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TO ASSESS AND COMPARE THE ANALGESIC EFFECT OF INTRATHECAL HYPERBARIC BUPIVACAINE VS MORPHINE AS AN ADJUVANT TO INTRATHECAL HYPERBARIC BUPIVACAINE IN ABDOMINAL HYSTERECTOMY SURGERY : A RANDOMISED DOUBLE BLIND INTERVENTIONAL STUDY

Anaesthesiology

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ABSTRACT

Background: The aim of this study is to assess and compare the analgesic effect of intrathecal hyperbaric bupivacaine vs morphine as an adjuvant to intrathecal hyperbaric bupivacaine in abdominal hysterectomy.

Methods: The study was done on 60 patients of (age 35-65 years, weight 45-70 kilograms) ASA grade 1&2. These were randomly allocated in 2 groups of 30 each. They were undergoing abdominal hysterectomy procedures. Group A patients received 3.5 ml of 0.5% hyperbaric bupivacaine+ 0.5 ml normal saline intrathecally (Total volume 4 ml). Group B patients received 3.5 ml of 0.5% hyperbaric bupivacaine + 150 mcg morphine diluted in 0.5 ml normal saline intrathecally (Total volume 4ml). Mean time of onset of sensory and motor block, mean time to first rescue analgesia, mean VAS score and proportion of cases with complications was recorded.

Conclusion: Morphine as adjuvant to hyperbaric bupivacaine provides longer duration of post-operative analgesia and significantly decreases requirement of total number of rescue analgesia in first 24 hours in compare to hyperbaric bupivacaine alone. It was also observed that onset of sensory block was earlier.

KEYWORDS

Spinal anaesthesia, Abdominal Hysterectomy, Morphine, Duration of analgesia.

INTRODUCTION

The word pain has been derived from "poena" which means penalty or punishment. Pain is defined by the International Association for the Study of Pain (IASP) is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage."

According to the American Board of Anaesthesiologist lists "relief and prevention of pain during surgical, obstetrics, therapeutic and diagnostic procedure", are one of the essential components of specialty. Post-operative pain is a major source of fear and anxiety.

Pain is frequently the result of nociception; an activity in the nervous system that results from the stimulation of nociceptors. This activity is carried to the brain, usually via the spinal cord, conveys information, without conscious awareness, about damage or near damage in body tissues. Pain is the conscious experience of sensorial information and a feeling of unpleasantness that manifests as a result of nociception. Relief of pain during surgery is the main aim of anaesthesia. Any expertise acquired in this field should be extended into the postoperative period.

Uncontrolled postoperative pain resulting from any kind of surgery may produce a range of detrimental acute and chronic effects. The transmission of nociceptive stimuli from the periphery to the central nervous system results in neuro-endocrine stress response resulting in increased sympathetic tone, increased catecholamine levels and catabolic hormone secretion. Shallow respiration and inadequate cough due to pain can result in postoperative pulmonary complications. In patients with underlying cardiac disease, severe postoperative pain may cause sympathetic stimulation and thus increase cardiac work and further pain can also cause constriction of the coronary vessels, leading to myocardial ischemia and infarction. Control of these pathophysiologic processes by administering adequate postoperative analgesia along with intraoperative anaesthesia may lead to improvement in morbidity and patient satisfaction.

Many options are available for the treatment of postoperative pain, including systemic (i.e. opioid and non-opioid) analgesics and regional techniques. Efficacy of intravenous opioids is typically limited by the development of tolerance or opioid related side effects. Intravenous opioids are commonly used for moderate to severe postoperative pain. Neuraxial and peripheral techniques can provide superior analgesia compared to systemic drugs.

Epidural and spinal blocks are the major techniques available in regional anaesthesia, with a long history of effective use for a variety of surgical procedure and pain relief.

