EFFECT OF ADDING DIFFERENT DOSES OF DEXAMETHASONE TO BUPIVACAINE ON INTRATHECAL ANESTHESIA IN CESAREAN SECTION

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ABSTRACT

Background: The cost-effectiveness and facility in the administration have been made the spinal anesthesia as the most used technique in cesarean section. However, the short-term duration of local anesthetic drugs’ action has created a matter of concern for anesthesiologists. The purpose of this investigation was to evaluate the effect of different doses of dexamethasone conjugated with bupivacaine on the duration of spinal anesthesia as the primary outcome, and their adverse effects were examined among patients underwent cesarean section as well.

Subject and Methods: In the current double-blind clinical trial, 90 pregnant women scheduled for cesarean section were randomly assigned into three groups after taking written consent. Patients assigned to the group A (n=30) received intrathecal bupivacaine 12.5mg (2.5 ml) of 0.5% hyperbaric bupivacaine diluted in preservative free normal saline (1 ml), group B (n=30): received 12.5 mg (2.5 ml) of 0.5% intrathecal hyperbaric bupivacaine and 2 mg (0.5 ml) preservative free dexamethasone, diluted in preservative free normal saline (0.5 ml), overall 3.5 ml volume intrathecally, and group C (n=30): received 12.5 mg (2.5 ml) of 0.5% hyperbaric bupivacaine and 4 mg (1 ml) preservative free dexamethasone, overall 3.5 ml volume intrathecally.

Results: In the present study the crude mean age of the patients was 26.49±5.49 (range: 18-40 years) and the patients’ age, weight, and body mass index were comparable among three groups (p>0.05). The study showed the sensory block (min) in patients was significantly higher in groups 2 and 4 mg dexamethasone; 284.63±64.85 and 313.37±70.53, respectively compared to the control or group control, 165.33±44.95 minutes. Similarly, the motor block (min) in patients assigned groups 2 and 4 mg dexamethasone was substantially higher; 223.43±52.67 and 227.20±47.17, respectively in comparison with it’s in group control, 126.33±34.62 minutes. However, the difference between groups 2 and 4 mg dexamethasone not substantial for both sensory and motor blocks (p>0.05). The patients of three groups had not substantial difference in frequency of post-operative adverse effects, including postoperative nausea & vomiting, hypotension, bradycardia, shivering, post-dural-puncture headache.

Conclusions: administration of 2 or 4 mg dexamethasone intrathecally prolongs the duration of sensory and motor block of bupivacaine substantially in patients underwent cesarean section under spinal anesthesia and the effect of adding 2 mg on the duration of sensory and motor blocks is same like adding 4 mg.

Keywords: Bupivacaine, dexamethasone, intrathecal, sensory block, motor block, spinal anesthesia

Cesarean section has been reported to be the most common surgeries selected by women1. Spinal anesthesia is the most commonly used technique for perioperative anesthesia and analgesia in the cesarean section owing to its cost-

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EFFECT OF ADDING DIFFERENT DOSES OF DEXAMETHASONE

effectiveness and facility in administration. It reduces mortality rate associated with cesarean section done under general anesthesia and it reduces immediate postoperative pain by sixteen times when compared with general anesthesia\(^2\) - \(^3\). Moreover, it is an effective, safe, easy to perform method with a low failure rate, cheap, no systemic toxicity of local anesthesia, and high maternal satisfaction\(^4\) - \(^6\). Spinal anesthesia enables to prevent unwanted general anesthesia risks like gastric contents aspiration, airway management difficulties, and distress of infant respiratory\(^3\) and tracheal intubation stress\(^2\). However, the short duration of action of local anesthetic drugs has created a matter of concern for anesthesiologists. It has been documented that bupivacaine is convenient for those clinical procedures lasting between 90-129 minutes\(^7\) - \(^8\).

To cope with the issue of short duration of action of local analgesic, currently a number of additives are used as conductive drugs to prolong the spinal anesthesia duration, such as epinephrine, phenylephrine, clonidine, opioids, etc\(^7\) - \(^10\). However, these additives may result in certain adverse effects like nausea, vomiting, sedation, respiratory depression, psychometric impacts, hypotension, pruritis, etc. Therefore, anesthesiologists are mostly concern about long acting local anesthetic drugs with least side effects. Adding epinephrine to the local anesthetics may lead to tachycardia, pallor, and hypertension. A risky factor in cardiovascular patient\(^3\). Opioids control postoperative pain well; however, they are followed by central and respiratory depression effects, nausea, vomiting, drowsiness, and pruritus. At present, there is no drug able to control pain specifically without having side effects\(^11\), \(^12\).

