Original Article

Study of effect of fentanyl and tramadol added to low dose bupivacaine in subarachnoid block for caesarean section – a comparative study

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Abstract

Background *Caesarean section is one of the most common operation. Adjuvent added to low dose bupivacaine for caesarean section is a better option.*

Objectives *The study was designed to observe the effects of fentanyl and tramadol added to low dose bupivacaine in subarachnoid block for caesarean section.*

Methods *Sixty parturient were randomly divided into three groups, 20 (twenty) parturient in each group. Group-A was received 0.5% bupivacaine 7.5 mg (one and half ml) in 0.5ml of 5% dextrose in water-total 2 ml, Group-B was received of 0.5% bupivacaine 5mg with fentanyl 5O µgm -total 2mL. and in Group-C was received 0.5% bupivacaine 5mg with tramadol 50 mg- total 2 ml were used for spinal anaesthesia. Height of sensory block was assessed by pin prick method and quality of motor block was assessed by Bromage scale. Duration of effective analgesia was recorded as the patients request for the first dose of analgesic. APGAR score was recorded at 1 and 5 minute after delivery of the baby.*

Result *The mean duration of block in group-A was 117,75± 22.96; in group-B was 166,00± 29-62 and group-C was 213.00± 27.35 min which was significant among three groups (P = 0.01). The mean change of systolic blood pressure among the three groups at 3 min., 4 min., 5 min., 6 min., 8 min., 9 mim, 10 min., 20 min. and 30 min. after SAB was found significant and the mean change of diastolic blood pressure was significant at 2, 3, 8, 9, 10, 20 min and p value was 0.020, 0.035, 0.058, 0.031, 0.040, 0.063 respectively after SAB. Hypotension occured 7 (seven) patients in group-A; 9 (nine) patients in group-B and 4 (four) patients in group-C. Itching was not found in group-A; 6 patients in group-B and no patient in group-C. Measurement of VAS after SAB was significant among the groups. There were also significant difference of VLAS among the groups in 1st hour (P =0.00049), 2nd hrs (P- 0.007) and 3rd hrs (P = 0.001) after of SAB, and interaction between groups were significant (P =0.001).*

Conclusion *Bupivacaine and tramadol combination may be a better choice for intrathecal anaesthetic agent in comparison to 0.5% of bupivacaine in 0.5ml of 5% dextrose with water or 0.5% of bupivacaine with fentanyl combination.*

Keywords *SAB, bupivacaine, fentanyl and tramadol*

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Introduction

Obstetric anaesthesia is a demanding but gratifying sub-specialty of anaesthesiology. The widespread acceptance and use of regional anaesthesia for labour has made obstetric anaesthesia is a major part of most anaesthetic practices. The common indications for anaesthesia for parturients are caesarean section. Regional anaesthesia for caesarean section become the preferred technique because general anaesthesia has been associated with higher maternal mortality. Regional anaesthesia is advantageous in terms of less neonatal exposure to potentially depressant drugs, decreased risk of maternal pulmonary aspiration

and an awaken mother at the birth of her child[1]. Hyperbaric bupivacaine is the most common local anaesthetic used in subaracnoid block for caesarian section. A variety of ways have been tried to improve the quality of spinal anaesthesia during caesarian section, injecting large dose of local anaesthetic, making hyperbaric local anaesthetic solutions, addition of adrenaline, morphine or fentanyl to local anaesthetic agents. Adding an adjunct (opioids or non opioids) has allowed reduction in the dose of bupivacaine and provides cardiovascular stability[2]. In the context of " augmentation stratagies" a wide variety of opioids and non opioids are used as an adjunct to subarachnoid block to improve the quality of anaesthesia and prolongation of analgesia in the post operative peroid[3]. Opioids added to local anaesthetic for subarachnoid block was first introduced into clinical practice in 1979 with morphine sulphate as a forerunner. Morphine is a hydrophilic agent, may not be optimal as intrathecal drug for intraoperative analgesia because of less lipid soluble drug have a slower rate of onset of action and the drug may reach the medulla and cause delayed respiratory depression[4]. Fentanyl , a lipophilic opioid, has rapid onset of action following intrathecal administration[5]. So, fentanyl is suitable as intrathecal drug for intraoperative analgesia and also prolongs analgesia in the postoperative peroid[6].

