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Intrathecal Hyperbaric Bupivacaine-Fentanyl Versus Hyperbaric Bupivacaine Saline in Appendicectomy Patients, Attending the Tertiary Care Centre, South India

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Abstract
The aim of the present study is to compare the effectiveness of intrathecal hyperbaric bupivacaine-fentanyl and intrathecal hyperbaric bupivacaine-saline in appendicectomy patients. Hospital based multi-centric randomized comparative double-blind study was carried out for the period of one year. 100 cases of appendicitis which attended the general surgery department and were posted for surgery under spinal anesthesia were included in this study. Both groups included mostly 41-50-year-old patients. Both groups had equal male and female representation. When subarachnoid block characteristics were examined, group S had a considerably reduced time reaching T10 level. The maximum degree of sensory block (T4 and T5), duration to attain it and bromage 3 onset showed no difference. Group S' relapse to bromage was greatly delayed. The mean systolic blood pressure was insignificant. Significant mean diastolic blood pressure findings were not found. In our research, nausea and pruritis were reported but negligible. Visual analog scale for postoperative pain. Rescue analgesic was administered and timed for VAS >6. Intrathecal hyperbaric bupivacaine-fentanyl provides a suitable spinal anesthetic alternative to saline. It improves perioperative/intra operative analgesia, hemodynamic stability, side effects and 24-hour rescue analgesic use.

INTRODUCTION

Spinal anesthesia is a very convenient kind of anesthesia that has several benefits compared to general anesthesia, such as decreased stress response and enhanced post-operative pain management. Spinal lignocaine has been eliminated due to its ability to produce temporary neurological symptoms in addition to providing a shorter duration of anesthetic blocking[1]. Spinal bupivacaine causes a significant and long-lasting loss of motor function, which leads to a delay in being able to go home following ambulatory surgery[2]. Ropivacaine, an amide local anesthetic, has just been developed and has been effectively utilized to provide epidural analgesia for women in labor, during cesarean birth and for post-operative pain relief[3]. It has been utilized intrathecally for day care treatments due to its ability to offer sufficient sensory block and promote early motor recovery[4].

Ropivacaine is increasingly preferred because to its enhanced safety characteristics compared to bupivacaine, including a lower risk of central nervous system and cardiovascular toxicity[1,5]. Intrathecal opioids are able to enhance the sensory block produced by local anesthetics without causing an increase in sympathetic block. This result in a tolerable level of spinal anesthesia at a lower dose of local anesthetic[6,7]. While intrathecal bupivacaine alone provides effective sensory blockage, a significant proportion of patients may encounter hemodynamic instability, pain and discomfort, necessitating the need for additional analgesic support during the early postoperative period[8].

In order to address these limitations, opioids are delivered intrathecally in conjunction with bupivacaine. There are many advantages to using this method, including steady hemodynamic, more concentrated pain relief, less lung problems, earlier patient mobility, faster recovery of bowel function and lower stress reaction. Combining other medications with local anesthetics might potentially reduce the required amount of local anesthetics, lessen negative side effects and prolong the duration of anesthesia[9]. Fentanyl, an opioid with a high affinity for fat, quickly takes effect after being injected into the spinal canal. When given intrathecally at doses that are substantial enough to elicit delayed respiratory depression, the likelihood of migrating to the fourth ventricle is reduced[10]. Combining fentanyl at a dose of 10 micrograms with hyperbaric bupivacaine at a dose of 10.5-12.5 mg improves the quality of subarachnoid block during surgery and immediately after[11]. Pruritus, nausea, vomiting and respiratory depression are common adverse effects associated with intrathecal opioids. Tramadol is a synthetic analgesic medication that works in the central nervous system. It has two separate and complementary modes of action: one is a mild opioid agonist and the other is a monoamine neurotransmitter reuptake inhibitor. The racemic combination of tramadol consists of two enantiomers that synergistically increase the effectiveness of pain relief and improve its tolerance profile. Tramadol has a far lower impact on respiration compared to centrally acting opioids due to its considerably lower affinity for μ receptors, which is 6000 times less than that of morphine. Tramadol is capable of delivering efficient pain management after surgery, with less chance of causing respiratory depression when administered via the central neuraxial pathway. However, the presence of itching, feelings of sickness, throwing up, difficulty in urinating, outbreak of cold sores and the possibility of unexpected breathing problems force medical professionals to give a lower amount of tramadol when using it intrathecally to provide efficient and long-lasting pain relief without these effects. Additionally, it hinders the reabsorption of serotonin and norepinephrine in the spinal cord, resulting in extended pain relief after surgery and without any harmful effects on the nerves[12].

