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# INTRATHECAL LOW DOSE OF HEAVY BUPIVACAINE WITH DEXMEDETOMIDINE FOR CESAREAN SECTION

By

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## ABSTRACT

**Background:** Different adjuvants have been used with local anesthetics to improve quality of regional anesthesia (sub-arachnoid, epidural or combined sub-arachnoid and epidural block) and to avoid intra-operative visceral and somatic pain and to provide prolonged post-operative analgesia. Dexmedetomidine is a highly selective $\alpha_2$-adrenergic agonist which has both analgesic and sedative properties when used as an adjuvant in regional anesthesia.

**Objective:** Evaluation of the effect of intrathecal hyperbaric bupivacaine plus dexmedetomidine on the onset and duration of sensory and motor block, intra-operative hemodynamic stability (changes), surgeon's satisfaction, intraoperative adverse effects and postoperative analgesia. **Patients and method:** Sixty females in childbearing period (22-40 years old), ASA physical status I scheduled for elective cesarean section. Patients were randomly allocated to receive intrathecal either 12.5 mg of (0.5%) heavy bupivacaine [B control group], or 7.5mg of (0.5%) heavy bupivacaine plus 8 ug dexmedetomidine [BD study group]. **Results:** Patients in BD group had a significantly rapid onset and longer duration of sensory and motor block than control B group. Onset of postoperative pain significantly delayed in BD group. Moreover, abdominal muscle relaxation was excellent clinically, with marked reduction in side effects as nausea, vomiting, hypotension and bradycardia compared with control B group. No side effects were recorded on babies as regard the neonatal assessment in both groups. **Conclusion:** The low dose of intrathecal anesthetic agent (Bupivacaine 7.5 mg) with 8 ug Dexmedetomidine had a significantly rapid onset and associated with prolonged motor and sensory block, hemodynamic stability and decreased postoperative analgesic consumption compared with (Bupivacaine 12.5 mg) alone.

**Keywords:** Dexmedetomidine, Bupivacaine, Spinal anesthesia, Cesarean Section.

## INTRODUCTION

Regional anesthesia (sub-arachnoid, epidural or combined sub-arachnoid and epidural block) is preferred for cesarean section as it allows a parturient to remain awake and participate in the birth of her baby. The administration of regional anesthesia not only avoids the maternal complications with general anesthesia, but also improves utero-placental blood flow and neonatal outcome, **(Ankichetty et al., 2013**). Local anesthetics are associated with relatively short duration of action. Thus, early analgesic intervention is needed in the postoperative period. So far, many adjuvants have been used to augment the analgesia produced by intrathecal local anesthetics and to reduce their adverse effects **(Kang et al., 1998)**. For cesarean section the approved intrathecal dose of hyperbaric bupivacaine

is 12 to 15 mg **(Choi et al., 2000 and Bogra et al., 2005**). Cesarean section delivery requires traction of peritoneum and handling of intra-peritoneal organs, resulting in intra-operative visceral pain. With higher doses of hyperbaric (heavy) bupivacaine, the incidence of intra-operative visceral pain is reduced **(Choi et al., 2000**). Dexmedetomidine is a highly selective $\alpha_2$-adrenergic agonist which has both analgesic and sedative properties when used as an adjuvant in regional anesthesia (**Mauro and Brand?o, 2004**). Intrathecally dexmedetomidine was used safely as 10 ?g or 15 ?g diluted to 0.5 ml with 0.9% saline, added to bupivacaine in the same syringe **(**Eid **et al., 2011**), and also dexmedetomidine 5 ug with hyperbaric bupivacaine 10 mg in 2.5 ml **(**Mahdy and Abdullah, **2011**), **Kanazi et al.2006** found that 3?g dexmedetomidine and 30 ?g clonidine are equipotent when added to bupivacaine intrathecally in patients undergoing uro-surgical procedures. In addition, dexmedetomidine has a sympatholytic effect that can attenuate the stress response to surgery, mitigating tachycardia and hypertension **(Taghinia et al., 2008**). Because of its analgesic properties "cooperative sedation" and lack of respiratory depression, dexmedetomidine is increasingly used as a sedative and adjuvant in anesthesia (Elbaradie **et al., 2004**). The rational of using dexmedetomidine in regional anesthesia, because dexmedetomidine is more selective $\alpha_2$-adrenoreceptor agonist has been evaluated as an adjuvant to intrathecal local anesthesia **(**Eid **et al., 2011**).

