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Original Research Article

A Randomized Clinical Assessment of Fentanyl and Tramadol as Adjuvants to Intrathecal Hyperbaric Bupivacaine 0.5% in Elective Caesarean Section

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Abstract

Aim: The aim of the present study was to evaluate the efficacy of intrathecal fentanyl and intrathecal tramadol as adjuvants to hyperbaric bupivacaine 0.5% in elective caesarean section patients in terms of duration of analgesia and intra-operative hemodynamic stability.

Methods: This prospective, randomised, double blinded study was done in the Department of Anesthesia and Critical Care, A. N. Magadh Medical College and Hospital Gaya, Bihar, India. All the 50 patients randomized were analysed for the study and there were no dropouts.

Results: The difference in terms of height, weight and BMI were comparable and was not statistically significant. Duration of analgesia in Fentanyl is 9.47 ± 2.08 hours compared to 6.40 ± 2.25 hours in Tramadol group. Difference between groups is statistically significant with a P value of 0.001. The onset of sensory blockade in Fentanyl group is 1.37 ± 0.49 minutes compared to 2 ± 0.69 minutes in Tramadol group and the difference is statistically significant with a P – value of 0.001. The onset of motor blockade in Fentanyl group is 1.73 ± 0.45 minutes compared to 2.3 ± 0.65 minutes in Tramadol group and the difference is statistically significant with a P – value of 0.001. The mean and standard deviation of the pulse rate of the fentanyl and tramadol group at various time intervals during the intra operative period was analysed. The mean and standard deviation of the mean arterial pressure of the fentanyl and tramadol group at various time intervals during the intra operative period was analysed.

Conclusion: Both the groups were effective in providing adequate surgical anaesthesia and hemodynamic stability, but fentanyl is the better alternative to tramadol as an adjuvant to spinal bupivacaine in elective caesarean section.

Keywords: Hyperbaric bupivacaine, Intrathecal, Fentanyl, Tramadol, Spinal anaesthesia, Caesarean deliveries, Analgesia, Muscle relaxation

Introduction

Spinal Anesthesia or intrathecal anesthesia is the first choice for infraumbilical and lower limb surgeries. In-order to further increase the duration of spinal local anesthetics, as well as to increase its safety profile, various adjuvants has been used. Since the isolation of opioids in the spinal cord in 1976, intrathecal administration of opioids in patients undergoing surgery has gained wide popularity [1]

Tramadol, a centrally acting analgesic drug is used mainly for treatment of moderate-to-severe pain. Tramadol is not a single-mechanism analgesic. In addition to μ-opioid agonist effect, it affects modulatory effects on central monoaminergic pathways, inhibiting neuronal uptake of noradrenaline and serotonin. [2] Fentanyl is a lipophilic opioid with rapid onset of action following intrathecal administration. It is commonly used as adjuvant to local anesthetics to improve the quality of blockade and also to prolong the duration of postoperative analgesia during spinal or other regional anesthesia. [3-4] However, there is not enough evidence for intrathecal tramadol to draw

meaningful conclusion on its ability to enhance the sensory and motor components of spinal anesthesia. The effective dose range for intrathecal tramadol for postoperative analgesia is still confusing till date. [5]

Spinal anesthesia is a preferred technique for day-care orthopedic, gynecological, and lower abdominal surgical procedures [6] Lignocaine was commonly used due to its short duration of action but reports of transient radicular irritation led to decline in its use [7] Intrathecal Ropivacaine offers shorter motor blockade duration hence, encouraging early mobilization in patient [8-10] Due to difficulty in maintaining pharmacological stability of hyperbaric Ropivacaine, presently only isobaric solution is available. But Ropivacaine, made hyperbaric with Dextrose, had produced more consistent block, prolonged the needed duration with quicker complete regression [11-12]

The aim of the present study was to evaluate the efficacy of intrathecal fentanyl and intrathecal tramadol as adjuvants to hyperbaric bupivacaine 0.5% in elective caesarean section patients in terms of duration of analgesia and intra-operative hemodynamic stability.

