MAR Anesthesia and Pain Management. (2024) 1:2
Research Article

Comparative Study of Intrathecal Bupivacaine versus Bupivacaine with Fentanyl for Cesarean Section

Darshana patel[1*], Ushma Baranda[2]

1Third Year Resident, Department of Anaesthesia, SMT NHL Medical College and SVP Hospital, Ahmedabad, Gujarat, India.

2 Assistant professor and PG guide Department of Anaesthesia, SMT NHL medical college and SVP Hospital, Ahmedabad, Gujarat, India.

[*]**Correspondence to: Dr. Darshana Patel,** Third Year Resident, Department of Anaesthesia, SMT NHL Municipal Medical College and SVP Hospital, Ahmedabad, Gujarat, India.

Copyright

Received: 05 June 2024

Published: 01 July 2024

Abstract

Intrathecal opioids for spinal anesthesia reducing the dose of local anesthetics during cesarean sections has become a favored approach among many anesthesiologists. This combination allows for effective spinal anesthesia while minimizing the occurrence of maternal hypotension, a common complication associated with spinal anesthesia during cesarean deliveries. By carefully adjusting the dosage of both local anesthetics and opioids, clinicians can achieve the desired level of anesthesia while mitigating the risk of hypotension, thus improving the overall safety and comfort of the procedure for both the mother and the baby.

Objectives: *To compare the efficacy of intrathecal plain bupivacaine with low dose bupivacaine plus fentanyl with respect to sensory and motor blockade, hemodynamic changes,side effect profile and post-operative analgesia after spinal anaesthesia.*

Material and methods:An observational,Prospective study involved 60 patients scheduled for elective cesarean section under spinal anesthesia, who were assigned to two equal groups. Group B includes patients who received 10 mg (2 mL) of 0.5% hyperbaric bupivacaine, while Group B + F includes patients who received 9 mg (1.8 mL) of 0.5% hyperbaric bupivacaine plus 10 µg (0.2 mL) of preservative-free fentanyl. The clinical characteristics of the subarachnoid block in both groups were assessed, and their impact on maternal and neonatal outcomes was evaluated. This design allowed for a direct comparison between the efficacy and safety profiles of plain bupivacaine and the combination of low-dose bupivacaine with fentanyl.

Results: *Our study findings indicate Mean Time required to reach peak sensory level was shorter in Group B + F. Mean time of two segment regression of sensory analgesia and complete sensory recovery was significantly earlier in Group B. Duration of motor recovery was earlier in Group B +F.*

Mean maximal heart rate was significantly more in Group B. Mean minimal systolic arterial pressure was significantly less in Group B compared to Group B + F.

The duration of effective analgesia was significantly more in Group B + F compared to Group B. The incidence of side effects was less in Group B + F than Group B.

These findings suggest that the combination of low-dose bupivacaine with fentanyl (Group B + F) offers advantages over plain bupivacaine (Group B) in terms of sensory and motor blockade characteristics, hemodynamic stability, duration of effective analgesia, and incidence of side effects in patients undergoing cesarean section under spinal anesthesia.

***Conclusion**: We can conclude that the addition of low-dose fentanyl with 0.5% hyperbaric bupivacaine for spinal anesthesia in cesarean section provides comprehensive benefits, including improved blockade quality, hemodynamic stability, reduced side effects, and effective post-operative pain relief.*

Introduction

Several advantages of regional anesthesia, particularly spinal anesthesia, compared to parenteral and inhalation techniques:Regional anesthesia techniques, such as spinal anesthesia, offer flexibility, effectiveness, and minimal depression compared to other anesthesia methods. They provide excellent sensory analgesia and motor blockade without significantly depressing vital functions. Spinal anesthesia provides rapid onset of sensory analgesia and profound motor blockade, which can shorten surgical time compared to epidural anesthesia.Spinal anesthesia is often the preferred technique for anesthetizing pregnant individuals undergoing cesarean section. It allows the mother to remain awake, avoids airway management issues, and reduces the risk of neonatal depression from general anesthetics.Spinal anesthesia is relatively simple to perform, with the appearance of cerebrospinal fluid as the definitive endpoint. This simplicity contributes to a higher success rate compared to epidural anesthesia.

