A Comparative Study on Three Different Doses of Fentanyl with Bupivacaine in Spinal Anaesthesia in Caesarean Section

Sonia Nahakpam[1], Laishram Dhanachandra[2], Ningombam Joenna Devi[3], Zarina Wahab[4], Linthoingambi Samjetsabam[5], Thangavelu Ravichandran Kumaragurubaran[6], Kalpana Thongram[7], Bishakha Keishab[8]

[1]Third Year Postgraduate Trainee, Department of Anaesthesia, Jawaharlal Nehru Institute of Medical Sciences, Porompat, Imphal. [2]Senior Resident, Department of Anaesthesia, Jawaharlal Nehru Institute of Medical Sciences, Porompat, Imphal. [3]Third Year Postgraduate Trainee, Department of Anaesthesia, Jawaharlal Nehru Institute of Medical Sciences, Porompat, Imphal. [4]Third Year Postgraduate Trainee, Department of Anaesthesia, Jawaharlal Nehru Institute of Medical Sciences, Porompat, Imphal. [5]Third Year Postgraduate Trainee, Department of Anaesthesia, Jawaharlal Nehru Institute of Medical Sciences, Porompat, Imphal. [6]Third Year Postgraduate Trainee, Department of Anaesthesia, Jawaharlal Nehru Institute of Medical Sciences, Porompat, Imphal. [7]First Year Postgraduate Trainee, Department of Anaesthesia, Jawaharlal Nehru Institute of Medical Sciences, Porompat, Imphal. [8]First Year Postgraduate Trainee, Department of Anaesthesia, Jawaharlal Nehru Institute of Medical Sciences, Porompat, Imphal.

ABSTRACT

BACKGROUND

Spinal anaesthesia is the technique of choice for caesarean section as it is devoid of many potential problems associated with general anaesthesia. The usual dose required for reaching the desired block height for hyperbaric bupivacaine is 10-12 mg. A lower dose of bupivacaine with an adjuvant is used as a reliable combination which produces synergistic effect, prolonging the duration of sensory block without increasing sympathetic block or delaying recovery.

METHODS

A total of 110 patients undergoing elective or emergency Caesarean section under spinal anaesthesia, were screened for eligibility and 105 were randomised in the trial, allocated to 3 groups to receive injection bupivacaine 7.5 mg along with fentanyl 15 mcg (Group BF1, n=35), fentanyl 20 mcg (Group BF2, n=35), fentanyl 25 mcg (Group BF3, n=35).

RESULTS

The average time required to reach the block height of T4-T6 was around 3.26 min in BF1, 3.97 min in BF2, 4.63 min in BF3. The two-segment regression time of BF1 was 68.06 min; BF2 72.17 min and BF3 80.06 min. The recovery time of sensory block for BF1 is around 129.71 min, for BF2, 193.43 min and for BF3 200.86 min. The time for onset of motor block was BF1 1.49 min, BF2 1.51 min and BF3 2.34 min. The time to maximum of motor block was 2.8 min for BF1, 3.69 min for BF2, 7.8 min for BF3. The recovery time of motor block for BF1, was 107.14 min; BF2, 91.57 min and BF3, 65.66 min.

CONCLUSIONS

All the three doses of fentanyl - 15mcg, 20mcg, 25mcg can be used as an adjuvant to 7.5 mg of 0.5% heavy bupivacaine for caesarean section to provide good quality surgical anaesthesia. Larger fentanyl dose group (25mcg) scores over small dose group in terms of sensory block with prolonged post-operative analgesia, early motor recovery and lesser incidence of hypotension.

KEYWORDS

Caesarean Section, Low Dose Bupivacaine, Fentanyl

Corresponding Author:
Dr. L. Dhanachandra,
Uripok Sorbon Thingeda,
Imphal West- 795001.
E-mail:
dhanachandralaishram1971@gmail.com
DOI: 10.18410/jebmh/2020/70

Financial or Other Competing Interests: None.

How to Cite This Article:
Nahakpam S, Dhanachandra L, Joenna Devi N, et al. A comparative study on three different doses of fentanyl with bupivacaine in spinal anaesthesia in caesarean section. J. Evid. Based Med. Healthc. 2020; 7(7), 327-332. DOI: 10.18410/jebmh/2020/70

Submission 16-01-2020,
Peer Review 21-01-2020,
Acceptance 30-01-2020,
Published 14-02-2020.