Materials and Methods

This prospective, randomised, double blinded study was done in the Department of Anesthesia and Critical Care, A. N. Magadh Medical College and Hospital Gaya, Bihar, India for one year. All the 50 patients randomized were analysed for the study and there were no dropouts. All the patients who underwent elective lower segment caesarean section under subarachnoid block between the age of 18-35yrs, body mass index between 18.5 to 24.9 Kg/m2 and belonging to ASA (American society of Anesthesiologists).

Patients who refused spinal anaesthesia, those who belonged to ASA class III and above, allergic to local anaesthetics and adjuvants, infection at needle site, any contraindications to subarachnoid block like bleeding tendencies, gross spinal deformities were excluded from the study. 62 patients were randomly allocated into two groups (N=31 each) by computer generated list of random numbers and were given adjuvants to 1.8ml of 0.5% hyperbaric Bupivacaine according to the groups: Group I - Fentanyl 0.2ml (10mcg), Group II- Tramadol 0.2ml (10mg). The patients as well as the anaesthetist involved in the assessment of the block were blinded to the drug used for spinal anaesthesia. Separate independent investigator prepared the syringes with drugs and handed them over to the performing anaesthetist. Both drugs were taken in identical 5ml syringes. Patients, anesthesiologists involved in intraoperative and postoperative care of the patient and investigator collecting the data were unaware of the group allocation. Pre anaesthetic checkup was done for all the patients. Patients were kept nil per oral 8 hours before surgery and given tablet Ranitidine 150mg and tablet Metoclopramide 10mg night before surgery as well as the morning of surgery at 7 AM with small sip of water. Patients were shifted to Operation Theatre (OT). Prior to shifting the patient, the operation theatre underwent routine inspection which included checking of Boyle's machine for any leaks, availability of emergency drugs, all necessary equipment for difficult airway and working standard monitors. Any deficiencies from standard requirements were rectified before shifting patient to the theatre. Standard monitors like pulse oximeter, electrocardiography and non invasive blood pressure were connected. An IV access was established with 18 gauge intravenous cannula. Patients were preloaded with 15ml/kg of lactated ringer's solution. Patients were positioned in left lateral position. Under strict aseptic precautions, L3-L4 intervertebral space was identified. Skin was infiltrated with 2ml of 2% Lidocaine. 25G Quincke's needle was inserted into the intervertebral space till subarachnoid space was reached which was confirmed by free flow of CSF on removing stylet. The labeled syringe which contained the corresponding drug as per which study group the patient belonged to was attached to the needle, aspirated for CSF and then entire volume of drug was injected. Time of injection of local anaesthetic solution was considered as 0 minutes. Patient was put in supine position and sensory level was checked by pin prick method. Level was checked every 2 minutes in first 20 minutes. Two consecutively same readings of 2 minute intervals were taken as maximum sensory level. Degree of motor blockade was assessed using Bromage scale (0 - able to lift legs, 1 - able to flex knees but not hips, 2 - unable to flex knees but can move ankle, 3 - no movement in legs). It was checked every 2 minutes till grade 3 is reached. Intraoperative parameters such as heart rate, blood pressure, and SpO2 were monitored every 5 minutes for 20 minutes, then every 10 minutes till the end of surgery. Duration of surgery and duration for rescue analgesia (Injection Diclofenac 75mg Intramuscularly on demand when patient complains of pain) was also monitored. Total analgesics required over 24 hours was also noted. Patients were monitored postoperatively for complications like nausea (treated with injection metoclopramide 10mg intravenously), pruritis (treated with injection chlorpheniramine 20mg intravenously), shivering, respiratory depression, hypotension (MAP fall > 20% treated with injection Ephedrine), bradycardia (heart rate < 50 beats/min, treated with Injection Atropine 0.6mg intravenously). Primary outcome of the study was duration of analgesia. Secondary outcomes were onset of sensory and motor block, intra- operative hemodynamic stability. Data was analyzed using

statistical package for social sciences (SPSS) VERSION 23, Microsoft USA, Armonk, NY: IBM Corporation and its licensors 2015. Continuous variables were expressed in standard deviation and mean. Data was analyzed by independent T- test, Mann Whitney U test or chi square tests whichever is applicable. Demographic parameters were assessed with analysis of variance between the groups and are expressed as Mean and standard deviation (SD). P value < 0.05 was taken as statistically significant.

