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Comparative Study Between Fixed Dose of Hyperbaric Bupivacaine and Dose Related to Height Used in Spinal Anesthesia for Caesarean Section in Normal and Pre-Eclamptic Patients

S. I. Saad [1], E. El S. Afifi [1], M. F. El Meligy [2], D. H. Abd El Hameed and N. El-S. M. Amer [1]
[1] anesthesia and ICU Dept., Faculty of Medicine, Benha Univ., Benha, Egypt
E-Mail: N.Amer@gmail.com

Abstract
Neuroaxial anesthesia has long been accepted as the standard practice for providing the safest anesthesia for cesarean section .Spinal anesthesia for CS should ideally last the duration of the procedure without producing maternal or fetal adverse effects. This study is to monitor the two techniques during cesarean section, fixed dose of bupivacaine not tailored to patient height and variable dose of bupivacaine tailored to patient height. We will compare the outcomes from the two different techniques regarding the level of anesthesia achieved, resulting hemodynamics (BP & HR) ,the requirements for fluids & pressors ,development of nausea & vomiting and the time needed to discharge from PACU**.** This study was conducted on 80 patients aged between 20 and 40 years old, ASA grade I and II . All patients were scheduled for elective cesarean section surgery. All cases were done in Benha university Hospitals after approved consent from the patients. The duration of sensory and motor block was significantly prolonged in fixed dose groups (A&C) than in adjusted dose groups (B&D).The amount of fluids and vasopressors needed were significantly much more in fixed dose groups (A&C) than in adjusted dose groups (B&D).The incidence of complications (hypotension , nausea and vomiting) were significantly higher in fixed dose groups (A&C) than in adjusted dose groups (B&D).we have shown that adjusting the dose of hyperbaric bupivacine (0.5%) according to height in both normal and pre-eclamptic patients , in combination with opioids (fentanyl 20 mcq) , provide adequate anesthesia for elective cesarean section in both normal and pre-eclamptic patients. This regimen associated with decrease in cephalic spread of anesthesia, decrease incidence and severity of maternal hypotention ,nausea ,vomiting , decrease the amount of fluids needed and the dosage of vasopressors used.

Keywords: analgesia, anesthesia, CS, AV, hyperbaric bupivacine (0.5%) and pre-eclamptic patients.

1. Introduction

Neuroaxial anesthesia has long been accepted as the standard practice for providing the safest anesthesia for cesarean section (CS). **(1).**

Spinal anesthesia for CS should ideally last the duration of the procedure without producing maternal or fetal adverse effects.In reality ,finding a spinal technique for CS that provides a reliable block without incurring adverse effects continues to be a challenge in the field of obstetric anesthesia. **(2).**

The most common side effects resulting from spinal anesthesia for CS is hypotension with a reported incidence of 20% - 100% in emergency CS.Often patients will experience a significant amount of nausea as a result of this drop in blood pressure. **(3).**

Anesthesia induced maternal hypotension can also impair utero-placental perfusion and can lead to fetal acidemia. **(4).**

Current strategies to help prevention and treatment of maternal induced hypotension resulting from spinal anesthesia, include giving supplemental intravenous fluids at the time the spinal is placed and with the use of pressor agents ,as phenylepherine or ephedrine ,to manage hypotension following spinal anesthesia. **(5).**

A research study has proven that the same dose of local anesthetic can be provided to patients with a large difference in their height with a reliable and consistent anesthetic level achieved. **(6).**

It has become a practice of many anesthesiologists to give a fixed dose of local anesthetic to all patients regardless their height. **(7).**

Many anaesthesiologists recommend varying the dose of local anesthetic depending on patient height by their clinical experience. **(8).**

Finding the best dose of intrathecal local anesthetic for patients with different heights undergoing CS would require stricking the ideal balance between the often conflicting demands of preventing patients discomfort while also avoiding adverse maternal effects ,particularly hypotension and nausea. **(9).**

