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A Comparison between Three Different Doses of Intrathecal Dexmedetomidine Added To Hyperbaric Bupivacaine for Infra Umbilical Surgeries

[1]Dr. V. A. Sabapathy Appavoo, [2]Dr. B. Arun Kumar, [3]Dr. P. Naveena, [4]Dr. Mohammed Jassim
[1]Professor, [2]Associate Professor, [3]Assistant Professor, [4]Postgraduate,
Department of Anesthesia & Critical Care, Vinayaka Missions Kirupananda Variyar Medical College & Hospital, Vinayaka Missions Research Foundation deemed to Be University, Salem, Tamil Nadu, India

***Corresponding Author:**
Dr. V. A. Sabapathy Appavoo
Professor, Department of Anesthesia & Critical Care, Vinayaka Missions Kirupananda Variyar Medical College & Hospital, Vinayaka Missions Research Foundation deemed to Be University, Salem, Tamil Nadu, India

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Abstract

Background: A common problem during lower abdominal surgeries under spinal anesthesia is visceral pain, nausea, and vomiting. The addition of fentanyl to hyperbaric bupivacaine improves the quality of intraoperative and early postoperative subarachnoid blocks. The addition of opioids to local anesthetic solutions has disadvantages, such as pruritus and respiratory depression. Dexmedetomidine, a new highly selective α2-agonist, is under evaluation as a neuraxial adjuvant as it provides stable hemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects.

Aim And Objectives: To compare the effects of 3 different doses of intrathecal dexmedetomidine added to hyperbaric bupivacaine for infra umbilical surgeries(Unilateral inguinal hernia and Vaginal Hysterectomies) concerning 1. The onset of sensory and motor blockade, 2. Duration of sensory and motor blockade, 3. Hemodynamic effects, 4. Duration of postoperative analgesia, 5. Post-operative sedation.

Materials And Methods: This was a randomized, prospective, parallel-group, a double-blinded study conducted in Vinayaka Missions Kirupananda Variyar Medical College, a Tertiary Care Hospital in Salem in 2019 Sample size: Sixty patients were studied the patients were randomly allocated into three groups. 1. Group A (n=20), 2. Group B (n=20), 3. Group C (n=20). Intervention: Spinal administration of the drug mixture 1. Group A (n=20) – 0.5% hyperbaric bupivacaine 2.4ml (12mg) + dexmedetomidine 5 µg in 0.6 ml normal saline. 2. Group B (n=20) – 0.5% hyperbaric bupivacaine 2.4ml (12mg) + dexmedetomidine 10 µg in 0.6 ml normal saline. 3. Group C (n=20) – 0.5% hyperbaric bupivacaine 2.4ml (12mg) + dexmedetomidine 15 µg in 0.6 ml normal saline. Masking: The anesthesiologist who administered the drug and the observer were blinded to the study. Sterile syringes containing 3.0 ml of the total volume of the drug were loaded by another anesthesiologist not participating in the study.

Results: The differences between them were interpreted by the Post hoc test of Bonferroni. Similarly, the onset time for sensory blocks and motor blocks were compared between groups by ANOVA. The intra and post-operative pulse rates, SBP, MAP, and SPO2 at different intervals were compared between groups by ANOVA and interpreted the difference by a Post hoc test of Bonferroni. The sensory level and sedation score between the three groups were analyzed and interpreted by $\chi 2$ test (Chi-square)

Conclusion: Intrathecal dexmedetomidine added to bupivacaine for lower abdominal surgeries, has a dose-dependent effect on the sensory and motor blockade, with earlier onset and increased duration of the blockade and prolonged postoperative analgesia, better level of sedation and stable hemodynamics

Keywords: Three Different Doses of Intrathecal Dexmedetomidine; Hyperbaric Bupivacaine