Tramadol a pseudo opioid drug when used intrathecally binds with opioids receptor in the spinal cord. The analgesia produced by combination of bupivacaine and tramadol reports rapid onset and less degree of motor blockade . Respiratory depression, retention of urine, pruritis and limited doses are main problem of opiods, which has been eliminated by use of tramadol[7]. Tramadol of induced antinociceptive activity is mediated by the both opioid (mu) and non- opioid (inhibition of monoamino uptake) mechanisms[8]. Tramadol is a synthetic analgesic as it has both opioid and non opioid mechanism of action and may produce analgesia with less respiratory depression, sedation, gastrointestinal stasis and abuse potential. In therapeutic doses, the effects on ventilation and the cardiovascular system are clinically insignificant[9]. In one study it is seen that intrathecal tramadol causes a dose related suppressive effects on both sensory (A 6, C) and motor neural conduction in the spinal cord[10]. Tramadol administered epidurally has demonstrated to decrease postoperative analgesic requirements. However, its effects on post operative analgesia after intrathecal administration has not been yet studied. The effect of intrathecal tramadol administration on pain control after TURP was studied[11]. There are no such reports yet published that compares the efficacy of bupivacaine fentanyl and bupivacaine tramadol mixture for caesarean section by intrathecal technique. Thus in this study, we have compared the anaesthetic effect with effectiveness and adverse effects of these two regimens with bupivacaine in 0.5 ml of 5% dextrose in water after applied intrathecally during caesarean section.

Methods

This randomized prospective study was carried out in the department of Anaesthesia, Analgesia and Intensive Care Medicine, Bangabandhu Sheikh Mujib Medical University, Shabagh, Dhaka. With approval from the hospital ethical committee and written informed consent, a total of sixty parturients of ASA class I and II undergoing caesarean section were included in the study. Any one who had contraindication for regional anaesthesia were excluded from the study. All parturient were randomly divided into three groups 20 (twenty) parturient in each group. Group-A : 0.5% bupivacaine 7.5 mg one and half ml in 0.5ml of 5% dextrose in water-total 2 ml. Group-B:Concentraton of 0.5% bupivacaine 5mg with fentanyl 50 µgm -total 2mL.Group-C:Concentraton of 0.5% bupivacaine 5mg with tramadol 50 mg- total 2 ml. After arrival of the patient to the operation theatre baseline parameter (pulse, blood pressure, rate, lungs, respiratory rate and Spo2) recorded and anesthetic procedure was explained again to each patient. A 18 Gauge indwelling iv. canula was inserted into a peripheral vein. All parturient preloading with a 20 ml per kg Hartmann's solution during the 10 min.presiding spinal block. Under all aseptic precaution spinal anesthesia was performed in the left lateral decubitus position with a 27 Gauge Quincke spinal needle. After subarachnoid injection, mothers were immediately turn supine with left uterine displacement. All patients were received supplementation of O_2 via face mask.

Immediately after spinal anaesthesia pulse, blood pressure and Spo2 was recorded. Then pulse, blood pressure, respiratory rate and Spo2 was recorded every 3 minute for first 20 minutes, at 5 minutes interval for remainder of peration and thereafter 30 minutes interval until the patients complaints of pain. The occurrence of discomfort and side effects like pruritus, nausea and vomiting, shivering, chest pain restlessness etc. were recorded upto 24 hours. Hypotension was defined as a decrease in systolic blood pressure to less than 20% from the baseline was treated with bolus of IV fluid and ephedrin as required. Height of sensory block was assessed by pin prick method at 20 minutes after administration of spinal anaesthesia. The quality of motor block was assessed by Bromage scale. The quality of anaesthesia was assessed depending on quality of motor lock (onset time, bromage scale) and quality of sensory block(onset time, level of block) and on incidence of side effects and by interviewing the parturient for their satisfaction, Verbal rating Scale(VRS). According to quality of anaesthesia was categorized as excellent / good / fair / poor. Duration of effective analgesia(first dose of rescue analgesic) was recorded as the patients request for the first dose of analgesic. APGAR score was recorded at 1 and 5 minute after delivery of the baby.

Values were expressed as mean ± SD. Analysis was done by one-way and two-way ANOVA; chi - square and student's t-test (unpaired). P value <0.05 was considered significant.