Intrathecal dose requirement is known to decrease during pregnancy.One reason for this ,is the epidural venous engorgement resulting from uterine enlargement and consequent venacaval compression ,displacing the CSF within the subarachnoid space and causing a decrease in the requirement for intrathecal drug or an increase in its intrathecal spread. **(10).**

The use of lower doses of intrathecal local anesthetic for spinal blockage is encouraged to minimize post spinal adverse effects during cesarean delivery. **(11).**

2. Subjects and methods

2.1 Ethics Committee: This study was conducted on 80 patients aged between 20 and 40 years old, ASA grade I and II . All patients were scheduled for elective cesarean section surgery. All cases were done in Benha university Hospitals after approved consent from the patients. **Type of**

Study: Prospective, comparative, double blind randomized clinical study.

2.2 Inclusion Criteria: 1- ASA physical status classes I ,II, 2- Age range between 20 -40 years, 3- Type of operation : elective cesarean section surgery and 4- Methods of randomization: Closed envelope.

2.3 Exclusion Criteria: Patient refusal, Parturients in labor, The patients with known history of allergy to amide local anesthetics or opioids, Extremes of height (<140 or >185 cm) , Infection at site of the injection, Any preexisting neurological disease, Failed spinal anesthesia, Obstetric complications like placenta previa and multiple pregnancies, ASA physical status classes III or IV and Patients receiving any anti-coagulant.

2.4 Group allocation:Patients were randomly allocated into four equal groups:

2.4.1 Group I : included 20 normal patients who were not suffering from any medical disease and received a fixed dose of bupivacaine that was 12.5 mg of bupivacaine 0.5% (2.5 ml).

2.4.2 Group II : included 20 normal patients who were not suffering from any medical disease and received variable doses of bupivacaine 0.5 % according to patient's height.

2.4.3 Group III: included 20 pre-eclamptic patients that received a fixed dose of bupivacaine that was 12.5 mg of bupivacaine 0.5% (2.5 ml).

2.4.4 Group IV : will include 20 pre-eclamptic patients that received a variable doses of bupivacaine 0.5% according to patient height

2.5 Methodology

2.5.1 Anesthetic management:

All patients were evaluated initially by medical history and a complete physical examination ,routine preoperative investigations were done (e.g CBC, PT, PTT, INR, liver function tests ,kidney function tests and ECG) for evaluation of the patient medical status. No premedication was administered .Patients was admitted to the operating room fasting for 6 h at least. A peripheral i.v. 18G catheter was inserted and rapid intravenous infusion of saline 10 ml/ kg over 15 minutes . Standard monitoring applied to the patients including continous electrocardiogram, pulse oximeter and non invasive blood pressure. Baseline blood pressure and maternal heart rate were recorded before lumbar puncture, recording continue at 1- minute intervals for the first 20 – minutes after spinal injection and then every 5 minutes till end of surgery.

I.V line was administered under complete aseptic conditions, all cases were injected in the sitting position, they were administered 3 ml (60 mg) 2 % lidocaine infiltration anesthesia at level L3-L4 or L 4-5 after disinfected with antiseptic solution. Patients received intrathecal injection of the previous drugs according to each group over 15 seconds using a 23-25G spinal needle at the level intervertbral disk L3-L4 or L 4-5. After injection Patients were immediately turned supine and wedge position maintained to minimize aortocaval compression.

Block profile assessed at 2 – min intervals for the first 20 minutes, thereafter the anesthesia onset time (time from end of injection of local anesthesia in subarachnoid to bilateral loss of pin – prick sensation at T6 level). Assessed in mid clavicular line using a 24 gauge sterile needle. During this period the following data was recorded : blood pressure, heart rate, oxygen saturation, respiratory rate, maximum sensory block level, time needed for maximum level to be reached, degree of motor block assessed by modified Bromage score (0 = no impairment, 1 = unable to raise extended legs but able to move knees and ankles; 2 = unable to extend legs or flex knees but able to move feet; 3 = unable to flex ankles, knees or hips), and time taken to reach maximum Bromage score. Also the following data were recorded: duration of surgery, fetal extraction time (time between start of surgery till delivery of fetus), total dose of oxytocin administrated post-delivery, frequency of hypotension episodes, total amount of ephedrine , other complications also recorded as nausea, vomiting, , total volume of fluids infused and blood loss (estimated in graded suction bottle and observation of soaked materials).