The use of corticosteroid compounds increases the duration of anesthesia and analgesia in peripheral nerve blocks. In addition, intravenous (IV) and oral dexamethasone considerably alleviate postoperative pain. Epidural and intrathecal steroids are used to reduce chronic pain\(^13\). In some studies, intrathecal dexamethasone increased the duration of sensory block and postoperative analgesia\(^1\) - \(^2\). Although intrathecal dexamethasone is used to control chronic pain; few studies have been performed on the sensory and motor block effects and postoperative side effects in patients undergoing cesarean section.

For example, Shalu and Ghodki \(^2\) assigned sixty patients into two groups in a randomized and double-blind method to receive injection dexamethasone 8 mg intravenously (intervention group) and group control received injection normal saline 2 cc immediately after spinal anesthesia and injection bupivacaine 0.5% heavy 10 mg through spinal anesthesia was received by all patients. They showed that dexamethasone administration of 8 mg intravenously was successful to prolong the postoperative analgesia and sensory block among patients underwent cesarean section under spinal anesthesia.

Although dexamethasone has been used intrathecally for many years, it has not been evaluated sufficiently when it was given in conjunction with bupivacaine intrathecally. The purpose of this investigation was to evaluate the effect of different doses of dexamethasone conjugated with bupivacaine on the duration of spinal anesthesia and to report
the adverse effects relevant to dexamethasone their adverse in patients underwent elective cesarean section.

**PATIENTS AND METHODS**

**Study design and eligibility criteria:** In the current comparative prospective study, 90 pregnant women aged between 18 years and 40 years old with class American Society of Anesthesiologist (ASA) I-II scheduled for Cesarean section under spinal anesthesia regardless of their socio-demographic aspects were randomly assigned into three groups. The patients were recruited in the theatre of Duhok maternity hospital in Duhok city after taking written consent forms between periods 1/6/2014 and 1/6/2015. The patients were divided into three groups in a blind random technique through selecting one of the written names of the three groups inside an opaque pocket by a colleague not-involved in the study and intervention.

The Patients met eligibility criteria if they were aged between 18 years and 40 years old and agree to participate, having no history of long-term steroid therapy (recognized through their medical records and confirmed by their gynecologist). Those patients with allergy to drugs (determined through the self-reported technique), uncontrolled hypertension, neurological or psychological disorders, spinal column surgery, low back pain, using of any drug that modifies pain perception were excluded from the study. In addition, the patients confirmed with bleeding diathesis, infection at the injection site, severe hypovolemia, severe pre-eclampsia, eclampsia, fetal distress were excluded from the study assignment.

**Clinical procedure:** A preanesthetic check-up including routine investigations were performed for all patients. Following procedure explanation to all patients (one by one), they were assigned into three mentioned above groups. The baseline clinical values of the patients, including heart rate, systolic and diastolic blood pressures, and oxygen saturation was recorded following shifting them to operating theater.

After patients’ assignment, group A or control (n=30) received intrathecal bupivacaine 12.5mg (2.5 ml) of 0.5% hyperbaric bupivacaine diluted in preservative free normal saline (1 ml), group B or group 2 mg dexamethasone (n=30): received 12.5 mg (2.5 ml) of 0.5% intrathecal hyperbaric bupivacaine and 2 mg (0.5 ml) preservative free dexamethasone, diluted in preservative free normal saline (0.5 ml), overall 3.5 ml volume intrathecally, and group C or group 4 mg dexamethasone (n=30): received 12.5 mg (2.5 ml) of 0.5% hyperbaric bupivacaine and 4 mg (1 ml) preservative free dexamethasone, diluted in preservative free normal saline (1 ml), overall 3.5 ml volume intrathecally.

Prior to subarachnoid block, all the patients were received 5 ml/kg lactated ringers solution after IV line preparation. Upon patients’ arrival into the operating room, peripheral oxygen saturation (SPO$_2$), ECG, pulse rate (PR), and systolic and diastolic blood pressures were monitored by the researcher and recorded in a pre-designed sheet every 5 minutes till the surgery completion.

