

MINIDOSE BUPIVACAINE – FENTANYL SPINAL ANESTHESIA FOR CESAREAN SECTION IN PREECLAMPTIC PARTURIENTS

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ABSTRACT

Background: Spinal anesthesia for cesarean section is associated with a high incidence of hypotension. The synergism between intrathecal opioids and local anesthetics may make it possible to achieve reliable spinal anesthesia with minimal hypotension using a minidose of local anesthetic.

Methods: Forty-four preeclamptic parturients undergoing cesarean section were randomized in two groups of 22 patients. Group A received a spinal anesthetic of bupivacaine 6 mg plus fentanyl 20 µg, and group B received 12 mg bupivacaine. Hypotension was defined as a 30% decrease in systolic and diastolic pressure from baseline. Hypotension was treated with intravenous ephedrine boluses 2.5-5 mg up to maximum 50 mg.

Results: All patients had satisfactory anesthesia. Five of 22 patients in group A required ephedrine, a single dose of 5 mg. Seventeen of 22 patients in group B required vasopressor support of blood pressure. The lowest recorded systolic, diastolic and mean blood pressures as fractions of the baseline pressures were 71.2%, 64.5% and 70.3% versus 59.9%, 53.5% and 60.2% respectively for group A versus group B.

Conclusion: A “minidose” of 6 mg bupivacaine in combination with 20 µg fentanyl may provide satisfactory spinal anesthesia for cesarean section in the preeclamptic patient. The minidose combination caused dramatically less hypotension than 12 mg bupivacaine and nearly eliminated the need for vasopressor support of blood pressure.

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Keywords: Hypotension, Preeclampsia, Spinal anesthesia, Bupivacaine, Fentanyl.

INTRODUCTION

Spinal anesthesia is often used for most cesarean sections and offers some advantages. Years ago, spinal anesthesia was considered contraindicated in patients with preeclampsia. The reason was a fear that the fast onset of anesthesia would possibly produce an undue degree of hypotension in volume-depleted, vasoconstricted patients with preeclampsia. Possible adverse effects on the fetus

owing to uncontrolled hypotension were feared.^{1,2} However, recent studies have not found these concerns.³

These patients present particular hazards with general anesthesia, such as concerns for rapid airway control and cerebral blood flow alterations during induction of general anesthesia and intubation.^{1, 2} Spinal anesthesia has only recently been recognized to have a place in operative management in preeclampsia.

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Minidose Bupivacaine – Fentanyl Spinal Anesthesia

Table I. Patient characteristics.

	Group A Bupivacaine 6 ^{mg} + Fentanyl 20 ^{µg}	Group B Bupivacaine 12 ^{mg}
Age	30.41 ± 5.23	29.32 ± 6.03
Weight	78.95 ± 9.28	76.62 ± 11.88
Gravidity	1.91 ± 1.15	1.79 ± 1.87
Gestational age	33.59 ± 2.57	33.52 ± 2.85
Operating time	62.11 ± 10.84	66.29 ± 14.73
Base line heart rate	102.91 ± 16.15	103.64 ± 12.38
Base line systolic pressure	155.23 ± 13.73	157.91 ± 16.92
Base line diastolic pressure	95.91 ± 10.30	99.86 ± 14.01

Data are mean ± SD unless otherwise indicated.
P was not significant for all variables.

Table II. Study data

	Group A	Group B	P Value
Peak level of block	T(5.7 ± 1.146)	T(5.7 ± 1.225)	0.058
Patients having pain during surgery	0	0	
Patients experiencing hypotension	6	14	0.34
Lowest systolic pressure	109.8 ± 14.5	100.8 ± 13.0	0.037
Lowest / baseline systolic pressure	0.712 ± 0.113 (71.2%)	0.645 ± 0.100 (64.5%)	0.042
Lowest diastolic pressure	57.1 ± 12.2	52.2 ± 7.6	0.117
Lowest / baseline diastolic pressure	0.599 ± 0.127 (59.97%)	0.535 ± 0.101 (55.5%)	0.072
Number of patients treated for hypotension	6	11	0.597
Number of ephedrine injections	5	19	0.0001

Data are mean ± SD unless otherwise indicated.
p<0.05 was significant.

