ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
Index Copernicus Value: 68 . 16
PubMed - National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 4, Issue – 4, July - 2019, Page No. : 76 - 86

Comparison of 5 Mg (1 Ml) And 4 Mg (0.8 Ml) 0.5% Hyperbaric Bupivacaine with 25 Microgms Fentanyl in CSE Technique for Caesarean Section- A RCT

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Type of Publication: Original Research Paper

Conflicts of Interest: Nil

Abstract

Background and Objectives Patients undergoing caesarean section in spinal anaesthesia are at greater risk of hypotension than those not undergoing-caesarean section. In addition to aortocaval compression, the total dose of local anaesthetic drug used in subarachnoid block also plays an important role in determining the magnitude of arterial hypotension. The combination of reduced dose of local anaesthetics with intrathecal opioids makes it possible to achieve adequate spinal anaesthesia with minimum hypotension. The use of a lower dose aims to decrease maternal and foetal side-effects (hypotension, intraoperative nausea/vomiting). Intrathecal opioid improves the quality of analgesia and reduces local anaesthetic requirements with favourable effects on haemodynamic stability. In this study we have compared two low doses of bupivacaine with Fentanyl as additive for subarachnoid block in CSE for caesarean section.

Methods: The study was carried out on 60 patients, 30 patients received subarachnoid 4mg(0.8 ml) of 0.5% hyperbaric bupvacaine with 25 microgms fentanyl **(Group A)** and 30 patients received Subarachnoid 5 mg(1 ml) of 0.5% hyperbaric bupvacaine with 25 microgms fentanyl **(Group B)** as a part of CSE technique for LSCS and hemodynamics and adequacy of anaethesia compared.

Result: Spinal block provided excellent surgical anaesthesia in all patients. The mean time to reach T6 sensory level in both the groups was similar. Less patients in group A had hypotensive episodes as compared to group B (3 out of 30 versus 7 out of 30). Onset of sensory block till T6 as well as grade of motor block was comparable.

Conclusions: We conclude that 4 mg of 0.5 % hyperbaric bupivacaine with 25 mcg fentanyl had better

hemodynamic stability as compared to 5 mg of 0.5 % hyperbaric bupivacaine with 25 mcg fentanyl. It was also associated with good sensory and motor blockade.

Keywords anaesthesia, obstetric, combined spinal epidural (CSE), bupivacaine, fentanyl, maternal hypotension.

Introduction

Spinal anaesthesia is the preferred anaesthetic technique for Caesarean deliveries, elective or emergency when balancing risks and benefits to the mother and her foetus. This is primarily due to increased maternal and foetal side effects due to general anaesthesia. While effective surgical anaesthesia is the primary objective of the spinal technique, it must be accomplished while minimizing maternal and neonatal side-effects. A major consideration is spinal anaesthesia-induced maternal hypotension, which occurs in up to 60%-70% of women in the absence of prophylactic measures [1]. The frequency, degree of hypotension and extent of sympathetic blockade is influenced by the dose of local anaesthetic in sub arachnoid block (SAB). The use of a lower dose aims to decrease maternal side-effects (hypotension, intraoperative nausea/ vomiting), reduce the time to discharge from the post anaesthesia care unit, and improve maternal satisfaction. However, such a strategy could compromise the adequacy of anaesthesia as although various factors influence the appropriate sensory nerve block for surgical anaesthesia, the local anaesthetic dose is the main determinant of its success [2]. Hence requirement of supplementary analgesia, either with epidural catheter (CSE technique) or conversion to general anaesthesia may be required. Use CSE (combined spinal epidural) technique, where the epidural catheter can be used to supplement either the level or duration of spinal blockade is recommended [3].

There have been various studies done to study low dose spinal anaesthesia in Caesarean Section but only a few have compared low doses in the same study[4]. The present study was carried out as an extension of a previous study done in the same institute comparing conventional dose of bupivacaine versus low dose bupivacaine for Caesarean Section [5].

