- 22.3 minutes. The time for first request analgesics was longer in Group D. The difference was statistically highly significant. Bradycardia was observed in 3 patients in Group C, 2 patients in Group D and 1 patient in Group F and Vomiting was observed in 1 patient in the Group D and 2 patients in the Group F without any significant difference.

Side Effects	Group C Clonidine		Group D Dexmedetomidine		Group F Fentanyl		Total	
	No.	%	No.	%	No.	%	No.	%
Bradycardia	3	7.5	2	5	1	2.50%	5	5
Vomiting	0	0	1	2.5	2	5.00%	3	2.5
No Side Effects	37	92.5	37	92.5	37	92.50%	112	92.5
df				4				
P-Value				> 0.05				
Inference				Not Significant				

Table 5. Incidence of Side Effects

Vaso-pressors	Group C Clonidine		Group D Dexmedetomidine		Group F Fentanyl		Total	
	No.	%	No.	%	No.	%	No.	%
Absent	16	40	18	45	17	42.5	51	42.5
Present	24	60	22	55	23	57.5	69	57.5
df				2				
P-Value				> 0.05				
Inference				Not Significant				
No. of times of Vasopressors								
1	18	85.7	17	89.5	17	89.5	52	88.1
2	3	14.3	2	10.5	2	10.5	7	11.9
Total	21		19		19		59	
df				2				
P-Value				> 0.05				
Inference				Not Significant				

Table 6. Requirement of Vasopressors

Incidence of hypotension and requirement of mephentermine with comparable in all the groups with no significant difference among them. The distribution of Mephentermine aliquots (1 dose= 6 mg) was slightly higher in the clonidine group but the difference was not statistically significant. After intrathecal bupivacaine with respective drug was given there was invariable fall in systolic blood pressure (SBP) in all three groups between first 15 to 20 minutes, followed by a gradual recovery. The difference of fall in SBP between the groups at different time intervals studied was statistically insignificant (p>0.05).

In the first 15 min. the drop in diastolic pressure in Group C and Group F is more than in Group D. The difference is statistically significant. (p<0.05). The difference between the pulse rates in three groups was statistically not significant. (p>0.05).

DISCUSSION

Our study compared three drugs fentanyl, clonidine and dexmedetomidine as adjuvants to spinal bupivacaine to studies of other investigators who have compared dexmedetomidine with either one of the adjuvants only. The results of our study show that supplementation of spinal bupivacaine with 5 µg dexmedetomidine significantly prolonged both sensory and motor block compared with intrathecal 25 µg fentanyl and 30 µg clonidine. Quality of analgesia significantly improved with use of dexmedetomidine as an adjuvant when compared to groups using fentanyl and clonidine.

The patients studied across the groups did not vary much with respect to age, weight or height. The types of surgeries performed were almost identical in all the groups. These parameters were kept identical in all the groups to avoid variations in the intraoperative and postoperative outcome of the patients.

The onset of sensory blockade was 4.2 +/- 1.2 minutes in Group C, 4.1 +/- 1.1 in Group D and in Group F was 4.3 +/- 1.1 minutes. The difference between the groups was statistically not significant These findings were in concordance with the results of Kanazi et al.,[5] when comparing 3 µg of dexmedetomidine with 30 µg of clonidine and Gupta et al.,[6] (2011) on comparison of 5 µg dexmedetomidine with 25 µg fentanyl when used as adjuvants to isobaric and hyperbaric bupivacaine, respectively.

The onset of motor blockade was 6.61 +/- 1.51 minutes in Group C, 5.42 +/- 1.33 in group D and in Group F was 6.66 +/- 1.41 minutes. The difference between groups was statistically highly significant and earlier in Group D. G. E. Kanazi, M. T. Aouad et al[5](2006) found that the supplementation of bupivacaine spinal block with a low dose of intrathecal dexmedetomidine or clonidine produces a significantly shorter onset of motor block. Gecaj-Gashi A et al [7](2012) conducted prospective, double-blinded study to investigate the effects of clonidine in co-administration with bupivacaine during spinal anaesthesia, regarding the onset and regression of motor and sensory block, postoperative analgesia and possible side effects.

The time for complete sensory recovery was 301 +/- 34.6 in group C, 342 +/- 44.2 minutes in Group D and in Group F was 303 +/- 33.34 minutes. The duration of sensory blockade was longer in Group D. The difference was statistically highly significant. The duration of sensory blockade was longer in Group D. The difference was statistically highly significant. This shows addition of dexmedetomidine to intrathecal bupivacaine increases the duration of sensory blockade more than that with clonidine and fentanyl. Both clonidine and fentanyl were however comparable producing almost similar duration of sensory blockade.

The time for complete motor recovery was 224 +/- 44.37 in group C, 270 +/- 44.1 minutes in Group D and in Group F was 221 +/- 42.1 minutes. The duration of motor blockade was longer in Group D. The difference was statistically highly significant. This shows addition of dexmedetomidine to intrathecal bupivacaine increases the duration of motor

blockade more than that with clonidine and fentanyl. G. E. Kanazi, M. T. Aouad et al[5] (2006) conducted a double-blind study on effect of intrathecal clonidine and dexmedetomidine, in 60 patients undergoing transurethral resection of prostate or bladder tumour under spinal anaesthesia.