Therefore, the use of single shot spinal anesthesia was considered acceptable by some experts, and they attempted to minimize Hypotension of Spinal Anesthesia (HAS). One approach has been to minimize HAS by using very small doses of local anesthetics. Although the use of a single shot low dose local anesthetic for spinal blockade may limit hypotension, it may not provide acceptable anesthesia.

Opioids and local anesthetics administered together intrathecally have a potent synergistic analgesic effect. Intrathecal opioids enhance analgesia from subtherapeutic doses of local anesthetic and make it possible to achieve successful spinal anesthesia using otherwise inadequate doses of local anesthetic.^{1,4} Yet because intrathecal fentanyl causes neither by itself nor in combination with bupivacaine any further depression of efferent sympathetic activity, it is possible to enhance the sensory blockade without altering the degree of sympathetic blockade.⁵

The goal of this study was to compare the hemodynamic and sensory effects of a minidose of bupivacaine – fentanyl spinal anesthetic versus a conventional dose of spinal bupivacaine in preeclamptic patients undergoing cesarean section.

PATIENTS AND METHODS

We studied 44 preeclamptic parturients with mean systolic and diastolic pressure higher than 140/90 mm Hg, chosen to have spinal anesthesia for cesarean section. Exclusion criteria were patient refusal or any other

relative contraindication to spinal anesthesia, patients with cardiovascular and pulmonary disease, diabetics and patients with CNS disorders, seizure, coagulopathy and HELLP syndrome. Parturients were randomly assigned to two groups defined by the spinal injectate. This study was done in Alzahra Hospital during 2004, for one year.

After obtaining written informed consent of the subjects, Group A were given 6 mg bupivacaine 0.5% in glucose, plus 20 µg fentanyl, and group B received 12 µg bupivacaine 0.5% in glucose. Bupivacaine 0.5% in glucose was prepared by adding 4 mg glucose 50% to 20 mL bupivacaine 0.5%. In both groups distilled water was added to drug mixture for making drug volume 2.5 mL in total. The syringe was prepared by one researcher and it was administered by a second anesthetist who performed subarachnoid blocks and remained blinded to its contents, and patient assessment, care, and data recording was done by a blind observer. The antepartum management include a seizure prophylaxis in patients with severe preeclampsia and consisted of magnesium sulfate (MgSO₄) administered as a loading dose of 4 g intravenously, followed by 1 g hourly intravenously. Hydralazine was administered intravenously as a vasodilator for additional blood pressure control against a standardized protocol that was identical in both groups. Previous use of other agents (α-methyl dopa, dexamethasone) was recorded. Before block, each patient received a rapid infusion of 8 ml/kg of Ringer's solution, in left lateral position during 15-30 minutes and the baseline blood pressure, and heart rate, was noted. After prep and drep of the back of the patient, subarachnoid injection was performed in the sitting

Table III. Side effects

	Group A (n=22)	Group B (n=22)	P
Nausea	3	12	P<0.01
Vomiting	0	5	0.29
Pruritis	3	0	

$p < 0.05$ was significant

position using a 25-gauge Quincke needle positioned midline at the L3 – L4 interspace. After aspiration of 0.5 mL of CSF the local anesthetic drug was injected in the spinal space during 10-15 seconds (if no blood was aspirated). After completion of injections the patients were immediately returned to the supine position and the operating bed positioned in 15-30 degrees head down, with left uterine displacement. The parturients head was rested on a pillow. Each patient received 6-8 lit/min O₂ by face mask. Standard monitoring included continuous ECG, pulse oximetry, maternal BP and HR.

The vital signs were recorded every one minute up to the birth of the neonate and then every five minutes using an automated noninvasive device. Pinprick testing in the right side of the body was used to establish onset and peak level of blockade. For the purpose of the study, hypotension was defined as a systolic blood pressure decrease of more than 30% from baseline. Hypotension was treated promptly by increasing uterine displacement and the rate of fluid administration. If hypotension persisted despite these measures, ephedrine 2.5-5 mg was injected and repeated as needed. Patients received 1500-2000 mL of ringer solution during surgery.

The vital signs, number of hypotension measurements, total ephedrine dose for each patient, and intraoperative patient complaints of pain, nausea, and vomiting were recorded. Metoclopramide 5-10 mg was used to treat nausea or vomiting. The condition of the neonate was assessed by APGAR score at 1 and 5 minutes after delivery. All mothers received oxytocin by continuous infusion after delivery. Return of sensory and motor function was assessed at 15 minute intervals until complete recovery from anesthesia. Statistical analysis was performed using SPSS. Analyses of variance was used to analyze demographic data. The nondependent t-test and chi-square test were used to analyze data. Results were considered significant at $p < 0.05$. The type of the study was interventional comparison.

