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A COMPARATIVE STUDY OF EFFICACY AND SIDE EFFECTS OF ADDITION OF VARYING DOSES OF FENTANYL INTRATHECALLY TO HYPERBARIC BUPIVACAINE IN PATIENTS UNDERGOING LOWER LIMB SURGERIES OR INGUINAL HERNIOPLASTIES

Anesthesiology

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ABSTRACT

Background And Aims: It is a common practice to add intrathecal opioids to local anesthetics to improve the quality of subarachnoid block. This study was designed to find an optimal dose of intrathecal Fentanyl, which can improve the quality of surgical anesthesia with minimal side effects in patients undergoing lower limb surgery or inguinal hernioplasties.

Material And Methods: In this prospective randomized double-blind study, 90 patients of either sex belonging to ASA grade I and grade II undergoing either lower limb surgery or inguinal hernioplasty under spinal anesthesia were randomly allocated to receive 10, 20, or 30 µg of intrathecal Fentanyl with 10 mg of 0.5% hyperbaric Bupivacaine. Patients were assessed for clinical efficacy by measuring onset and duration of sensory , and motor block and duration of analgesia. The side effects assessed were sedation, pruritus, nausea, vomiting and decrease in saturation and respiratory rate.

Results: Patients who received 20 µg of fentanyl have significantly prolonged sensory and motor block ($P < 0.05$) than the lower dose group. All patients in three groups have no statistically significant difference in the onset of sensory or motor block and hemodynamic variables.Patients who received 30 µg of fentanyl have a significantly higher incidence of pruritus, nausea, sedation and decrease in oxygen saturation compared to other group ($P < 0.05$).

Conclusion: Intrathecal Fentanyl in a dose of 30 µg did not improve anesthesia or analgesia compared to the two lower doses (10 and 20 µg), but increased the incidence of pruritus and nausea, while 10 µg was associated with earlier occurrence of pain in the recovery room. Therefore it was concluded that 20 µg of Fentanyl is the optimal dose of intrathecal Fentanyl to supplement intrathecal hyperbaric Bupivacaine (10 mg) for patients undergoing lower limb surgery or inguinal hernioplasty under spinal anesthesia.

KEYWORDS

Fentanyl, Bupivacaine, Modified Bromage scale, Ramsay Sedation Score

INTRODUCTION

Lumbar subarachnoid block is commonly employed for Inguinal Hernioplasty and lower limb surgeries because of its rapid onset, less failure rates and cost-effectiveness but it has the drawbacks of shorter duration of block and a lack of postoperative analgesia [1]. There is increasing interest in using various adjuvants to spinal local anaesthetics with the goal of decreasing the dose of local anaesthetics, enhancing the duration of action and minimising the side effects of local anaesthetics.

Various adjuvants have been used to prolong the action of intrathecal Bupivacaine like Clonidine, Dexmedetomidine, Opioids [2] (Fentanyl, Butorphanol), Ketamine, Midazolam etc. Neuraxial Opioids are widely used in conjunction with local anesthetics as they permit the use of lower dose of local anaesthetics while providing adequate anaesthesia and analgesia[3].

Fentanyl is highly lipophilic short-acting opioids which when added to local anaesthetics not only improves the quality of intra operative analgesia but also prolongs the duration and effectiveness of post operative analgesia[4]. It is preferred as an adjuvant in spinal anaesthesia because of its rapid onset of action, less risk of hypotension, absence of active metabolites and short duration of action with minimal cephalic spread[5]. Intrathecal Fentanyl is, however, associated with side effects such as pruritus, nausea, vomiting, oxygen desaturation and respiratory depression[6]. The effects associated with intrathecal Fentanyl appears to be influenced by dose of administration, as higher doses (50 microgram) causes respiratory depression while 40 microgram increases the incidence of itching, nausea and vomiting [7].

Bupivacaine is an amide-type, long-acting local anesthetic which is a equimolar racemic mixture of R(+) Bupivacaine and S(-) Bupivacaine . Bupivicaine reversibly binds to specific sodium ion channels in the neuronal membrane, resulting in a decrease in the voltage-dependent membrane permeability to sodium ions and membrane stabilization; inhibition of depolarization and nerve impulse conduction; and a reversible loss of sensation [8].

In this study we attempted to get an optimal dose of Intrathecal Fentanyl (10mcg, 20mcg or 30mcg) in patients undergoing Lower limb surgeries or Inguinal Hernioplasties.

MATERIAL AND METHODS

The study was carried out in Swaroop Rani Nehru Hospital associated with Moti Lal Nehru Medical College, Prayagraj over a period of one year from June 2019 to May 2020 after approval from Ethical Committee of the Institution and obtaining written and informed consent from all the patients.