Results

Table-I *Demographic data of study subject*

Chracter (s)	Groups			P	
	Group -A	Group-B	Group-C		
n	20	20	20		
Age (yr)	30.30+7.01	31.85±6.80	29.8515.60	0.597	NS
Height (cm)	150.95±3.61	151.70±1.41	150.4511.35	0.228	NS
Weight (kg)	56.7518.48	56.1013.80	56.6515.56	0.942	NS
Duration of Pregnancy	38.30±0.923	38.0011.076	38.601.820	0.120	NS

Legend : NS = Not Significant P > 0.01, VS = Very Significant P < 0.01, S = Significant p<0.05, HS= Highly Significant P<0.001.

Value are expressed as mean ± SD. Within parenthesis are percentage over column total. Between groups analysis were done by student's t' test (unpaired) and chi-squared one way or *two* way ANOVA as applicable. Values are regarded as significant if P< 0.05 (CI=95%).

There were no statistically significant differences in mean age, weight, height and gestational age between the three groups.

Hemodynamic changes during preoperative preriod

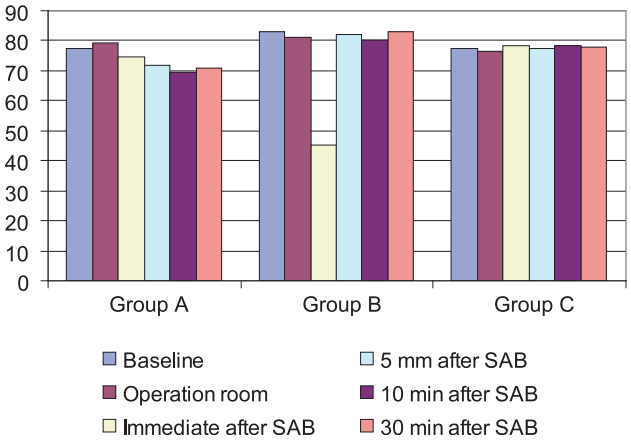

Fig 1 *Changes of heart rate during perioperative peroid*

Change of blood pressure

The mean change of systolic blood pressure of three groups are shown in Figure 2.

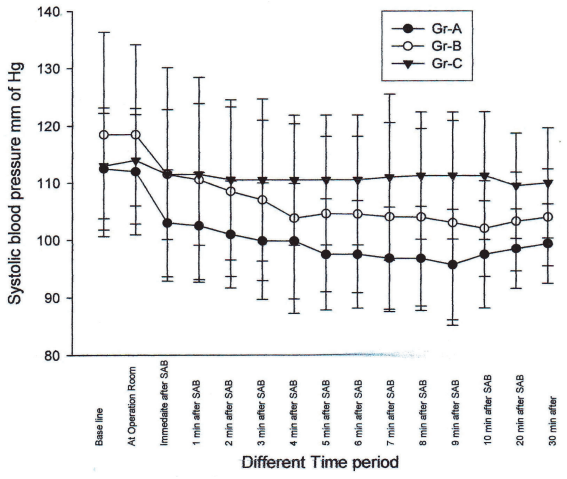

Fig 2 *Showing changes of systolic blood pressure in three groups at different time period*

The mean change of systolic blood pressure among the three groups were compared by ANOVA and found mean systolic bood pressure at preanaesthetic level was not significant (P=0.285), at operation room before SAB was not significant (P=O.209); at immediate after SAB was not significant (P=O.111) and at 1 min., 2 min., 7 min. was also not significant but at 3 min., 4 min., 5 min., 6 min., 8 min., 9 mim, 10 min., 20 min. and 30 min. after of SAB was found significant. P < 0.05.

The mean change of diastolic blood pressure of all groups are shown in Figure 3.

The mean change of diastolic blood pressure among the three groups were .compared by using ANOVA and founded mean diastolic blood pressure at immediate after SAB was not significant (P =0.268) at 1 min, 4 min, *5* min, 6 min, 7 min, 30 min and p value was 0,632,0.251,0.206,0.516, 0.167 respectively but it was significant at 2, 3, 8, 9, 10, 20 and p value was 0.020, 0.035, 0.058, 0.031, 0.040, 0.063 of after SAB.