BACKGROUND

Spinal anaesthesia is anaesthetic technique of choice for caesarean delivery worldwide as it is devoid of many potential problems associated with general anaesthesia like failed intubation, aspiration of gastric contents, neonatal depression, etc. Spinal anaesthesia has the added advantage of rapidity of onset,[1] production of dense neural block, effective sensory and motor blockade in an awake patient, minimal risk of drug toxicity, and transfer of drugs to foetus. It has been found to be a well-known technique as it is easy to perform, safe and cost effective. Some of the disadvantages include a limited duration of anaesthesia which cannot be manipulated once set. The use of lower dose aims to decrease the side effects (hypotension, intraoperative nausea, vomiting), reduce the time to discharge from the post anaesthesia care unit. However, such a strategy could compromise the adequacy of anaesthesia, require supplementary analgesia, and may necessitate conversion to general anaesthesia. Bupivacaine, an amide type of local anaesthetic has high potency, slow onset (5-8 min) and long duration of action (1.5-2 hours). Hyperbaric bupivacaine hydrochloride 0.5% is most commonly used for spinal anaesthesia for caesarean delivery. Its duration of 1.5-2 hours is well matched with the duration of surgery in most cases. For caesarean section, the usual dose required for reaching the desired block height (i.e. T4) is 10-12 mg. Caesarean section requires traction of peritoneum and handling of intraperitoneal organs resulting in intraoperative visceral pain. With higher doses of hyperbaric bupivacaine, the incidence of intraoperative visceral pain is reduced but may be associated with hemodynamic derangements leading to prolonged intensive care monitoring postoperatively, delayed recovery and thus delayed discharge. A common complication of spinal anaesthesia is maternal hypotension which may lead to nausea and vomiting, shock and even cardiac arrest to the mother and acidosis to the foetus. Bigger the dose more is the incidence of maternal hypotension. A lower dose of bupivacaine with an adjunct, intrathecal fentanyl[2] is used as a reliable combination in an attempt to improve the quality of spinal anaesthesia. This combination produces synergistic effect [3,4,5,6] prolonging the duration of sensory block[4,6,7] without increasing sympathetic block or delaying recovery[7] and also the quality of analgesia[8] during and after surgery. Fentanyl, a lipophilic opioid, has rapid onset of action, as compared to morphine following intrathecal administration. It doesn't tend to migrate to the fourth ventricle in sufficient concentration to cause delayed respiratory depression when given intrathecally.[7,9] Sowmya et al[10] in a study using two different doses of fentanyl 10 µg and 15 µg added to 10 mg bupivacaine for spinal anaesthesia for caesarean section found a better result with 15 µg fentanyl in having rapid onset of sensory blockade, hemodynamic stability and prolongation of post-operative analgesia. In another study conducted by Ali et al,[11] he used three different doses of fentanyl 10 µg, 15 µg, 25 µg along with 10 mg of 0.5% hyperbaric bupivacaine for caesarean section. All the three groups had adequate surgical anaesthesia, but incidence of side effects was more with 25 µg of fentanyl. It was concluded that 10 µg or 15 µg of intrathecal fentanyl provided adequate surgical anaesthesia and analgesia with minimal side effects. We planned to undertake the present study by reducing the dose of bupivacaine to 7.5 mg with the addition of three varying doses (15 µg, 20 µg, 25 µg) of fentanyl keeping in mind that opioid fentanyl has a local anaesthetic sparing effect.[8]

This study was conducted to compare the effects of low dose (7.5 mg) hyperbaric bupivacaine in combination with different doses of fentanyl (15 µg, 20 µg, 25 µg) on the onset and duration of sensory and motor block and to assess the quality of anaesthesia, analgesia and incidence of undesirable complications.

METHODS

The study was a prospective, randomised and double-blinded one, conducted in the Department of Anaesthesiology, JNIMS, Imphal over a period of 2 years. Patients undergoing elective or emergency Caesarean section under spinal anaesthesia and fulfilling the inclusion criteria were enrolled.