Introduction

Spinal anesthesia using local anesthesia is associated with a relatively short duration of action and hence early analgesic intervention is needed in the postoperative period. A common problem during infra umbilical surgery under spinal anesthesia is visceral pain, nausea, and vomiting. [1]Adjuvants are added to improve the quality, accelerate the onset of action, and also overcome the problems which occur during spinal analgesia. Adrenaline was the first spinal adjuvant used.[2] Adrenaline reduces its toxicity but does not greatly prolong its effect. Various adjuvants like morphine, fentanyl, sufentanil, clonidine, midazolam, ketamine, neostigmine, sodabicarbonate were added to local anesthetics and the latest inclusion is dexmedetomidine. Adjuvants are administered by various routes like an epidural, intrathecal and intravenous. In our study adjuvant is added to local anesthetic through intrathecal route . Alpha2 adrenergic receptor agonists like dexmedetomidine gain the focus of interest for their sedative, analgesic, perioperative sympatholytic, and hemodynamic stabilizing properties.[3] Dexmedetomidine is a new highly selective drug among the alpha 2 adrenergic receptor agonist. It has-beens approved by food and drugs administration for short-term sedation for mechanically ventilated ICU patients. No neurological defects have been reported to date in both human and animal studies during intrathecal use. [4,5]

Materials And Methods

This was a randomized, prospective, parallel-group, a double-blinded study conducted in Vinayaka Missions Kirupananda Variyar Medical College, a Tertiary Care Hospital in Salem in 2019 Sample size: Sixty patients were studied the patients were randomly allocated into three groups. 1. Group A (n=20), 2. Group B (n=20), 3. Group C (n=20). Intervention: Spinal administration of the drug mixture 1. Group A (n=20) – 0.5% hyperbaric bupivacaine 2.4ml (12mg) + dexmedetomidine 5 µg in 0.6 ml normal saline. 2. Group B (n=20) – 0.5% hyperbaric bupivacaine 2.4ml (12mg) + dexmedetomidine 10 µg in 0.6 ml normal saline. 3. Group C (n=20) – 0.5% hyperbaric bupivacaine 2.4ml (12mg) + dexmedetomidine 15 µg in 0.6 ml normal saline. Masking: The anesthesiologist who administered the drug and the observer were blinded to the study. Sterile syringes containing 3.0 ml of the total volume of the drug were loaded by another anesthesiologist not participating in the study.

Inclusion Criteria: Age between 18-60 years of both sex.ASA I and II patients.Elective surgeries(Inguinal herniorrhaphy and Vaginal hysterectomies)

Exclusion Criteria: Known hypersensitivity to any of study drugs.Known contraindication to Regional Anesthesia.Known or suspected coagulopathy.Renal disorders.Hypertension, IHD, Heart blocks, Arrhythmias, Cardiac valvular abnormalities.Patients on β blockers, Patients on any long term analgesic therapy, Patient on medications known to interact with study drugs. The anesthesiologist who administered the drug and the observer were blinded to the study. Sterile syringes containing 3.0 ml of the total volume of the drug were loaded by another anesthesiologist not participating in the study. The intraoperative monitoring and postoperative observation were done by the same anesthesiologist who administered the drug but was unaware of the content of the syringes. Emergency drugs and equipment were kept ready. Pre-loading did with 20 ml/kg of intravenous infusion of Ringer lactate. Monitors were connected to the patients and baseline values of heart rate, systolic, diastolic, mean arterial pressure, oxygen saturation was noted. Pulse rate, systolic blood pressure, mean blood pressure, diastolic blood pressure, respiratory rate, SPO2 were recorded before starting the procedure and thereafter 5, 10, 15, 20, mins interval till the end of the surgery and thereafter at hourly second and fourth hourly interval till 24 hours. Hypotension was defined as a systolic blood pressure less than 90mm Hg or a decrease in the MAP below 20%of the baseline value. Hypotension, if any occurred was treated with Inj.Ephedrine(6mg) incremental boluses.

