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Original research article

A comparision between three different doses of intrathecal dexmedetomidine added to hyperbaric bupivacaine for lower abdominal surgeries

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Abstract

Local anaesthesia combined with spinal anaesthesia has a substantially shorter period of action, necessitating early analgesic management in the postoperative phase. Visceral pain, chills/shivering, nausea, and vomiting are frequent issues after lower abdomen procedures performed under spinal anaesthesia. The study was blinded from the observer and the anaesthesiologist who gave the medicine. Another anaesthesiologist not involved in the study loaded the complete volume of the medicine into sterile syringes. The anaesthesiologist who administered the medication also performed the intraoperative monitoring and the postoperative observation, but he was not aware of the medication's composition. VAS (Visual analogue scale) score was compared and significant seen at 4hours and 8hours and slightly decreased after that and time required for rescue analgesia was early in groups with less drug whereas in groups with more dose was sustained for a longer duration. Sedation score was compared among the groups in a intergroup manner and significant difference was seen in groups with higher drug doses. And difference between Group C and Group A was seen in a significant manner and between Groups B and C also.

Keywords: Intrathecal dexmedetomidine, hyperbaric bupivacaine, lower abdominal surgeries

Introduction

Leonard Corning, a neurologist, first used the term "spinal anaesthesia" in 1885. On August 16, 1898, at Kiel, August Karl Gustav Bier administered the first spinal analgesia, for which he was recognised. The lumbar puncture process was described by Heinrich Quincke of keil, Germany [1].

Local anaesthesia combined with spinal anaesthesia has a substantially shorter period of action, necessitating early analgesic management in the postoperative phase. Visceral pain, chills/shivering, nausea, and vomiting are frequent issues after lower abdomen procedures performed under spinal anaesthesia.

Adjuvants are typically added to local anaesthetic medications to enhance their quality, quicken their start of action and lengthen their duration, The first spinal adjuvant employed was adrenaline. Although it does not significantly extend its effect, adrenaline lessens its toxicity [2].

The most recent adjuvant to be added to local anaesthetics is Dexmedetomidine. Other adjuvants include morphine, fentanyl, Sufentanil, clonidine, midazolam, ketamine, neostigmine, soda bicarbonate, and others. There are many ways to give adjuvants, including intravenous, intrathecal, and epidural. In our study, the intrathecal route is highlighted by the addition of adjuvant to local anaesthetic [3].

In some regions of the brain, Dexmedetomidine acts as an agonist of Alpha2 - adrenergic receptors. Due to its sedative, analgesic, perioperative sympatholytic, and hemodynamic stabilising effects, Dexmedetomidine has recently gained prominence. A novel medicine that is well regarded among alpha 2 adrenergic receptor agonists is Dexmedetomidine.

It has food and drugs administration approval for short-term sedation of ICU patients who are on mechanical ventilation. Dexmedetomidine is used by veterinarians to treat cats, dogs, and horses for conditions that are comparable. In investigations using intrathecal medication on both humans and animals, no neurological abnormalities have yet been reported. In this study, three different doses of intrathecal Dexmedetomidine along with Hyperbaric bupivacaine for lower abdominal surgeries, will be compared [4].

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Methodology
This was a randomised, prospective, parallel group, double-blinded study.

Randomisation
Simple randomised sampling was done by computer generated random numbers.

Sample size
Ninety patients were studied.

Inclusion criteria
- Age between 18-60 years of both sexes
- ASA I and II patients
- Lower abdominal surgeries

Exclusion criteria
- Known hypersensitivity to any of study drugs
- Known contra indication to Regional Anaesthesia
- Known or suspected coagulopathy
- Renal disorders
- Hypertension, IHD, Heart blocks, Arrhythmias, Valvular abnormalities.
- Patients on β blockers
- Patient on any long-term analgesic therapy
- Patient on medications known to interact with study drugs

Allocation
After obtaining Institutional Research and Ethical Committee (TIREC) approval and written informed consent, the patients were randomly allocated into three groups.
1. Group A (n=30)
2. Group B (n=30)
3. Group C (n=30)

Intervention
Spinal administration of the drug mixture
1. Group A (n=30) – 0.5% hyperbaric Bupivacaine + Dexmedetomidine 5 µg in 0.6 ml normal saline.
2. Group B (n=30) – 0.5% hyperbaric Bupivacaine + Dexmedetomidine 10 µg in 0.6 ml normal saline.
3. Group C (n=30) – 0.5% hyperbaric Bupivacaine + Dexmedetomidine 15 µg in 0.6 ml normal saline.