Hypotention defined as SBP < 100 mmHg or MBP decrease > 20% from baseline, treated with intravenous ephdedrine 5 – 10 mg boluses , bradycardia defined as heart rate < 50 bpm and treated with intravenous atropine 0.6 mg.

Surgery via transverse lower abdominal incision was allowed to start once sensory block reach or exceed bilateral T6 sensory dermatomes. If this was not achieved after 10 minutes, the patient were positioned in the 10^0 head down tilt to reach desirable block level T6. After delivery, patients were given 20 unit oxytocin in 500 ml saline at rate 10 unit / h and uterine repair was performed by surgeon. If patients reported pain or discomfort during surgery as assessed by VAS ≥ 40, bolus of intravenous fentanyl 1.5 ug/kg given (repeated once), if discomfort continue protocol allow for general anesthesia conversion.

Pain intensity was recorded during skin incision, uterus incision, and closure of peritoneam, postoperative 30 min, and postoperative 60 min and when there is pain. In assessment of pain intensity, 10 cm visual analogue scale (VAS) is used. Before operation, VAS was explained to patients as; "0" no pain,"10"intolerable-pain

Postoperative, in PACU, haemodynamics and block profile monitoring were continued till sensory level regressed below L1 and patients can freely move lower limb.

2.6 Statistical Analysis: Data were analyzed by using SPSS version 21.

3. Results

All groups were similar in regard to age, weight, height and BMI with no significant differences between fixed dose groups (A&C) and adjusted dose groups(B&D).(Fig. 1)

On a dose adjustment for height, significantly (P < 0.001) smaller amount of hyperbaric bupivacine, median IQR; 2.3{1.8-2.7 ml}, 2.05(1.8-2.9 ml)were given intrathecally in adjusted dose group B and D respectively than given to fixed dose group patients A and C; 2.5 ml. This table shows Spinal anesthetic was placed L3-4 interspace in 25% of patients in group A, 35% of patients in group B, 50% of patients in group C and 55% in group D ,with the reminder of patients received spinal anesthesia at L4-5 interspace. (table 1).

The Time of the block to reach T6 level was significantly (P < 0.001) prolonged in group B (adjusted dose) than in group A (fixed dose) (4.70±1.129 vs 2.95±0.887min) (P = 0.000003). Also it was significantly prolonged in group D (adjusted dose) than in group C (fixed dose) (3.80±0.768 vs 3.35±0.489 min), (P = 0.033),. . (table 2).

Peak sensory level reachs T6 level in 2 patients in group A (fixed dose) and 6 patients in group B (adjusted dose), reaches T4 level in 2 patients in group A and 9 patients in group B and the level was above T4 level in 16 patients in group A and 5 patients in group B. Table (3)

The time for block to regress below L1 was significantly (P < 0.001) prolonged in group A (fixed dose) than in group B (adjusted dose) (130.25±7. 518 vs 115.10±8.252 min). Also,it was significantly (P < 0.001) prolonged in group C (fixed dose) than in group D (adjusted dose) (132.20±19.917 vs 109.20±18.272 min) . Table (4)

Duration of sensory block was significantly (P <0.02) prolonged in group A (fixed dose) than in group B (adjusted dose) (164.52±12.533 vs 154.33±8.342 min). it Also, it was significantly(P <0.04) prolonged in group C (fixed dose) than in group D (adjusted group) (172.75±25.138vs 146.46±11.64min) .Table (5)

Duration of motor block was significantly (P < 0.017) prolonged in group A (fixed dose) than in group B (adjusted dose) (134.25±10.422 vs 126.50±9.191min). Also, it was significantly prolonged (P < 0.001) in group C (fixed group) than in group D (adjusted dose) (141.75±19.076 vs 118±12.814min). Table (6)