Statistical Analysis:

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The statistical procedures were performed by the statistical package IBM SPSS statistics - 20. The P - values less than 0.05 (P<0.05) were treated as significant in two tail conditions. The Randomization of three groups was done by matching their ages, demographic factors, and hemodynamic factors such as pulse rate, SBP, MAP SPO2, and duration of surgery by ANOVA (Analysis of Variance). The differences between them were interpreted by the Post hoc test of Bonferroni. Similarly, the onset time for sensory blocks and motor blocks were compared between groups by ANOVA. The intra and post-operative pulse rates, SBP, MAP, and SPO2 at different intervals were compared between groups by ANOVA and interpreted the difference by a Post hoc test of Bonferroni. The sensory level and sedation score between the three groups were analyzed and interpreted by $\chi 2$ test (Chi-square). The duration of analgesia between the groups was analyzed and interpreted by Kaplan- Mayer Survival Function.

Results:

Randomization by group matching:

Table-1 Matching Of Three Groups According To Their Age.

Variables	Group	n	Mean	SD	ANOVA 'F'	df	Significance
Age	A	20	44.4	10.7	0.249	2, 57	P>0.05
	B	20	46.0	5.6			
	C	20	44.4	8.1			

Table :1 The three groups were matched according to their age for randomization and found that there was no difference between the mean ages between them (44.4 ± 10.7 ≈46.0±5.6 ≈ 44.4±8.1 and P>0.05).

Table-2:Matching Of Three Groups According To Their Preoperative Hemodynamic Characteristics And Duration Of Surgery

Variables	Group	n	Mean	SD	ANOVA 'F'	df	Significance
Pre Pulse rate	A	20	82.2	4.4	2.015	2, 57	.143
	B	20	85.7	7.3			
	C	20	82.4	6.6			
Pre SBP	A	20	120.5	10.9	1.610	2, 57	.209
	B	20	119.9	10.1			
	C	20	125.4	10.7			

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Pre MAP	A	20	91.1	6.9	0.620	2, 57	.541
	B	20	89.8	8.1			
	C	20	92.6	9.1			
Pre SPO2	A	20	99.8	0.4	2.375	2, 57	.102
	B	20	99.8	0.4			
	C	20	100.0	0.0			
DOS	A	20	97.6	34.1	0.620	2, 57	.542
	B	20	100.9	30.3			
	C	20	108.1	26.1			

Table – 2 shows the hemodynamic variables and the duration of surgery of three groups. The mean pre-op pulse rate, SBP, MAP, SPO2, and duration of surgery were matched, and found that no significant differences were observed between the three groups (P>0.05).

Table – 3: Comparison Of Onset Of Blockade Between Groups

Block	Groups	N	Mean (Sec.)	SD	ANOVA 'F'	df	Sig (P)
OTSB	A	20	226.1	28.7	8.903	2, 57	.000
	B	20	206.8	14.9			
	C	20	197.2	20.2			
OTMB	A	20	233.0	23.3	31.733	2, 57	.000
	B	20	228.2	16.8			
	C	20	190.4	14.2			

Table – 3 shows the comparison of onset of sensory and motor blockade between the three groups. The mean onset time of the A group was significantly higher than the other two groups B&C (A>B&C; 226.1±28.7>206.8±20.2&197.2±14.9 and P<0.05). The mean values of the B& C groups were approximately equal (206.8±20.2≈197.2±14.9 and P>0.05). The mean onset time of motor blockade of the C group was significantly lower than the other two groups (190.4±14.2< 233.0±23.3 & 228.2±16.8 and P<.001). The onset

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time for a motor block of the other two groups namely A and B were not significant (233.0±23.3 ≈ 228.2±16.8 and P>0.05).

Table 4: Level Of Blockade: Comparison Of Maximum Sensory Levels Of Three Groups

Sensory level	A	B	C	Total	$\chi 2$	df	Sig
T4	0	1	8	9	25.046	6	.000
T6	5	5	7	17			
T7	2	6	4	12			
T8	13	8	1	22			
Total	20	20	20	60			

Table 4. The highest sensory level achieved for the A group was T6 and the C group was T4. Among the A&B group subjects, 65% and 40% were associated with T8 sensory level, and among the C group subjects, 40% were associated with T4 sensory level. The above levels were statistically very highly significant (P<0.001).