Spinal anaesthesia, a common technique in anaesthesia practice, has got inherent advantages like intense motor and sensory blockade, good relaxation, reliability, avoids side effects of multiple drugs used in general anaesthesia, no postoperative respiratory depression, nausea, vomiting, drowsiness etc. It also has good patient and surgeon acceptability as well as safe enough for early discharge from the hospital.

Bupivacaine, an amide type of local anaesthetic, has high potency, slow onset and long duration of action is commonly employed for spinal anaesthesia. However, postoperative pain control is still a major problem as spinal anaesthesia using only local anaesthetics is associated with relatively short duration of action. Neuraxial adjuvants are used to improve or prolong analgesia and decrease the adverse effects associated with high doses of a single local anaesthetic agent. In addition to their dose sparing effects, neuraxial adjuvants are also utilized to increase the speed of onset of neural blockade (reduce latency), improve the quality and prolong the duration of neural blockade.

Intrathecal opioids added to local anaesthetics enhance analgesia without intensifying motor and sympathetic block, and make it possible to achieve successful anaesthesia in spite of the use of a low dose local anaesthetic. Among opioids morphine (long acting, hydrophilic, natural opioid analgesic) adjudged as the most effective due to its potent and prolonged effect. Till date no consensus has been reached regarding the optimal dose of single shot intrathecal morphine but appears to be 100–250 mcg. In our study we decided to use 150 mcg of morphine.

METHODS

The present study was carried out in the Department of Anaesthesiology at SMS Medical College and Hospital, Jaipur, Rajasthan. After obtaining institutional ethical committee approval and patients written informed consent, the study was conducted in 60 patients, aged 35-65 years of ASA Grade 1&2 scheduled for abdominal hysterectomy. The patients were randomly allocated using sealed envelope method in 2 groups (30 of each).

- Group A (n=30) :Patients received 3.5 ml of 0.5% hyperbaric bupivacaine + 0.5 ml normal saline intrathecally.(Total volume 4 ml)

- Group B (n=30) :Patients received 3.5 ml of 0.5% hyperbaric bupivacaine + 150 mcg morphine diluted in 0.5 ml normal saline intrathecally.(Total volume 4ml)

Patients with cardiovascular, respiratory, neurological and liver diseases, patients who are on narcotic therapy were excluded from study. A detailed pre-anaesthetic evaluation including history and a thorough general and systemic examination and all relevant investigations were done for all the patients.

After taking written informed consent and confirming overnight fasting, patient was taken on OT table patient was connected to monitors and baseline vitals like BP, pulse rate, respiratory rate was recorded 18 gauge intravenous (IV) cannula had been inserted and lactated Ringer's solution was administered as a bolus of 10 ml/kg before sub-arachnoid block to all patients. Vitals were noted just before lumbar puncture. Spinal anaesthesia was performed at L3- L4 interspace with the patient in left lateral position by using a 25 Gauge Quincke needle under strict aseptic conditions. Free flow of cerebrospinal fluid was verified before injection of the anaesthetic solution. All patients was immediately placed in a supine position following the injection with a head down tilt to achieve desired level of block of T6-T8. Patients were given 6.0 L/min of oxygen by face mask. Intra-operatively pulse rate, non-invasive BP, respiratory rate and Spo2 was monitored. Episodes of intra-operative hypotension were managed with crystalloids and if required with incremental doses of Inj. Mephentermine 6 mg intravenously. Bradycardia was treated with 0.6mg of Inj. Atropine intravenously. Intra-operative nausea was treated with inj. Ondansetron 4mg and any pruritus was treated using anti-histamines.

The onset of sensory block was defined as the time from the intrathecal injection of the bupivacaine to the time taken to achieve the desired level of block. This was assessed by pin prick test bilaterally in midclavicular line by using 25G hypodermic needle. The level of sensory block was assessed every 2 minutes till the highest level of the block was reached and the time to achieve the same was also noted.

Regression of sensory block was defined as the time taken for the sensory block to regress up to 2 segments of dermatome from the highest level achieved.