The principal objective of the present study was to compare two low doses of bupivacaine-fentanyl i.e, 4mg bupivacaine + 25 mcg fentanyl versus 5mg bupivacaine + 25 mcg fentanyl in subarachnoid block in CSE technique with respect to intraoperative hemodynamics, onset of sensory and motor block, and necessity of supplementation of subarachnoid block. The secondary objectives were to compare the incidence of side-effects like nausea, vomiting, and pruritus.

Methodology

The study was carried out at a tertiary care centre of a Medical College in central India as a hospital based, prospective, randomized controlled trial after obtaining the Institutional Ethics Committee's approval. Randomization was done by systematic randomization method.The study was carried out on 60 patients, 30 patients in each group (sample size is calculated using **EPR** info. Software on basis of ref. study[6] using criteria of blood pressure for calculation). Inclusion criteria were patients with singleton uncomplicated pregnancy of gestational age more than 36 weeks, belonging to American Society of Anaesthesiologists (ASA) physical status I-II, height in 150-170 cm range and BMI up to 26 posted for elective caesarean section. Patient with severe pre-eclampsia, with coagulation abnormalities or on therapeutic anticoagulants, those having kyphoscoliosis, pre-existing neurological deficit, any infection at site of injection, altered mental status, known allergies to

medications used in the study and patients not willing for the procedure were excluded from the study.

All patients were operated under Combined Spinal Epidural (CSE) anaesthesia. After thorough preoperative evaluation a written informed consent was taken from the patients. Patients were explained about the procedure and divided randomly into two groups:

1) **Group A** (Study group):– Subarachnoid 4mg (0.8 ml) of 0.5% hyperbaric bupvacaine with 25 microgms fentanyl.

2) **Group B** (Control group):- Subarachnoid 5 mg(1 ml) of 0.5% hyperbaric bupvacaine with 25 microgms fentanyl.

After confirming fasting status patients were taken in operation theatre, multichannel monitor for SpO_2, ECG, ETCO2 and NIBP was attached. 4L/min oxygen was supplied by Hudson's mask. Intravenous line was established with a 20G cannula. Co-loading was done with ringer lactate 500ml. Antacid prophylaxis was given with Inj. Ranitidine 1mg/kg IV and inj. Ondansetron 0.1mg/kg IV 30min. prior to the procedure. Basal values for BP, pulse rate and SpO_2 were noted.

CSE procedure was carried out in left lateral position. Under all aseptic precautions, 18G epidural catheters was inserted at L2-L3 level using loss of resistance to air technique and 4-5 cm was kept inside epidural space. Subarachnoid Block was given with 23 G Quincke's needle using 0.8 ml (4mg) or 1ml (5 mg) 0.5% heavy Bupivacaine + 25 micrograms Fentanyl as per the group allotment in lower space preferably L3-L4.Patient was made supine, with wedge below right buttock, table tilted to 15 degree head down position.

Further in both groups onset of block was assessed by pinprick in mid line every minute till same reading is observed thrice. If the block did not reach T10 level it was considered a failure. Surgery was allowed to start when block achieved level of T6. If the block height was between T10 and T6, further plan was as follows - an epidural test dose with 3 ml Lignocaine (2%)+Adrenalin (1:200,000) would be given and then supplemented with 0.5% Bupivacaine epidurally in incremental dose of 2ml for blockade upto T6. Blood pressure and pulse rate was noted immediately after spinal was given (T0) and then every 2 minute till 10 mins (time T1 to T5) and thereafter every 5 mins. Till end of surgery (time T6 onwards). Bradycardia defined as HR<60/min was treated with Inj. Atropine 0.6mg and hypotension defined as MAP less than 20% of the baseline values was treated with Inj. Ephedrine 6mg in incremental doses. Intraoperative pain occurring in spite of a level of blockade upto T6 would be treated with allequots of Inj. Fentanyl 25 mcg till a maximum of 100 mcg. After surgery patient was shifted to PACU for further monitoring.Intraoperative dose of IV ephedrine, atropine and fentanyl required, failure of procedure and side-effects such as nausea, vomiting, pruritus and shivering were noted.