Table-5.Comparison Of Pulse Rate Between Groups At Different Time Intervals

Pulse rate	Group	n	Mean	SD	F	Df	Sig (P)
5 Minutes	A	20	79.9	3.7	0.481	2, 57	.621
	B	20	81.8	6.4			
	C	20	80.3	8.3			
10 Minutes	A	20	78.3	3.2	1.619	2, 57	.207
	B	20	82.3	7.6			
	C	20	78.5	10.8			
15 Minutes	A	20	76.6	3.4	2.872	2, 57	.065
	B	20	83.9	11.7			
	C	20	78.0	12.7			
	A	20	78.1	4.5			

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30 Minutes	B	20	81.2	9.8	1.345	2, 57	.269
	C	20	76.5	11.9			
1 Hour	A	20	75.8	4.2	1.477	2, 57	.237
	B	20	80.7	9.9			
	C	20	77.1	12.0			
2 Hours	A	20	75.6	4.1	2.825	2, 57	.068
	B	20	81.7	8.3			
	C	20	76.9	11.4			
3 Hours	A	20	75.7	4.1	2.428	2, 57	.097
	B	20	81.4	6.8			
	C	20	77.9	11.8			
8 Hours	A	20	76.5	6.1	1.368	2, 57	.263
	B	20	81.2	8.7			
	C	20	78.3	11.4			
12 Hours	A	20	77.3	5.7	1.472	2, 57	.238
	B	20	81.8	8.6			
	C	20	79.2	10.2			
18 Hours	A	20	79.1	5.0	0.640	2, 57	.531
	B	20	82.0	8.6			
	C	20	79.6	11.1			
24 Hours	A	20	79.7	6.2	0.342	2, 57	.712
	B	20	82.0	8.7			

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	C	20	80.6	10.9			

Table:5 The Pulse rates at different intervals such as at 5,10,15,30 minutes, 1, 2, 3,8,12, 18, and 24 hours are shown in the above Table-5. The mean pulse rates at the above different times between the three groups are not significantly different (P>0.05).

Table-6 Comparison Of Sbp Between Groups At Different Time Interval

SBP	Group	n	Mean	SD	F	df	Sig (P)
5 Minutes	A	20	111.5	10.3	1.723	2, 57	.188
	B	20	110.4	9.4			
	C	20	118.7	22.5			
10 Minutes	A	20	107.0	9.2	2.842	2, 57	.067
	B	20	106.5	7.4			
	C	20	113.8	14.5			
15 Minutes	A	20	102.0	9.5	1.515	2, 57	.228
	B	20	102.5	8.5			
	C	20	107.8	15.6			
30 Minutes	A	20	104.0	9.9	3.044	2, 57	.055
	B	20	104.8	9.3			
	C	20	113.1	17.7			
1 Hour	A	20	107.1	15.4	0.073	2, 57	.930
	B	20	108.3	15.1			
	C	20	108.8	12.7			
2 Hours	A	20	111.3	14.8	0.157	2, 57	.855
	B	20	112.3	14.1			
	C	20	109.9	11.6			
3 Hours	A	20	111.3	14.8	0.046	2, 57	.955
	B	20	112.5	14.4			
	C	20	112.6	16.1			
8 Hours	A	20	107.5	7.8	0.084	2, 57	.919
	B	20	108.5	8.1			

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	C	20	107.8	7.7			
12 Hours	A	20	109.1	9.5	0.199	2, 57	.820
	B	20	109.7	9.7			
	C	20	108.0	6.1			
18 Hours	A	20	109.1	9.5	0.233	2, 57	.793
	B	20	109.8	9.7			
	C	20	111.0	7.1			
24 Hours	A	20	108.8	9.6	0.597	2, 57	.554
	B	20	109.5	10.5			
	C	20	112.0	8.9			

Table:6 The SBP at different intervals such as at 5,10,15,30 minutes, 1, 2, 3,8,12, 18, and 24 hours are shown in the above Table The mean SBP at the above different times between the three groups are not significantly different (P>0.05).