Onset of motor block was defined as the time taken from intrathecal injection to the time taken to achieve complete motor block (grade-3)

Immediately after operation patients were shifted to recovery room. Following observations were recorded:-

Vitals parameters – Regular check-up of blood pressure, pulse rate, saturation and respiratory rate were done at 5, 10, 15, 20, 25,30,40,50 ,60, 70,80,90 min interval and post operatively until first rescue analgesia given , patient monitored for 24 hours.

TOTAL DURATION OF ANALGESIA: Time from completion of surgery to patient's first demand of rescue analgesia. (On VAS 3)

Visual Analog Score: Postoperatively, the pain was assessed by using visual analogue pain scale (VAS) between 0 and 10 (0 = no pain, 10 = most severe pain). It was assessed at every 30 min. postoperatively.

The incidence of adverse effects such as nausea, vomiting, bradycardia, hypotension, respiratory depression and urinary retention were noted.

Side effects – The following side effects were looked for:-

1- Bradycardia (PR<60bpm) and hypotension (defined as a decrease of MAP by more than 20% from baseline or a fall of SBP below 90 mmHg).
2- Nausea and vomiting – assessed by three point scale. (0= no nausea and vomiting, 1= mild to moderate nausea or vomiting not needing treatment, 2= severe nausea or vomiting needing treatment).
3- Respiratory depression
4- Shivering

STATISTICALANALYSIS

All Statistical analysis was performed with the SPSS. The Categorical variables were summarized as percentage and were analysed using Chi square test. The quantitative data was presented as mean and standard deviation were compared by student t-test. A Probability (p value) less than 0.05 was considered as statistically significant.

Observations

A total of 60 patients who underwent abdominal hysterectomy surgery were enrolled for the study and were randomly divided into 2 groups. The demographic profiles with regard to age and weight was comparable. The distribution as per ASA status was similar. The duration was surgery in both the groups was also similar and statistically insignificant.

Pre-induction heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, spo2 were comparable in both the groups with a statistically no significant difference between them ($p<0.05$).

Table 1: Mean time to onset of sensory block (min)

	Group A		Group B	
	Mean	SD	Mean	SD
Sensory Block	6.93	1.36	5.67	1.06
Median	6		6	
P VALUE	0.0001 (S)			

Above table shows mean time to onset of sensory block in both the groups. Mean time to onset of sensory block in patients of group A was 6.93±1.36 (min) and the Mean time to onset of sensory block in patients of group B was 5.67±1.06 (min). Difference was statistically significant ($p = 0.0001$).

Table 2: Mean time to onset of motor block (min)

	Group A		Group B	
	Mean	SD	Mean	SD
Motor Block (Bromage grade III)	9.37	1.00	8.80	0.85
Median	9		9	
P VALUE	0.021 (NS)			

As depicted in above table the mean time of onset of motor block. The mean time of onset of motor block in group A was 9.37±1.00 (min) in group A and in group B it was 8.80±0.85 (min). Difference in mean time of onset of motor block was statistically not significant ($p>0.001$). In both group in cases achieved highest degree of motor blockage was bromage grade 3.

Table 3: Comparison of VAS among two groups

	Group A		Group B		Result (P value)
	Mean	SD	Mean	SD	
0 min	0.00	0.00	0.00	0.00	-
30 min	0.77	0.90	0.77	1.04	1.00 (NS)
1 hr	0.97	1.00	0.87	1.01	0.701(NS)
2 hr	2.83	1.21	2.60	1.22	0.459 (NS)
4 hr	3.83	0.53	3.33	0.96	0.015 (S)
6 hr	3.90	0.40	3.60	0.62	0.030 (S)
12 hr	3.93	0.37	4.00	0.00	0.321 (NS)
18 hr	3.97	0.18	4.00	0.00	0.321 (NS)
24 hr	3.97	0.18	4.00	0.00	0.321 (NS)

Comparison of the mean VAS between the groups which is statistically significant at 4 and 6hours ($p <0.05$).