Study Variables

Dependent variables: Severity of postoperative pain, first analgesia request time and total analgesia consumption.

Independent Variables

A. Socio-demographic variables: {age, weight, height}, Parity, gestational age, duration of surgery, ASA category, time from intrathecal injection to delivery of the child.

B. Factor related to related with spinal anaesthesia: Level of sensory block, onset of sensory block, grade of motor block, onset of motor block, duration of motor block to recover,

C. Factor related with perioperative side effects of spinal anaesthesia: Nausea/vomiting, hypotension, shivering, pruritis, hemodynamic changes, maternal respiratory depression, APGAR score and bradycardia.

Results

Table 1: Segregation of height, weight, BMI

	Group	N	Mean	SD	P value(by 't' test)
Height	Fentanyl	25	158.50	4.19	0.480
	Tramadol	25	157.70	4.51	
Weight	Fentanyl	25	59.43	4.56	0.187
	Tramadol	25	57.97	3.92	
BMI	Fentanyl	25	23.61	0.99	0.246
	Tramadol	25	23.29	1.10	

The difference in terms of height, weight and BMI were comparable and was not statistically significant.

Table 2: Segregation of time duration for analgesia

	Groups	N	Mean	SD	P value
Analgesia duration	Fentanyl	25	9.47	7.08	0.001
	Tramadol	25	6.40	2.25	

Duration of analgesia in Fentanyl is 9.47 ± 2.08 hours compared to 6.40 ± 2.25 hours in Tramadol group. Difference between groups is statistically significant with a P value of 0.001.

Table 3: Segregation of time for onset of sensory and motor blockade

	Groups	N	Mean	SD	P value
Onset of sensory	Fentanyl	25	1.37	0.49	<0.001
	Tramadol	25	2.00	0.69	
Onset of motor	Fentanyl	25	1.73	0.45	<0.001
	Tramadol	25	2.30	0.65	

The onset of sensory blockade in Fentanyl group is 1.37 ± 0.49 minutes compared to 2 ± 0.69 minutes in Tramadol group and the difference is statistically significant with a P – value of 0.001. The onset of motor blockade in Fentanyl group is 1.73 ± 0.45 minutes compared to 2.3 ± 0.65 minutes in Tramadol group and the difference is statistically significant with a P – value of 0.001.

Table 4: Pulse rate in both the groups at various time intervals during the intra operative period

Pulse Rate	Groups	N	Mean	SD	P value
0 minutes	Fentanyl	25	93.47	17.51	0.549
	Tramadol	25	90.87	15.85	
5 minutes	Fentanyl	25	89.37	17.36	0.897
	Tramadol	25	89.93	16.31	
10 minutes	Fentanyl	25	89.80	15.18	0.885
	Tramadol	25	90.37	14.95	
15 minutes	Fentanyl	25	88.67	13.62	0.623
	Tramadol	25	90.33	12.48	
20 minutes	Fentanyl	25	90.07	14.66	0.670
	Tramadol	25	91.53	11.73	

30 minutes	Fentanyl Tramadol	25 25	85.63 88.47	13.13 12.19	0.390
40 minutes	Fentanyl Tramadol	25 25	80.96 84.48	12.86 14.40	0.364
50 minutes	Fentanyl Tramadol	25 25	80.94 88.67	14.79 12.14	0.148

The mean and standard deviation of the pulse rate of the fentanyl and tramadol group at various time intervals during the intra operative period was analysed.