RESULTS

There were 22 patients in each of the two groups. There were no differences between the demographic characteristics of the two groups (Table I). Though baseline systemic blood pressure was slightly higher in group B, this was not a significant difference. (157.91 ± 16.92 in group B versus 155.23 ± 13.73 in group A). No patients in either group complained of intraoperative pain or required supplemental analgesics intraoperatively. Peak sensory block level was similar in both groups.

The lowest recorded systolic and diastolic blood pressures are reported in Table II as well as their

percentages of the baseline pressures. For group A these were 71.2% and 59.5% versus 64.5% and 53.5% respectively for group B.

In Group A, 5 of 22 patients and in group B, 17 of 22 patients experienced hypotension according to the protocol definition of hypotension. Seventeen patients in group B and 5 patients in group A required treatment with ephedrine. However numbers of ephedrine administration in incremental doses were 19 times in group B versus 5 times in group A and this difference is significant ($p = 0.0001$). Nausea was seen in 12 patients of group B and 3 patients of group A. Also 8 patients in group B and no patient in group A had vomiting. Postoperative follow up revealed uneventful recovery in all patients, except for 3 patients of group A, which complained of pruritis and were treated with antihistamine.

DISCUSSION

This study demonstrates that the use of minidose bupivacaine plus fentanyl spinal anesthetic (6 mg bupivacaine plus 20 µg fentanyl) for cesarean section in preeclamptic parturients provides successful anesthesia and incurs minimal hypotension. In the minidose group 5 of 22 patients experienced hypotension and in these patients a single dose of 5 mg ephedrine sufficed. This was in contrast to the marked reduction in blood pressure and the significant vasopressor requirements seen in the group receiving spinal anesthetic of bupivacaine 12 mg (17 of 22 patients in group B). Numbers of ephedrine administration showed a significant difference ($p = 0.0001$) between the two groups. (5 times in group A versus 19 in group B) and means that the incidence of blood pressure drop in group B was higher, more severe, and required more ephedrine injection in incremental doses than patients of group A.

Ben-David et al. showed that minidose bupivacaine – fentanyl spinal anesthesia caused dramatically less hypotension than 10 mg bupivacaine and nearly eliminated the need for vasopressor support of blood pressure for surgical repair of hip fracture in the elderly⁵.

An intravenous fluid preload of 8 mL/kg Ringer's solution was used in this study. Fluid administration may prevent a decrease in central venous pressure and may diminish or even reverse the decrease in cardiac index, but blood pressure falls nevertheless because of a substantial decrease in systemic vascular resistance⁶. But on the other hand excessive administration of crystalloid or colloid may also result in pulmonary or cerebral edema in preeclamptic patients, and is therefore to be avoided.^{1,6} Pouta et al. demonstrated that an intravenous fluid bolus resulted in a greater increase in CVP in preeclamptic women than in normotensive controls undergoing spinal anesthesia.^{1,7}

Ephedrine is probably the most commonly used drug in cesarean section. It does not have detrimental effects on uterine blood flow, thus, it is widely used as a pressor for hypotension of spinal anesthesia in parturients,¹ but systemic vasoconstriction and accelerated response to

vasopressors in preeclamptic parturients⁷ limited it to use in large doses in these patients. In this study ephedrine was used in incremental doses and started with 5 mg. Nausea and vomiting during spinal anesthesia may be related to postural hypotension and hypoxemia of the vomiting center. Excessive elevated blood pressure following administration of a vasopressor, also results in nausea.

This problem is unpleasant during surgery. In this study the incidence of nausea and vomiting in group A (mini dose group) was 3 and 0, and in group B was 12 and 5 respectively (Table III) and the differences were significant ($p < 0.05$). This difference showed that nausea and vomiting were higher in group B than group A, which were more hypotensive following administration of spinal anesthesia. We conclude that the most possible cause of nausea and vomiting is hypotension, compared to other causes such as intrathecal fentanyl especially in lower doses.

