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# POST OPERATIVE ANALGESIC EFFECT OF INTRATHECAL FENTANYL ON HYPERBARIC BUPIVACAINE FOLLOWING TOTAL ABDOMINAL HYSTERECTOMY

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**ABSTRACT**

**Objective:** This prospective, randomised, double blinded study was carried out to evaluate the post-operative analgesic effect of intrathecal fentanyl mixed with hyperbaric bupivacaine following total abdominal hysterectomy.

**Methods:** This study was conducted on sixty adult patients who underwent elective total abdominal hysterectomy. They were randomised into two groups to receive intrathecal bupivacaine heavy 0.5% plus normal saline 0.25 ml (Group I) and equal amount of intrathecal bupivacaine plus 0.25 ml of fentanyl citrate (Group II).

**Results:** There was no significant differences in the duration of surgery between the groups. However, the duration of post-operative analgesia was significantly longer in the fentanyl. Intraoperative hemodynamic stability was better in the fentanyl group though it was not statistically significant.

**Conclusion:** The addition of fentanyl to intrathecal bupivacaine significantly increases the intraoperative hemodynamic stability and the duration of post-operative analgesia without significant side effects.

**KEYWORDS :** Spinal anaesthesia, intrathecal, fentanyl, hysterectomy

**Introduction :**

Spinal anaesthesia with hyperbaric bupivacaine is widely used for lower abdominal and lower limb surgeries because of simplicity of technique, rapid onset of action and reliability in producing uniform sensory and motor blockade. But the main disadvantage is its limited duration of action and hence lack of long lasting postoperative analgesia. Many adjuvant drugs may be added to local anaesthetic solution not only to prolong the duration of the block but also to provide postoperative analgesia. Administration of local anaesthetics in combination with opioids intrathecally[1,2] is an excellent technique for managing postoperative pain. Opioids have been a choice in regional anaesthesia to improve the antinociceptive effect of local anaesthetics. Morphine[3] and Fentanyl [4] are being used intrathecally together with local anaesthetics in caesarean section. Fentanyl , a lipophilic opioid not only improves intraoperative analgesia following intrathecal administration but also enhances early postoperative analgesia[5,6,7,8] without delayed respiratory depression[9].

The present study was designed to evaluate the post operative analgesic effect and the associated complications of intrathecal Fentanyl as an adjunct to hyperbaric bupivacaine in patient undergoing total abdominal hysterectomy.

**Methods:**

A prospective randomised double blinded study was conducted in the Department of Anaesthesiology, RIMS, Imphal. After obtaining approval from the Institutional Ethical Committee and Informed consent, 60 (sixty) patients of ASA (American Society of Anaesthesiologists)- I and II grades, aged between 35 to 65 years, undergoing total abdominal hysterectomy under spinal anaesthesia were included in the study. All the patients were randomly divided into two groups of 30(thirty) each.

1. Group I (Control group) patients received Inj.0.5% bupivacaine (heavy) 2.75ml mixed with 0.25ml of normal saline.
2. Group II (Fentanyl group) patients received Inj.0.5% bupivacaine (heavy) 2.75ml mixed with 0.25ml (12.5µg) of Fentanyl citrate.

Patients with neurological deficit, bleeding disorder, psychiatric disorder, chronic pain, obvious skeletal deformity and patients on antihypertensive medication were excluded.

Age, weight, heart rate, arterial blood pressure, peripheral oxygen saturation, duration of surgery and duration of postoperative analgesia and any adverse effects or complications were recorded. All the patients were kept overnight fasting and received diazepam 10mg and ranitidine 150mg orally as premedication in the night before surgery. On arrival at the operation theatre, baseline heart rate (HR), non-invasive blood pressure (NIBP), continuous electrocardiogram (ECG) and peripheral oxygen saturation of haemoglobin ($SPO_2$) were recorded. All the patients were preloaded with Inj. Ringer's lactate 15ml per kg body weight about 15minutes before the intended time of intrathecal drug administration. Under adequate aseptic precaution lumbar puncture was performed at $L_{3-4}$ intervertebral space using midline approach with a 25 gauge quincke spinal needle in the lateral decubitus position.