**The aim of this study** was to evaluate the effect of intrathecal 7.5mg of (0.5%) hyperbaric bupivacaine plus 8ug dexmedetomidine on the onset and duration of sensory and motor block, intraoperative hemodynamic stability (changes), surgeon's satisfaction, intra-operative adverse effects and postoperative analgesia.

## PATIENTS AND METHODS

The study was designed as prospective randomized double blind study, and was conducted at Al-Azhar University's Hospital over a period of three months from the beginning of March 2014 to the end of May 2014. In that period, sixty cases were selected for the study. The study was done after obtaining the approval of Al-Azhar University Hospitals`s Ethical Committee and written consent was taken from patients who participated in this study. The total injected volume in both groups was 2.5ml diluted in normal saline 0.9% for each participant. The participants, those had pregnancy induced medical diseases like pregnancy induced hypertension, gestational diabetes mellitus, or other medical diseases like rheumatic heart diseases, renal impairment, respiratory disease, liver disease or history of drug allergy for the planned drugs were excluded from the study. The participants were assigned randomly into two groups equally using computer-generated randomization code that were placed in sealed, sequentially numbered envelops: The first group was control which included 30 cases (B group), received intrathecal 12.5mg of (0.5%) heavy bupivacaine, and the second group include 30cases (BD group) which was the study group, received intrathecal 7.5mg of (0.5%) heavy bupivacaine plus 8ug dexmedetomidine.

An intravenous normal saline solution (10-15 ml /kg) was used as the preload fluid therapy, to reduce the hypotensive effect of spinal anesthesia. No special premedication was added, (except the routine premedication before cesarean section as anti-acid, ranitidine and metoclopramide half an hour before surgery. The anesthetic agent was 2.5ml of prepared solution which was injected in the sitting position through 25 gauge Whitacre spinal needle at L3-4 intervertebral space. The participant had lain in supine position with left tilting 45$^{o}$ to avoid aorto-caval syndrome effects (hypotension, bradycardia …..etc) then oxygen (4-6 L/min) was supplied by oxygen mask via Drager Fabius GS anesthesia machine. All participants were anesthetized by the same technique with the same anesthetic tools, same anesthesia and obstetrician teams.

Heart rate, arterial blood pressure and oxygen saturation were monitored every 5minutes from time of injection of local anesthetics till the end of operation by automated non-invasive blood pressure monitor machine (Datex Ohmeda S /5 Light Monitor).

Sensory block was assessed by pinprick method using a blunt 27G hypodermic needle and cold alcohol swap along the midclavicular line bilaterally. Motor block was assessed according to the modified Bromage scale before surgery and rated as the patient is able to move the hip, knee and ankle, unable to move the hip but is able to move the knee and ankle, unable to move the hip and knee but able to move the ankle or unable to move the hip, knee and ankle and score of 0, 1, 2 or 3 was given for each description respectively **(Bromage, 1965)**. Muscle relaxation during surgery was assessed clinically by the obstetrician and rated as poor, fair, good or excellent, and score of 1, 2, 3 or 4 was given for each description respectively (**Bogra et al., 2005**).

The regression times for sensory and motor block were recorded. All durations were calculated considering the time of spinal injection as time zero. All intra-operative and postoperative complications as respiratory bradypnea or apnea and / or cardiovascular bradycardia or hypotension were recorded. Hypotension, defined as a decrease in systolic blood pressure > 25 % of the baseline value was treated with increasing left uterine displacement, increasing rate of intravenous crystalloid fluids, then 6 mg ephedrine bolus if no response to previous measures and repeated if needed. Bradycardia, defined as a pulse rate of < 50 beat/min. was treated with boluses of 0.5 mg atropine. Other side effects as nausea, vomiting and pruritus were recorded. Neonatal outcome was assessed by APGAR scores at 1$^{st}$ and 5$^{th}$ min and by analyzing umbilical artery samples for pH and base deficit (**Finster and Wood, 2005)**.