Inclusion Criteria

- Patients aged 20-40 years
- Have an ASA I or II
- Scheduled for elective or emergency caesarean section
- Has signed a written informed consent

Exclusion Criteria

- Patient with contraindication for subarachnoid block (spinal deformity, local sepsis)
- Refusal for study
- Patient with known allergy to study drugs
- Patients put on epidural anaesthesia
- Patient on opioid
- Patient with neurological or psychiatric disease on concurrent medication
- Patient with cardiopulmonary disease, hepatorenal disease, coagulation disorder
- Patient at risk of developing wound infection, bacteraemia, intracranial pressure increase
- Any patient requiring sedation or conversion to GA

Operational Definition

Hypotension-defined as a systolic BP <100 mmHg or lower by more than 20% of baseline reading or MAP <70 mmHg. Bradycardia-heart rate <50/min. Respiratory depression-defined as respiratory rate <10/min.

Procedure and Data Collection

All patients were assessed for anaesthetic fitness and adequate preparation was made for spinal anaesthesia. A peripheral venous access was secured with 18G canula.

Intravenous infusion of Ringer's lactate solution was started for volume loading and thereafter was maintained at 6 ml/kg/hr. Injection ranitidine 50 mg was given intravenously 45 minutes before and injection ondansetron 4 mg intravenously 30 minutes before spinal block. The drugs were prepared in identical syringes containing either 15 µg (0.3 ml), 20 µg (0.4 ml), 25 µg (0.5 ml) of fentanyl with bupivacaine heavy 7.5 mg (1.5 ml) making it to a total volume of 2 ml by adding distilled water by an anaesthesiologist blinded to the study. Patients were randomly distributed into 3 groups BF1 (15 µg), BF2 (20 µg), BF3 (25 µg). Spinal anaesthesia was administered in L2-L3 orL3-L4 interspace with patient in left lateral position with 25G Quincke's spinal needle, with direction of needle aperture towards cranial end during injection, after confirming free and clear flow of CSF and the whole drug was injected in 10 seconds without barbotage. All patients were placed in supine position immediately. After injecting the spinal drug for the operation- a block was placed underneath right flank, table tilted 15°head down and then, straightened after the sensory block reached the sub coastal margin in the epigastrium.

All patients were monitored for ECG, BP, SpO2, heart rate, sensory level (pin prick in midclavicular line), motor level (modified Bromage scale), and for complaints like nausea, vomiting, shivering, pruritus, and sedation from the time of spinal injection. BP, pulse rate were recorded every 3 minutes for the first 15 minutes thereafter for every 5 minutes till the end of the operation. Injection mephentermine IV was given to treat hypotension and injection atropine IV for bradycardia. Monitoring was continued in the postoperative period. The patient was shifted to the post-operative ward after complete recovery from motor and sensory blocks.

Statistical Analysis

The data was analysed using SPSS Version 20. All difference was considered significant at p value <0.05. Motor block was assessed using modified Bromage Scale as follows: Grade 0- No motor block with full flexion of knees and feet, Grade 1 – Just able to flex knees, full flexion of feet, Grade 2 – Unable to flex knees, but some flexion of feet Possible, Grade 3 – Unable to move legs or feet.

Ethical Issues

Ethical clearance was obtained from the Institutional Ethics Committee of JNIMS, Imphal before conducting the study. Informed consent from the patient concerned was obtained.

RESULTS

A total of 110 patients were screened for eligibility and 105 were randomised in the trial. Allocated to 3 groups (Figure 1).