The objective of this study is to assess the effects of intrathecal hyperbaric bupivacaine-fentanyl versus intrathecal hyperbaric bupivacaine-saline in individuals undergoing appendicectomy.

MATERIALS AND METHODS

Hospital based multi-centric randomized comparative double-blind study carried out for the period of one year and which included 100 ASA I, II patients scheduled for elective appendicectomy surgery under spinal anesthesia.

Inclusion Criteria:

- ASA physical status class I and II.
- Age between 18-60 years of either sex.

Exclusion Criteria:

- ASA grade III and IV.
- Infection at the site of injection.
- Coagulopathy or anticoagulation.
- Congenital anomalies of lower spine.
- Active disease of CNS.
- History of allergy to local anesthetics.

Patients were allocated into two groups by simple randomization technique, based on study drugs assigned to each group.

Group F (50): Intrathecal hyperbaric bupivacaine-fentanyl.

Group S (50): Intrathecal hyperbaric bupivacaine saline.

At the time of preanaesthetic assessment, all patients were evaluated and investigated for systemic diseases. Participants were explained about SAB procedure and educated about using 'VAS'. A written and informed consent was obtained from all participants in the study. Pre-op preparation of patients included overnight NPO, premedication -Tab. Rantidine 150 mg, Tab. Alprazolam 0.5 mg.

Procedure: On day of surgery, anesthesia work station and emergency cart were kept ready in OR. On arrival of patient on OR table, 18G iv access was secured on left forearm, patient was connected to multi parameter monitor and baseline vitals were recorded, pre loading was done with 15ml /kg Ringer's Lactate 15 min prior to start of procedure. Subarachnoid block was performed under aseptic precautions with patient in right lateral position using 26G Quincke's spinal needle, test drugs assigned to study groups were deposited intrathecally and patient turned supine immediately. Time of onset of T10 sensory block and peak sensory block was noted using pin prick method, Motor block was assessed with Modified Bromage scale and time of onset of bromage 3 motor block was noted. NIBP, ECG NIBP, ECG, HR and SpO2 were recorded every 2 minutes for first 10 minutes, every 10 minutes for next 50 min and every 15 minutes till end of surgery.

Bromage Scale
Bromage 0: Patient is able to move the hip, knee and ankle.

Bromage 1: Patient is unable to move the hip but is able to move the knee and ankle.

Bromage 2: Patient is unable to move the hip and knee but able to move the ankle.

Bromage 3: Patient is unable to move the hip, knee and ankle.

Intra Operatively All the Patients were Observed For:

- Hypotension described as >20% fall of baseline blood pressure, treated with 200 ml Ringer's Lactate bolus and 6mg ephedrine i.v.
- Bardycardia defined as HR < 50 bpm, treated with 0 5 mg atropine iv.
- Respiratory depression defined as respiratory rate <9 breaths/min and SpO2<90% on room air, incidence was recorded in data sheet for analysis.

Side Effects: Regression time of sensory block and motor blockade to reach modified Bromage 0 was noted. Visual analogue scale used for assessing postoperative pain. VAS >6 rescue analgesic was given and time noted.

Statistical Methods: Statistical analysis was done by Statistical package for social sciences (SPSS) version 22.0, (SPSS Inc, Chicago, IL) statistical analysis software.

RESULTS AND DISCUSSIONS

Majority of the patients belonged to 41-50 years age group in both the groups. There was equal distribution of male and female in both the groups.

The variables of subarachnoid block were compared in both groups it was found the time to attain T10 level significantly lower in group S. The difference in highest level of sensory block (T4 and T5), time to reach highest level, time to onset of bromage 3 was insignificant. Time to regression to bromage was significantly delayed in Group S.