However, it's important to note a significant disadvantage of spinal anesthesia, which is the finite duration of anesthesia and a higher incidence of hypotension. These drawbacks need to be carefully managed to ensure patient safety and comfort during the procedure. Overall, despite its limitations, spinal anesthesia remains a preferred and effective choice for cesarean section anesthesia due to its numerous benefits.

Bupivacaine, an amino-amide has been the local anaesthetic of choice for spinal anaesthesia in parturient. The use of lignocaine for spinal anaesthesia has become controversial due to concerns related to transient radicular irritation. The incidence is greater with lignocaine than with bupivacaine..Addition of opioids to local anaesthetic for spinal

anaesthesia was first introduced in 1979 with intrathecal morphine.the efficacy of intrathecal fentanyl as an adjuvant to bupivacaine in cesarean section anesthesia. This study is prompted by the advantages offered by opioids, such as fentanyl, when added to local anesthetics for spinal anesthesia. Opioids act synergistically with local anesthetics, enhancing sensory block while minimizing sympathetic block. They also prolong post-operative analgesia and offer hemodynamic stability by allowing for reduced doses of local anesthetics, thus minimizing side effects. Fentanyl, specifically, is known for its rapid onset and offset of action,improves post operative analgesia and offers hemodynamics stability, making it a promising adjuvant for spinal anesthesia in cesarean sections.

Material and Methods

This was a comparative,observational,and prospective study conducted in SVP hospital,NHL Municipal Medical College,Ahmedabad,India.After patients informed, written consent, 60 female patients posted for elective cesarean section under spinal anaesthesia were enrolled in the study.

Inclusion criteria:

1)ASA physical status I or II

2)Age between 18 to 35 years

3)Elective cesarean section

Exclusion criteria:

1)Patients classified as ASA III or IV

2) The patient refuses for spinal anesthesia

3) Active infection at the site of injection,

4)Coagulopathy or those taking anticoagulant medications

5)Patients with pre-existing neurological disease, severe cardiac or respiratory failure and patients with

musculoskeletal deformities

6)Patients who are uncooperative or unable to remain still during the procedure

7) Patients with allergy to local anaesthetics

8)Complicated pregnancy such as pregnancy induced hypertension, placenta previa

Study plan: The patients were divided into two equal groups;

30 patients each:Group B and Group B+F.

Preoperative assessment and preparation protocol for patients undergoing spinal anesthesia for cesarean section.

Clinical Examination: Patients undergo a thorough general and systemic examination to assess their overall health status.

Airway Assessment: Evaluation of the patient's airway is conducted to ensure that spinal anesthesia can be safely administered without compromising airway management.

Spine Examination: Examination of the spine helps identify any anatomical abnormalities or conditions that may affect the administration of spinal anesthesia.

Routine Preoperative Investigations: Standard preoperative tests are performed, including complete blood count, blood sugar, kidney function tests, coagulation profile, urine analysis, and electrocardiogram, to assess the patient's baseline health and identify any potential risk factors.

Confirmation of Nil-By-Mouth Status: Patients' fasting status is confirmed to minimize the risk of aspiration during anesthesia induction.

Application of Monitors: Non-invasive monitors, including blood pressure, electrocardiogram, and pulse oximeter, are applied to continuously monitor vital signs during the procedure.

Recording Baseline Parameters: Baseline vital signs, including systolic and diastolic blood pressure, heart rate, respiratory rate, and oxygen saturation, are recorded before anesthesia induction.

Preparation of Emergency Drugs and Equipment: Emergency drugs and resuscitation equipment are readily available in case of any unforeseen complications during the procedure.