Statistical analysis: Data were expressed as mean ± SD or frequency and percentages as appropriate. Unpaired Student's t-test was used to determine statistical significance difference for interval variables. P value of 0.05 (two tailed) was considered as statistically significant. SPSS 19.0. Statistical Package was used for the analysis but Obstetrician`s satisfaction and Abdominal relaxation was determined statistically by Mann-Whitney U test.

## RESULTS

The demographic data of the patients regarding age, weight, and height were comparable among the two groups with no statistical significant difference (Table 1).

**Table (1):** Patient demographic data (mean ± SD**).**

| Groups / Parameters | B group (n=30) | BD group (n=30) | P value |
|---|---|---|---|
| Age (years) | 35.0±13.1 | 34.5±10.8 | 0.65 |
| Weight (kg) | 77.0±9.01 | 78.2±11.5 | 0.77 |
| Height (cm) | 173.1±9.5 | 172.1±8.8 | 0.61 |

Onset of sensory block to the 5$^{th}$ thoracic level ($T_5$) was faster in BD group (2± 0.74 min) than control (B) group which recorded a statistically significant late onset (4.67± 0.66). The time to two-segment regression of sensory block was significantly longer in BD group (115.3± 7.6min) compared with control (B) group (100.6±6.2 min). Time to full sensory recovery to S1 (estimated as the time to full skin sensibility) was significantly longer in BD group (292.8± 26.4 min) than control (B) group (163.7± 9.3min) (Table 2).

**Table (2): Characteristics of spinal block (**mean ± SD).

| Groups / Parameters | B group (n=30) | BD group (n=30) | P value |
|---|---|---|---|
| Onset of sensory block (min) | 4.67±0.66 | 2.0± 0.74 | <0.001 |
| Onset of motor block (min) | 8.5±3.00 | 4.7±2.10 | <0.001 |
| Two segment regression time (min) | 100.6± 6.2 | 115.3 ± 7.6 | <0.001 |
| Sensory recovery time to S1 (min) | 163.7± 9.3 | 292.8± 26.4 | <0.001 |
| Motor recovery time (min) | 88.4±6 | 176.2± 9.4 | <0.001 |

As regard to the motor characteristics of spinal block, level was thoracic 7$^{th}$ ($T_7$), all patients achieved Bromage 3 motor block after (4.7 ± 2.1 min) in BD group compared to significant delay (8.5 ± 3.0 min) in control (B) group (Table 2). Regarding motor recovery time, BD group showed significantly longer time than the observed as in control (B) group (Table 2). Intraoperative abdominal muscle relaxation (clinically assessed by same Obstetrics' team in all cases) was excellent (Score 4) in (BD) group compared significantly to fair (Score 2) in control (B) group (Table 3).

**Table (3):** Results of Obstetrician`s satisfaction and Abdominal relaxation score that done by Mann-Whitney U test (median (range) and P-value).

| Groups / Parameters | BD group (n=30) | B group (n=30) | P- value |
|---|---|---|---|
| Abdominal relaxation | 4(4-4) | 2(2-2) | <0.0001 |
| Obstetrician`s satisfaction | 4(4-4) | 2(2-2) | <0.0001 |

As regard to the adverse effects of spinal block and additives, no significant difference as regard hypotension and bradycardia. Nausea and vomiting were recorded more in control (B) group especially at peritoneal manipulation than (BD) group ,the suffering participants had treated by reassurance and midazolam 2mg in control group (B), with no statistical significant difference (Table 4).