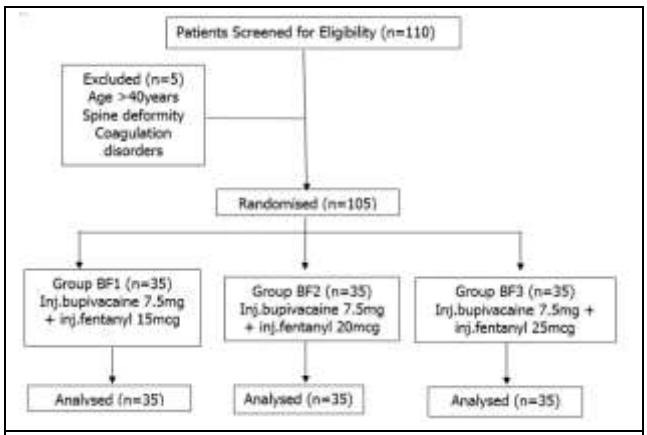

Figure 1. Consort Flow Chart for Randomisation

Parameters	mean± SD			P
	BF1	BF2	BF3	
Age (Years)	28.26 ± 5.35	27.83 ± 5.87	28.86 ± 5.18	0.733
Weight (Kg)	53.77± 4.94	54.49 ± 5.23	53.97 ± 4.23	0.815
Duration of surgery (min)	48.0± 5.45	48.57 ± 4.62	47.29 ± 6.34	0.622
Duration of anaesthesia (min)	129.71± 18.70	193.43± 18.46	279.43± 31.61	0.000

Table 1. Patient Characteristics

In group BF1, the block never increased to more than T 4 but in group BF2 and BF3, 4 (11.4%) patients has sensory block higher than T4 which indicates that more dose of fentanyl was associated with more incidence of higher block

Characteristics	Mean ± SD (min)			p
	BF1	BF2	BF3	
Time to onset of sensory block	1.29± 0.45	1.20± 0.4	1.09± 0.28	0.103
Time from onset to reach T 10	2.23±0.59	2.26± 0.7	2.11±0.75	0.657
Time for sensory block to reach the maximum-T4-T6	3.26± 0.61	3.97± 1.24	4.63±1.41	0.001
Two segment regression time	68.06± 3.67	72.17± 2.57	80.06± 3.39	0.001
Recovery time of sensory block	129.71±18.7	193.43± 18.46	279.43± 31.61	0.001

Table 2. Various Characteristics of Sensory Blockade Among the Three Groups

Characteristics	mean± SD (min)			p
	BF1	BF2	BF3	
Time to onset of motor block	1.49±0.5	1.51±0.56	2.34±0.96	0.001
Time to maximum of motor block	2.8±0.71	3.69±0.9	7.8±2.12	0.001
Recovery time of motor block	107.14±22.79	91.57±11.09	65.66±15.47	0.001

Table 3. Various Characteristics of Sensory Blockade Among the Three Groups

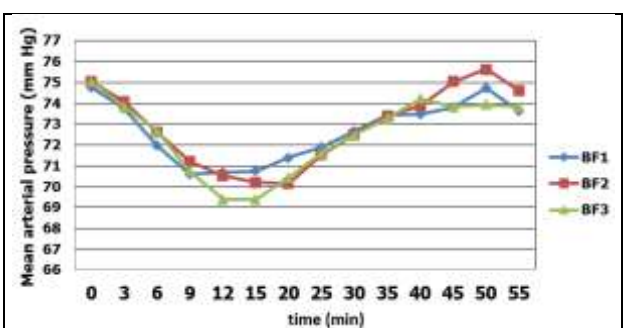

Figure 2. Line Diagram Showing the Trend of Mean Arterial Pressure Intraoperatively

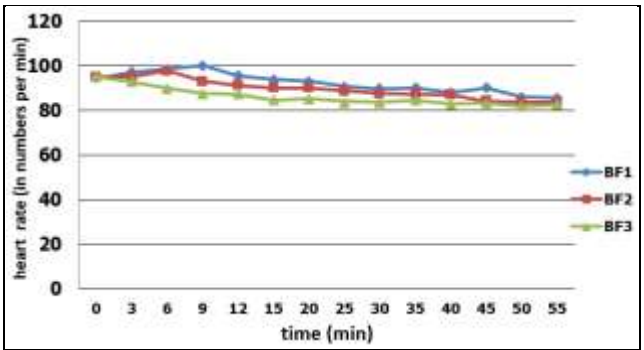

Figure 3. Line Diagram Showing the Recording of Heart Rate Intraoperatively

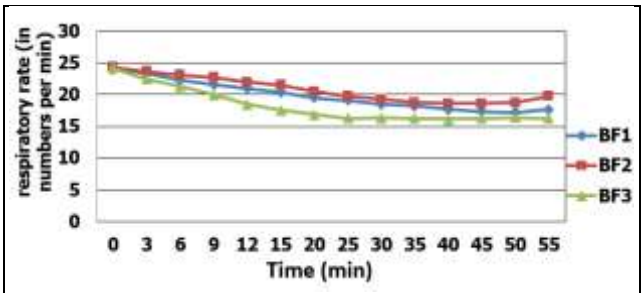

Figure 4. Line Diagram Showing the Recordings of the Respiratory Rate Intraoperatively