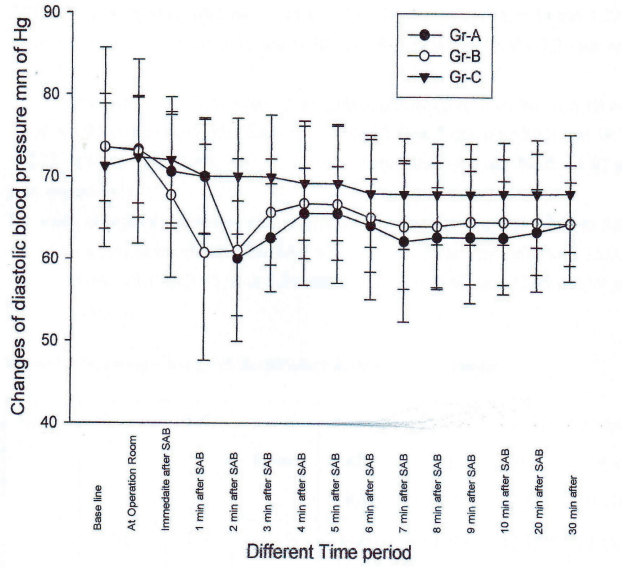

Fig 3 *Showing changes of diastolic blood pressure in three groups at different time period*

Table II *Showing occurence of hypotension in three groups.*

Group	Number	Yes	No	x^2	P
Gr-A	20	7	13		
Gr-B	20	9	11	2.85	0.230
Gr-C	20	4	15		

Values are expressed as mean + SD. Between groups analysis were done by student 'st' test (unpaired). Values are regarded as significant if p<0.05 (% = 2.85).

Hypotension occur 7 (seven) patients in group-A; 9 (nine) patients in group-B and 4 (four) patients in group-C.

Table III *Showing Occurrence of itching in three groups.*

Group	Number	Yes	'No	X^2	P
Gr-A	20	00	20	13.333	0.001
Gr-B	20	06	14		
Gr-C	20	00	20		

Values are expressed as mean ±SD. Between groups analysis were done by student's t' test (unpaired). Values are regarded as significant if p<0.05.

Itching was experienced no patient in group-A; 6 patients in group-B and no patient in group-C.

Table IV *Showing duration of block in min. between study groups.*

Group	Number	Mean± SD
Gr-A	20	117.75 ±22.96
Gr-B"	20	1 66.00 ± 29.629
Gr-C	20	213.00 ±27.357
f		63.187
P		0.000

Values are expressed as mean ± SD. Between groups analysis were done by student's 't'test (unpaired). Values are regarded as significant if p<0.05.

The mean duration of block in group-A was 117,75± 22.96; in group-B was 166,00± 29-62 and group-C was 213.00± 27.35 It was significant among three groups (P = 0.01).

Quality of analgesia:

Quality of analgesia was assessed by visual linear analogue scale (VLAS) and as well as by interviewing the patient intraoperatively. Datas have been shown in Table V.

Table V *Showing analysis of intensity of pain by VLAS in Three groups.*

Groups	First hour	Second hour	Third hour	F	P	
Gr-A	21.95 ±	18.65±	14.44 ±	11.96	0.004	vs
Cr-B	1.5423.30 ±	5.4523.00±	3.2414.38 ±	40.815	0.001	vs
Gr-C	1.1321.90 ±	5.1924.30±	1.5427.00±	39.047	0.001	vs
f	1.685.8491	1.418.2522	0.87114.5740			
P	0.0049VS	0.0007HS	0.001HS			

Values are expressed as mean ± SD. Between groups analysis were done by student's 't test (unpaired). Legend : NS = Not Significant P > 0.01, VS = Very Significant P < 0.01, S = Significant p<0.05, HS=Highly Significant P<0.001.

VAS after SAB significantly felt in group-A, group-B (P - 0.001) and group-C (P=0.001). There were also significant difference of VLAS among the groups in 1st hour (P =0.00049), 2nd hr (P= 0.007) and 3rd hr (P = 0.001) after of SAB, and interaction between groups was significant (P=0.001).

Discussion

Regional anaesthesia has become the preferred technique because general anaesthesia (G/A) has been associated with high maternal mortality. Preservation of conciousness and early postoperative analgesia is considered to be an advantage of regional anaesthesia.

The one cause limiting the choice of spinal anaesthesia for caesarean section is the possibility of neonatal depression because of severe hypotension after spinal anaesthesia. A variety of ways have been tried, to improve the quality\and reduce the complication of regional anaesthesia like the addition of adrenaline , morphine[12] or fentanyl[13]added to hyperbaric bupivacaine solution. More over the apparent synergistic effect between the two types of agents decreases dose requirements and provides excellent analgesia with few maternal side effects and little or no neonatal depression[14].

Fentanyl is a unique drug can be used intrathecally which binds with the poioid receptors and in combination with low dose bupivacaine provide adequate analgesia and decrease need of large volume of local anaesthetic agents when as a soal agent it does not.