Peripheral Vein Cannulation: A suitable peripheral vein is cannulated to facilitate the administration of intravenous fluids and medications as needed.

Preloading with IV Fluids: Intravenous Ringer's solution is administered to all patients as a preload before the procedure to optimize hemodynamic stability.

Patient Positioning: Patients are positioned in the left lateral position to facilitate spinal anesthesia administration and minimize the risk of aortocaval compression. Proper sterilization techniques are employed to reduce the risk of infection during the procedure. Spinal anesthesia is performed using a 23-gauge Quincke spinal needle at the L3-4 or L4-5 interspace, guided by anatomical landmarks.

Group B (n=30): Received intrathecal injection of 0.5% hyperbaric bupivacaine 2 mL (10 mg).

Group B + F (n=30): Received intrathecal injection of 1.8ml (9mg) of 0.5% hyperbaric bupivacaine plus 0.2ml (10 ug) fentanyl.

Immediately after intrathecal injection the patients were placed in supine position with a wedge under the right hip to maintain left uterine displacement. Oxygen supplementation was done If needed by face mask at 5 L/min. Administered Inj. Oxytocin 10 units via drip after delivery of baby is a common practice to help prevent postpartum hemorrhage by stimulating uterine contractions, aiding in the expulsion of the placenta, and promoting uterine tone. Continuous monitoring of the patients conscious level and oxygen saturation.

Parameters recorded intra-operatively:

sensory and motor blockade, hemodynamic changes, side effect profile and post-operative analgesia after spinal anaesthesia.

Level of sensory block:

The sensory level assessment described involves using a pin prick method with a hypodermic needle to evaluate the extent of anesthesia provided by the subarachnoid injection. **Onset of Analgesia**: This is the time interval from the completion of the subarachnoid injection (time '0') to the loss of pin prick sensation at the knee joint (L4 dermatome). It indicates when the anesthesia begins to take effect. **Peak Sensory Dermatome Level**: After the onset of analgesia, the peak sensory dermatome level is assessed by pin prick in the midline every minute until the level stabilizes for two consecutive tests. This determines the highest

level of anesthesia achieved. **Surgery Initiation**: Surgery typically begins when the block height reaches the T5 dermatome, indicating an adequate level of anesthesia for the intended procedure. **Two Segment Regression**: This refers to the point at which the sensory level regresses by two dermatomal segments from its peak level. It signifies the gradual decrease in anesthesia effect. **Complete Sensory Recovery**: Complete sensory recovery is defined as the return of sensation to the great toe (L5 dermatome). This indicates the resolution of anesthesia effects.

The time taken to achieve peak sensory level, two segment regression, and complete sensory recovery are all noted to assess the duration and efficacy of anesthesia. The duration of anesthesia is recorded from the onset of analgesia to complete sensory recovery, providing important information about the duration of anesthesia provided by the procedure.

Motor block assessment:

The inability to raise extended legs suggests that the lower extremity muscles are affected by the anesthesia, leading to a loss of motor function. This assessment helps determine the onset and effectiveness of motor block, which is important for ensuring adequate anesthesia for surgical procedures while minimizing the risk of unintentional patient movement during surgery.

The degree of motor block was assessed with

Bromage scale.

Grade 0 – No motor block

Grade I – Inability to raise the extended leg

Grade II – Inability to flex the knee, able to flex the ankle

Grade III – Inability to flex the ankle (complete motor block)

Recovery from motor blockade was recorded every 15minutes. Duration of motor blockade was calculated from the time ‘0’ to the recovery of motor blockade.Heart rate and blood pressure measured every 2 min for first 20 min, then at 15 min interval till the end of surgery and thereafter at 30 min interval until the patient complained of pain.

Visual analogue scale (VAS) was recorded. It ranges from 0 indicating no pain and 10 indicating severe intolerable pain with variable degrees of ascending pain in between. If VAS > 4, general anaesthesia was given and the patient was excluded from the study.