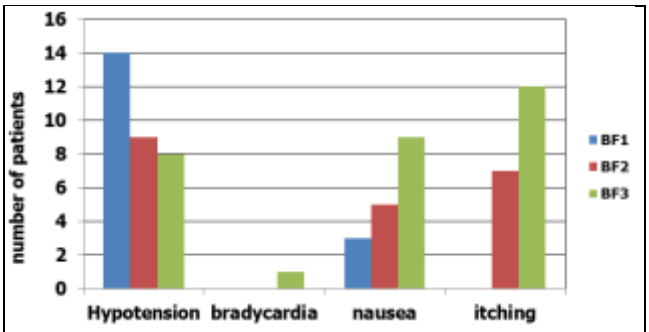

Figure 5. Bar Diagram Showing Incidence of Hypotension, Bradycardia, Nausea, Itching Among the Three Groups

*There were no episodes of headache, vomiting and respiratory depression in any of the groups

DISCUSSION

Spinal anaesthesia has gained more widespread popularity[12,13,14,15,16,17,18] for caesarean section than general anaesthesia due to the associated risk and complications of the latter. For caesarean section, the usual intrathecal dose of hyperbaric bupivacaine is 10-12 mg. But even with recommended dose, there have been reports of long duration of motor block and sensory block along with hemodynamic derangements[19] due to high dose of intrathecal bupivacaine resulting in delayed recovery[20,21,15] and hence, discharge from post anaesthesia care unit. In order to avoid these, a low dose bupivacaine with several adjuncts has been tried. Use of lipophilic opioid like fentanyl intrathecally as an adjuvant to local anaesthetic bupivacaine reduces the requirement of mephentermine doses to combat hypotension. Hunt et al[1] suggested that the addition of ≥6.25 mcg fentanyl to hyperbaric bupivacaine for spinal anaesthesia in parturients undergoing elective repeat caesarean delivery improves intraoperative as well as immediate postoperative analgesia with no adverse effects on the mother or neonate. Bogra et al[22] also concluded that bupivacaine- fentanyl combination leads to abolishment of visceral pain, reduction in nausea incidence, increased hemodynamic stability and that fentanyl was able to reduce the dose of bupivacaine and therefore, its harmful effects. Overall the combined effect of fentanyl – bupivacaine was found to be superior[3,12,20,23,17] over just bupivacaine alone as fentanyl apart from positive effects, retards the negativity as well as reduces the doses of bupivacaine too.[24] Fentanyl being more lipophilic than morphine is readily eliminated from the CSF making late respiratory depression less likely.[17] There have been various studies regarding the dosage of fentanyl and bupivacaine combinations for spinal anaesthesia in caesarean section. Seewal et al[25] compared the effects of addition of various doses of fentanyl (10, 20, 30, 40 mcg) intrathecally to 0.5% hyperbaric bupivacaine on perioperative analgesia and subarachnoid block characteristics in lower abdominal surgery, in which they concluded that addition of 10 mcg fentanyl improves the quality and duration of analgesia and no further advantage occurs if the dose of fentanyl is increased up to 40 mcg. Mani et al[26] conducted a randomised controlled study comparing three different doses of bupivacaine (5 mg, 7.5 mg, 10 mg) with fentanyl 25 mcg for TURP surgeries in which addition of 25 mcg of fentanyl to 5 mg of bupivacaine provides reliable and satisfactory surgical anaesthesia with stable hemodynamic status, reduced duration of sensory and motor blockade and without any significant adverse effects when compared to 7.5 mg and 10 mg bupivacaine with fentanyl, facilitating early discharge of patients. Arikan et al[27] compared the effects of two different doses of fentanyl (10 mcg, 25 mcg) given intrathecally in addition to 0.5% levobupivacaine for caesarean section and concluded that the addition of 25 mcg fentanyl decreases the ephedrine requirement without additional side effects and adverse neonatal outcomes. Sowmya et al[10] compared 10 mcg of fentanyl with 15 mcg of fentanyl as an adjuvant in 10 mg bupivacaine in which there was faster onset of sensory blockade, better hemodynamic stability and prolonged post-operative analgesia in patients administered with 15 mcg of fentanyl and 10 mg bupivacaine. Ali et al[11] conducted a study on three different doses of fentanyl (10 mcg, 15 mcg, 25 mcg) as an adjuvant to 10 mg of 0.5% hyperbaric bupivacaine in which there was no significant difference in the onset of block, quality of surgical anaesthesia, pain scores, neonatal APGAR score, hemodynamic variables, etc., but 10 mcg or 15 mcg provided adequate surgical analgesia with minimal side effects. In our study, we have used three different doses of fentanyl (15 mcg, 20 mcg, 25 mcg) along with 0.5% bupivacaine heavy 7.5 mg for spinal anaesthesia. While choosing fentanyl doses, reports of previous studies in the review of literature were taken into consideration. It was quite clear that fentanyl dose lesser than 10 mcg and larger than 25 mcg when used as an adjuvant to low dose