Table 5: Mean arterial pressure in both the groups at various time intervals during the intra-operative period

Mean arterial pressure at given time	Groups	N	Mean	SD	P value
0 minutes	Fentanyl Tramadol	25 25	85.57 83.07	11.86 15.19	0.480
5 minutes	Fentanyl Tramadol	25 25	76.93 79.07	9.70 12.89	0.472
10 minutes	Fentanyl Tramadol	25 25	72.43 78.80	11.02 17.25	0.095
15 minutes	Fentanyl Tramadol	25 25	71.03 77.70	10.67 17.78	0.085
20 minutes	Fentanyl Tramadol	25 25	72.23 71.37	10.82 8.74	0.734
30 minutes	Fentanyl Tramadol	25 25	76.63 76.57	15.84 11.50	0.985
40 minutes	Fentanyl Tramadol	25 25	77.13 77.19	12.14 11.01	0.987
50 minutes	Fentanyl Tramadol	25 25	80.06 69.83	8.22 10.76	0.007
60 minutes	Fentanyl Tramadol	25 25	81.33 72.44	12.42 9.02	0.131

The mean and standard deviation of the mean arterial pressure of the fentanyl and tramadol group at various time intervals during the intra operative period was analysed.

Discussion

Spinal anesthesia is a preferred method of anesthesia for surgery on lower half of body due to its efficacy, rapidity, reduction in blood loss, and protection against thromboembolic episodes. When the patient is receiving spinal anesthesia with local anesthetic agents like bupivacaine, addition of another drug intrathecally which will prolong analgesia is a logical choice. Hyperbaric bupivacaine is the most common drug used in spinal anaesthesia for caesarean section. Bupivacaine belongs to amide group of local anaesthetics with high potency, slow onset (5-8 minutes) and long duration of action. For caesarean section intrathecal dose of hyperbaric bupivacaine is 12 to 15 mg. [13] Addition of opioids to local anaesthetics is routinely done in central neuraxial blockade as it provides better intraoperative and early postoperative analgesia. [14] Spinal anaesthesia is often used for both emergency and elective caesarean section. The advantages of spinal anaesthesia are its rapidity in onset, safety and reliability. Caesarean delivery requires traction of peritoneum and handling of intraperitoneal organs, resulting in intraoperative visceral pain. With higher doses of hyperbaric bupivacaine, incidence of intraoperative visceral pain associated with organ manipulation is reduced. [15,16]

The difference in terms of height, weight and BMI were comparable and was not statistically significant. Duration of analgesia in Fentanyl is 9.47 ± 2.08 hours compared to 6.40 ± 2.25 hours in Tramadol group. Difference between groups is statistically significant with a P value of 0.001. The onset of sensory blockade in Fentanyl group is 1.37 ± 0.49 minutes compared to 2 ± 0.69 minutes in Tramadol group and the difference is statistically significant with a P – value of 0.001. The onset of motor blockade in Fentanyl group is 1.73 ± 0.45 minutes compared to 2.3 ± 0.65 minutes in Tramadol group and the difference is statistically significant with a P – value of 0.001. The mean and standard deviation of the pulse rate of the fentanyl and tramadol group at various time intervals during the intra operative period was analysed. The mean and standard deviation of the mean arterial pressure of the fentanyl and tramadol group at various time intervals during the intra operative period was analysed. Alfolayan et al studied the same two drugs as adjuvants to bupivacaine in appendicectomies by assessing intra-operative pain and discomfort along