Masking
The study was blinded from the observer and the anaesthesiologist who gave the medicine.
Another anaesthesiologist not involved in the study loaded the complete volume of the medicine into sterile syringes. The anaesthesiologist who administered the medication also performed the intraoperative monitoring and the postoperative observation, but he was not aware of the medication's composition.

Pre-anaesthetic evaluation
The following pre-operative evaluations were conducted on all of the research participants.

History
History of co-morbid medical illness, any previous history of surgery under anaesthesia evaluated.

Results
In C group 200.40secs and in B group 212secs and in A group 216.50secs and by increasing the dose, Earlier onset of sensory block was seen in group C>B>A with significant P value of 0.01. By increasing the dose, onset of motor block was also earlier. Onset of motor and sensory block is dose dependent and more earlier with group c (15microgram).

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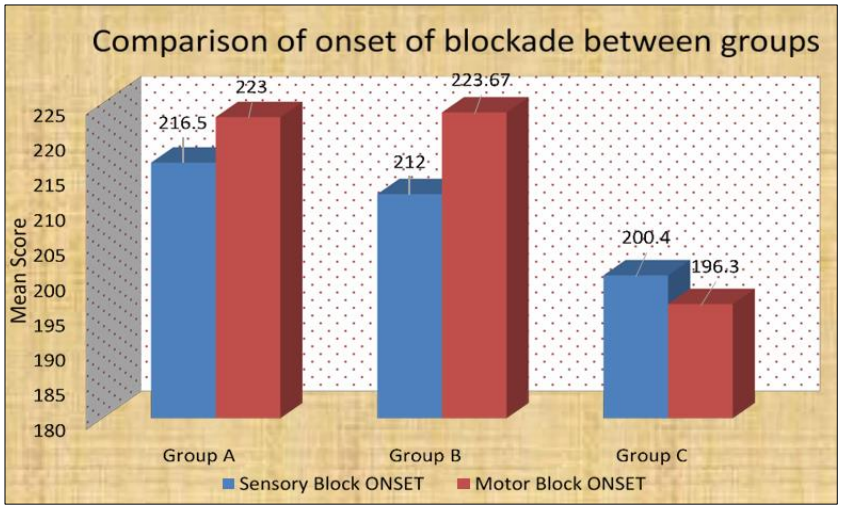


Graph 1: Comparison of onset of blockade between groups

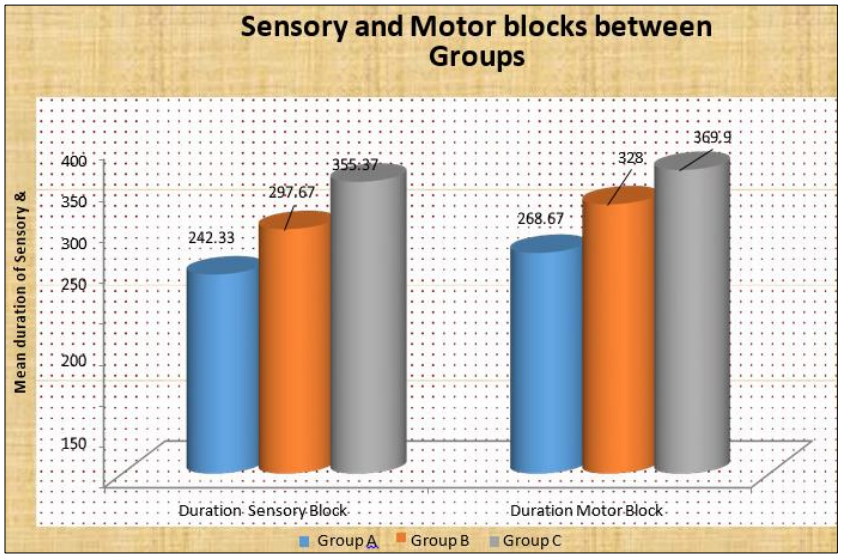
Table 1: Comparison of onset of motor & sensory block between the groups