Degree of motor block was assessed every 2 minutes for first 10 minutes or till the surgery started and later after the incision was sutured by Bromage scale [7] as:

1. Unable to move legs and feet.
2. Unable to flex knees, but with free movement of feet.
3. Just able to flex knees with free movement of feet.
4. Free movement of legs and feet.

Onset of analgesia, highest level of subarachnoid block, degree of motor blockade, haemodynamic parameters like pulse rate, blood pressure, episodes of hypotension, requirement of epidural local anaesthetic and IV Fentanyl as additional analgesic, and recovery of motor blockade postoperatively were noted.

Statistical Analysis

The demographic characteristics and clinical parameters were compared using t-test of independent samples respectively. Difference in the means of above parameters between groups was also evaluated for statistical significance at different time points after SAB, using t-test for independent samples. Time to achieve T6 level was compared using t-test. Frequency distribution for hypotension episodes were studied using Chi-square test. Entire analysis was performed using R-3.0.0 programming language with pre-validated scripts. The level of significance was fixed at 5% throughout the analysis.

Results

There were 30 patients in each group of total 60 patients and age, BMI data was collected, analysed and the groups were found to be comparable using Student's t- test.

Table 1 – Demographic characteristic of two groups-

Demographics									
Variables	Group	N	Mean	SD	Std. Error Mean	t value	df	P value	Inference
Age	0.8ml	30	26.867	3.071	0.561	0.899	58	0.372	NS
	1ml	30	26.133	3.246	0.593				
BMI	0.8ml	30	22.571	1.889	0.345	0.142	58	0.888	NS
	1ml	30	22.499	1.998	0.371				

The baseline parameters MAP and pulse rate were tested using Student's t- test and the difference was found statistically insignificant as indicated by the P-value ($p > 0.05$) shown in the table 2 .

Table 2- Baseline parameters of two groups-

Baseline parameters									
Variables	Group	N	Mean	SD	Std. Error Mean	t value	df	P value	Inference
MAP_0	0.8ml	30	84.200	8.961	1.636	0.595	58	0.554	NS
	1ml	30	82.767	9.680	1.767				
Pulse rate_0	0.8ml	30	92.833	13.889	2.536	0.586	58	0.560	NS
	1ml	30	90.633	15.151	2.766				

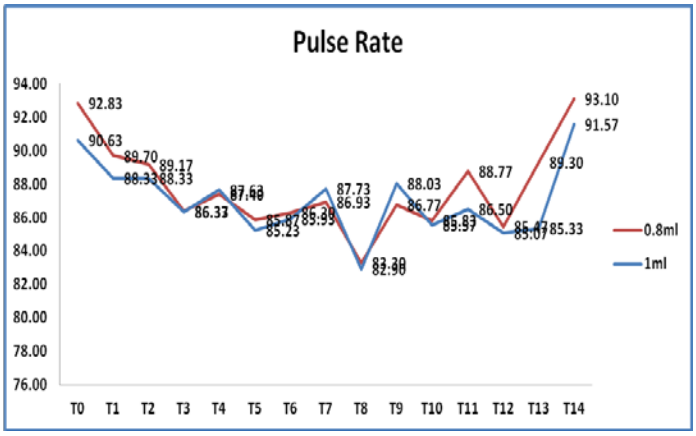
The pulse rate of patients of both groups were observed at different point of the time after administration of SAB and presented as below.