The haemodynamic parameters such as HR, NIBP, ECG and $SPO_2$ were monitored periodically and recorded at 2minutes interval for the first 10minutes and thereafter at 5minutes interval until the end of surgery. All the patients were also observed for the presence of side effects/complications (dry mouth, dizziness, anxiety, restlessness, pruritus, sedation, nausea). Intravenous fluid was administered in the form of Ringer's lactate (RL) at the rate of 10ml per kg body weight per hour. A decrease in systolic blood pressure of >20% from baseline was treated with rapid infusion of 500ml of RL and 5mg of Inj. Mephentermine intravenously and bradycardia (HR< 60 per mins) was also treated with intravenous atropine sulphate.

All the patients were observed in the post anaesthetic recovery room and then in the ward for 24 hrs. Duration of post-operative analgesia was taken as the time from the end of the surgery upto the patients first analgesic request and rescue-analgesia was provided by Inj. Tramadol hydrochloride 100mg intravenously.

**Results:**

The weight of the patients ranged from 56.4 to 57 kg and their age range was between 44.8 to 46.7 years. The duration of surgery (minutes) in both the groups were similar (64.17 Vs. 62.67) but the duration of analgesia (minutes) in the Fentanyl group was significantly longer than the control group (265.67 Vs. 138.83) ($p<0.001$) as shown in Fig. 1.

At the pre-operative stage, no significant differences in the heart rate and blood pressure were observed among the groups. Fig. 2 shows the distribution of mean arterial blood pressure over the groups and it was found that the pressure in the Fentanyl group was normally higher in all the stages than the corresponding value for the control group. These variations were tested by independent sample t-test, it was concluded that there was no significant variations between the groups statistically except from 2 minutes to 15 minutes. Peripheral oxygen saturation were comparable in both the groups.

Pruritus was found in only 1 patient in the Fentanyl group which was mild and self-limiting. There were no side effects like dry mouth, sedation, nausea, etc. It shows that the pattern of side effects were similar in both the groups.

**Discussion :**

Many workers had attempted to prolong the effects of spinal anaesthesia and provide postoperative analgesia with the use of adjuvant drugs. Adequate post operative pain control is essential to prevent adverse consequences of surgical insult.

The administration of local anaesthetics in combination with opioids intrathecally is an excellent technique for managing postoperative pain following abdominal, pelvic, thoracic or orthopaedic procedures on lower extremities. Discovery of opioid receptors in spinal cord triggered the usage of intrathecal opioids. Local anaesthetics with opioids demonstrate significant synergy. They provide excellent analgesia with fewer drug requirements and decreased side effects.

Opioids and local anaesthetics exert their antinociceptive effect in the spinal cord by different mechanisms. The μ agonist, Fentanyl , exerts its action by opening $K^+$channels and reducing $Ca^{+2}$ influx, resulting in inhibition of transmitter release. The μ agonists also have a direct postsynaptic effect, causing hyperpolarisation and a reduction in neuronal activity. Local anaesthetic, bupivacaine, acts mainly by the blockade of voltage-gated $Na^+$ channels in the axonal membrane. Local anaesthetics may also interfere with synaptic transmission by a presynaptic inhibition of $Ca^{+2}$ channels in addition to their effects on nerve conduction. A combination of these effects may explain the observed synergism between bupivacaine and Fentanyl in our study group.

In the present study, duration of analgesia in the Fentanyl group (265.67±28.85min) was significantly longer than the control group (138.83±13.17 min). The mean BP in the Fentanyl group was higher than the control group but was statistically insignificant. HR was statistically not significant. One patient in the Fentanyl group had pruritus but it was mild and self-limiting. Peripheral O2 saturation in both the groups was comparable.

Our findings were in agreement with the study by BN Biswas et al[10] in which 40 healthy women of ASA grade 1 scheduled for elective caesarean section were randomly allocated to receive either 2ml of 0.5% Inj bupivacaine with 0.25ml NS (group A, n=20) or 0.25ml (12.5μg) Fentanyl with 2ml of 0.5% inj bupivacaine (group B, n=20) it was found that Fentanyl prolonged the duration of both sensory and motor block. Time to first rescue analgesia was longer 248±11.76 min in the Fentanyl group which was comparable with the present study. There was no difference in the frequency of hypotension or bradycardia between the groups. Pruritus was only 15% in the Fentanyl group. Hence, addition of Fentanyl to bupivacaine improves the quality of spinal anaesthesia.