bupivacaine in spinal anaesthesia for caesarean section did not provide any added advantage in terms of quality of surgical anaesthesia.[5,25,22,28,23] The difference in onset of sensory block and time to onset to reach T10 of the three study groups was not found to be statistically significant (p >0.05). The average time required for sensory block to reach T4-T6 was significantly increased in group bupivacaine 7.5 mg+ fentanyl 25 mcg as compared to other two study groups (p <0.05). The two segment regression time was more in group bupivacaine+ fentanyl 25 mcg with a mean value of 80.06 min. Recovery of sensory block was significantly longer (p<0.05) in group using 25 mcg fentanyl resulting in prolonged post-operative analgesia.[29,17] Thus, it was seen that with higher dose of fentanyl the sensory block was denser than the lower doses. These findings are consistent with the studies conducted by Sowmya et al.[10] Block intensity was assessed by the degree of motor block. The time of onset of motor block and time needed to reach maximum of motor block was significantly more with the group using 25 mcg fentanyl (p<0.05). The recovery time of motor block was significantly shorter in the group using 25 mcg of fentanyl which may be attributed to the early ambulation of the patients (p <0.05). This may be due to the intensity of motor block which depends only on the dose of bupivacaine and fentanyl dose only intensifies sensory block but not motor block. These results are similar to the results observed by Ben David et al.[4] The intraoperative hemodynamic parameters were more stable in group using 25 mcg of fentanyl compared to the other two study groups using 15 mcg and 20 mcg of fentanyl as adjuvant. In this study, we also assessed the occurrence of side effects of fentanyl in the various dosages. Hypotension was found in all the 3 groups but less frequently seen in group using 25 mcg of fentanyl, but it was not statistically significant (p>0.05) Bradycardia was seen in only one patient in the study group using 25 mcg of fentanyl. Nausea was complained by some patients from all the 3 groups, most commonly by patients receiving 25 mcg of fentanyl. There were no incidences of vomiting. There was no respiratory depression among the three study groups which was in accordance with the studies of Belzarena et al,[30] Singh et al,[3] Ben David et al[4] and Kotwani et al.[31] Itching was significantly seen in patients receiving 25mcg of fentanyl (p value<0.05) which was also seen in the study conducted by Hunt et al,[1] Belzarena et al,[30] Ali et al.[11] The incidence of side effects except hypotension were more commonly seen in group using 25 mcg of fentanyl. The strength of the study is that this study is one of the few studies which compared the effect of three doses (15 mcg, 20 mcg, 25 mcg) of fentanyl as an adjuvant with bupivacaine heavy (7.5 mg) as local anaesthetic during spinal anaesthesia for caesarean section. Proper blinding was done during the administration of drug. There were few limitations of the study. Firstly, the study does not include pregnant women of age >40 years, weight >60 Kg. So, the result cannot be applied to the pregnant women as a whole. Secondly, the sample size taken for the study was small (110) and were chosen from pregnant women for elective or emergency caesarean section in our hospital. Hence, it may not be feasible to apply to the general population of different geographical regions. Third, height of the patient was not considered as one of the criteria for administering the drugs as volume of drug required varies with height and may be the reason for hypotension in short stature patients. In spite of these limitations, it must be noted that there were some significant results which can be derived from the study. Furthermore, prospective studies on the use of different doses of fentanyl as adjuvant and low dose bupivacaine in neuraxial block for pregnant women as well as adults undergoing different types of lower abdominal and lower limb surgeries are needed.