Table 3

	Group	N	Mean	SD	Std. Error Mean	t	df	P value	Inference
T0	0.8ml	30	92.83	13.889	2.536	0.586	58	0.560	NS
	1ml	30	90.63	15.151	2.766				
T1	0.8ml	30	89.70	15.068	2.751	0.352	58	0.726	NS
	1ml	30	88.33	14.972	2.734				
T2	0.8ml	30	89.17	14.904	2.721	0.213	58	0.832	NS
	1ml	30	88.33	15.410	2.813				
T3	0.8ml	30	86.37	11.159	2.037	0.010	58	0.992	NS
	1ml	30	86.33	13.379	2.443				
T4	0.8ml	30	87.40	10.988	2.006	-0.068	58	0.946	NS
	1ml	30	87.63	15.212	2.777				
T5	0.8ml	30	85.87	12.173	2.223	0.195	58	0.846	NS
	1ml	30	85.23	13.022	2.377				
T6	0.8ml	30	86.30	12.457	2.274	0.109	58	0.914	NS
	1ml	30	85.93	13.567	2.477				
T7	0.8ml	30	86.93	13.025	2.378	-0.229	58	0.819	NS
	1ml	30	87.73	13.973	2.551				
T8	0.8ml	30	83.30	11.432	2.087	0.129	58	0.898	NS
	1ml	30	82.90	12.595	2.300				
T9	0.8ml	30	86.77	11.619	2.121	-0.411	58	0.683	NS
	1ml	30	88.03	12.240	2.235				
T10	0.8ml	30	85.83	11.948	2.181	0.087	58	0.931	NS
	1ml	30	85.57	11.898	2.172				
T11	0.8ml	30	88.77	11.172	2.040	0.770	58	0.444	NS
	1ml	30	86.50	11.617	2.121				
T12	0.8ml	30	85.47	12.937	2.362	0.117	58	0.907	NS
	1ml	30	85.07	13.468	2.459				
T13	0.8ml	30	89.30	12.946	2.364	1.089	58	0.281	NS
	1ml	30	85.33	15.187	2.773				
T14	0.8ml	30	93.10	16.635	3.037	0.358	58	0.721	NS
	1ml	30	91.57	16.498	3.012				

The difference between the two groups was statistically not significant as seen from Table 3 and Figure 1.

Figure 1



MAP was observed for both the groups at different point of the time and the mean values were compared using t-test and difference was found to be statistically non significant at each point of the time as seen in Table 4.

Table 4- showing changes in MAP in both the groups-

MAP Analysis									
Variables	Group	N	Mean	SD	Std. Error Mean	t value	df	P value	Inference
T0	0.8ml	30	84.200	8.961	1.636	0.595	58	0.554	NS
	1ml	30	82.767	9.680	1.767				
T1	0.8ml	30	83.533	11.741	2.144	0.345	58	0.731	NS
	1ml	30	82.467	12.193	2.226				
T2	0.8ml	30	82.100	9.455	1.726	1.853	58	0.069	NS
	1ml	30	77.167	11.099	2.026				
T3	0.8ml	30	81.500	9.070	1.656	1.936	58	0.058	NS
	1ml	30	76.367	11.340	2.070				
T4	0.8ml	30	78.967	11.090	2.025	0.922	58	0.360	NS
	1ml	30	75.967	13.944	2.546				
T5	0.8ml	30	79.367	12.067	2.203	0.856	58	0.395	NS
	1ml	30	76.633	12.648	2.309				
T6	0.8ml	30	79.367	10.969	2.003	0.024	58	0.981	NS
	1ml	30	79.300	10.253	1.872				
T7	0.8ml	30	78.500	11.717	2.139	0.108	58	0.914	NS
	1ml	30	78.200	9.736	1.778				
T8	0.8ml	30	80.767	7.650	1.397	0.804	58	0.425	NS

	1ml	30	78.967	9.590	1.751				
T9	0.8ml	30	82.100	9.579	1.749	0.592	58	0.556	NS
	1ml	30	80.600	10.057	1.836				
T10	0.8ml	30	81.200	10.453	1.908	0.566	58	0.574	NS
	1ml	30	79.700	10.076	1.840				
T11	0.8ml	30	82.267	9.969	1.820	0.588	58	0.559	NS
	1ml	30	80.667	11.071	2.021				
T12	0.8ml	30	82.233	10.254	1.872	0.109	58	0.913	NS
	1ml	30	81.933	10.979	2.005				
T13	0.8ml	30	83.667	9.967	1.820	0.635	58	0.528	NS
	1ml	30	81.933	11.148	2.035				
T14	0.8ml	30	83.533	9.194	1.679	0.114	58	0.909	NS
	1ml	30	83.233	11.038	2.015				