Table-7. Comparison Of Spo2 Between Groups At Different Time Intervals

SPO2	Group	n	Mean	SD	F	df	Sig (P)
5 Minutes	A	20	99.5	0.5	1.354	2, 57	.266
	B	20	99.4	0.6			
	C	20	99.2	0.5			
10 Minutes	A	20	98.8	0.5	2.146	2, 57	.126
	B	20	99.0	0.6			
	C	20	99.2	0.5			
15 Minutes	A	20	98.9	0.6	2.678	2, 57	.077
	B	20	99.0	0.6			
	C	20	99.3	0.4			
30 Minutes	A	20	99.6	0.5	1.004	2, 57	.373
	B	20	99.8	0.3			
	C	20	99.8	0.4			
1 Hour	A	20	99.8	0.4	0.377	2, 57	.687
	B	20	99.9	0.3			

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	C	20	99.8	0.3			
2 Hours	A	20	99.8	0.3	0.138	2, 57	.872
	B	20	99.9	0.3			
	C	20	99.8	0.3			
3 Hours	A	20	99.9	0.2	1.000	2, 57	.374
	B	20	100.0	0.0			
	C	20	100.0	0.0			
8 Hours	A	20	100.0	0.0	1.000	2, 57	.374
	B	20	99.9	0.2			
	C	20	100.0	0.0			
12 Hours	A	20	99.9	0.2	1.000	2, 57	.374
	B	20	100.0	0.0			
	C	20	100.0	0.0			
18 Hours	A	20	99.9	0.2	0.500	2, 57	.609
	B	20	99.9	0.2			
	C	20	100.0	0.0			
24 Hours	A	20	99.90	0.2	1.000	2, 57	.374
	B	20	100.0	0.0			
	C	20	100.0	0.0			

Table:7 The SPO2 at different intervals such as at 5,10,15,30 minutes, 1, 2, 3,8,12, 18, and 24 hours are shown in the above Table-8. The mean SPO2 at the above different times between the three groups is not significantly different (P>0.05).

Table – 8 Comparison Of Duration Of Sensory And Motor Blocks Between Groups.

Block	Groups	N	Mean (min.)	SD	ANOV A 'F'	df	Sig (P)
DSB	A	20	241.0	48.9	19.371	2, 57	.000
	B	20	290.0	56.2			
	C	20	341.5	47.6			
	A	20	260.6	41.5	52.839		

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DMB	B	20	318.0	31.0		2, 57	. 000
	C	20	362.5	16.5			

Table -8. The duration of the sensory block of the C group was significantly longer than the B and B group was significantly longer than the A group (341.5±47.6>290±56.2>241.0 ±48.9 and P<0.001). Similarly the duration of the motor block of the C group was significantly longer than B and the B group was significantly longer than the A group (362.5±16.5>318.0 ±31.0>260.6±41.5 and P<0.001).