Table-4: Mean time of first rescue analgesia

	Group A		Group B	
	Mean	SD	Mean	SD
Mean Time to first rescue analgesia	227.33	17.06	387.17	26.96
Median	228		393	
P value	P <0.001 (S)			

As depicted in above table, the mean time of first rescue analgesia in patients of group A was 227± 17.06(min) and in group B was 387.17±26.96 (min). Difference was statistically significant. (p value <0.001). Mean time of first rescue analgesia was longer in group B as compared group A.

Table 5: Number of rescue analgesia in 24 hours (Number)

	Group A (N=30)		Group B (N=30)	
	No.	%	No.	%
1 time	2	6.67	30	100.00
2 times	14	46.67	0	0

3 times	13	43.33	0	0
4 times	1	3.33	0	0
RESULT (P VALUE)	p<0.001 (S)			

In group A 6.67% of the patients were given one time rescue analgesia, 46.67% of the patients were given twice times rescue analgesia and 43.33% were given thrice times rescue analgesia and 3.33% were given four times rescue analgesia, While in group B 100% of the patients were given only once rescue analgesia which is significantly less than group A (p<0.001).

Table 7: Adverse Effects

	Group A (N=30)		Group B (N=30)		P value
	No.	%	No.	%	
Hypotension	3	10.00	2	6.67	1.000(NS)
Bradycardia	2	6.67	3	10.00	1.000(NS)
Nausea & Vomiting	7	23.33	8	26.67	0.760 (NS)
Respiratory Depression	0	0.00	0	0.00	-
Shivering	0	0.00	1	3.33	1.000(NS)
Pruritis	0	0.00	0	0.00	-

Above table shows comparison of the incidence of side effects in both groups. Hypotension occurred in 3 patients (10.0%) in group A while in 2 patients (6.67%) in groups B. Bradycardia occurred in 2 patients (6.67%) in group A whereas and in 3 patients (10.0%) in groups B. Nausea occurred in 7 patients (23.33%) in group A whereas in 8 patients (26.67%) in groups B, Shivering occurred in 1 patient (3.33%) in group B. None of patient in both the groups complained of respiratory depression and pruritis.

DISCUSSION

Spinal anaesthesia is the most commonly used technique for abdominal hysterectomy surgeries, as it is cost effective and easy to administer. However, postoperative pain control is a major concern, because spinal anaesthesia uses only local anaesthetic drugs associated with relatively short duration of action and thus early rescue analgesic is needed in the post-operative period. Various drugs such as dexmedetomidine, clonidine, midazolam, fentanyl and others have been used as an adjuvant for prolongation of the effect of spinal anaesthesia and duration of analgesia.

It is important to manage post-operative pain judiciously and adequately. Postoperative pain may delay recovery, increase hospital stay and patient's expenditure. Good analgesic techniques minimizes patient's discomfort, facilitates early mobilization and discharge from hospital. It also prevents acute pain developing into chronic pain.

Intrathecal opioids added to local anesthetics enhance analgesia without intensifying motor and sympathetic block. Among opioids, morphine is the very effective due to its potent and prolonged effect. Analgesia is long lasting due to its hydrophilicity, decreased systemic absorption, and slow rate of clearance from the opioid receptors. Till date no consensus has been reached regarding the optimal dose of single shot intrathecal morphine but appears to be 100–250 mcg considering the ceiling dose for analgesic efficacy of intrathecal morphine we decided to study 150 mcg of morphine.

This study was conducted to compare the analgesic effects of intrathecal hyperbaric bupivacaine with morphine in patients undergoing abdominal hysterectomy.

Peri-operative hemodynamic variables, duration of post-operative analgesia, block characteristics and any adverse effects were observed in both the groups at different time interval.

