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A COMPARATIVE STUDY OF INTRATHECAL DEXMEDETOMIDINE WITH 0.5% HYPERBARIC BUPIVACAINE AND INTRATHECAL FENTANYL WITH 0.5% HYPERBARIC BUPIVACAINE IN INFRA UMBILICAL SURGERIES

Anaesthesiology

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ABSTRACT

INTRODUCTION: Regional anaesthesia is the preferred technique for most infra-umbilical surgeries. It allows the patient to remain awake, minimizes or completely avoids the problem associated with airway management. With spinal anaesthesia, the onset of anaesthesia is more rapid allowing the surgical incision to be made sooner and also provides post operative analgesia.

AIM: To determine the duration of analgesia determined by the first demand for rescue analgesia in two groups of a defined study population. To compare intraoperative hemodynamics between two groups of population. To note the incidence of any complications in either group, specifically sedation and pruritus.

MATERIALS AND METHODS: This study was undertaken in Command Hospital (EC), Kolkata (West Bengal, India) during the period Mar 2017 to Feb 2018. One hundred twenty patients, scheduled for infra-umbilical surgeries belonging to ASA I and II were included in the study. The study population was randomly divided into two groups with 60 patients in each group.

RESULT: Association of ASA vs. group was not statistically significant (p=0.6985). Association of Comorbidity vs. group was not statistically significant (p=0.9833). Association of diagnosis/surgery vs. group was statistically significant (p=0.0301). We found that in group-I, the mean duration of motor block (mean ± s.d.) of patients was 359.3333 ± 34.3431 min. In group-II, the mean duration of motor block (mean ± s.d.) of patients was 265.7167 ± 28.4737 min. Difference of mean duration of motor block vs. group was statistically significant (p<0.0001).

CONCLUSION: Intrathecal dexmedetomidine with 0.5% hyperbaric bupivacaine produces excellent surgical analgesia and an extended analgesia in postoperative period. Intrathecal dexmedetomidine with 0.5% hyperbaric bupivacaine increases the duration of sensory and motor blockade.

KEYWORDS

Dexmedetomidine, Bupivacaine, Fentanyl, Spinal Anaesthesia.

INTRODUCTION

Pain and its alleviation have been a challenge for humans for centuries. No other problem in medicine has proved so elusive. Surgical trauma causes severe tissue damage and surgical pain is aggravated by associated muscle spasm and visceral distension. Anaesthesiologists have succeeded to considerable extent in rendering the patient pain free during surgery, but once the luxury of pain free surgery is over, the patient has to face the misery of postoperative pain.

Regional anaesthesia is the preferred technique for most infra-umbilical surgeries and is simple to perform. With spinal anaesthesia, onset of anaesthesia is more rapid allowing the surgical incision to be made sooner and also provides post operative analgesia. Spinal anaesthesia with cocaine was initially produced inadvertently by J Leonard Corning in 1885 and first used deliberately by August Bier in 1898.[1]

Since dose of local anaesthetics used for spinal anaesthesia is small; there is less chance of drug toxicity. For decades, lignocaine had been the local anaesthetic of choice for spinal anaesthesia. Its advantages were rapid onset of action and good motor block manifested as good muscle relaxation. However, its use got limited by its short duration of action and has been implicated in transient neurologic symptoms and cauda equina syndrome following intrathecal injection.[2]

Bupivacaine is 3-4 times more potent than lignocaine and has longer duration of action. Its disadvantages are slow onset of action and decreased motor block. Though the duration of action of bupivacaine is prolonged, it will not produce prolonged post operative analgesia. Hence another adjuvant is required for producing prolonged post operative analgesia. The identification of opioid receptors has opened new horizons in pain management. In 1976, Yaksh and Rudy were the first investigators to demonstrate direct opioid analgesia at the spinal cord level.[3]

Morphine was the first opioid administered intrathecally to augment neuraxial blocks.[4] Opioid analgesic drugs produce intense, prolonged analgesic action without gross autonomic changes, loss of motor power or impairment of sensation other than pain when injected into subarachnoid or epidural space.

Opioid analgesics can produce side effects like post operative nausea and vomiting, pruritus, urinary retention, late and unpredictable respiratory depression[5].