Variables	Group A - Group B		Group A - Group C		Group B - Group C	
	Difference	P-value	Difference	P-value	Difference	P-value
Sensory Block On set	4.500	0.423	16.100**	0.002	11.600*	0.011
Motor Block Onset	0.667	0.892	26.700**	0.000	27.367**	0.000

*significant at 0.05 level; **significant at 0.01 level;

Comparison of onset of sensory and motor block between the groups was mentioned in this table and the difference was significant between the Group A and Group C with a difference value of 16.1 in case of sensory block onset whereas in case of motor block onset, the difference was 26.7.

Duration of sensory and motor blocks are more with group C> group B > group A. The P value was highly significant. And duration of the action was increasing by increasing the dose of the drug among the groups. And the group with higher dose will show the good amount of increase in the duration of the action.



Graph 2: Comparison of sensory and motor block between groups

Table 2: Comparison of Duration of motor and sensory between the groups

Variables	Group A - Group B		Group A - Group C		Group B - Group C	
	Difference	P- value	Difference	P- value	Difference	P-value
Duration	55.333**	0.000	113.03	0.000	57.700**	0.000
Sensory Block						
Duration Motor Block	59.333**	0.000	101.23	0.000	41.900	0.000

*significant at 0.05 level; **significant at 0.01 level;

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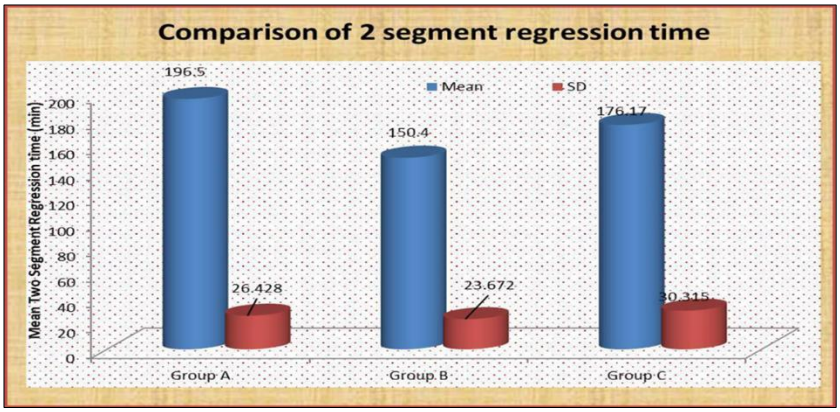
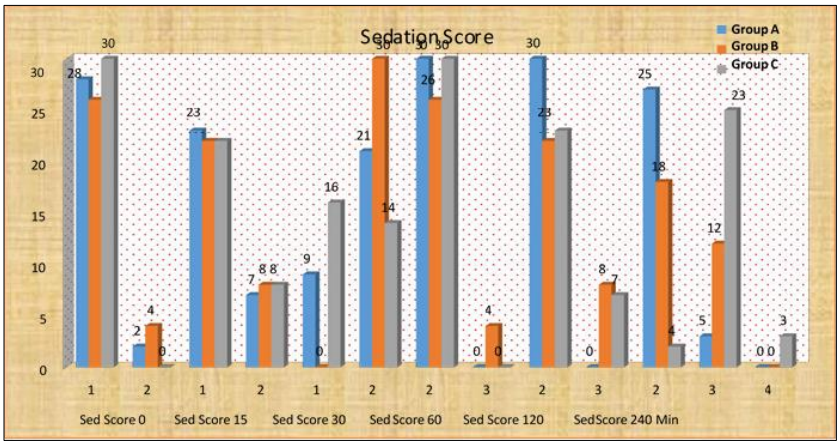
In this table duration of motor and sensory block was compared among the groups in a intergroup manner and significant difference was seen between groups A and C and significance was decreasing among the groups B and C and groups A and B.
In this table comparison of 2 segment regression was compared among the groups and significant amount of difference was seen among the group A and C.