Study Design:

This was a Prospective, Randomized, Interventional, Double blind and Non- Placebo study.

Selection Of Cases:

A total of 90 adult patients of either sex, belonging to ASA grade I and II, posted for either Inguinal Hernioplasties or Lower limb surgeries were included in this study.

Inclusion Criteria:

1. Patients with valid informed and written consent.
2. Patients of either sex aged between 18 to 60 years.
3. Patients of ASA grade I and grade II.
4. Patients undergoing elective Inguinal Hernioplasty or Lower Limb Surgery.

Exclusion Criteria:

1. Patients refusal.
2. ASA Class III and above.
3. Duration of Surgery exceeding 120 minutes.
4. Local site infection or sepsis.
5. Patients with spinal deformities.
6. Patients with bleeding disorder(s).
7. Patients having severe cardiovascular disease(s), hypertension or hypotension.
8. Patients having compromised reserves of respiratory system.

9. Patients having prior history of allergy to study drug.

Group Allocation:
Patients were randomly allocated and divided into three groups (30 patients in each group) using computer generated random number table.

Group A	30 Patients	Intrathecal 0.5% hyperbaric Bupivacaine (10mg,2.0ml) administered with Fentanyl 10µg (0.2 ml diluted to 0.6ml).
Group B	30 Patients	Intrathecal 0.5% hyperbaric Bupivacaine (10mg,2.0ml) administered with Fentanyl 20µg (0.4 ml diluted to 0.6ml).
Group C	30 Patients	Intrathecal 0.5% hyperbaric Bupivacaine (10mg,2.0ml) administered with Fentanyl 30µg (0.6 ml)

Double Blinding:
Double blinding was achieved by two different anaesthesiologists – one for preparation of the study drug, second for administration of the drug and data collection. Hence the observer and patient, both were unaware of the study drug.

METHODOLOGY:
A detailed Pre-Anaesthetic evaluation was done one day before surgery. A written informed consent was taken. All patients were kept nil per oral from 12 midnight and received Tab. Ranitidine 150mg and Tab. Alprazolam 0.5 mg as pre-medication on night prior to surgery.

In the operation theatre, intravenous access was established and 10-20 ml/kg of intravenous Ringer Lactate was infused over 20 - 25 min prior to subarachnoid block. Patients were attached to standard ASA monitors and baseline parameters were recorded.

The intrathecal adjuvant solutions were prepared under strict aseptic technique using 0.9% normal saline where dilution was required.

In left lateral position or sitting position, skin was cleaned and draped. After informing the procedure to the patient, following strict aseptic techniques, following series of steps for **4 P's (Preparation, Position, Projection and Puncture),** the subarachnoid space was entered using 25-gauge Quincke Babcock spinal needle. After ensuring free flow of cerebrospinal fluid, the study drug was administered over 20–30 seconds. The patients were placed in the supine position later on.

All patients received a total volume of 2.6 ml containing 2 ml of 0.5% hyperbaric Bupivacaine with 0.6 ml of solution containing either 10 µg (Group A), 20 µg (Group B) or 30 µg (Group C) of preservative-free Fentanyl. One of the investigators who was blind to group allocation recorded Pulse rate, Mean arterial pressure, Respiratory Rate and peripheral O2 saturation (SpO_2) at baseline (i.e. 5 min after stabilization of patient in the operation room), at the time of institution of spinal anesthesia i.e. 0 minute, at every 5 min interval for first 15 minutes and at 15 minute intervals for the rest of surgery.

Sensory level was assessed by loss of sensation to pinprick in the mid-clavicular line bilaterally. Time to reach sensory level of T6 on the operating side was taken as the time of onset of sensory block.

Motor block was assessed using **Modified Bromage scale**[9]. Time taken to reach Bromage 3 was taken as the time of onset of motor block. Sedation score was assessed using **Ramsay sedation score**[10].

Occurrence of side effects, such as nausea, vomiting, pruritus, decrease in saturation to <90, and respiratory rate of <8 per minute was recorded. Any patient who complained of nausea, vomiting, pruritus were treated according to the hospital protocols.

All the patients were shifted to post anaesthesia recovery room for next 4 hours and were observed. **Duration of Sensory Block was measured from the time** from achieving T6 block height to the time when same regresses to S2 level. **Duration of Analgesia** was measured from the time of achieving the T6 block to the first request of analgesia. At this time, intravenous opioid infusion was started after a bolus dose of opioid. **Duration of Motor Block** was measured from the time from achieving Bromage 3 to regaining Bromage 0.