Fentanyl is the most frequently intrathecal lipophilic opioid used as analgesic agent with minimal cephalad spread making it least likely of all intrathecal opioids to cause delayed respiratory depression. Fentanyl exhibits close structural similarities to local anaesthetics and has demonstrable effect on sensory C primary afferent nerve fibers, which may facilitate analgesic effects.[7]

Dexmedetomidine, an alpha2 adrenergic agonist, has a variety of different actions via alpha2 adrenergic receptors in spinal cord and locus coeruleus in brain. Its highly lipophilic nature allows rapid absorption in cerebrospinal fluid and binding to alpha2 adrenergic receptors prolongs its analgesic action after spinal anaesthesia. Addition of intrathecal dexmedetomidine to bupivacaine prolongs analgesia and decreases morphine consumption postoperatively.[7] (Clonidine also has antihypertensive properties and the ability to potentiate the effects of local anaesthetics but causes hypotension more than dexmedetomidine).[8]

Dexmedetomidine has been shown to result in the prolongation of the sensory blockade and the reduction in the amount or the concentration of local anaesthetic required to produce post operative analgesia. It also has the ability to prolong motor blockade produced by bupivacaine without causing respiratory depression. (Large doses of intrathecal clonidine as much as 450µg without local anaesthetics provide sedation with intense and long lasting postoperative analgesia[9] but are inadequate for surgical anaesthesia, due to which it has been replaced as an adjuvant to local anaesthetics rather than alone by dexmedetomidine).[10]

Optimal doses of dexmedetomidine as an adjuvant to local anaesthetic producing prolonged post-operative analgesia with minimal side effects would be a true alternative to opioids.

Though studies have been conducted with various opioids and dexmedetomidine as additives to bupivacaine to prolong the intra and postoperative analgesia, none of them reported that they were devoid of side effects. Hence, the present study is being undertaken to compare the effects of dexmedetomidine and fentanyl as additives to intrathecal hyperbaric bupivacaine for spinal anaesthesia in infra-umbilical surgeries.

- **Primary Outcome :** To determine the duration of analgesia determined by the first demand for rescue analgesia in two groups of a defined study population.

- **Secondary Outcome :**

1. To compare intraoperative hemodynamics between the two groups.
2. To note the incidence of any complications in either group, specifically sedation and pruritus.

MATERIALS AND METHODS

A study entitled "A comparative study between intrathecal dexmedetomidine with 0.5% hyperbaric bupivacaine and intrathecal fentanyl with 0.5% hyperbaric bupivacaine in infra umbilical surgeries." was undertaken in Command Hospital (EC), Kolkata during the period Mar 2017 to Feb 2018. The study was undertaken after obtaining ethical committee clearance as well as informed consent from all patients.

One hundred twenty patients, scheduled for infraumbilical surgeries belonging to ASA I and II were included in the study. The study population was randomly divided into two groups with 60 patients in each group.

Group A (n=60) - Received 2.5 ml of intrathecal hyperbaric bupivacaine with 5 µg of preservative free dexmedetomidine.
Group B (n=60) - Received 2.5 ml of intrathecal hyperbaric bupivacaine with 25 µg of preservative free Fentanyl.

Inclusion criteria for the Study :

a) Patients of either sex
b) ASA I & II patients
c) Planned for Elective Infra-umbilical Surgery
d) Aged between 20 to 60 years
e) Body weight between 45 to 85 kgs

EXCLUSION CRITERIA:

a) Patient refusal
b) Local infection of the back
c) Coagulopathy or anticoagulant therapy
d) Any cardiovascular disease
e) Increased intracranial tension.
f) Pre-existing neurological disease & severe deformity of spine.

STATISTICAL METHODS :

Explicit expressions that can be used to carry out various *t*-tests are given below. In each case, the formula for a test statistic that either exactly follows or closely approximates a *t*-distribution under the null hypothesis is given. Also, the appropriate degrees of freedom are given in each case. Each of these statistics can be used to carry out either a one-tailed test or a two-tailed test.

Once a *t*-value is determined, a *p*-value can be found using a table of values from Student's t-distribution. If the calculated *p*-value is below the threshold chosen for statistical significance (usually the 0.10, the 0.05, or 0.01 level), then the null hypothesis is rejected in favour of the alternative hypothesis.

p-value ≤ 0.05 was considered as statistically significant.

RESULT AND DISCUSSION

We found that in group-I, the mean age (mean ± s.d.) of patients was 41.6000 ± 11.1571 years. In group-II, the mean age (mean ± s.d.) of patients was 44.4333 ± 12.3293 years. Difference of mean age vs. group was not statistically significant (p=0.1894). Thus age was matched in this study. In group-I, 18(30.0%) patients had female and 42(70.0%) patients had male. In group-II, 18(30.0%) patients had female and 42(70.0%) patients had male. Association of sex vs. group was not statistically significant (p=1.0000). In group-I, 41(68.3%) patients had ASA I and 19(31.7%) patients had ASA II. In group-II, 39(65.0%) patients had ASA I and 21(35.0%) patients had ASA II. Association of ASA vs. group was not statistically significant (p=0.6985). Association of Comorbidity vs. group was not statistically significant (p=0.9833). Association of diagnosis/surgery vs. group was statistically significant (p=0.0301).