Graph 3: Comparison of 2 segment regression time between groups

In this table sedation score among the groups was compared and by increasing the dose of the drug and the time required for the rescue analgesia was increasing in a significant manner compare with Group A In Group C longer time was required for the rescue analgesia.



Graph 4: Comparison of sedation score

Table 3: Pair-wise comparison of Sedation Score

Variables	Group A - Group B		Group A - Group C		Group B - Group C	
	Difference	P- value	Difference	P- value	Difference	P-value
T0 Min	0.067	0.398	0.067	0.155	0.133*	0.039
T15 Min	0.033	0.770	0.033	0.770	0.000	1.000
T30 Min	0.300**	0.001	0.233	0.069	0.533**	0.000
T60 Min	0.133	0.039	-	-	0.133	0.039
T120 Min	0.267	0.002	0.233**	0.004	0.033	770
T240 Min	0.300	0.007	0.933	0.000	0.633**	0.000

In this table sedation score was compared among the groups in a intergroup manner and significant difference was seen in groups with higher drug doses. And difference between Group C and Group A was seen in a significant manner and between Groups B and C also.

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Table 4: VAS scores among three groups

		N	Mean	S.D	S.E	F-value (p-value)	Sig.
Vas0Min	Group A	30	.00	.000	.000	-	-
	Group B	30	.00	.000	.000		
	Group C	30	.00	.000	.000		
	Total	90	.00	.000	.000		
Vas1HR	Group A	30	.00	.000	.000	-	-
	Group B	30	.00	.000	.000		
	Group C	30	.00	.000	.000		
	Total	90	.00	.000	.000		
Vas2hr	Group A	30	.00	.000	.000	-	-
	Group B	30	.00	.000	.000		
	Group C	30	.00	.000	.000		
	Total	90	.00	.000	.000		
Vas4hr	Group A	30	2.80	.997	.182	33.833** (0.000)	P<0.001 Highly Significant
	Group B	30	1.20	.997	.182		
	Group C	30	.80	.997	.182		
	Total	90	1.60	1.314	.138		
Vas8hr	Group A	12	3.00	.000	.000	7.181** (0.002)	P<0.01 Significant
	Group B	30	3.20	.997	.182		
	Group C	30	2.40	.814	.149		
	Total	72	3.00	1.007	.119		
Vas12hr	Group A	0	.	.	.	3.478@ (0.070)	P>0.05 Not Significant
	Group B	12	4.00	.000	.000		
	Group C	30	3.53	.860	.157		
	Total	42	3.67	.754	.116		

In this table VAS (Visual analogue scale) score was compared and significant seen at 4hours and 8hours and slightly decreased after that and time required for rescue analgesia was early in groups with less drug whereas in groups with more dose was sustained for a longer duration.
Duration of analgesia is about 747.33minutes for group C > 464.33minutes for group B >298.67minutes for group A. The difference is highly significant.

Table 5: Comparison of duration of analgesia between three groups

Variables	Group A - Group B		Group A - Group C		Group B - Group C	
	Difference	P-value	Difference	P-value	Difference	P-value
duration of analgesia	165.667	0.000	448.667**	0.000	283.000*	0.0000

Table 6: Mean and Median for Survival Time

Meana					Medians			
Group	Estimate	Std. Error	95%Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound			Lower Bound	Upper Bound
GroupA	321.803	10.509	301.204	342.401	310.000	8.771	292.808	327.192
GroupB	478.168	6.056	466.297	490.038	480.000	11.787	456.898	503.102
GroupC	785.567	11.021	763.967	807.167	800.000	19.419	761.939	838.061
Overall	597.128	24.457	549.193	645.064	680.000	121.697	441.474	918.526

a. If it is censored Estimation is limited to the largest survival time.