Techanivate A et al[11] had demonstrated the addition of 20μg Fentanyl in 0.5% hyperbaric bupivacaine increases the duration of analgesia following its placement in subarachnoid space as compared to bupivacaine with NS. Time to first required postoperative analgesia in Fentanyl group was significantly higher than in the saline group ($p< 0.001$). It was comparable with our study in which the duration of post operative analgesia was increased and demand for rescue analgesic was reduced in the Fentanyl group. There was no significant difference in the incidence of nausea, vomiting, hypotension and urinary retention which was comparable with our study. No patient developed respiratory depression or PDPH. Shivering was less frequently found in the Fentanyl group.

Jaishri Bogra et al[12]performed synergistic effect of intrathecal Fentanyl and Bupivacaine in spinal anaesthesia for caesarean section on 120 patients divided into six groups, identified as $B_8$ , $B_{10\ and}$ $B_{12.5}$ 8; 10 and 12.5 mg of bupivacaine mg & $FB_8$, $FB_{10}$ and $FB_{12.5}$ recieved a combination of 12μg intrathecal Fentanyl respectively. Blood pressure declined with the increasing concentration of bupivacaine & Fentanyl . Incidence of nausea & shivering reduces significantly whereas, postoperative pain relief & hemodynamics increased by adding Fentanyl which was similar with our study.

Intrathecal Fentanyl with small-dose dilute Bupivacaine has been proved to provide better anaesthesia without prolonging recovery by Bruce Ben-David et al.[13] Pruritus was a common complication in the patients receiving intrathecal Fentanyl , although in most cases, it was so mild as to not require treatment. Consistent with the previous work that has shown the side effects of intrathecal Fentanyl to be dose related we found that the pruritus after 12.5μg Fentanyl to be much less prominent. Respiratory depression is a known complication of intrathecal opioids[14] , but we found no clinical manifestations of respiratory depression. This is not surprising , because it has been shown that even a much larger dose of 25μg of intathecal Fentanyl in elderly patients did not lead to respiratory depression**.** Intrathecal opioids are known to inhibit bladder function[15] . However , we found no influence of this small dose of Fentanyl in delaying return of bladder function.

One observation we have made in our study is that there is notable hemodynamic stability in Fentanyl group although it is not statistically significant. It has been postulated that the decrease in sympathetic efferent activity (spontaneous & evolved ) after spinal anaesthesia is dose-related to the bupivacaine, and that intrathecal Fentanyl causes neither by itself nor in combination with Bupivacaine any further depression of efferent sympathetic activity.[16] On the other hand, there is contrary evidence to show an effect of neuraxial opioids in reducing sympathetic outflow[17] and clinical study has shown that the addition of Fentanyl to epidural anaesthesia is associated with increased likelihood of hypotension after epidural blockade.[18]

In conclusion, this study demonstrates that the use of intrathecal Fentanyl to hyperbaric Bupivacaine significantly increases the duration of postoperative analgesia, decreases the rescue analgesic, a relative better hemodynamic stability and without significant side effects.

**Conclusion :**

In the present study, changes in peripheral oxygen saturation were comparable in the control and Fentanyl groups. However, mean arterial blood pressure and heart rate in the control group was lower than the Fentanyl group throughout the operation but not statistically significant. Duration of postoperative analgesia in the Fentanyl group (265.67±28.85min) was significantly longer than the control group( 138.83±13.17 min) even though the duration of surgery( 62.67± 3.41 vs 64.17±3.49 min) were statistically not significant. There was no significant side effects of intrathecal Fentanyl during the study. It may be concluded that intrathecal Fentanyl significantly prolongs the postoperative pain free period without significant side effects.

**Fig. 1 Distribution of duration of analgesia (minutes) in the two groups**

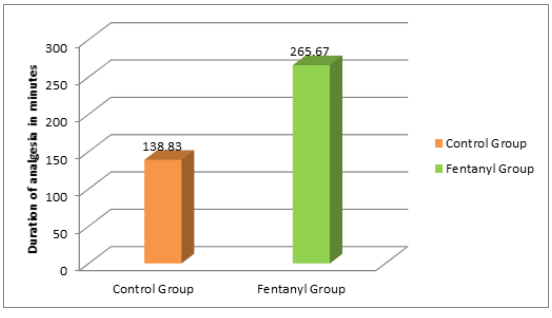
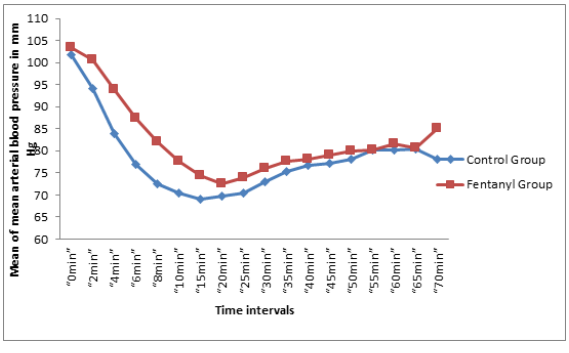