Anesthesiology is a branch of medicine that focuses on the management of pain and comprehensive care of patients undergoing surgery during the preoperative period. Pain is characterized as a disagreeable sensory and emotional encounter linked to real or prospective harm to bodily tissues[13]. Local anesthetics have a limited duration of effect and there is an early need for rescue analgesics. Adjuvants are included to enhance the quality and length of the treatment, as well as to provide improved postoperative pain relief and patient comfort[14,15]. Local anesthetic adjuvants include a diverse collection of medicines with different modes of action, including traditional opioids. Adjuvants reduce the dosage of local anesthetic and mitigate its adverse effects. The patient had myocardial depression, resulting in hypotension, bardycardia, heart block and ventricular arrhythmia. Visceral discomfort, nausea and vomiting are often encountered issues with lower abdominal procedures performed under spinal anesthesia[16]. Fentanyl is an analgesic that acts as a µ receptor agonist and is 80 times more powerful than morphine[17,18]. The addition of 0.5% heavy bupivacaine enhances the effectiveness of spinal analgesia, while also decreasing both visceral and somatic pain[17].

The majority of patients in both groups were between the ages of 41 and 50. Both groups had a balanced gender distribution, with an equal number of males and females. Upon comparing the variables of subarachnoid block in both groups, it was seen that the time required to reach the T10 level was much shorter in group S. The disparity in the maximum degree of sensory block (T4 and T5), the duration to achieve the highest level and the duration until beginning of

Table 1: Age, gender, height and weight distribution of the study participants

	Group F		Group S	
	No	Percentage	No	Percentage
Age				
18-20yrs	2	4	0	0
21-30yrs	3	6	4	8
31-40yrs	14	28	27	54
41-50yrs	21	42	13	26
51-60yrs	8	16	5	10
>60yrs	2	4	1	2
Gender				
Male	25	50	25	50
Female	25	50	25	50
Total	50	100	50	100
Height	158.64±5.15		157.13±5.85	
Weight	60.14±12.36		58.92±10.18	

Table 2: Comparison of variables in subarachnoid block among the study participants

Variables	Group F	Group S	'p' value
Time from injection to T10(min)	03.39±0.86	02.64±0.58	<0.001
Time from injection to highest Sensory (min)	11.48±1.24	11.77±1.25	0.316
Onset of Bromage 3 (min)	10.40±1.09	10.58±1.00	0.325
Regression to bromage 0 (min)	152.90±8.31	419.70±16.85	<0.001

Table 3: Comparison of systolic blood pressure (mmHg) between two groups

SBP (mmHg)	Group F	Group S	'p' value
Pre op	128.60±11.70	126.20±9.54	0.268
2 minutes	125.1±12.11	119.40±10.65	0.014
4 minutes	119.10±11.34	114.84±10.85	0.060
6 minutes	115.24±9.77	112.72±10.84	0.230
8 minutes	112.42±9.04	110.92±10.86	0.450
10 minutes	110.2±9.87	110.50±10.50	0.898
20 minutes	109.46±9.70	109.38±10.77	0.950
30 minutes	107.66±9.49	108.34±10.57	0.736
40 minutes	106.64±9.98	107.32±10.20	0.743
50 minutes	106.82±10.18	107.12±9.75	0.881
60 minutes	108.98±9.74	107.82±9.20	0.542
75 minutes	111.24±9.57	108.60±8.88	0.156
90 minutes	114.58±8.32	110.56±8.55	0.019

The mean systolic blood pressure did not show significant results.

Table 4: Comparison of diastolic blood pressure (mmHg) between two groups

DBP (mmHg)	Group F	Group S	'p' value
Pre op	80.10±8.58	80.78±7.81	0.679
2 minutes	77.38±9.68	74.18±9.22	0.094
4 minutes	72.46±8.56	71.06±9.48	0.440
6 minutes	69.04±8.65	69.44±9.56	0.827
8 minutes	65.76±7.87	67.74±10.31	0.285
10 minutes	62.30±8.39	66.68±10.31	0.022
20 minutes	60.92±9.23	65.12±9.96	0.032
30 minutes	61.36±7.40	64.80±9.66	0.048
40 minutes	60.90±8.25	64.94±9.62	0.026
50 minutes	61.28±8.50	64.76±9.28	0.053
60 minutes	62.98±8.79	65.16±8.90	0.221
75 minutes	65.75±7.53	65.62±8.30	0.933
90 minutes	69.00±7.54	67.18±8.42	0.258

The mean diastolic blood pressure did not show significant results.