The Neonatal APGAR score at 1 min and 5 min after baby delivery was calculated by an attending paediatrician.

Assessment of additional analgesia: Need for additional analgesia was noted using Bromage scale as degree of analgesia.

I: Required general anaesthesia for completion of surgery.

II: Pain that required addition of analgesic drug.

III: Mild discomfort but did not required systemic analgesic.

IV: No discomfort at all during the procedure.

Hemodynamic variables: The mean maximum heart rate was significantly more in Group B than Group B + F. The decrease in systolic blood pressure in Group B was significantly more than in Group B + F.More patients in Group B required additional fluid and vasopressors as compared to patients in Group B + F.

The difference in respiratory rate and SpO2 was not significant in both the Groups.

Monitoring and treatment of side effects: side effects such as hypotension, bradycardia, respiratory depression,nausea, vomiting, shivering and sedation were noted till complete recovery.

Hypotension was defined as a decrease in systolic blood pressure of more than 20% of baseline value or < 100 mm Hg. It was treated with leg elevation, IV fluids, oxygen supplementation or Inj.Mephenteramine 3mg intravenous as needed. Bradycardia was defined as fall in heart rate < 60 beats per minute. Inj.Atropine 0.01 mg/kg was kept ready. Respiratory depression was defined as respiratory rate less than 10 per minute and hypoxia was defined as an oxygen saturation of < 95%. Inj.Naloxone was kept ready for respiratory depression.

Inj.Ondansetron 4mg intravenous was given for nausea and vomiting.

Inj.Pheniramine maleate 45.5 mg intravenous for pruritis

Parameters recorded post-operatively

Continuous monitoring of the conscious level,respiratory rate and oxygen saturation every 15 min till complete recovery.

Sensory level and motor block every 15 min till complete recovery.

Heart rate and non-invasive blood pressure every30 min till complete recovery.

Intra-operative patients comfort was assessed in recovery room 30 min after surgery with visual linear analogue scale.Time taken from the administration of subarachnoid block to the time patients first dose of rescue analgesic. Non-steroidal anti-inflammatory drugs were given to all patients with VAS >4.

Statistical analysis: Results were expressed as mean+standard deviation of the means (SD) or number(%). Comparison between different parameters in the two studied groups was performed using unpaired t test. Comparison between categorical data was performed using Chi square test

The data was considered significant if p value < 0.05 and highly significant if p value < 0.01.

Results

Demographic data: There was no statistical difference among groups as far as age, weight, height and duration of surgery (Table 1).

Table 1: Demographic Data and duration of surgery among the two groups Parameters

Parameters	Group B Mean+ SD	Group B + F Mean+SD	P value
Age(years)	23+3.24	23.40+3.56	> 0.05
weight(kg)	54.06+4.85	52.3+5.80	> 0.05
height(cm)	152.83+4.06	151.36+5.20	> 0.05
Duration of surgery(min)	55.60+9.02	57.12+5.63	> 0.05

Sensory blockade:

Time required for the 'onset of sensory analgesia' was comparable in both the groups. Peak level of sensory analgesia was comparable in both the groups ($p > 0.05$). Thus the addition of fentanyl to 0.5% hyperbaric bupivacaine did not change the height of block. The mean time required to reach 'peak sensory level' was earlier in Group B + F than Group B and this was statistically significant ($p < 0.001$). Mean time of 'two segment regression' of sensory analgesia and duration of 'complete sensory recovery' was statistically significant.