Gupta R, Verma R Bogra J, et al.[6] (2011) studied as Patients in dexmedetomidine group (D) had a significantly longer sensory and motor block time than patients in fentanyl group (F). The mean time of sensory regression to S1 was 476±23 min in group D and 187±12 min in group F (P<0.001). The regression time of motor block to reach modified Bromage 0 was 421±21 min in group D and 149±18 min in group F (P<0.001). They concluded that Intrathecal dexmedetomidine is associated with prolonged motor and sensory block, hemodynamic stability, and reduced demand for rescue analgesics in 24 hrs as compared to fentanyl. Gecaj-Gashi A et al[7] (2012) concluded that the intrathecal application of clonidine in combination with bupivacaine improves the duration and quality of spinal anaesthesia.

Gecaj-Gashi A et al[7] (2012) conducted prospective, double-blinded study to investigate the effects of clonidine in co-administration with bupivacaine during spinal anaesthesia, regarding the onset and regression of motor and sensory block, postoperative analgesia and possible side effects. They concluded that the intrathecal application of clonidine in combination with bupivacaine improves the duration and quality of spinal anaesthesia and also provides longer duration of postoperative analgesia.

Similarly, significantly improved analgesic efficacy was seen by Gupta et al.,[3] on comparison of dexmedetomidine and fentanyl as intrathecal adjuvants (P < 0.001).

Al-Mustafa et al,[8] observed dose dependent prolongation of motor and sensory blockade with reduced analgesic requirement with increasing dosages of intrathecal dexmedetomidine (5, 10, and 15 µg).

Regarding Haemodynamic stability, in the present study, the incidence of hypotension and requirement of mephentermine with comparable in all the groups with no significant difference among them. Hypotension was corrected by administration of injection mephentermine 6 mg IV in incremental doses, giving IV fluids and raising the foot end side of the operating table to facilitate venous return. The distribution of Mephentermine aliquots (1 dose= 6 mg) was slightly higher in the clonidine group but the difference was not statistically significant. In the first 15 min. the drop-in mean arterial pressure in bupivacaine + clonidine is more than bupivacaine + dexmedetomidine group and the difference is statistically significant. Bradycardia was observed in 3 patients in Group C, 2 patient in Group D and 1 patient in Group F. A. M. El-Hennawy, A. M. Abd-Elwahab et al (2009)[9] they concluded that addition of dexmedetomidine or clonidine to caudal bupivacaine significantly promoted analgesia in children and no significant difference was observed in incidence of hemodynamic changes or side effects.

The most significant Side effects reported about the use of intrathecal α2 adrenoreceptor agonists are bradycardia and hypotension. In the present study, these side effects were not significant probably because we used small doses of intrathecal dexmedetomidine, clonidine, and fentanyl with high dose local anaesthetic. These doses of adjuvants used in this study did not affect the near maximal sympatholysis caused by local anaesthetics.

Vomiting was observed in 1 patient in the Group D and 2 patients in the Group F without any significant difference. Respiratory depression is one of the major side effect of intrathecal opioids. None of our patients experienced respiratory depression and maintained SpO_2 of 98-100% in all the groups. Pruritus is a frequent complication (49-100%) of intrathecal fentanyl but it was not observed in the present study. Buvanendran et al[10] found that addition of small dose of bupivacaine to intrathecal fentanyl reduces the incidence of pruritis from 95% to 36%, on all parts of body.

CONCLUSIONS

Addition of dexmedetomidine to intrathecal bupivacaine will prolong the duration of sensory and motor blockade when compared to clonidine and fentanyl. Onset of motor blockade is earlier with dexmedetomidine. Dexmedetomidine provides prolonged postoperative analgesia. All the three drugs provide stable haemodynamics. There are no significant side effects by adding clonidine, dexmedetomidine or fentanyl.

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REFERENCES

[1] Marri SR. Adjuvant agents in regional anaesthesia. Anaesthesia and Intensive Care Medicine 2012;13(11):559-562.
[2] Zhang C, Li C, Pirrone M, et al. Comparison of dexmedetomidine and clonidine as adjuvants to local anesthetics for intrathecal anesthesia: a meta-analysis of randomized controlled trials. J Clin Pharmacol 2016;56(7):827-834.
[3] Gupta R, Bogra J, Verma R, et al. Dexmedetomidine as an intrathecal adjuvant for postoperative analgesia. Indian J Anaesth 2011;55(4):347-351.
[4] Owen MD, Ozsaraç O, Sahin S, et al. Low-dose clonidine and neostigmine prolong the duration of intrathecal bupivacaine-fentanyl for labor analgesia. Anesthesiology 2000;92(2):361-366.
[5] Kanazi GE, Aouad MT, Jabbour-Khoury SI, et al. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anesthesiol Scand 2006;50(2):222-227.
[6] Gupta R, Bogra J, Verma R, et al. Dexmedetomidine as an intrathecal adjuvant for postoperative analgesia. Indian J Anaesth 2011;55(4):347-351.

[7] Gecaj-Gashi A, Terziqi H, Pervorfi T, et al. Intrathecal clonidine added to small-dose bupivacaine prolongs postoperative analgesia in patients undergoing transurethral surgery. Can Urol Assoc J 2012;6(1):25-29.
[8] Al-Mustafa MM, Badran IZ, Abu-Ali HM, et al. Intravenous dexemedetomidine prolongs bupivacaine spinal analgesia. Middle East J Anesth 2009;20(2):225-31.
[9] El-Hennawy AM, Abd-Elwahab AM, Abd-Elmaksoud AM, et al. Addition of clonidine or dexmedetomidine to bupivacaine prolongs caudal analgesia in children. Br J Anaesth 2009;103(2):268-274.
[10] Buvanendran AL, Newman M, McCarthy RJ, et al. Intrathecal bupivacaine reduces pruritus and prolongs duration of fentanyl analgesia during labor: a prospective randomized controlled trial. Anaesth Analg 1988;87(6):1309-1315.