Table 5: Side-effects noted in study groups

Side-effects	Group F		Group S	
	N	Percentage	N	Percentage
Nausea	3	6	0	0.0
Vomiting	1	2	0	0.0
Pruritus	3	6	0	0
Hypotension	8	16	14	28
Bardycardia	0	0.0	7	14
Urinary retention	0	0.0	0	0.0
Respiratory depression	0	0.0	0	0.0

Incidence of nausea vomiting and pruritus was known in our study but was insignificant.

Table 6: Comparison of visual analogue scale

VAS	Group F	Group S	p-value
6 hours	3.50±0.51	0.00±0.00	<0.001
12 hours	5.90±0.97	3.50±0.51	<0.001
18 hours	7.28±0.95	5.52±0.51	<0.001
24 hours	7.24±0.96	3.62±0.69	<0.001

Visual analogue scale used for assessing postoperative pain. VAS > 6 rescue analgesic was given and time noted.

bromage 3 were not significant. The use of intrathecal Fentanyl as an adjunct to bupivacaine is a well -established technique[19,20]. It has a fast onset and improves pain relief during and after surgery without causing a prolonged loss of motor function[21,22]. Fentanyl has higher lipid solubility and is efficiently cleared from the cerebrospinal fluid, reducing the likelihood of delayed respiratory depression. The present text describes the acquired clinical knowledge on the intrathecal usage of α2adrenoreceptor agonists, namely clonidine. However, more clinical trials are required to establish the effectiveness, safety and appropriate dosage of dexmedetomidine as an adjunct to spinal local anesthetics. α2-agonists attach to presynaptic C-fibers and postsynaptic dorsal horn neurons. The combined effect of local anesthetics and α2 agonists at the spinal level is responsible for the strong pain-relieving capabilities. Intrathecal administration of α-2 receptor agonists has been shown to considerably extend the duration of spinal anesthesia. Additionally, these agonists have analgesic effects for both somatic and visceral pain[23].

The time it took for reversion to bromage was greatly delayed in Group S. The average systolic blood pressure did not provide statistically meaningful findings. The average diastolic blood pressure did not exhibit statistically significant findings. The occurrence of nausea, vomiting and pruritus was seen in our research., however, it was deemed minor. A visual analogue scale is used to evaluate postoperative pain. An analgesic medication called VAS >6 rescue was administered and the time was recorded[24]. Singh H[25] shown that intrathecal administration of Fentanyl at a dosage of 25μ (o.3μ/kg) resulted in a decreased need for analgesics without an increase in the occurrence of adverse effects such as nausea, pruritus and denaturation during the early postoperative period. Multiple investigations have confirmed the efficacy of the 25μ dosage. In the current research, it was revealed that Fentanyl offers the longest duration of pain relief after surgery, while causing minor side effects such as respiratory depression and itching. However, the occurrence of itching was negligible and only detected in a few individuals. In a study conducted by Varrassi[26], it was seen that the administration of 25μg of Fentanyl during spinal anesthesia in senior men who were not premeditate did not have any effect on respiratory rate end-tidal carbon dioxide ($ETCO_2$) levels, minute ventilation, respiratory drive, or the reaction to carbon dioxide. However, the study found that the administration of 50μg of Fentanyl resulted in early respiratory depression. Hello EA Eid conducted a study where they administered 15μg of dexmedetomidine intrathecally. The results revealed

that this treatment led to considerably greater sedation ratings. This finding suggests that using dexmedetomidine intrathecally might be advantageous for patients who are enduring lengthy difficult procedures, as it can be used as an alternative to epidermal or extended general anesthetics.

CONCLUSIONS

Ultimately, the use of intrathecal hyperbaric bupivacaine-fentanyl serves as a viable substitute for intrathecal hyperbaric bupivacaine saline in spinal anesthesia. It offers superior preoperative /intra operative pain relief, stable blood flow, fewer adverse effects and decreased need for further pain medication during a 24-hour period.

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