Demographic variables were comparable in the both the groups.
The mean duration of surgery was comparable in both the groups. It was 65.00±15.92 min in group A and 68.67±15.97 min in group B (p value =0.376).

The mean time of onset of motor block in group B was 8.80±0.85 min and in group A was 9.37±1.00 min. The mean time of onset of motor block was earlier in group B as compared to group A. It was statistically significant as p value = 0.021. **Darshan Ashvine Trivedi and coworker (2013)**[1] found that mean time onset of motor block was significantly earlier in group B as compared to group A. Results of this study coincides with the results of study done by **Monica brunschwiler and coworker** (1998). They also found that mean time onset of motor block was statistically earlier in group B as compared to group A. **Xiaofei Qi and co- worker (2016)**[8] found that mean time onset of motor block was significantly earlier in group B as compared to group A. In both groups A and B all patients achieved degree of motor block grade 3.

None of the patients experienced pain in both the groups up to 30 minutes post-operatively. Difference in mean VAS score was significantly higher in group A as compared to group B at 90, 120, 150, 180, 210, 240, 270,300 and 360 minutes postoperatively (p-value was statistically significant at 4 and 6 hr).

It was observed that VAS score was significantly less in group B as compared to group A for 300 minutes post-operatively. Observations of this is consistent with previous studies conducted by **Grace Det et al (1995)**[3]. They also found that VAS score was significantly high group A as compared to group B. They used 0.5 gm morphine as an adjuvant to hyperbaric bupivacaine. **D.J.Fogarty et al (1995)**[4] also reported that intrathecal bupivacaine with morphine significantly prolongs the mean duration of motor block as compared to intra intrathecal bupivacaine.

The mean time for first rescue analgesia i.e time from intrathecal injection to patients demand for analgesic was 227.33±17.06 in min in group A while 387.17±26.96 min in group B. Difference in mean time for first rescue analgesia was significantly more in group B (p<0.001). The duration of analgesia was longer in group B as compared to group A. **D.J. Fogarty et al (2015)**[4] found that duration of analgesia was prolonged in morphine group as compared to bupivacaine group.

Jacobson and coworker (1988) found that duration of analgesia was prolonged in morphine group as compared to bupivacaine group. **Rath mall and Associates (2003)**[7] found that duration of analgesia was prolonged in morphine group as compared to bupivacaine group. They used 100-300 mcg morphine as an adjuvant to hyperbaric bupivacaine. **Xiaofei Qi and coworker (2016)**[8] found that duration of analgesia was prolonged in morphine group as compared to bupivacaine group.

The heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and SpO2 were statistically insignificant in the both groups at different time interval peri-operatively. **Abdel Ghaffer HS Mohammed S A and co worker (2016)**[5] observed insignificant difference in hemodynamic variations in both groups. They used 0.5 gm morphine as an adjuvant to hyperbaric bupivacaine. Similar Results was observed by studied done by **Brunschwiler M et al (1998)**[6] they find out their was no statistically significant hemodynamic variation in both groups. They used 0.15 gm morphine as an adjuvant to hyperbaric bupivacaine.

Occurrence of nausea and vomiting during perioperative period was 8 (26.67%) patients in group B and 7 (23.33%) patients in group A. Difference of occurrence of nausea and vomiting in both groups was statistically insignificant (P value = 0.760)

None of the patients experienced shivering, pruritus in both the groups. Though the occurrence of side effects were more in group B than in group A and side effects were statistically insignificant in both the groups. **Brian D Sites (2003)** found that incidence of side effect in bupivacaine group and morphine group were comparable It was statistically insignificant.

CONCLUSION

We concluded that morphine as adjuvant to hyperbaric bupivacaine provides longer duration of post-operative analgesia and significantly decreases requirement of total number of rescue analgesia in first 24 hours in compare to hyperbaric bupivacaine alone. It was also observed that onset of sensory block was earlier.

Hence, we conclude that group B (morphine) is better for post-operative analgesia and it can be used safely.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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