Statistical Analysis:
All data was entered into Microsoft Excel spreadsheet and analyzed by SPSS (Statistical Package for the Social Sciences) version 20.0 statistical analysis software. Data was summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. Significance was assessed at 5% level of significance. A "p" value of <0.05 was considered as significant. ANOVA test was used to analyze the quantitative variables. Tukey's honestly significant difference (Tukey HSD) *post-hoc* test was used to compare among groups if *P* was found to be statistically significant. Qualitative data (Demographic variables, Gender and complications) were compared using Chi-square test.

Observations
Following observations were drawn from the study.

Table-1 : Comparison Of Demographic Profile And Clinical Characteristics

Variables	Group A	Group B	Group C	P-value
Age (in years)	41.26 ± 13.42	39.56± 13.57	35.66 ± 11.63	0.219
Height (in cms)	166.40 ± 7.28	167.06 ± 6.98	167.60 ± 6.66	0.784
Weight (in kg)	63.16 ± 9.50	65.20± 10.39	65.83 ± 9.62	0.549
BMI (kg/m^2)	22.66 ± 2.13	23.30 ± 2.45	23.33 ± 2.08	0.482
PR	78.66 ± 10.57	77.93 ± 10.83	77.60 ± 5.92	0.899
MAP	91.40 ± 2.64	89.63 ± 3.66	87.00 ± 3.76	0.114
SPO_2	98.63 ± 1.03	98.80 ± 0.84	98.73 ± 0.78	0.751
RR	13.10 ± 1.12	13.36 ± 1.24	13.13 ± 1.16	0.657

Patients in three groups were comparable in their baseline demographic and clinical parameters [Table 1]. The mean values of mean arterial pressure (MAP) and heart rate (HR) were comparable between the three groups throughout the intraoperative and postoperative periods. None of the patients experienced respiratory distress at any point of time [Table 1].

Table-2 : Comparison Of Mean Time Of Onset And Duration Of Sensory And Motor Blocks And Duration Of Analgesia:

				P-value		
Variables	Group A	Group B	Group C	A v/s B	A v/s C	B v/s C
Onset of Sensory Block	5.13 ± 0.93	5.03 ± 1.09	5.00 ± 0.90	0.706	0.578	0.899
Onset of Motor Block	5.90 ± 1.06	5.86 ± 0.89	5.80 ± 1.18	0.807	0.896	0.732
Duration of Sensory Block	140.50 ± 9.22	152.00 ± 14.59	157.00 ± 13.49	0.001	0.000	0.174
Duration of Motor Block	140.55 ±8.35	143.50 ± 11.60	143.71 ± 12.10	0.552	0.501	0.997
Duration of Analgesia	214.00 ± 22.98	248.16 ± 13.16	254.00 ± 27.49	0.000	0.000	0.299

When compared , the time of onset of both sensory and motor block was statistically insignificant in all the three groups ($P > 0.05$) . The duration of sensory block was significantly prolonged in group B and group C as compared to group A ($P \leq 0.001$) . The duration of analgesia was significantly prolonged in group B and group C as compared to group A ($P < 0.001$). However, duration of sensory block and analgesia for group B and C were comparable with no statistical differences between these two groups ($P > 0.05$). The duration of motor block were comparable between the three groups ($P > 0.05$). [Table 2]

Table-3: Comparison Of Side Effects Among Groups :

				P- value		
COMPLICATIONS	Group A	Group B	Group C	A Vs B	A Vs C	B Vs C
Sedation Score	2.16 ± 0.37	2.23 ± 0.43	2.56 ± 0.50	0.527 (NS)	0.001 (Sig)	0.008 (Sig)
Hypotension	2 (6.66%)	2 (6.66%)	4 (13.33%)	1.000 (NS)	0.398 (NS)	0.398 (NS)
Bradycardia	1 (3.33%)	2 (6.66%)	4 (13.33%)	0.561 (NS)	0.167 (NS)	0.398 (NS)

Oxygen Desaturation	0 (0%)	1 (3.33%)	5 (16.66%)	0.321 (NS)	0.019 (Sig)	0.088 (NS)
Pruritis	0 (0%)	1 (3.33%)	8 (26.66%)	0.321 (NS)	0.002 (Sig)	0.011 (Sig)
Nausea	2 (6.66%)	4 (13.33%)	9 (30.00%)	0.398 (NS)	0.039 (Sig)	0.020 (Sig)
Vomitting	2 (6.66%)	4 (13.33%)	8 (26.66%)	0.398 (NS)	0.019 (Sig)	0.018 (Sig)

The mean maximum sedation score was higher in Group C as compared to Group B and Group A ($p<0.05$). The incidence of oxygen desaturation, pruritus , nausea and vomiting was higher in group C as compared to other two groups ($p<0.05$). There was no statistically significant difference in the greatest decrease in mean HR, mean SBP and MAP in the three groups($P > 0.05$). [Table 3]

RESULT

Following results were drawn from our study:

1. Demographic data and clinical characteristics were comparable among the three groups in respect of age, height, weight, BMI, sex and baseline vital parameters in terms of Pulse rate, Mean Arterial Pressure, Oxygen saturation and Respiratory rate with no statistically significant difference ($p> 0.05$). {Table – 1}
2. Time of onset of both sensory and motor block was statistically insignificant in all the three groups ($P > 0.05$). {Table – 2}
3. The duration of sensory block was significantly prolonged in group B and group C as compared to group A ($P \leq 0.001$). {Table – 2}
4. The duration of analgesia was significantly prolonged in group B and group C as compared to group A ($P < 0.001$) {Table – 2}
5. The duration of motor block were comparable between the three groups ($P > 0.05$). {Table – 2}
6. The incidence of side effects was higher in Group C as compared to Group B and Group A. {Table – 3}

DISCUSSION

In our study, the dose of intrathecal fentanyl used was 10 µg, 20 µg, 30 µg. The patients studied across the group did not vary much with respect to age, sex, height or BMI. Baseline vitals were comparable among the groups.

Previous studies have shown significantly higher number of failed blocks in patients receiving intrathecal fentanyl in the doses of 7.5 µg.[4] . **Chu *et al.*** found that all patients receiving 12.5 and 15 µg of intrathecal fentanyl with 0.5% hyperbaric bupivacaine experienced excellent intraoperative and postoperative analgesia contrary to patients receiving 7.5 µg of fentanyl[4]. Therefore, most of the authors prefer to use doses of intrathecal fentanyl higher than 10 µg.

In our study, the time of achieving sensory block of T6 and motor block was similar in all three groups, indicating that it is the presence of opioid and not the dose of opioid that affects the onset of block, which is in accordance with the previous studies.

Ali MA *et al.*[11] in their study used 10µg, 15µg, 25µg intrathecal Fentanyl and found that there was no significant difference in time of onset of sensory and motor blockade. However, the duration of sensory block increased with the increase in dose of intrathecal Fentanyl.

There was significant difference in the duration of surgical blockade provided by using 20 µg (152.00 ± 14.59 minutes) as compared to 10 µg(140.50 ± 9.22 minutes) but no such significance was seen when the dose was increased to 30 µg (157.00 ± 13.49 minutes) which is in accordance with the findings of previous studies. Also, in our study, the duration of analgesia was significantly higher by using 20 µg (248.16 ± 13.16) as compared to 10 µg(214.00 ± 22.98 minutes) but no such significance was seen when the dose was increased to 30 µg (254.00 ± 27.49 minutes).

The duration of motor blockade in group A was (140.55 ±8.35minutes), in group B was (143.50 ± 11.60 minutes) and in group C (143.71 ± 12.10 minutes) which was comparable and did not differ significantly. This is also in accordance with the previous studies.

The side effects observed in the study were pruritus, nausea, and vomiting, sedation, oxygen desaturation and respiratory depression. The incidence of pruritus was highest in the patients from Group C (26.66%) compared to Group A (0%) and Group B (3.33%). Previous studies have shown similar findings. **Hunt *et al.*** observed a significant increase in the overall incidence of itching in patients who received 25 and 50 µg of intrathecal fentanyl [12] . Nausea and vomiting are other frequent complications of intrathecal fentanyl administration. In our study, the incidence of nausea was highest in the patients from Group C (26.66%) compared to Group A(6.66%) and Group B (13.33%) and also the incidence of vomiting was highest in the patients from Group C (30.00%) compared to Group A(6.66%) and Group B (13.33%). The high incidence of nausea in this study is not comparable to other studies which showed either less[13] or no differences[14].

In our study, the incidence of oxygen desaturation was highest in the patients from Group C (16.66%) compared to Group A(0) and Group B (3.33%) but none of the patients had respiratory rate less than 8/minute. **Khanna MS *et al.*[15]** in 2002 used 25 µg Fentanyl intrathecally along with Bupivacaine in elderly patients undergoing dynamic hip screw fixation (hip replacement) surgeries, found no change in the respiratory rate but slight reduction in SpO2 was observed. Most authors used doses below 25 µg in later studies and did not find respiratory depression in any patient[(76,82)]. The findings of our study were consistent with the previous studies.

CONCLUSION

In this study we found that duration of sensory block and duration of analgesia was longer in Group B (20µg). Group C (30µg) was associated with higher incidence of pruritus, nausea, vomiting ,sedation and oxygen desaturation with no improvement in anaesthesia or analgesia while Group A (10µg) was associated with early occurrence of pain in recovery room. Therefore it was concluded that Intrathecal Fentanyl in dose of 20 µg is the optimal dose to supplement Hyperbaric Bupivacaine (10mg) for patients undergoing lower limb surgeries or inguinal hernioplasties under spinal anaesthesia.

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