Figure 2

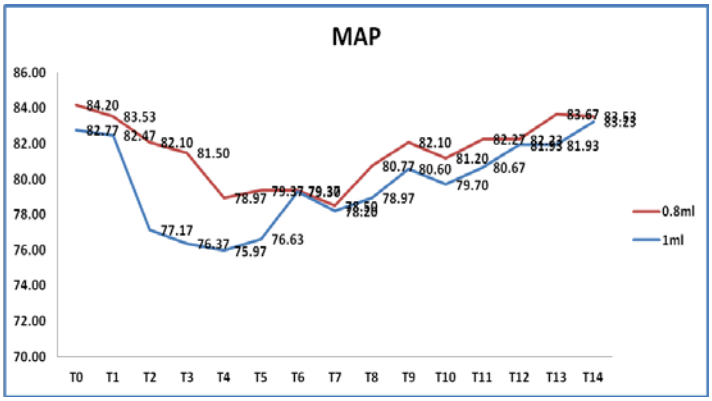


Figure 2 shows that 0.8ml bupivacaine plus fentanyl(group A) lowered the MAP less in comparison to 1 ml bupivacaine plus fentanyl(group B),though it was not statistically significant.

Hypotension was defined as MAP less than 20% of the baseline values. Number of hypotension episodes in group A was less (i.e. 3 out of 30) as compared to groups B (i.e.7 out of 30) as seen in table 5. Though the difference in the results was statistically not significantly different but the table shows less incidences of hypotension in patients of group A, clinically which is good for safety of both mother and foetus.

Table 5- incidence of hypotension in both groups

Hypotension incidence					
Groups	No. of hypotension episodes			Total	P value
	1	2	>3		
0.8ml	2	1	0	3	0.344
1ml	6	1	0	7	
Total	8	2	0	10	
Chi-Sq = 0.476, DF = 1, p value = 0.491					

Table 6- Median and mode of Bromage score

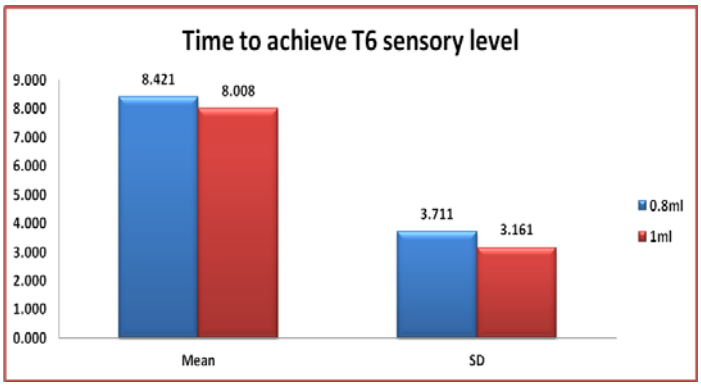
	Median		Median test	Mode	
	0.8ml	1ml		0.8ml	1ml
T0	4	4		4	4
T1	4	3	0.194	4	3
T2	3	3	1.000	3	3
T3	3	3	0.313	3	3
T4	2	2	0.795	2	2
T5	2	2	0.787	2	2
At the end of surgery	3	3	0.559	3	3

Table 6 provides the median value and the mode of Bromage scores and its comparison at each time point between two groups and it was found that the difference was not statistically significant (P >0.05).

Table 7: Time to achieve T6 sensory level

Time to achieve T6 sensory dermatomal level in mins									
Variables	Group	N	Mean	SD	Std. Error Mean	t value	df	P value	Inference
Time to achieve T6 sensory level	0.8ml	30	8.421 min.	3.711	0.587	0.457	58	0.650	NS
	1ml	30	8.008 min.	3.161	0.689				

Figure 7-



The mean time to achieve sensory block to pinprick at T6 was compared and the difference was not statistically significant (P value>0.05).