The 'duration of effective analgesia' was prolonged in Group B + F as compared to Group B ($p < 0.05$) and was statistically significant

Table 2

Parameter	Group B Mean+SD	Group B + F Mean+SD	p value
Time for onset of sensory blockade (sec)	68+9.22	65+8.55	>0.05
Time to reach peak sensory level (min)	6.36+1.33	5.02+ 1.42	<0.001
Time for two segment regression (min)	68.0+17.53	88.66 + 18.78	< 0.05
Time for complete sensory recovery (min)	113.66+9.06	132.4 + 11.36	< 0.05
Duration of effective analgesia	122.33+9.98	236.33 + 28.15	< 0.05

Motor blockade:

The 'onset of motor blockade' was clinically earlier in Group B than Group B + F but statistically was not significant. All patients in both the groups had complete motor blockade. The mean 'duration of motor recovery' was shorter in Group B + F than Group B and was statistically significant ($p < 0.05$).

Table 3

Parameter	Group B Mean+SD	Group B + F Mean+SD	p value
Onset of motor blockade (sec)	71.5+11.77	77.33+12.65	> 0.05
Time required for motor recovery (min)	107.80+8.91	86.16+14.72	< 0.05

Maternal and foetal outcome: Mean uterine incision to delivery time and neonatal APGAR score at 1 and 5 minute

Table 4

Parameter	Group B Mean+SD	Group B + F Mean+SD	p value
Uterine incision to delivery time (sec)	86+15.84	80.83+16.05	> 0.05
APGAR score at 1 min	9.56+0.81	9.8+0.30	> 0.05
APGAR score at 5 min	9.7+0.55	9.43+0.73	> 0.05

Hemodynamic variables: The mean maximum heart rate was significantly more in Group B than Group B + F ($p < 0.05$). The decrease in systolic blood pressure in Group B was significantly more than in Group B + F ($p < 0.05$).More patients in Group B required additional fluid and vasopressors as compared to patients in Group B + F.

The difference in respiratory rate and SpO2 was not significant in both the groups.

Table 5

Parameter	Group B Mean+SD	Group B + F Mean+SD	p value
Basal Heart Rate (min)	84.6+6.34	87+5.08	>0.05
Minimal Heart Rate (min)	85.33+5.86	85.27+4.22	>0.05
Maximal Heart rate (min)	108.73+5.65	102.53+4.35	<0.05
Basal systolic arterial blood pressure (mm Hg)	124.73+6.92	123.53+6.62	>0.05
Minimal systolic arterial blood pressure (mm Hg)	97.66+9.69	106.8+8.50	<0.05
No. of patients additional crystalloid	6	1	<0.05
No. of patients requiring vasopressor (Mephenteramine)	8	2	<0.05

Adverse effects

Table 6: The incidence of adverse effects

Adverse effects	No. of patients (%) Group B	No. of patients (%)Group B+F
Nausea	4	-
Vomiting	3	-
Bradycardia	0	-
Hypotension requiring treatment	10	3

Pruritus	0	4
Shivering	4	0
Respiratory depression	0	0

Discussion

The appropriate anesthesia method for cesarean sections, especially considering the risks associated with general anesthesia compared to regional anesthesia. Regional anesthesia, such as spinal anesthesia, is preferred due to its lower risk of fatality compared to general anesthesia. Intrathecal fentanyl is often used as an adjuvant to enhance the quality and duration of spinal anesthesia.The aim seems to be improving the safety and efficacy of regional anesthesia techniques, ultimately reducing maternal mortality associated with cesarean sections. Both the groups were comparable with respect to age, weight, height and duration of surgery.Intrathecal fentanyl acts on mu receptors present in substantia gelatinosa of spinal cord. Analgesic effects of opioids arise from the ability of these drugs to inhibit the ascending transmission of nociceptive information from the spinal cord dorsal horn and to activate the descending inhibitory pathway.

Sensory blockade: the study found that the addition of intrathecal fentanyl to hyperbaric 0.5% bupivacaine did not significantly alter the onset or peak level of sensory blockade compared to using hyperbaric bupivacaine alone. This suggests that fentanyl does not affect the height of the block because opioid-induced analgesia is not associated with sympathetic nervous system denervation.