The patient was located in a sitting position and with antiseptic techniques, 26- gauge Quincke needle was inserted.
intradurally at L3–L4 or L4–L5 interspace through midline approach. An anesthesiologist not-involved in the study prepared the medication in order to establish the double-blind method. Subsequently, the patients were located in the supine position when the drug was administered and were given oxygen for 2-3 L minutes by a nasal prongs.

**Measurement Criteria:** Level of sensation was assessed through a pin prick test by a needle with a short bevel along the mid-axillary line bilaterally. Every 30 seconds for a 20 minutes duration, the sensory block level was checked and then every 5 minutes was evaluated until the end of surgery. Time from intrathecal administration till the peak of sensory and motor block (highest dermatome level) was defined as onset of time action. The duration of sensory block was calculated from the peak of sensory block till the patients feel pain at the site of surgery. A 30% decrease in systolic blood pressure (SBP) from the baseline or SBP < 100 mm Hg was defined as hypotension, bradycardia determined as heart rate (HR) <50 beats/min and were managed with IV ephedrine 5-10 mg plus crystalloid fluids; and IV atropine 0.5 mg respectively. Postoperative nausea and vomiting (PONV) were assessed and treated with 0.15 mg /kg IV metoclopramide.

**STATISTICAL ANALYSIS**

The homogeneity of patients’ age, weight, and BMI was examined through the One-way ANOVA statistical tests. The differences between sensory and motor duration among three study groups were evaluated through the One-Way ANOVA and post-hoc statistical tests and chi-squared tests for adverse effects of different doses of dexamethasone. The p-value less than 0.05 was considered as statistically significant and less than 0.01 as a clinically substantial difference. The Statistical Package for Social Sciences version 23:00 (SPSS: IBM) was used for statistical calculations.

**RESULTS**

The homogeneity in patients’ characteristics of three study groups was examined in Table 1, and showed that the patients were comparable in mean age (p=0.632), weight (p=0.486), and BMI (p=0.922). The effects of the two doses of dexamethasone (2 mg and 4mg) on the duration of sensory and motor nerve block in pregnant women underwent elective cesarean section is shown in the Table 2. This study revealed that those patients assigned into the treatment groups (2mg and 4mg dexamethasone) had a longer sensory blocking duration; 284.63±64.85 and 313.37±70.53 minutes, respectively compared to those in the control group; 165.33±44.95 minutes (P<0.001). Similarly, the patients assigned into treatment groups had longer motor blocking duration (min); 223.43±52.67 and 227.20±47.17, respectively in comparison to the control group, 126.33±34.62 minutes (P<0.001). However, there was no statistically significant difference between the two treatment groups—in sensory and motor blocking effect, as shown in the Table 2 and Figure 1.

The frequency of adverse effects reported among the three groups were varies some adverse effects were higher in treatment groups in comparison to the control group.
like post-operative shivering, bradycardia and hypotension, while PONV were less frequent in treatment groups in comparison to the control, however there were no statistically significant differences between treatment groups and control (Table 3).

Table 1: Baseline information for the women underwent cesarean section

<table>
<thead>
<tr>
<th>Patients' Characteristics</th>
<th>Control (n=30)</th>
<th>2 mg dexamethasone (n=30)</th>
<th>4 mg dexamethasone (n=30)</th>
<th>p-value (Two-sided)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>25.70±5.55</td>
<td>26.93±5.47</td>
<td>26.83±5.56</td>
<td>0.632</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>88.43±6.30</td>
<td>89.37±7.59</td>
<td>87.20±6.99</td>
<td>0.486</td>
</tr>
<tr>
<td>BMI</td>
<td>60.57±1.73</td>
<td>60.45±1.79</td>
<td>60.63±1.75</td>
<td>0.922</td>
</tr>
</tbody>
</table>

*One-Way ANOVA was performed for all statistical analyses.

Table 2: Comparison between treatments and control group in regards to duration of sensory and motor nerve block.

<table>
<thead>
<tr>
<th>Anesthetic Duration</th>
<th>Frequency Distribution (Mean ± S.D.)</th>
<th>p-value (Two-sided)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensory Duration (min)</td>
<td>Control: 165.33±44.95</td>
<td>2 mg dexamethasone: 284.63±64.85</td>
</tr>
<tr>
<td>Motor Duration (min)</td>
<td>Control: 126.33±34.62</td>
<td>2 mg dexamethasone: 223.43±52.67</td>
</tr>
</tbody>
</table>

*One-Way ANOVA was performed for all statistical analyses.