CONCLUSIONS

All the three doses of fentanyl – 15 mcg, 20 mcg, 25 mcg can be used as an adjuvant to 7.5 mg of 0.5% heavy bupivacaine for caesarean section deliveries to provide good quality surgical anaesthesia without maternal complications and other intolerable side effects. Larger fentanyl dose group (25 mcg) scores over small dose group in terms of sensory block with prolonged post-operative analgesia, early motor recovery and lesser incidence of hypotension.

REFERENCES

[1] Hunt CO, Naulty JS, Bader AM, et al. Perioperative analgesia with subarachnoid fentanyl- bupivacaine for caesarean delivery. Anaesthesiology 1989;71(6):535-540.
[2] Lee BB, Kee WDN, Hung VY, et al. Combined spinal-epidural analgesia in labour: comparison of two doses of intrathecal bupivacaine with fentanyl. British Journal of Anaesthesia 1999;83(6):868-871.
[3] Singh H, Yang J, Thornton K, et al. Intrathecal fentanyl prolongs sensory bupivacaine spinal block. Can J Anaesth 1995;42(11):987-991.
[4] Ben-David B, Solomon E, Levin H, et al. Intrathecal fentanyl with small-dose dilute bupivacaine: better anesthesia without prolonging recovery. Anesthesia & Analgesia 1997;85(3):560-565.
[5] Shende D, Cooper GM, Bowden MI. The influence of intathecal fentanyl on characteristics of subarachnoid block for caesarean section. Anaesthesia 1998;53(7):706-10.
[6] Karakan M, Tahtaci N, Goksu S. Synergistic effect of intrathecal bupivacaine and fentanyl in spinal anaesthesia. Gazi Medical Journal 1999;10:100-105.
[7] Kuusniemi KS, Pihlajamaki KK, Pitkanen MT, et al. The use of bupivacaine and fentanyl for spinal anesthesia for urologic surgery. Anesth Analg 2000;91(6):1452-1456.