However, the time required to reach the peak level of sensory analgesia was earlier in the group that received the combination of bupivacaine and fentanyl. This may be attributed to the synergistic effect of fentanyl enhancing the analgesic effect of bupivacaine on the afferent pathway without affecting sympathetic outflow.The quality of sensory analgesia was reported to be superior in the group that received both bupivacaine and fentanyl, with no patients experiencing intra-operative discomfort requiring analgesic supplementation.

However, it's worth noting that the time for sensory recovery, indicated by the onset of sensory regression and complete sensory recovery, was longer in the group that received fentanyl along with bupivacaine compared to the group that received bupivacaine alone. This could imply that the addition of fentanyl prolongs the duration of sensory blockade.

These findings are consistent with similar studies Agarwal et al8And Dahlgren et al 9 found similar results.suggesting that the addition of intrathecal fentanyl to bupivacaine may enhance the quality of sensory analgesia during cesarean sections but might also prolong the time for sensory recovery.

The 'duration of effective analgesia' was prolonged in Group B + F than Group B. Bano F10,Tolia G6 and Agarwal A8 also found similar results.Fentanyl due to its synergistic effect with bupivacaine prolongs the duration of analgesia thus decreasing the analgesic requirement post operatively. This contributes to patients comfort and satisfaction.

Motor Blockade: the onset of motor blockade was earlier in the group that received only bupivacaine (Group B) compared to the group that received both bupivacaine and fentanyl (Group B + F), although this difference was not statistically significant. The majority of patients in both groups experienced motor onset between 50-70 seconds. This suggests that fentanyl did not have a significant effect on the onset of motor blockade.It's also noted that patients in Group B received a higher dose of bupivacaine (10 mg) compared to those in Group B + F (9 mg), yet both groups achieved a similar level of motor blockade, categorized as grade III.Overall, these findings suggest that while the addition of fentanyl did not significantly impact the onset of motor blockade, it allowed for achieving similar motor blockade levels with a slightly lower dose of bupivacaine.

Maternal and foetal outcome: There was no neonatal depression observed, and the mean APGAR scores at 1 minute and 5 minutes were similar in both groups. These findings align with previous research by Bogra et al., Agarwal et al., and Dahlgren et al., all of whom reported good neonatal outcomes when using intrathecal fentanyl as an additive to bupivacaine for cesarean sections.

Overall, these results suggest that the addition of intrathecal fentanyl to bupivacaine does not compromise fetal safety and may contribute to positive neonatal outcomes. However, it's essential to continue monitoring and researching to ensure the safest and most effective anesthesia practices for both mother and baby during cesarean sections.

Hemodynamic variables: Baseline and minimal heart rates were similar between both groups, indicating that neither group experienced bradycardia. This absence of bradycardia contrasts with the potential for

fentanyl-induced bradycardia due to its stimulation of the central vagal nucleus. The authors attribute this lack of bradycardia to the low dose of intrathecal fentanyl used in the study.Although there was no significant change in heart rate overall, there was a significant difference in maximum heart rate between the groups. The group that received fentanyl along with bupivacaine showed less of an increase in maximum heart rate. This observation could be attributed to fentanyl efficacy in providing visceral pain relief, ensuring better surgical analgesia, and potentially reducing the incidence of hypotension.In case of hypotension, maintaining normal maternal blood pressure during cesarean sections under spinal anesthesia is crucial for adequate neonatal outcomes. The study revealed that the fall in systolic blood pressure was statistically significant in the group that received bupivacaine alone compared to the group that received bupivacaine with fentanyl. This finding aligns with previous research indicating that the incidence of hypotension is higher with increasing concentrations of bupivacaine.Despite using a lower dose of bupivacaine in combination with fentanyl, fewer patients in the fentanyl group experienced hypotension compared to the bupivacaine-only group. Moreover, those who did experience hypotension in the fentanyl group required less additional intervention compared to the bupivacaine-only group, suggesting that fentanyl may have a protective effect against hypotension during spinal anesthesia for cesarean sections.Overall, these findings highlight the potential hemodynamic benefits of adding intrathecal fentanyl to bupivacaine for cesarean sections, including the mitigation of hypotension and its associated complications. However, further research is warranted to elucidate the optimal dosing and safety profile of this combination in clinical practice.