The dose of ephedrine used was significantly different (P < 0.001) between group A (fixed dose) and group B (adjusted dose), (25.125±14.7585vs 5.850±4.4665 min). Also, it was significantly different (P < 0.001) between group C (fixed dose) and group D (adjusted dose) (28.050±11.2553vs 5.150±5.5656min) More doses of ephedrine were needed in fixed groups (A & C) than in adjusted groups (B & D) .Table (7)

Apgar scores of newborns was similar in group A (fixed dose) and B (adjusted dose), at 1 and 5 minutes interval, with no significant differences . Also,it was similar in group C (fixed dose) and D (adjusted dose), at 1 and 5 minutes interval, with no significant differences.Table (8)

No significant differences were identified between the groups A (fixed group) and B (adjusted dose) or between group C (fixed group) and D (adjusted dose) regarding the urine output (UOP),estimated blood loss and duration of surgery.Table (9)

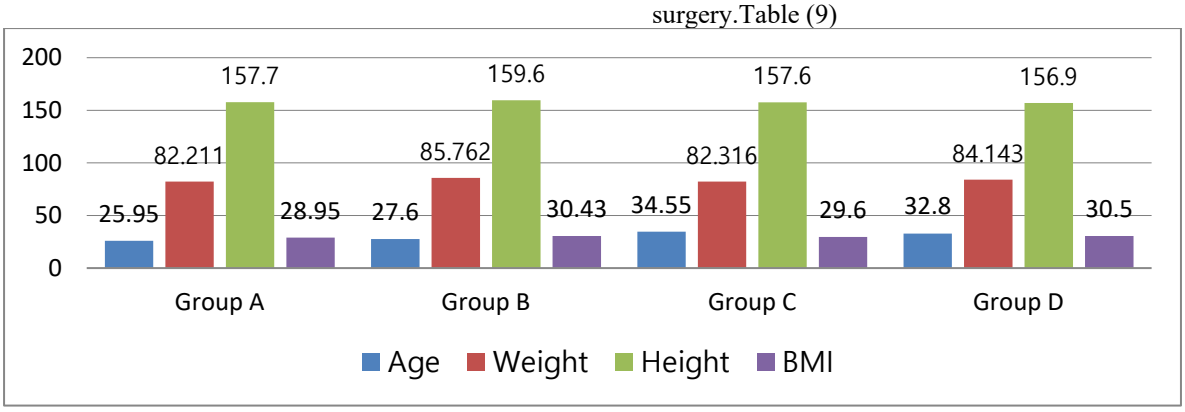

Fig (1) Mean of Demographic data of studied groups

Table (1) : Total volume of injectant (ml) and Level of injection in studied groups :

		Group A	Group B	*p*- value	Group C	Group D	*p*- value
Total volume injectant (LA dose) (ml)		2.5	2.3{1.8-2.7}	<0.001**	2.5	2.05(1.8-2.9)	<0.001**
Level of injec Tion	between L3&4	5(25%)	7(35%)	.114	10(50%)	11(55%)	.752
	L4&5	15(75%)	13(65%)		10(50%)	9(45%)	

Table (2) :Time (min) to reach T6 level (onset) :

	Group A	Group B	P- value	Group C	Group D	P-value
Time to reach T6(Onset) (min)	2.95±0.887	4.70±1.129	.000003 <0.001**	3.35±0.489	3.80±0.768	0.033*

Table (3) :Peak sensory level in studied groups :

		Group A	Group B	*p*- value	Group c	Group d	*p*- value
Peak sensory level	At T6	2(10%)	6(30%)	<0.001**	1(5%)	6(30%)	<0.001**
	At T4	2(10%)	9(45%)		6(30%)	10(50%)	
	Above T4	16(80%)	5(25%)		13(65%)	4(20%)	

Table (4) : Time to regression below L1 (min) in studied groups :