[8] Lane S, Evans P, Arfeen Z, et al. A comparison of intrathecal fentanyl and diamorphine as adjuncts in spinal anaesthesia for Caesarean section. Anaesthesia 2005;60(5):453-457.
[9] Biswas BN, Rudra A, Bose BK, et al. Intrathecal fentanyl with hyperbaric bupivacaine improves analgesia during caesarean delivery and in early post-operative period. Indian J Anaesth 2002;46(6):469-472.
[10] Sowmya N, Ravi M, Sujatha MP, et al. Intrathecal fentanyl in different doses (10mcg, 15mcg) with hyperbaric bupivacaine (10mg) for caesarean section: a comparative study. IOSR Journal of Dental and Medical Sciences 2016;15(11):40-43.
[11] Ali MA, Ismail S, Sohaib M, et al. A double blinded randomised control trial to compare the effect of varying doses of intrathecal fentanyl on clinical efficacy and side effects in parturients undergoing caesarean section. Journal of Anaesthesiology, Clinical Pharmacology 2018;34(2):221-226.
[12] Bogra J, Arora N, Srivastava P. Synergistic effect of intrathecal fentanyl and bupivacaine in spinal anesthesia for cesarean section. BMC Anesthesiology 2005;5(1):5.
[13] Arzola C, Wieczorek PM. Efficacy of low-dose bupivacaine in spinal anaesthesia for Caesarean delivery: systematic review and meta-analysis. British Journal of Anaesthesia 2011;107(3):308-318.
[14] Gauchan S, Thapa C, Prasai A, et al. Effects of intrathecal fentanyl as an adjunct to hyperbaric bupivacaine in spinal anesthesia for elective caesarean section. Nepal Med Coll J 2013;15(3):156-159.
[15] Venkata HG, Pasupuleti S, Pabba UG, et al. A randomised controlled prospective study comparing a low dose bupivacaine and fentanyl mixture to a conventional dose of hyperbaric bupivcaine for caesarean section. Saudi Journal of Anaesthesia 2015;9(2):122-127.
[16] Gopichand K, Suresh T. Effects of fentanyl on hyperbaric bupivacaine in spinal anaesthesia for caesarean section. J Med Sci & Clin Res 2016;4(8):11714-11719.
[17] Yesuf KA, Gebremedhn EG, Melkie TB. Analgesic effect of intrathecal fentanyl as an adjuvant to spinal anaesthesia in comparison with spinal anaesthesia with bupivacaine only for mothers delivered by emergency caesarean section. J Anaesth Crit Care: Open Access 2017;7(5):00278.
[18] Ahmad M, Ahmad M, Atif N. Haemodynamic preservation in caesarean sections by low dose 0.5% hyperbaric bupivacaine. J Ayub Med Coll Abbottabad 2017;29(2):211-214.
[19] Nofal WH, Abdelaal WA, Elfawal SM. Minimum effective volume of bupivacaine in spinal anesthesia for elective cesarean section. Does it differ with height? A non-randomized parallel study. Egyptian Journal of Anaesthesia 2017;33(1):67-72.
[20] Unal D, Ozdogan L, Ornek HD, et al. Selective spinal anaesthesia with low-dose bupivacaine and bupivacaine + fentanyl in ambulatory arthroscopic knee surgery. Journal of Pakistan Medical Association 2012;62(4):313-318.
[21] Akanmu ON, Soyannwo OA, Sotunmbi PT, et al. Analgesic effects of intrathecally administered fentanyl in spinal anaesthesia for lower limb surgery. Macedonian Journal of Medical Sciences 2013;6(3):255-260.
[22] Seyedhejazi M, Madarek E. The effect of small dose bupivacaine-fentanyl in spinal anesthesia on hemodynamic nausea and vomiting in cesarean section. Pak J Med Sci 2007(Part-I);23(5):747-750.
[23] Uike S, Choudhary S, Jain A. Comparative study of analgesic effect of intrathecal bupivcaine and bupivacaine with fentanyl during and after caesarean delivery. International Journal of Medical Research and Review 2015;3(3).
[24] Singh BN. Assessment of efficacy of bupivacaine plain versus bupivacaine with fentanyl in spinal anaesthesia in geriatric patients undergoing hip replacement surgery: a comparative study. International Journal of Contemporary Medical Research 2017;4(7):1614-1616.
[25] Seewal R, Shende D, Kashyap L, et al. Effect of addition of various doses of fentanyl intrathecally to 0.5% hyperbaric bupivacaine on perioperative analgesia and subarachnoid-block characteristics in lower abdominal surgery: a dose-response study. Reg Anesth Pain Med 2007;32(1):20-26.
[26] Mani SM, Srinivasagam KK, Manthiramoorthy N, et al. Randomized clinical comparison of three different doses of bupivacaine with fentanyl for TURP-search for optimal dose to be used in day care urological procedures. Annals of International Medical and Dental Research 2016;2(5):10-14.
[27] Arikan M, Aslan B, Horasanli E, et al. Comparison of two different doses of fentanyl combined with levobupivacaine for elective cesarean section. J Anesth Clin Res 2016;7:687.
[28] Chavan G, Chavan A, Ghosh A. Effect of Intrathecal fentanyl on subarachnoid block with 0.5% hyperbaric bupivacaine. International J of Healthcare and Biomedical Research 2014;2(4):67-76.
[29] Weigl W, Bieryło A, Wielgus M, et al. Analgesic efficacy of intrathecal fentanyl during the period of highest analgesic demand after cesarean section. A randomized controlled study. Medicine (Baltimore) 2016;95(24):e3827.
[30] Belzarena SD. Clinical effects of intrathecally administered fentanyl in patients undergoing cesarean section. Anesthesia & Analgesia 1992;74(5):653-657.
[31] Kotwani MB, Rupwate K, Shivananda P, et al. Comparison between high dose hyperbaric bupivacaine (12.5 mg) alone versus low dose hyperbaric Bupivacaine (7.5 mg) with fentanyl (25 µg) in spinal anaesthesia for inguinal hernia surgery. Int J Clin Trials 2016;3(3):140-146.