In the study of Varcauteran, on small-dose bupivacaine versus plain bupivacaine spinal anesthesia for cesarean section, a low incidence of hypotension and nausea was seen.⁸

Thus intrathecal fentanyl in combination with bupivacaine causes further depression of efferent sympathetic blockade and increases the efficacy of intraoperative analgesia, therefore decreasing the incidence of nausea and vomiting. In this study none of the patients complained of pain intraoperatively. Pregnant patients require less local anesthetic because of increased sensitivity of nerve fibers for local anesthetics, the reduced amount of CSF and the effect of the gravid uterus on cephalad spread of intrathecally injected substances.^{1,8} Although the use of single shot low dosage local anesthetic (lower than 10mg bupivacaine) for spinal blockade can limit hypotension, it may not develop a reliable anesthesia even in parturients. However the addition of an opioid intrathecally to the local anesthetic, because of a potent synergistic analgesic effect, can reduce the dose requirements and provide satisfactory anesthesia.

CONCLUSION

Minidose of 6 mg bupivacaine in combination with 20 µg fentanyl provides acceptable spinal anesthesia for cesarean section in preeclamptic patients. The minidose bupivacaine – fentanyl caused less hypotension than 12 mg bupivacaine and nearly eliminated the need for vasopressor supports of blood pressure, and decreases the incidence of nausea and vomiting.

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Case Report

HEPATITIS B VIRUS INFECTION IN AN ANTI-HBc NEGATIVE PATIENT: A CASE REPORT

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ABSTRACT

One of the best reliable markers of hepatitis B virus infection is antibodies to the core antigen (Anti-HBc).

A first-time blood donor with HBsAg positivity was identified as an HBV carrier that was anti-HBc negative. The patient was followed for 24 months in order to investigate the evolution of his HBV serological profiles and HBV-DNA (PCR).

In the follow-up for 24 months, HBsAg, HBeAg and HBV-DNA (PCR) were positive but all the time anti-HBc remained negative. HBV DNA viral load was 3.4×10^6 copies per mL. In the immunohistochemical study on the needle liver biopsy, the hepatocytes were positive for HBcAg and HBsAg.

For this immunological situation, the most probable hypothesis is an immunotolerance to HBV due to an in utero HBV infection. This situation does not impose a risk of HBV transmission by blood transfusion, because HBsAg positive donations are excluded and discarded by HBsAg screening tests.

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INTRODUCTION

Hepatitis B virus produces several protein antigens such as HBsAg and HBeAg. HBcAg is produced by hepatitis B virus and is detected in liver tissue.¹⁻² Antibodies to each of these antigens can be measured in blood.¹⁻⁴ 3-4 weeks after the appearance of HBsAg, anti-HBc can be detected and persists for many years.⁵⁻⁸

In the Iranian Blood Transfusion Organization a sample from each donation is tested for HBsAg, Anti-HIV, anti-HCV and a serologic test for syphilis like RPR. All positive donation units are excluded and discarded. The positive results are confirmed, then donors are notified and they are followed-up by the Iranian Blood Transfusion Organization hepatitis clinic.

CASE REPORT

The first-time blood donor was a man. He was 30 years old, born and living in Tehran. At his first donation on June 2001 he was positive for HBsAg and negative for anti-HIV, anti-HCV and RPR so this unit was discarded.

Four blood samples were obtained during nearly 24 months. The results obtained from the HBV serological markers included HBsAg, anti-HBc, HBeAg, HBeAb that are shown in detail in Table I. The results remained stable through-out the follow-up.

HBV DNA was analyzed using polymerase chain reaction (PCR). HBV DNA was positive by PCR method and detected by gel electrophoresis (Fig 1). The HBV DNA viral load was 3.4×10^6 copies per ml.

The needle liver biopsy on August 2001 was studied, and no significant pathologic changes were observed.

The histological activity index, according to modified HIA score was A: 0, B: 0, C: 1, D: 0, Total=1 and stage: 0.⁹

Immunohistochemical studies were performed using HBcAg and HBsAg markers and detected by avidin-biotin-peroxides complex method. The needle liver biopsy demonstrated strong nuclear reactivity for HBcAg and cytoplasmic positivity for HBsAg^{10,11} (Fig. 2 and 3).

In order to evaluate the status of the immune system especially an efficient antiviral cellular and humoral immune response, several serological markers were studied. The results of immunoglobulin G, A and M were in references interval according to age and sex. The patient