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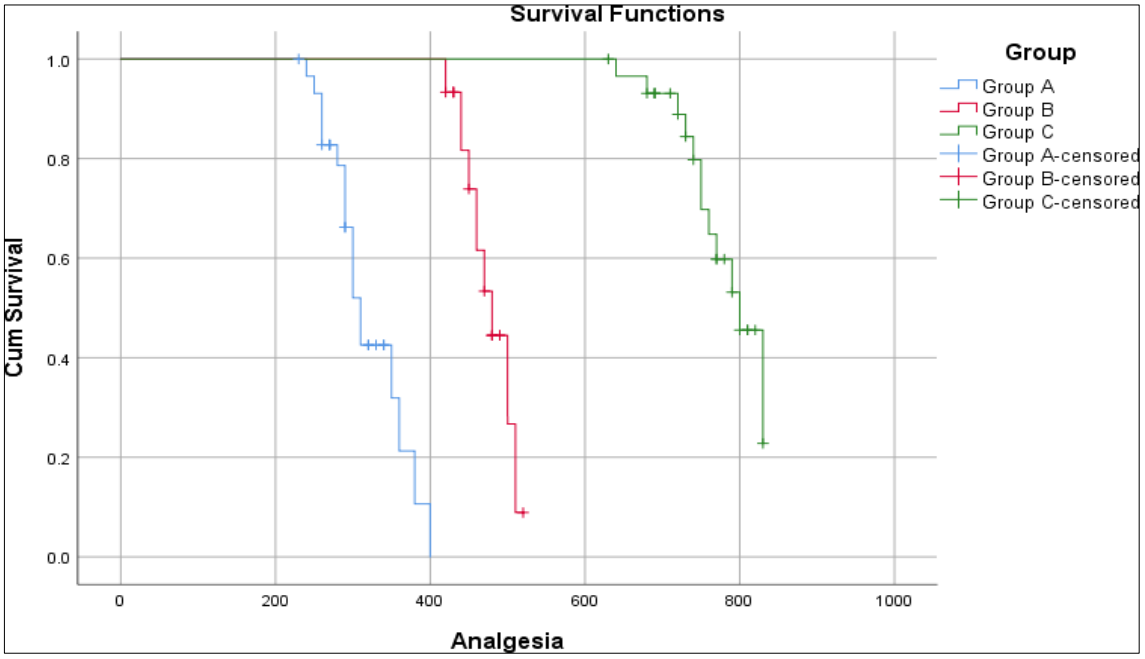

Graph 5: Survival functions

Discussion

This current study shows that there was a minimal difference of cephalad segmental dermatomal level of sensory blockade.but the onset of sensory blocking is faster in 15 µg compared to 5 and 10 µg groups.

Dexmedetomidine enhances the intrathecal blockade of local anaesthetics. There is strong correlation between concentration of Dexmedetomidine and sensory blockade. Intrathecal injection of 15µg of Dexmedetomidine yields analgesia for 6 to 7 hours.

Rajni Gupta *et al* (2011) 27 investigated the impacts by using Dexmedetomidine as an adjuvant for post-operative analgesia along with isobaric ropivacaine. Their research revealed that the Dexmedetomidine group had a considerably longer mean time of regression to S1 and longer mean analgesic duration. It was shown that the duration of both motor and sensor effects are lengthened by the intrathecal administration of Dexmedetomidine to ropivacaine.

Rajni Gupta *et al* (2011) [5] studied the comparative effect of Intrathecal Fentanyl and Dexmedetomidine as a Bupivacaine adjuvant. They had discovered that long-lasting motor and sensory block is related with intrathecal Dexmedetomidine.

M Mahmoud M Al -Mustafa *et al* (2009) [6] studied the effects of varying Dexmedetomidine doses administered to spinal isobaric Bupivacaine during urological operations. They discovered that, in a dose-dependent way, the Dexmedetomidine group dramatically increased motor and sensory block duration and greatly accelerated its onset. They came to the conclusion that when Dexmedetomidine is used as an adjuvant to Bupivacaine in spinal anaesthesia, it has a dose-dependent influence on the development and regression of sensory and motor block.