Arnab Paul[11] et al showed that mean age of group BD was 45.27 ± 10.52 years and 47.2 ± 8.29 years in group BF. Difference of mean age in two groups was not statistically significant.

Soliman R et al [12] showed that 171 patients had female in group-D and 166 patients had female in group-F. 43 patients had male in group-D and 42 patients had male in group-F. That was not statistically significant. **Arnab Paul et al [11]** showed that male : female ratio was not statistically significant.

We found that in group-I, the mean weight (mean ± s.d.) of patients was 62.9667 ± 6.7797 kg. In group-II, the mean weight (mean ± s.d.) of patients was 63.6500 ± 8.3703 kg. Difference of mean weight vs. group was not statistically significant (p=0.6241).

We found that in group-I, the mean height (mean ± s.d.) of patients was 162.8833 ± 6.1784 cm. In group-II, the mean height (mean ± s.d.) of patients was 162.9000 ± 7.5615 cm. Difference of mean height vs. group was not statistically significant (p=0.9895).

It was found that in group-I, the mean duration of surgery (mean ± s.d.) of patients was 68.0667 ± 13.4994 min. In group-II, the mean duration of surgery (mean ± s.d.) of patients was 67.8833 ± 19.8230 min. Difference of mean duration of surgery vs. group was not statistically significant (p=0.9529).

It was found that group-I, the mean PSB (mean ± s.d.) of patients was 1.4975 ± 0.3221 min. In group-II, the mean PSB (mean ± s.d.) of patients was 2.4767 ± 0.5104 min. Difference of mean PSB vs. group was statistically significant (p<0.0001).

It was found that in group-I, the mean PMB (mean ± s.d.) of patients was 1.9933 ± 0.6722 min. In group-II, the mean PMB (mean ± s.d.) of patients was 3.2217 ± 0.9292 min. Difference of mean PMB vs. group was statistically significant (p<0.0001).

We found that in group-I, the mean duration of motor block (mean ± s.d.) of patients was 359.3333 ± 34.3431 min. In group-II, the mean duration of motor block (mean ± s.d.) of patients was 265.7167 ± 28.4737 min. Difference of mean duration of motor block vs. group was statistically significant (p<0.0001).

Arnab Paul [11] et al showed that onset of sensory block (min) 7.5 ± 1.25 mins in group-BD and 8.9 ± 1.52 mins in group BF. They found that difference of mean time onset of sensory block in two groups was statistically significant. But **Gupta K [13]** et al showed that onset of sensory block (min) 7.25 ± 2.3 mins in group-LD and 9.27 ± 2.79 mins in group LF. They found that difference of mean time onset of sensory block in two groups was not statistically significant.

We found that in group-I, Difference of mean BSBP vs. group was not statistically significant (p=0.4227). Difference of mean SBP at 2 min vs. group was not statistically significant (p=0.8434). Difference of mean SBP at 4 min vs. group was not statistically significant (p=0.1882). Difference of mean SBP at 6 min vs. group was statistically significant (p=0.0091). Difference of mean SBP at 8 min vs. group was statistically significant (p=0.0001). Difference of mean SBP at 13 min vs. group was statistically significant (p<0.0001). Difference of mean SBP at 18 min vs. group was statistically significant (p<0.0001). Difference of mean SBP at 23 min vs. group was statistically significant (p=0.0001). Difference of mean SBP at 33 min vs. group was statistically significant (p=0.0257). Difference of mean MSBP vs. group was statistically significant (p=0.0004).

We found that difference of mean BDBP vs. group was not statistically significant (p=0.1885). Difference of mean DBP at 2 min vs. group was not statistically significant (p=0.7672). Difference of mean DBP at 4 min vs. group was statistically significant (p=0.0319). Difference of mean DBP at 6 min vs. group was statistically significant (p=0.0020). Difference of mean DBP at 8 min vs. group was statistically significant (p<0.0001). Difference of mean DBP at 13 min vs. group was statistically significant (p<0.0001). Difference of mean DBP at 18 min vs. group was statistically significant (p<0.0001). Difference of mean DBP at 23 min vs. group was statistically significant (p=0.0047). Difference of mean DBP at 33 min vs. group was not statistically significant (p=0.2847). Difference of mean MDBP vs. group was statistically significant (p=0.0004).