	Group A	Group B	*p*- value	Group c	Group d	*p*- value
Time to regression below L1. (min)	130.25±7.518	115.10±8.252	.000 <0.001**	132.20±19.917	109.20±18.272	.001 <0.001**

Table (5) :Duration of sensory block(min) in studied groups:

	Group A	Group B	*p*- value	Group c	Group d	*p*- value
Duration of sensory block (min)	164.52±12.533	154.33±8.342	<0.02	172.75±25.138	146.46±11.64	<0.04

Table (6) : Duration of motor block (min) in studied groups :

	Group A	Group B	*p*- value	Group C	Group D	*p*- value
Duration of motor block (min)	134.25±10.422	126.50±9.191	<0.017*	141.75±19.076	118±12.814	<0.001**

Table (7) :Total dose (mg) of vasopressors (ephedrine) used in studied groups :

	Group A	Group B	*p*- value	Group C	Group D	*p*- value
Dose of ephedrine (mg)	25.125±14.7585	5.850±4.4665	.0001*	28.050±11.2553	5.150±5.5656	.0001*

Table (8):APGAR score in studied groups :

APGAR score	Group A	Group B	Test	P-value	Group C	Group D	Test	P-value
1 min.	7.16±0.624	7.36±0.64	1.12	0.26	7.24±0.72	7.4±0.70	0.79	0.43
5 min.	9.36±0.49	9.44±0.5	0.56	0.57	9.4±0.5	9.52±0.51	0.84	0.4

Table (9) :UOP (ml) ,Estimated blood loss (ml) and duration of surgery (min) in studied groups :

	Group A	Group B	*p*-value	Group c	Group d	*p*-value
UOP (ml)	154.500±94.282	164.000±128.2534	.791	122.00± 42.128	128.00± 54.734	.700
Estimated blood loss (ml)	692.50±87.772	725±75.219	0.216	680 ±102.8	710±127.37	0.36
Duration of surgery (min)	50.900±5.6559	49.750±5.9549	.535	59.88±14.73	53.52±13.87	0.12

4. Discussion

Recent trends of obstetric anesthesia show increased popularity of regional anesthesia among obstetric anaesthetists. General anesthesia is associated with higher mortality rate in comparison to regional anesthesia**.** Regional anesthesia has some risks; deaths are primarily related to excessive high regional blocks and toxicity of local anesthetics. Reduction in doses and improvement in technique to avoid higher block levels and heightened awareness to the toxicity of local anesthetics have contributed to the reduction of complications related with regional anesthesia ***(12)***

Addition of opioids to local anesthetics intrathecally potentiate surgical anesthesia, making the patients more satisfied with their anesthetic. Opioids have selective site of action in spinal cord, synergistically it enhances L.A effect on efferent pathway without effect on sympathetic pathway so enhance pain relief without haemodynamic changes[18]. In our study all patients had received intrathecal fentanyl in a dose of 20 mcq to potentiate the block. ***(13).***

In the current study, eighty female patients were randomly allocated into four equal groups. Each group includes 20 patients. Group A : included 20 normal patients who were not suffering from any medical disease and received a fixed dose of bupivacaine that was 12.5 mg of bupivacaine 0.5% (2.5 ml).Group B : included 20 normal patients who were not suffering from any medical disease and received variable doses of bupivacaine 0.5 % according to patient's height. Group C : included 20 pre-eclamptic patients that received a fixed dose of bupivacaine that was 12.5 mg of bupivacaine 0.5% (2.5 ml).Group D : included 20 pre-eclamptic patients that received variable doses of bupivacaine 0.5% according to patient height.All patients in all groups received a dose of 20 microgram of fentanyl.

Our study is to adjust dose of intrathecal local anesthetic for elective cesarean section according to height using concentrations of bupivacaine commonly used in clinical practice in both normal and pre-eclamptic patient. The aim of the study to get best balance between adequate analgesia and the need to decrease dosage to avoid maternal and fetal adverse effects.