Discussion

Administering anaesthesia in obstetric patient is a great challenge as here anaesthetist has to take care of two lives, mother and her unborn baby. Numerous factors determine the type of anaesthesia chosen for caesarean section like urgency of operation, indication of the operation, maternal preference, any coexisting medical problems etc. Caesarean section performed under general anaesthesia has greater risks and side effects for both mother and baby. Most of the deaths occurring during general anaesthesia are airway or aspiration related [8]. This has increased popularity of spinal and epidural anaesthesia in surgical obstetric practice. Spinal anaesthesia is simple,

has rapid onset and produces excellent surgical anaesthesia but it has various limitations including fixed duration of anaesthesia, lesser control of block height, post-dural puncture headache and hypotension [1].Maintenance of normal maternal blood pressure after spinal anaesthesia in caesarean section is key factor for adequate neonatal outcome too. The mature placenta is high capacitance organ with no auto regulatory ability, so uteroplacental perfusion pressure is dependent on systemic blood pressure. Spinal anaesthesia with adequately maintained blood pressure results in better neonatal blood gas and acid-base measurements in Caesarean delivery. Hypotension is associated with nausea, vomiting, dizziness, maternal morbidity and influences the neonatal well-being by reducing utero-placental blood flow [9]. Apart from modalities to limit hypotension after spinal anaesthesia like left uterine displacement, head-down tilt, I.V fluids and ephedrine boluses, lowering the dose of LA agent which improves maternal haemodynamic stability can also be an important strategy. Addition of opioids as adjuvants along with local anaesthetic drug in neuraxial anaesthesia improves the quality of the sensory block without producing higher level of analgesia and improves maternal haemodynamic stability [10,11]. Studies have shown a more favourable haemodynamic profile in patients when decreased dose of LA was used along with upload [12, 13].

Lower anaesthetic doses cannot be recommended unless an epidural catheter is in place (CSE) to rescue the block if anaesthesia is inadequate or becomes inadequate during surgery [3].

In our study the mean pulse rate and mean arterial pressure were comparable at all time points throughout the study with $p>0.05$. When the incidence of hypotensive episodes were compared, they occurred in 3 out of 30 patients in group A (Table 5)as compared to 7 out of 30 patients in group B. 1patient in both groups had 2 episodes of hypotension and no patient in either group had >2 episodes. The difference was not statistically significant but clinically it does indicate more haemodynamic stability in group A. [6,14]. Time of onset of block upto T6, the degree of Bromage score at different time points were all found to be comparable statistically at all time points with $p>0.05$. This means that lessening the dose of local anaesthetic neither adversely affected the time required to start the Caesarean section, nor the degree of motor blockade and hence the relaxation.

All patients in both the groups maintained adequate oxygen saturation (SpO_2 >98%), we had supplemented all the patients with 4L/min of oxygen on Hudson mask.

There was no incidence of nausea and vomiting in either group. The finding of less nausea in the groups may be surprising in that nausea is generally considered a side effect of intrathecal opioids. Palmer et al. also found a lower incidence of perioperative nausea and vomiting when 15 µgms fentanyl was added to lidocaine spinal anesthesia for Caesarean delivery [12]. Also, Dahlgren et al. found that either fentanyl or sufentanil added to the spinal anaesthetic for Cesarean delivery led to reduced need for intraoperative antiemetics [13].

Duration and intensity of motor blockade was almost same in both the groups at time points after 2 min of spinal anaesthesia and at the end of surgery. None of the patient in either of the groups required epidural activation in our study and there were no failure.

None of our patient complained of intraoperative pain which could be explained by the synergistic action of fentanyl and bupivacaine[15].