Adverse effects: The addition of intrathecal fentanyl to bupivacaine appears to have contributed to a reduction in some adverse effects such as nausea, vomiting, and shivering, while also potentially mitigating the incidence of hypotension requiring treatment. However, it's note worthy that pruritus was more common in the Group B + F, which is a known side effect of opioids like fentanyl. The absence of respiratory depression in both groups is reassuring, indicating the safety of the anesthesia protocols used in the study.

Conclusion

Thus we conclude that the addition of intrathecal fentanyl to hyperbaric bupivacaine to spinal anesthesia for cesarean sections, providing adequate analgesia, improved hemodynamic stability, and a reduced risk of complications like nausea, vomiting and shivering, without compromising the safety of mother and the foetus.

Reference

1. Pollock JE, Neal JM, Stephenson CA, Wiley CE. Prospective study of the incidence of transient radicular irritation in patients undergoing spinal anaesthesia. Anaesthesiology 1996;84:1361-1367.

2. Tan PH, Chia YY, Lo Y, Yang LC, Lee TH. Intrathecal bupivacaine with morphine or neostigmine for postoperative analgesia after total knee replacement. Can J Anesth 2001;48(6):551-6.

3. Panchal S, Arria AM, Labhsetwar SA: Maternal mortality during hospital admission for delivery: Aretrospective analysis using a state-maintained database. Anesth Analg 2001;93:134-141.

4. Hawkins JL, Koonin LM, Palmer SK, et al: Anaesthesia related deaths during obstetric delivery in the united states, 1979-1990. Anesthesiology 1999;86:277-284.

5. Bogra J, Arora N, Srivastava P. Synergistic effect of intrathecal fentanyl and bupivacaine in spinal anaesthesia for caesarean section. BMC Anesthesiol 2005;5:5.

6. Geetanjali T, Ajay K, Aruna J. Low dose intrathecal bupivacaine with fentanyl for caesarean delivery. J Anaesth Clin Pharmacol 2008;24(1):201-204.

7. 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. Anaesthesiology 1993;79;766-73.

8. Agarwal A, Agarwal S, Asthana V, Payal YS. Comparison of intrathecal fentanyl and sufentanil in addition to bupivacaine for caesarean section under spinal anaesthesia. J Anaesth Clin Pharmacol 2009;25(2):154- 56.

9. Dahlgren G, Hulstrand C, Jakobson J, Norman M. Intrthecal sufentanil, fentanyl or placebo added to bupivacaine for caesarean section. Anesth Analg 1997;85:1288-93.

10. Bano F, Sabbar S, Zafar S, Rafeeq N, et al. Intrathecal fentanyl as adjunct to hyperbaric bupivacaine in spinal anaesthesia for caesarean section. JCPSP 2005;16(2):87-90.

11. Seyedhejazi M, Madarek E. The effect of small dose bupivacaine – fentanyl in spinal anaesthesia on hemodynamic, nausea and vomiting in caesarean section. Pak J Med Sci 2007;23(5):747-50.

12.De Witte, Jan MD, Sessler. Perioperative shivering: physiology and pharmacology. Anaesthesiology 2002;96,467-84.

13. Techanivate A, Rodanant O, Somsiri T. Intrathecal fentanyl for prevention of shivering in caesarean section. J Med Assoc Thai 2005;88:1214-21.

14. Szarvas S, Harmon D, Murphy d. Neuraxial opioid- induced pruritis: a review. J Clin Anesth 2003;15(3):234- 9. PMID:12770663.

15. Belzarena S.D. Clinical effect of intrathecal administered fentanyl in patient undergoing caesarean section. Anaesth Analg 1992;74:653-7.

Medtronic