**The Tukey test did show that the differences between groups control and 2 mg dexamethasone and groups control and 4 mg dexamethasone is substantially significant in both sensory and motor blocks duration except the difference between groups 2 and 4 mg dexamethasone in both categories.

Figure 2: Difference in sensory and motor block durations
EFFECT OF ADDING DIFFERENT DOSES OF DEXAMETHASONE

Table 3: Frequency of adverse events reported among three study groups.

<table>
<thead>
<tr>
<th>Adverse Effects</th>
<th>Frequency Distribution F (%)</th>
<th>p-value (Two-sided)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control 2 mg dexamethasone 4 mg dexamethasone</td>
<td></td>
</tr>
<tr>
<td>PONV</td>
<td>6 (20.0) 4 (13.3) 3 (10.0)</td>
<td>0.654**</td>
</tr>
<tr>
<td>Hypotension</td>
<td>8 (26.7) 7 (23.3) 9 (30.0)</td>
<td>0.843*</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>5 (16.7) 7 (23.3) 7 (23.3)</td>
<td>0.766*</td>
</tr>
<tr>
<td>Shievring</td>
<td>7 (23.3) 8 (26.7) 10 (33.3)</td>
<td>0.679*</td>
</tr>
<tr>
<td>PDPH</td>
<td>3 (10.0) 4 (13.3) 5 (16.7)</td>
<td>0.925**</td>
</tr>
</tbody>
</table>

*Chi-squared and **Fishers’ Exact tests were performed for statistical analyses.
PDPH: Post-dural-puncture headache; PONV: Postoperative Nausea & Vomiting

DISCUSSION
The researcher aim in conducting this study was to examine the effect of two doses of dexamethasone conjugated with bupivacaine on pregnant patients underwent elective cesarean section. This study showed that supplementing spinal bupivacaine with 2 and 4 mg dexamethasone substantially prolonged sensory and motor block compared to intrathecal bupivacaine in cesarean section with no significant difference in adverse events frequencies.

A few researches have been conducted on the effects of combination of dexamethasone with bupivacaine on prolongation of the duration of action of local anesthetic in patients undergoing cesarean section under spinal anesthesias. Shalu and Ghodki (2017) reported that administration of 8 mg of dexamethasone intravenously prolong the duration of of postoperative analgesia and sensory nerve block. Sachdeva et al (2016) also reported that adding 8mg dexamethasone to ropivacaine in transversus abdominal plane (TAP) block prolonged the duration of the block without any complication.

Adding of dexamethasone as an adjunct anesthetic material for peripheral nerve blocks were effective in prolonging the postoperative analgesia in interscalene brachial plexus blockade and caudal analgesia for pediatric orchiopexy. A similar finding were reported that dexamethasone injection perineurally in nerve block, including epidural, brachial plexus, femoral, sciatic, facial, and dental block can prolong the duration of both sensory and motor nerve block.

The exact mechanism of action of dexamethasone in prolonging the analgesic effects of local anesthestic remain unclear. However, dexamethasone and through its effects on reducing inflammatory mediator and probably by blocking transmission in nociceptive C-fibers and through suppressing ectopic neural discharge. Dexamethasone is a potent and selective glucocorticoid with a minimal mineralocorticoid action. May be its anti-inflammatory and immunosupressive inherencement is responsible for the analgesia prolongation, or it leads to vasoconstriction and slower the absorption anesthetic drugs and finally prolonging its action.

According to the finding of this study 2 mg dexamethasone combined with bupivacaine showed the same clinical effects compare to the higher dose of dexamethasone (4mg), which is in contrary...
to other studies were larger doses of dexamethasone was used as additive to local anesthetics\textsuperscript{17}. There were no significant difference in adverse effects reported in treatment groups and in agreement with the present study, other investigators showed no substantial difference in adverse events following adding dexamethasone as an adjunct drug to bupivacaine under spinal anesthesia\textsuperscript{2,14}. The current study showed that the sensory and motor block durations in patients underwent cesarean section under spinal anesthesia and having comparable age, weight, and BMI were significantly longer in those groups received 2 and 4 mg dexamethasone compared to the patients did not receive dexamethasone as an adjunct drug with out substantial difference in adverse effects frequencies. It is recommended to the anesthesiologist to use 2 mg dexamethasone as an adjunct drug rather than 4 and 8 mg dexamethasone. However, the optimal dose of dexamethasone needs further investigation to be used in spinal anesthesia.