**Fig. 2 Distribution of Mean arterial blood pressure (mm Hg) in the two groups at different time intervals.**




**References**

1. Torda TA, Hann P, Mills G, Leon De: Comparison of extradural Fentanyl ,Bupivacaine and two Fentanyl -Bupivacaine mixtures for pain relief after abdominal surgery. British Journal of Anesthesia 1995;74:35-40.
2. Tan Ping-Heng, Chia Yuan-Yi, Lo Yuan, Liu Kang, Yang Lin-Chang: Intrathecal Bupivacaine with Morphine or Neogstigmine for post operative analgesia after total knee replacement surgery. Canadian Journal of Anesthesia 2001;48:551-56.

3. Abouleish E, Rawal N, Fallon K, Harnandez D: Combined intrathecal morphine and bupivacaine for caesarean section. Anesth Analg 1988;67:370-374
4. Benhamou D, Jhorin D, Brichant JF, DaillanD P, Milon D, Schneider M, et al: Intrathecal clonidine and Fentanyl with hyperbaric bupivacaine improves analgesia during caesarean section. Anesth Analg 1998;87:609-613.
5. Belzariena S :Clinical effects of intrathecally administered Fentanyl in patients undergoing caesarean section. Anesth Analg 1992;74:53-57.
6. Dahlgren G, Hultstrand C, Jakobsson J, Norman M, Eriksson EW, Marrin H, et al: Intrathecal sufentanil,Fentanyl and placebo added to bupivacaine for caesarean section. Anesth Analg 1997;85:1288-1293.
7. Shende D, Cooper GM, Bowden MI: The influence of intrathecal Fentanyl on the characteristics of subarachnoid block for caesarean section. Anaesthesia 1998;53:706-710.
8. Bon-David B, Miller G, Gavriel R, Gurevitch A: Low dose bupivacaine - Fentanyl spinal anaesthesia for caesarean delivery. Reg Anaesth and Pain Med.2000;25:235-239.
9. Hunt CO, Naulty JS, Bader AM: Perioperative analgesia with subarachnoid Fentanyl - bupivacaine for CS delivery. Anesth 1989;71;535-40.
10. Dr BN Biswas, Dr A Rudra, Dr B K Bose, Dr S Nath, Dr S Chakrabarty, Dr S Bhattacharjee, et al: Intrathecal Fentanyl with hyperbaric bupivacaine improves analgesia during caesarean delivery and in early post-operative period. Indian Journal Anesthiology 2002;46(6) :469-472.
11. Techanivate A, Urusopine P, Kiatgungwanglia P, Kosawaboonpol R: Intrathecal Fentanyl in spinal anesthesia for appendicectomy. J Med Assoc Thai 2004May;87(5):525-30.
12. Jaishri Bogra, Namita Arora, Pratima Srivastava: Synergistic effect of intrathecal Fentanyl and bupivacaine in spinal anesthesia for caesarean section. BMC Anesthesiology 2005,5:5.
13. Bruce Ben-David, Eric Solomon, Hilton Levin, Hillel Admoni, Zeev Goldik: Intrathecal Fentanyl with small-dose dilute bupivacaine: Better Anesthesia without prolonging recovery. Anesth Analg 1997;85:560-5.
14. Etches RC, Sandler AN, Daley MD. Respiratory depression and spinal opioids. Can J Anaesth 1989;36:165-85.
15. Rawal N, Mollefors K, Axelsson K: An experimental study of urodynamic effects of epidural morphine and of naloxone reversal. Anesth Analg 1983;62:641-7.
16. Wang C, Chakrabarti MK, Whitwam JG: Specific enhancement by fentanyl of the effects of intrathecal bupivacaine on nociceptive afferent but not on sympathetic efferent pathways in dogs. Anesthesiology 1993;79:766-73.
17. Caffrey JL, Gu H, Barron BA, Gaugl JF: Enkephalin lowers vascular resistance in dog hindlimb via a pheripheral nonlimb site. Am J Physiol 1991;260:H386-92.
18. Curatolo M, Scaramozzino P, Venuti FS: Factors associated with hypotension and bradycardia after epidural blockade. Anaesth Analg 1996;83:1033-40.