We found that difference of mean BMAP vs. group was not statistically

significant (p=0.6511). Difference of mean MAP at 2 min vs. group was not statistically significant (p=0.7347). Difference of mean MAP at 4 min vs. group was not statistically significant (p=0.1256). Difference of mean MAP at 6 min vs. group was statistically significant (p=0.0019). Difference of mean MAP at 8 min vs. group was statistically significant (p=0.0002). Difference of mean MAP at 13 min vs. group was statistically significant (p<0.0001). Difference of mean MAP at 18 min vs. group was statistically significant (p<0.0001). Difference of mean MAP at 23 min vs. group was statistically significant (p=0.0002). Difference of mean MAP at 33 min vs. group was not statistically significant (p<0.0001). Difference of mean MMAP vs. group was statistically significant (p=0.0002).

It was found that difference of mean BHR vs. group was not statistically significant (p=0.6005). Difference of mean HR at 2 min vs. group was not statistically significant (p=0.1100). Difference of mean HR at 4 min vs. group was not statistically significant (p=0.1115). Difference of mean HR at 6 min vs. group was statistically significant (p=0.0131). Difference of mean HR at 8 min vs. group was statistically significant (p=0.0563). Difference of mean HR at 13 min vs. group was statistically significant (p=0.0240). Difference of mean HR at 18 min vs. group was statistically significant (p=0.0189). Difference of mean HR at 23 min vs. group was not statistically significant (p=0.1087). Difference of mean HR at 33 min vs. group was not statistically significant (p=0.2685). Difference of mean MHR vs. group was statistically significant (p=0.0497).

In group-I, the mean BVAS (mean ± s.d.) of patients was 16.5000 ± 19.2067. In group-II, the mean BVAS (mean ± s.d.) of patients was 16.1667 ± 20.3438. Difference of mean BVAS vs. group was not statistically significant (p=0.9266).

According to VAS10 in two groups all patients had 0. According to VAS20 in two groups all patients had 0. According to VAS30 in two groups all patients had 0. According to VAS120 in two groups all patients had 0. According to VAS180 in two groups all patients had 0.

It was found that in group-I, the mean rescue analgesia (mean ± s.d.) of patients was 408.8333 ± 45.2305. In group-II, the mean rescue analgesia (mean ± s.d.) of patients was 286.8814 ± 30.0964. Association of mean rescue analgesia vs. group was statistically significant (p<0.0001).

In group-I, 1(1.7%) patient had T10 SBH, 11(18.3%) patients had T7 SBH, 39(65.0%) patients had T8 SBH and 9(15.0%) patients had T9 SBH. In group-II, 31(51.7%) patients had T10 SBH, 21(35.0%) patients had T8 SBH and 8(13.3%) patients had T9 SBH. Association of SBH vs. group was statistically significant (p<0.0001).

It was found that in group-I, 20(33.3%) patients had T10 MBH, 1(1.7%) patient had T6 MBH, 22(36.7%) patients had T8 MBH, 17(28.3%) patients had T9 MBH. In group-II, 49(81.7%) patients had T10 MBH, 5(8.3%) patients had T8 MBH, 5(8.3%) patients had T9 MBH and 1(1.7%) patient had T10 MBH. Association of MBH vs. group was statistically significant (p<0.0001). Association of side effects vs. group was statistically significant (p=0.0043).

Arnab Paul [11] et al showed that time to attain complete motor block (min) 19.65 ± 3.57 mins in group-BD and 21.9 ± 3.59 mins in group BF. They found that difference of mean time onset of motor block in two groups was statistically significant. **Gupta K** [13] **et al** showed that time to attain complete motor block (min) 19.27 ± 4.7 mins in group-LD and 22.78 ± 5.5 mins in group LF. They found that difference of mean time onset of sensory block in two groups was statistically significant.

Gupta K [13] **et al** showed that time to total duration of sensory analgesia (min) 187.7 ± 6.9 mins in group-LD and 146.7 ± 8.3 mins in group LF. They found that difference of mean total duration of sensory analgesia in two groups was statistically significant.

Arnab Paul [11] **et al** showed that time to total duration of sensory analgesia (min) 380.32 ± 35.93 mins in group-BD and 315.16 ± 25.39 mins in group BF. They found that difference of mean total duration of sensory analgesia in two groups was statistically significant.

CONCLUSION

The present study entitled "A comparative study of intrathecal dexmedetomidine with 0.5% hyperbaric bupivacaine and intrathecal fentanyl with 0.5% hyperbaric bupivacaine in infra umbilical surgeries" was undertaken to compare the efficacy of these drugs in Indian population.