In summary, the findings of this study suggest that spinal anaesthesia for caesarean delivery using both the low

doses of bupivacaine was with equal haemodynamic stability statistically. Subarachnoid 4mg (0.8 ml) of 0.5% hyperbaric bupivacaine with 25 microgms fentanyl in CSE technique in LSCS was associated with clinically less episodes of hypotension as compared to Subarachnoid 5mg(1ml) 0.5% hyperbaric bupivacaine with 25 microgms fentanyl in CSE technique in LSCS. Hence 4 mg of 0.5% bupivacaine could be used when low dose spinal anaesthesia is considered for Caesarean Section in presence of epidural catheters. There are a few limitations of this study. The study's sample size was calculated as per incidence of hypotension and so it may not be adequately to compare the requirement for additional intraoperative analgesia in the form of activation of epidural catheter or IV Fentanyl. Secondly this study was carried out in patients with uncomplicated pregnancies, so the results may not be applicable in other patients (e.g, PIH or multiple gestations).

References

1. Rout CC, Rocke DA, Levin J, Gouws E, Reddy D. A reevaluation of the role of crystalloid preload in the prevention of hypotension associated with spinal anesthesia for elective Cesarean section. Anesthesiology 1993; 79: 262–9.
2. Hocking G, Wildsmith JA. Intrathecal drug spread. Br J Anaesth 2004; 93: 568–78
3. McNaught AF, Stocks GM. Epidural volume extension and low-dose sequential combined spinal-epidural blockade: two ways to reduce spinal dose requirement for caesarean section. International Journal of Obstetric Anesthesia 2007; 16: 346–53
4. C. Arzola, Wieczorek PM. Efficacy of low-dose bupivacaine in spinal anaesthesia for Caesarean delivery: systematic review and meta-analysis. British Journal of Anaesthesia 2011;107 93 0:308-18.
5. Deshmukh S, Jibhkate R, Gadkari C, Borkar N, Bawa J. Comparative evaluation of subarachnoid block with conventional dose bupivacaine versus low dose bupivacaine and Fentanyl for Caesarean Section. International Journal of Biomedical and Advance Reseach 2019: 10(2):e5082
6. Jain G, Singh DK, Bansal P, Ahmed B, Dhama SS. Comparison of low doses of intrathecal bupivacaine in combined spinal epidural anaesthesia with epidural volume extension for caesarean delivery. Anesthesia, essays and researches. 2012 Jan;6(1):47.
7. Bromage PR. Epidural Analgesia, 1st ed. Philadelphia: W.B. Saunders Company, 1978: 144– 5.
8. Hawkins JL, Koonin LM, Palmer SK, et al. Anesthesia-related deaths during obstetric delivery in the United States. Anesthesiology 1997; VT: 277-84.
9. De Santiago J. The effects of the pregnant uterus on the extradural venous plexus in the supine and lateral positions, as determined by magnetic resonance imaging. Br J Anaesth 1997;78:317.
10. Roofthooft E, Van de Velde M. Low-dose spinal anaesthesia for Caesarean section to prevent spinal-induced hypotension. CurrOpinAnaesthesiol 2008; 21: 259–62.
11. Kaur M, Katyal S, Kathuria S, Singh P. A comparative evaluation of intrathecal bupivacaine alone, sufentanil or butorphanol in combination with bupivacaine for endoscopic urological surgery. Saudi J Anaesth 2011;5:202-7
12. Palmer C. M., Voulgaropoulos D., Alves D. (1995): Subarachnoid fentanyl augments lidocaine spinal anesthesia for cesarean delivery. RegAnesth; 20: 389–394.
13. Dahlgren G., Hultstrand C., Jakobsson J., Norman M., Eriksson E. W., Martin H. (1997): Intrathecal

sufentanil, fentanyl, or placebo added to bupivacaine for cesarean section. ObstetAnesth; 85: 1288–1293. 8

14. Nayagam HA, Singh NR, Singh HS. A prospective randomised double blind study of intrathecal fentanyl and dexmedetomidine added to low dose bupivacaine for spinal anesthesia for lower abdominal surgeries. Indian journal of anaesthesia. 2014 Jul;58(4):430
15. Belzarena S. D. (1992): Clinical effects of intrathecally administered fentanyl in patients undergoing cesarean section. AnesthAnalg; 74: 653–657.