with postoperative analgesia and concluded that both provided better analgesia than bupivacaine alone but were equipotent with each other. This may be due to the fact that they used a higher dose of 25mcg Fentanyl and 25mg Tramadol with 3ml of 0.5% Bupivacaine compared to our lower dose of 10mcg, 10mg and 1.8ml respectively. [17] Subedi et al performed a similar study with 10mg Tramadol and 10mcg Fentanyl but ended up using 2ml of 0.5% Bupivacaine for the subarachnoid block whereas we only used 1.8ml. Perhaps this difference in volume and dose of local anaesthetic intrathecally might have led to their opposing conclusion of Tramadol providing better postoperative analgesia than Fentanyl as an adjuvant. [18] Chakraborty et al studied the effect of adding 20mg of Tramadol intrathecally with 3ml 0.5% Bupivacaine for major gynaecological surgeries in relation to postoperative analgesia and came to the conclusion that it significantly prolonged the postoperative duration of analgesia. This would seem to support our findings of Tramadol providing a good postoperative analgesia duration. However it would be difficult to say for sure since we did not have a control group like they did of Bupivacaine alone to compare with. [19] Sanjul Dandona et al, conducted a study consisting of 50 patients belonging to ASA 1 and 2 posted for lower abdominal and lower limb surgeries under subarachnoid block. They compared efficacy of tramadol and fentanyl as adjuvant to local anaesthetics in these patients and concluded that duration of sensory and motor block and duration of postoperative analgesia was significantly prolonged in fentanyl group compared to tramadol group which would concur with the findings of our study. [20] Dalvi et al also compared 25mcg Fentanyl and 25mg Tramadol just like Alfolayan et al, but concluded favouring our results by proving that intrathecal Fentanyl provided longer duration of sensory and motor blockade than Tramadol. [21]

Both the previous mentioned studies concluded in favour of Fentanyl like our study. The former based it on intraoperative analgesia whereas the latter would also stress upon postoperative analgesia duration. Choi DH et al compared the efficacy of different doses of 0.5% heavy bupivacaine with different dose combination of 0.5% bupivacaine plus fentanyl in patients posted for caesarean section. They concluded that high dose of local anaesthetics are required to produce surgical anaesthesia compared to local anaesthesia with fentanyl group. They inferred that adding opioid to local anaesthetics reduces the dose local anaesthetic agent by increasing the block density. [22] Combination of adjuvants with local anaesthetics allows for a reduction in doses of both classes of drugs, thus lessening the likelihood of side effects attributable to each. [23]

Conclusion

Both the groups were effective in providing adequate surgical anaesthesia and hemodynamic stability, but fentanyl is the better alternative to tramadol as an adjuvant to spinal bupivacaine in elective caesarean section.

References

1. Pöpping DM, Elia N, Marret E, Wenk M, Tramèr MR. Opioids added to local anesthetics for single-shot intrathecal anesthesia in patients undergoing minor surgery: a meta-analysis of randomized trials. PAIN®. 2012 Apr 1;153(4):784-93.
2. Jou IM, Chu KS, Chen HH, Chang PJ, Tsai YC. The effects of intrathecal tramadol on spinal somatosensory-evoked potentials and motor-evoked responses in rats. Anesthesia & Analgesia. 2003 Mar 1;96(3):783-8.
3. Biswas BN, Rudra A, Bose BK, Nath S, Chakrabarthy S, Bhattacharjee S. Intrathecal fentanyl with hyperbaric bupivacaine improves analgesia during caesarean delivery and in early post-operative period. Indian Journal of Anaesthesia. 2002 Nov 1;46(6):469-72.
4. Shang AB, Gan TJ. Optimising postoperative pain management in the ambulatory patient. Drugs. 2003 May; 63:855-67.
5. Chakraborty S, Chakrabarti J, Bhattacharya D. Intrathecal tramadol added to bupivacaine as spinal anesthetic increases analgesic effect of the spinal blockade after major gynecological surgeries. Indian journal of pharmacology. 20 08 Jul 1;40(4):180-2.
6. Kuthiala G, Chaudhary G. Ropivacaine: A review of its pharmacology and clinical use. Indian journal of anaesthesia. 2011 Mar 1;55 (2):104-10.
7. Fettes PD, Hocking G, Peterson MK, Luck JF, Wildsmith JA. Comparison of plain and hyperbaric solutions of ropivacaine for spinal anaesthesia. British journal of anaesthesia. 20 05 Jan 1;94(1):107-11.
8. Singh AP, Kaur R, Gupta R, Kumari A. Intrathecal buprenorphine versus fentanyl as adjuvant to 0.75% ropivacaine in lower limb surgeries. Journal of Anaesthesiology Clinical Pharmacology. 2016 Apr 1;32(2):229-33.
9. Campora E, Merlini L, Pace M, Bruzzone M, Luzzani M, Gottlieb A, Rosso R. The incidence of narcotic-induced emesis. Journal of pain and symptom management. 1991 Oct 1;6(7):428-30.
10. HA H. Spinal anesthesia by magnesium sulfate. JAMA. 1906; 46:647-50.
11. Herroeder S, Schönherr ME, De Hert SG, Hollmann MW, Warner DS. Magnesium—essentials for anesthesiologists. The Journal of the American Society of Anesthesiologists. 20 11 Apr 1;114(4):971-93.