The study was conducted in a prospective randomized double-blind fashion on 120 patients divided in two groups of 60 each.

ASA grade I and II patients in the age group of 20 to 60 years in the Department of Anaesthesiology & Critical Care, Command Hospital (EC), Kolkata (West Bengal, India) scheduled to undergo elective surgeries were selected.

The observations were discussed in terms of vital parameters, onset and duration of sensory and motor block, intra and post operative pain defined by VAS and side effects. The results of the study indicates that addition of 5µg dexmedetomidine with 0.5% hyperbaric bupivacaine for spinal anaesthesia intensifies and increases the duration of sensory blockade and increases the intensity and duration of motor blockade with insignificant intra-operative hypotension and bradycardia in comparison to addition of 25µg fentanyl with 0.5% hyperbaric bupivacaine heavy for spinal anaesthesia

Table: Distribution of Mean Duration of surgery (min), PSB (min), PMB (min), Duration of motor block (min), BVAS and RESCUE ANALGESIA : Group

		Number	Mean	SD	Minimum	Maximum	Median	p-value
Duration of surgery (min)	Group-I	60	68.0667	13.4994	40.0000	115.0000	67.0000	0.9529
	Group-II	60	67.8833	19.8230	30.0000	130.0000	66.5000	
PSB (min)	Group-I	60	1.4975	.3221	0.7500	2.5000	1.5000	<0.0001
	Group-II	60	2.4767	.5104	1.2000	4.0000	2.5000	
PMB (min)	Group-I	60	1.9933	.6722	1.0000	5.0000	1.9000	<0.0001
	Group-II	60	3.2217	.9292	2.0000	6.0000	3.0000	
Duration of Motor Block (min)	Group-I	60	359.3333	34.3431	310.0000	456.0000	348.0000	<0.0001
	Group-II	60	265.7167	28.4737	226.0000	348.0000	260.0000	
BVAS	Group-I	60	16.5000	19.2067	0.0000	60.0000	10.0000	0.9266
	Group-II	60	16.1667	20.3438	0.0000	70.0000	0.0000	
RESCUE ANALGESIA	Group-I	60	408.8333	45.2305	298.0000	540.0000	400.0000	<0.0001
	Group-II	60	286.8814	30.0964	240.0000	360.0000	280.0000	

Association of SBH and MBH : Group

		GROUP				
		Group-I	**Group-II**	**TOTAL**	**Chi-square value**	**p-value**
SBH	**T10**	1	31	32	44.5838	<0.0001
	Row%	3.1	96.9	100.0		
	Col %	1.7	51.7	26.7		
	T7	11	0	11		
	Row%	100.0	0.0	100.0		
	Col %	18.3	0.0	9.2		

	T8 Row% Col %	39 65.0 65.0	21 35.0 35.0	60 100.0 50.0		
	T9 Row % Col %	9 52.9 15.0	8 47.1 13.3	17 100.0 14.2		
	TOTAL Row % Col %	60 50.0 100.0	60 50.0 100.0	120 100.0 100.0		
MBH	**T10** Row % Col %	20 29.0 33.3	49 71.0 81.7	69 100.0 57.5	31.4376	<0.0001
	T6 Row % Col %	1 100.0 1.7	0 0.0 0.0	1 100.0 0.8		
	T8 Row % Col %	22 81.5 36.7	5 18.5 8.3	27 100.0 22.5		
	T9 Row % Col %	17 77.3 28.3	5 22.7 8.3	22 100.0 18.3		
	TI0 Row % Col %	0 0.0 0.0	1 100.0 1.7	1 100.0 0.8		
	TOTAL Row % Col %	60 50.0 100.0	60 50.0 100.0	120 100.0 100.0		

On the basis of present study, the following conclusions were drawn :

1. Intrathecal dexmedetomidine with 0.5% hyperbaric bupivacaine produces excellent surgical analgesia and an extended analgesia in postoperative period.
2. Intrathecal dexmedetomidine with 0.5% hyperbaric bupivacaine makes faster onset of sensory and motor block.
3. Intrathecal dexmedetomidine with 0.5% hyperbaric bupivacaine increases the duration of sensory and motor blockade.
4. This method can be considered as a method of pre-emptive analgesia to avoid the multiple pricks for analgesia in the immediate postoperative period.
5. Intrathecal dexmedetomidine with 0.5% hyperbaric bupivacaine does not cause significant intra-operative hypotension and bradycardia.

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