Our results are in accordance with these previous studies. However most of these investigations used Dexmedetomidine at doses up to 10µg but in our study it was done with 5 10 and 15µg with reasonable sensory blockade.

Sensory block prolonged in all groups which has statistical significance with group A and B, B and C, C and A. (C = 355.37 > B = 297.67 > A = 242.33 mts) Sensory block regressed less rapidly in all groups A, B and Group C. Our investigation supported each of these characteristics and confirmed.

Complete blockade of lower limbs is observed in all groups but prolonged in all three groups. But more in 15µg group in comparison with other groups.

When compared analgesic action of Dexmedetomidine, it produces a dose dependent duration of analgesia. The duration of the motor and sensory blockade is extended with Dexmedetomidine. The motor blockade was complete and no-one had incomplete motor blockade. At 5 minutes all of them had motor blockade. Motor action of spinal anaesthetics was prolonged by the binding of 2-adrenoceptor agonists with motor neurons which are present in the dorsal horn, the prolongation of the sensory block may be caused by synergism between local anaesthetic and 2- adrenoceptor agonist. Additionally, it may lead to local vasoconstriction and slow the elimination of local anaesthetics. Dexmedetomidine has been demonstrated in numerous studies to prolong motor and sensory blockade. These conclusions are supported by our research.

Hala E A Eid *et al* (2011) [7] studied the Dexmedetomidine intrathecal dosage-related effect when added to hyperbaric Bupivacaine. Dexmedetomidine was observed to considerably lengthen the time it took for the 2-segment regression, sensory, motor block regression to modified Bromage 0, and time required to

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rescue analgesia. Also it was linked with decreased post-operative pain score. Hence it was determined that spinal 0.5%hyperbaric Bupivacaine's analgesic and sedative effects are prolonged by intrathecal Dexmedetomidine at dosages of 10 and 15µg.

Eisenach, Dekock *et al* [8] have studied that when Clonidine is administered intrathecally with Bupivacaine and the prolongation in the action was observed. Fukushima *et al* [9] administered 2 µg/kg Dexmedetomidine was administered via an epidural in humans for post-operative analgesia, but no neurologic impairments were noted. According to the results of our investigation, the combination of 5µg of Dexmedetomidine with 0.5%hyperbaric bupivacaine greatly lengthens both the motor and the sensory block.

In our investigation, group C demonstrated stable hemodynamic conditions, higher patient satisfaction, and sensory and motor blockage lasting longer.

Dexmedetomidine produce cooperative sedation. It does not interfere with the respiratory drive hence it facilitates early weaning from ventilator, thus reducing ICU stay costs. Sedation is usually present during regional anaesthesia when Dexmedetomidine is utilised, which is consistent with the known sedative/anesthetic- sparing effects of alpha2 -adrenergic agonists due to their activities present in locus-coeruleus.

Anand *et al* [10] studied the results of using caudal Dexmedetomidine with Ropivacaine to give children post-operative analgesia and also established its safety in pediatric population. It was concluded that caudal Dexmedetomidine (2µg/kg) with 0.25% Ropivacaine (1 ml/kg) for lower abdominal pediatric procedures result in significant post-surgical pain relief and better quality of sleep and a prolonged duration of arousable sedation with less incidence of emergence agitation.

Prem kumara *et al* in their investigation of various Dexmedetomidine dosages intrathecally along with Bupivacaine concluded that Dexmedetomidine has dose dependant effect on both motor and sensory blockade with earlier onset and time required for post-surgical analgesia was increased, better level of sedation and stable hemodynamics.

Comparable results are there on present study from other studies. Different doses of Dexmedetomidine produced mild sedation with higher doses produced slightly higher sedation and have minimal influence on hemodynamic changes.

Our studies also on par with their studies and dose dependent effect.

Conclusion

For lower abdominal procedures, intrathecal Dexmedetomidine administered to Bupivacaine has a dose-related effect on both the motor and sensory blockade, with earlier onset and increased duration of blockade and prolonged post-operative analgesia, better level of sedation and stable hemodynamics.

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