12. James MF. Magnesium: an emerging drug in anaesthesia. British Journal of Anaesthesia. 20 09 Oct 1;103(4):465-7.
13. Dahlgren G, Hultstrand C, Jakobsson J, Norman M,Eriksson EW, Martin H. Intrathecal sufentanil, fentanyl, or placebo added to bupivacaine for cesarean section. Anesthesia and Analgesia. 1997 Dec 1;85(6):1288-93.
14. Dalvi NP, Patil N. Comparison of effect of intrathecal fentanyl bupivacaine and tramadol-bupivacaine combination on postoperative analgesia in lower abdominal surgeries. Research and Innovation in Anesthesia. 2016; 1(2):35-40.
15. De Simone CA, Leighton BL, Norris MC. Spinal anesthesia for cesarean delivery: a comparison of two doses of hyperbaric bupivacaine. Reg Anesth Pain Med. 1995 Mar 1;20(2):90-4
16. Dixit S. Postoperative analgesia after caesarean section: an experience with intrathecal buprenorphine. Indian J Anaesth 2007;51(6): 515-518.
17. Pedersen H, Santos AC, Steinberg ES, Schapiro HM, Harmon TW, Finster M. Incidence of visceral pain during cesarean section: the effect of varying doses of spinal bupivacaine. Anesthesia and analgesia. 1989 Jul;69(1):46-9.
18. Pradhan M, Amatya SP, Shrestha A, Piya R, Hirachan N. To compare the effect of intrathecal Fentanyl with hyperbaric Bupivacaine on the quality of subarachnoid blockade in cesarean section. Journal of Advanced Medical and Dental Sciences Research. 2017 Aug 1;5(8):4-7.
19. Sanjul Dandona, NehaBatra SS. Comparison of Intrathecal tramadol and fentanyl as adjuvant in abdominal and lower limb surgeries: A randomized clinical study. Int J Med Heal Res.2017;3(2):46-9.
20. Scott LJ, Perry CM. Tramadol. Drugs. 2000 Jul 1;60(1):139- 76.
21. Srivastava U, Kumar A, Gandhi NK, Saxena S, Dutta D, Chandra P, Singh S. Hyperbaric or plain bupivacaine combined with fentanyl for spinal anaesthesia during caesarean delivery. Indian J Anaesth. 2004 Jan 1;48(1):44-6.
22. Tejswani GA, Rattan AK. The role of spinal opioid receptors in antinociceptive effects produced by intrathecal administration of hydromorphone and buprenorphine in the rat. Anesth Analg 2002 Jun;94(6):1542-1546.
23. Upadya M, Neeta S, Manissery JJ, Kuriakose N, Singh RR. A randomized controlled study comparing intrathecal hyperbaric bupivacaine-fentanyl mixture and isobaric bupivacaine-fentanyl mixture in common urological procedures. Indian journal of anaesthesia. 2016 Jan;60(1):44 - 9.