Respiratory depresion effect of opioid commonly used interthecally can be attenuated by tramadol. Jones et al. used bupivacanine with fentalyl 37.5 µ.g without any adverse effect to neonate [13]. Reyburn et al. 1989 administered up to 600 µg of fentanyl in pregnant women during labour without any harmful effect on newborn[15]. Respiratory depression, retention of urine, pruritis and limited doses are main problem of opioids, which has been eliminated by use of tramadol[7]. Tramadol a pseudo-opioid drug when used intrathecaly binds with opioids receptors in the spinal cord. The analgesia produced by combination of bupivacaine and tramadol reports rapid onsest less degree of motor blockade[7].

During examination of the neuro chemical profile of tramadol revealed that, unlike morphine it also inhibited the uptake of norepinephrine (Ki=0.79 micro M) and serotonin (0.99 micro M)[8].

In therapeutic doses, the effects on ventilation and the cardiovascular system are clinically insignificant[9].

In one study it is seen that intrathecal tramadol causes a dose related supprcssive effects on both sensory (A S, C) and motor neural conduction in the spinal cord[10]. This result indicate that tramadol exerts a dose-related cental neural blockade. Antinociception is mediated by opioid (mu) and non-opioid (inhibition of monoamine uptake) mechanisms is advantage of tramadol.

Bupivacaine is longer acting commonly used local anaesthetic with no tachyphylaxis. As plain bupivacaine is unpredictable in dose requirement and achieving the block for pain fibres supply along the proposed operative field. Severeal reports[16] have suggested that the total dose of bupivacaine is more important than volume or concentration of anaesthetic solution in determining spread of

anaesthetic solution in cerebrospinal spinal fluid (CSF). To get the advantage of hyparbaric solution of local anaesthetic, 0.5 ml of 5% dextrose with water was added.

Bupivacaine alone on the otherhand is longer acting drug and have found analgesia for operative condition was good with minimal motor block with a dose of 7.5mg to 10 mg for spinal anaesthesia in casarean section required supplementary analgesia because of visceral pain during sergery[17].

Petersen and co-workers[17] reported that similar spread of sensory block to above T_3 developed in patients who received 7.5-10 mg and 10-12.5 mg of 0.5% hyperberic bupivacaine solution, but the use of a larger dose of bupivacaine resulted in a lesser frequency of moderate to severe visceral pain. In other study, the frequency of visceral pain and the requirement for supplementary opioid were significantly less in the 3-4 ml and 4-4.4 ml groups than in the 13.6 ml group (Chung, et al 1996)[18]. In our study, the duration of block (Group-A, Group-B, Group-C) were significantly difference among three groups. In Group-C, shown longer duration of block (sensory. and motor) than other groups. In this study, change of heart rate in Group-A, was significantly decreased from preanaesthetic value at immediately after SAB, at 5 min, at 10 min and at 30 min of after SAB.

But the change of of heart rate in group-B and group-C was not significant as group-A It is found that change of heart rate of group-C was more stable than other groups.

The change of blood pressure in group-A and group-B was significantly decreased immediate after SAB at 2 min, 3 min, 8 min, 9 min, 10 min, 20 min and at 30 min after block but the change in group-C was not significant as for as group-A and group-B.

The result of haemodynamic changes in our study consistent with the report of Lee B.Bet al[19].

The respiratory rate of group-B has significant changes at 5 min, immediate and at 30 min after performing the SAB. But in other groups change was not that much significant.

In this study, hypotension, bradycardia, nausea, vomiting and itching were found more-in gronp-B and group-A but a few in group-C, In groop-A, few patients had been shown-bradycardia and hypotension.

It has been shown, in this prospective experimental, randomized blind-envelop study that the benefit of lower incidence of motor block; equal effective anaesthesia is achievable for operative procedure using the combination of smaller dose[1] of bupivacaine in dextrose with water, or with bupivacaine and fentanyl, or the combination of bupivacaine-tramadol. No undue respiratory depression to both mother and neonate was recorded.

The result consistent with the result of Vaughan, et al 2001 they have been shown pruritus occur in some patient out of 62 on which one required treatment[20]. There were two incidence of nausea and vomiting requiring no treatment.

This study concluded that bupivacaine and tramadol combination may be a better choice for intrathecal anesthetic agent in comparison to 0.5% of bupivacaine in 0.5ml of 5% dextrose with water or concentration of 0.5% of bupivacaine with fentanyl combination.

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