**Table (4):** Adverse effects *(*number and %,)

| **Groups** / **Parameters** | **B group** (n=30**)** | | **BD group** (n=30**)** | | **P-value** |
|---|---|---|---|---|---|
| | **N.** | **%** | **N.** | **%** | |
| Hypotension | 7 | (23.3%) | 3 | (10.0%) | 0.33 |
| Bradycardia | 5 | (16.6%) | 2 | (6.66%) | 0.45 |
| Nausea\Vomiting | 4 | (13.3%) | 2 | (6.66%) | 0.63 |
| Need for analgesia | 3 | (10.0%) | 0 | (0.0%) | 0.05 |

There were no significant differences regarding different parameters of neonatal assessments among the two groups regarding 1st min and 5th min APGAR score as well as umbilical artery samples (Table 5).

**Table (5):** Neonatal assessment ***(***mean± SD).

| **Groups** / **Parameters** | **B group** (n=30 ) | **BD group** (n=30 ) | **P value** |
|---|---|---|---|
| 1st min. Apgar score | 7.80 ± 0.77 | 8.00±0.78 | 0.61 |
| 5th min. Apgar score | 8.3 ± 0.66 | 8.8±0.67 | 0.06 |
| Umbilical PH | 7.26 ± 0.12 | 7.28±0.10 | 0.85 |
| $PCO_2$ | 44.69 ± 0.56 | 44.57±0.55 | 0.17 |
| Base deficit | 4.95 ± 0.55 | 4.77±0.08 | 0.36 |
| $HCO_3$ | 21.20 ± 1.97 | 20.93±1.89 | 0.85 |

## DISCUSSION

Obstetric anesthesia has evolved substantially in the last two decades, with regional techniques becoming increasingly popular for cesarean sections. Spinal anesthesia has evolved as the preferred anesthetic technique for most cases of cesarean section (**Bogra et al., 2005**). Local anesthetics are commonly used for intrathecal anesthesia, but the major problem is the relatively short duration of action. Thus early analgesic intervention is needed in the postoperative period. A number of adjuvants, such as clonidine and midazolam, and others have been studied to prolong the effect of spinal anesthesia **(Elia et al., 2008).**

Dexmedetomidine, an imidazole compound, is the pharmacologically active dextro-isomer of medetomidine that displays specific and selective $\alpha_2$-adrenoceptor agonism. Its activation of the receptors in the brain and spinal cord inhibits neuronal firing and results in symoatholytic effect, causing hypotension, bradycardia, sedation, and analgesia (**Boussofara et al., 2006).**

Dexmedetomidine have been used in animal studies intrathecally with no adverse neurotoxicity or neurologic deficits (**Mohamed et al., 2012). Kanazi et al. (2006)** used a small intrathecal dose of dexmedetomidine in combination with bupivacaine on humans for spinal anesthesia. Results showed a shorter onset of motor block and a prolongation in the duration of motor and sensory block with hemodynamic stability and lack of sedation (**Shimode et al., 2003**). Reduction in doses of anesthetic agent (Bupivacaine) 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 (**Courtney et al., 1992).** Spinal anesthesia among the neuraxial blocks in obstetric patients needs more strict dose calculations as the drugs are directly injected in the intrathecal space. Visceral pain is a common problem in cesarean section under spinal anesthesia and visceral pain was not fully abolished with lower doses of bupivacaine. Incidence of hypotension as well as fall in the systolic BP increases with high dose of bupivacaine (**Bogra et al., 2005**). The spinal bupivacaine 10 mg with 5 ug dexmedetomidine significantly prolonged both sensory and motor block compared with intrathecal 25ug fentanyl and bupivacaine 10 mg in spinal anesthesia for cesarean section **(**Mahdy and Abdullah, **2011**).

The present study showed that combination of dexmedetomidine 8ug with low dose of bupivacaine 7.5mg produced satisfactory spinal block, rapid onset of sensory and motor blockage with hemodynamic stability, reduced visceral pain, excellent abdominal muscle relaxation (clinically assessment). They also made good intraoperative sedation (patient were calm, have no nausea or vomiting during peritoneal manipulation like that occurred in control group), and patients did not need intraoperative sedation or supportive hypnosis.