Discussion

Recent researches have revealed that the administration of an α2- agonist in the center-neuraxial blockade produces prolonged postoperative pain relief without undue sedation. This effect is due to the sparing of supraspinal CNS sites from excessive drug exposure, resulting in analgesia without heavy sedation. [6]The mechanism by which intrathecal α2-adrenergic agonists prolong the motor and sensory block of local anesthetics is still not clearly understood. Intrathecal α2-adrenergic agonists produce analgesia by depressing the release of C-fiber transmitters and by hyperpolarization of postsynaptic dorsal horn neurons.[7] This anti-nociceptive effect may explain the prolongation of the sensory block when added to spinal anesthetics. The prolongation of the motor block of spinal anesthetics may result from the binding of α2-adrenergic agonists to motor neurons in the dorsal horn. Most of the clinical experience gained in the use of intrathecal α2- adrenoceptor agonists have been described with clonidine, which has a potent synergistic effect with local anesthetics.[8] There is only a few research available using a combination of intrathecal dexmedetomidine and local anesthetics. The dose of epidural/ caudal dexmedetomidine reported is in the range of 1.5 - 2 µg/kg. Compared with clonidine, dexmedetomidine has 10 times higher receptor binding affinity. [10]Extrapolations led to the calculation of an equipotent dose of intra-ethically administered dexmedetomidine. Several clinical studies have established that intrathecal clonidine increases the duration of the sensory and motor spinal block when added to spinal local anesthetics and this effect of clonidine is dose-dependent.[11] Doses of more than 75 µg are accompanied by excessive sedation, hypotension, and bradycardia. Intrathecal dexmedetomidine up to 10µg added to local anesthetics has not produced any major adverse effects during the studies conducted by these authors discussed above.[12] Greene NM et al, who pioneered using dexmedetomidine in humans for spinal anesthesia, hypothesized that intrathecal dexmedetomidine 3 µg or clonidine 30 µg would be equipotent and would produce a similar effect on the characteristics of bupivacaine spinal anesthesia. These conclusions were arrived, pondering over previous animal studies using intrathecal dexmedetomidine. The authors added a low dose of 3 µg of dexmedetomidine or 30 µg of clonidine to 12 mg of intrathecal bupivacaine. They found no significant difference between the groups concerning blockade characteristics, analgesia, and sedation. They confirmed their hypothesis that the intrathecal doses of dexmedetomidine and clonidine used in the study are equipotent.[13] Gupta R et.al compared 10µg of intrathecal dexmedetomidine to magnesium sulfate as adjuvants to bupivacaine and concluded that dexmedetomidine provided earlier onset and prolonged duration of sensory and motor blockade, without any significant hemodynamic alterations [14].In the present study, we observed that the onset time of sensory and motor blockade was dose-dependent. Group A (226.1±28.7 seconds) significantly differed (P<0.001) with group B (197.2±14.9 seconds) & C (206.8±20.2 seconds) in respect of their sensory onset time. This means that the onset of sensory blockade was earlier with higher doses. The onset time of motor block was also earlier with increasing doses. Group C (190.4±14.2 seconds) significantly differed (P<0.001) with group A (233.0±23.3 seconds) & group B (228.2±16.8 seconds). A dose-related increase in the level of sensory blockade (C>B>A) was noted.[15] The duration of sensory and motor blocks between the groups was also dose-dependent, and significantly (P<0.001) differed from each other. The duration of both sensory and motor blockade was highest with group C (sensory mean-341.5±47.6 minutes, motor mean-362.5±16.5 minutes). P<0.001). The

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postoperative sedation was also dose-dependent with group C exhibiting a minimum score of 3 and a maximum score of 4. None of the patients showed signs of respiratory depression. [16]From the present study, it is clear that intrathecal dexmedetomidine with spinal bupivacaine not only shortens the onset of anesthesia but also prolongs the duration of the blockade and achieves a longer duration of analgesia. Bradycardia required no treatment, and correction of hypotension required less than 12-18 mg of ephedrine in incremental boluses.[17] Otherwise, the patients remained hemodynamically throughout. The statistical analysis of the pre, intra, and post-op hemodynamic variables such as PR, SBP, MAP, and SPO2 between the three groups showed no statistically significant hemodynamic fluctuation. [18]The results of the present study, when compared to the studies of the authors discussed above, have a similar outcome concerning the onset and duration of sensory and motor block, the duration of analgesia, and hemodynamic profile.[19,20]

Conclusion

Intrathecal dexmedetomidine added to bupivacaine for lower abdominal surgeries, has a dose-dependent effect on the sensory and motor blockade, with earlier onset and increased duration of the blockade and prolonged postoperative analgesia, better level of sedation, and stable hemodynamic . To summarize, intrathecal dexmedetomidine added to bupivacaine had a dose-dependent effect on the sensory and motor block characteristics showing. Earlier onset of sensory and motor blockade. Increased initial segmental level of sensory blockade .Increased duration of sensory and motor blockade. Increased duration of post-op. analgesia. Increased level of sedation. Three different doses (5, 10, and 15µg) did not vary in their effect on the hemodynamic stability or adverse effects.

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