The dose adjustment of intrathecal bupivacine (0.5%) was done according to table 1 modified from local anesthetics commonly used for cesarean section with subarachnoid block table of ***(14).***

As regards to the time for onset of motor blockade (min) and the duration of it (min); The time of motor block to reach T6 level was significantly ($P < 0.001$) prolonged in adjusted dose groups (B&D) than in fixed dose groups (A&C). While the duration of motor block was significantly shorter in adjusted dose groups (B&D) than in fixed dose groups (A&C). These results were in agreement with the study done by ***(15)*** , who made a comparative study between fixed dose of intrathecal hyperbaric bupivacaine 0.5% and height adjusted dose of intrathecal hyperbaric bupivacaine 0.5% during caesarean section and found that group FD (Fixed dose) was with earlier onset and more prolonged duration of motor block than in adjusted dose group according to height.

As regards to time to maximum Bromage scale; The time to reach maximum Bromage scale was significantly prolonged in adjusted dose groups (B&D) than in fixed dose groups (A&C). This is in agreement with the study of ***(16)*** who had a study on two groups of patients undergoing cesarean section,the first group received a fixed dose of intrathecal bupivacaine 0.5% and the other group received an adjusted dose of intrathecal bupivacaine 0.5% according to height. They found that the time to reach maximum Bromage scale was more prolonged in adjusted dose group than in the other group.

As regards to the need for vasopressors (ephedrine) ;The incidence of the need for vasopressors was markedly higher in fixed dose groups (group A and C) than in adjusted dose groups (group B and group D). Only 7 patients in fixed dose groups did not need the use of ephedrine (17.5%) while 30 patients in adjusted dose groups did not need the use of vasopressors (75%). There was improvement of maternal haemodynamics in adjusted dose groups than fixed dose groups reflected by marked decrease in the need for vasopressors. The current study coincides with study done by ***(17).*** 120 patients scheduled for elective caesarean section under spinal anaesthesia were included. The patients were divided into two groups; fixed Dose group (FD group**)** received fixed dose of intrathecal 0.5% hyperbaric bupivacaine and the other group received variable doses according to height .They found that hyperbaric bupivacaine (0.5%) dosing regimen based on patient's height achieved adequate anaesthesia for cesarean sections with reduced use of vasopressors than in fixed dose group.

As regards to neonatal APGAR score ; Mature placenta is a highly capacitance organ with no autoregulation and so uteroplacental flow is dependent on systemic blood pressure. Although the incidence and severity of maternal hypotention were decreased in adjusted dose groups (group B&C), we can not prove any difference in fetal outcome using Apgar score at 1 and 5 minutes which is specific but not highly sensitive test. Future studies measuring umbilical cord blood gases and uteroplacental blood flow may prove that. The current study coincides with study done by ***(18)***. One hundred patients scheduled for elective caesarean section under spinal anaesthesia were included.. The patients were divided into two groups.Fixed Dose *group* received intrathecal 10mg of 0.5% hyperbaric bupivacaine and the adjusted Dose group received height based doses of

intrathecal injection of 0.5% hyperbaric bupivacaine. Neonatal outcome using APGAR score at 1 and 5 mins were noted. They found that there was no differences between the two groups regarding neonatal outcome.

While using of fixed dose of bupivacaine 0.5 % (2.5 ml) in a tall patient nearly had the same effects as the use of the adjusted dose of bupivacaine 0.5% according to height regarding the decrease in incidence and severity of maternal hypotention ,nausea and vomiting, decrease the amount of fluids needed and the dosage of vasopressors used. And that`s because the volume of the injectant not extending high resulting in no high sympathetic block.

4. Conclusion

we have shown that adjusting the dose of hyperbaric bupivacine (0.5%) according to height in both normal and pre-eclamptic patients , in combination with opioids (fentanyl 20 mcq) , provide adequate anesthesia for elective cesarean section in both normal and pre-eclamptic patients. This regimen associated with decrease in cephalic spread of anesthesia, decrease incidence and severity of maternal hypotention ,nausea ,vomiting , decrease the amount of fluids needed and the dosage of vasopressors used.

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