## CONCLUSION

Dexmedetomidine is an adjuvant to spinal analgesia with bupivacaine in cesarean section giving good quality of spinal anesthesia (relaxation, controlled the visceral pain with hemodynamic

stability) with low dose of anesthetic agent (bupivacaine 7.5 mg ) and sedation with minimal side effects and no adverse effects on the mothers and babies.

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**قسم التخدير والعناية المركزة بطب الأزهر**

**خلفية البحث :** كثر إستخدام المساعدات المحقونة مع أدوية (عقاقير) التخدير الموضعية لتحسين أثر وجودة التخدير الجزئى (التخدير النصفى اوتخدير ما فوق الام الجافية او الاثنين معا ) لتجنب الشعور بالألم من الاحشاء والجسم المراد تخديرهم أثناء العملية الجراحية وكذلك طول فترة الشعور بالمسكنات بعد ها . ويعد عقار الدكسميديتوميدين واحدا من أعلى العقاقير المنشطة والمنحازة لمستقبلات الادرينالين الفا 2وهذه المستقبلات لها خاصيات التهدئة والمسكنات عند تنبيهها كمساعد لعقار التخدير الموضعى .

**الهدف من هذه الدراسة :** تقييم تأثير هذا الخليط من عقار الدكسميديتوميدين 8 ميكروجرام والجرعة المنخفضة من عقار البيوبيفاكيين ذو الكثافة العالية 7.5 مليجرام ذو التركيز 0.5% على بداية حدوث التخدير على عصبى الإحساس والحركة ، وتأثيره على استقرار الدورة الدموية للمريض ، وقياس مدى رضاء الجراح عن اثر المخدر وكذلك قياس الآثار غير المرضية أثناء إنجاز الجراحة وأخيرا تقييم اثر المسكن فى فترة ما بعد الجراحة .

**المرضى وطرق البحث :** ستون سيدة فى فترة الإنجاب (22-40 سنة)، من المعيار الأول على مقياس جمعية التخدير الأمريكية وضعوا فى جدول الجراحة لقسم النساء والتوليد لعمل ولادة قيصرية اختياريا وبعد اخذ موافقة كتابية منهن على إجراء البحث،وقد وزعوا عشوائيا فى مجموعتين لأخذ 12.5 مليجرام من عقار البيوبيفاكيين ذو الكثافة العالية بتركيز 0.5 % بالسائل المحيط بالحبل المرجعية . والمجموعة محل الدراسة كانت تأخذ 7.5 مليجرام من عقار البيوبيفاكيين ذو الكثافة العالية بتركيز 0.5 %مضافا إليه 8 ميكروجرام من عقار الدكسميديتوميدين.

**النتائج :** المرضى بمجموعة البحث حدث معهن سرعة واضحة فى بداية اثر التخدير وطول فى وقت عدم الإحساس بالألم وعدم القدرة على الحركة عنه مع المرضى بالمجموعة المرجعية . كما أثبتت الدراسة تأخر الإحساس بالألم بعد الجراحة بالمجموعة محل الدراسة عنه مع المرضى بالمجموعة المرجعية. وكذلك إرتخاء عضلات البطن ورضاء الجراح مع تراجع واضح فى الآثار الجانبية مثل الشعور بالغثيان والقيء والهبوط بالدورة الدموية وإنخفاض نبض القلب عنه مع المرضى بالمجموعة المرجعية و لم تسجل آثاراً جانبية فى المواليد فى المجموعتين .

**الاستنتاج :** الجرعة المنخفضة 7.5 مليجرام من عقار البيوبياكيين ذو الكثافة العالية بتركيز 0.5 %مضافا إليه 8 ميكروجرام من عقار الدكسميديتوميدين كانت مصاحبة ببداية سريعة للتخدير وطول فى فترة التخدير مع إستقرار فى الدورة الدموية وتأخر فى حاجة المريض للمسكنات فى فترة ما بعد الجراحة بالمقارنة بالجرعة 12.5 مليجرام من عقار البيوبيفاكيين ذو الكثافة العالية بتركيز 0.5 %.