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EFFECT OF ADDING DIFFERENT DOSES OF DEXAMETHASONE


گورنیتن تخمین شانه‌ی بین مه‌سوز لدف کورنیتن عوامل بین که بی‌جهت‌زایی‌خوری و برای‌مایلی‌داور همی. فکولینکا یک‌پاشته‌ی لسر 105 نخوشان

پیش‌خوان

پیشنهدی: تابوریک بون و ساناتی بون ل کارکردنی‌ها (کامپیوتر) بی‌پدیدگی و درک گفتنی که ویک تکنیکی که برای ل نمک‌کاری فیزیکی برای بی‌پدیدگی انحراف. هر یک از برتریت مینا گروهی یا فیزیکی شاکر به برابریان ل همی. همگیان که بی‌پوستی گذشته بند. لک، کوره بونی بی‌پوستی یک گروهی شاکر بازی بی‌پوستی. نتایج نهایی فکولینکا

وکاتینیکی خرید نانه زنی که تهیه‌گر فیزیکی کردن.

ریکینگ فکولینکا: ل فکولینکا ۱۰۲ گیله به‌ردست ۹۰ زنی دوگیاگ که نمک‌زهگری فیزیکی پیدا می‌گرند که بین‌رونشینگ چوئی

پیشن واهنگنیت از هر منادی به‌سنگرد خود جنگ دانه‌ی کردن. نخوششان ل گروهی (کنترل) (۳۰ ساعت) (۱۲.۵ مگ. (۰.۵ مل) ز ۰.۵٪ بیکاتین، گروهی گیا (۲ مگ. دیکسانتارین (دیکسانتارین (۲ مگ. ۰.۵٪ بیکاتین، دوگیاگ ۲ مگ. دیکسانتارین و گروهی ۴ مگ. دیکسانتارین ۲۰ مگ. (۰.۵ مل) (۰.۵٪ بیکاتین، گروهی ۴ مک. دیکسانتارین و گروهی ۴ مک. دیکسانتارین و گروهی)

نتایج: ل فکولینکا به‌ردست نخوششان ۵.۴۹±۲۶ سال (۸ حاکی ۰۰ سالی) و هم‌سن گروهی خودان نمی‌توان;

ظنه‌گر شدن (۰.۲) (۱ بی‌پوستی فیزیکی هم‌سن گروهی خودان نمی‌توان;

۱۵ گروهی (۲۸.۴ مگ. دیکسانتارین و گروهی ۴ مگ. دیکسانتارین و گروهی ۴ مگ. دیکسانتارین و گروهی ۴ مگ. دیکسانتارین و گروهی ۴ مگ. دیکسانتارین و گروهی)

هر گروهی (۰.۵ مل) ۵۰٪ بیکاتین، گروهی ۴ مگ. دیکسانتارین و گروهی ۴ مک. دیکسانتارین و گروهی ۴ مک. دیکسانتارین و

دیره‌گرایی: فکولینکا دارک‌کر گروهی خودان ۴ و ۸ مگ. ر گروهی و دوگیاگ گروهی دوگیاگ دوگیاگ و دوگیاگ دوگیاگ

برچه‌ی لانه زنی دوگیاگ درازکردن.
الخلاصة

تأثير إضافة جرع مختلفة من الدكساميثازون إلى البوبيفاكائيين في العمليات القيصرية باستخدام التخدير داخل القراب

الخلفية والأهداف: يعد التكلفة المناسبة وسهولة العطاء من أهم العوامل التي جعلت التخدير داخل القراب (التخدير النصفي) من أكثر طرق التخدير شيوعاً أثناء عمليات الولادة القيصرية. كما تقلل التخدير تحت القراب 16 مرة مقارنةً بالتخدير العام. وهكذا تعتبر المدة القصيرة نسبياً لفعالية أدوية أدوية التخدير المستخدمة في التخدير تحت القراب. الهدف من هذه الدراسة هو تقييم تأثير إضافة جرع مختلفة من الدكساميثازون إلى البوبيفاكائيين على مدة التخدير داخل القراب وقياس التأثيرات الجانبية المصاحبة للتخدير لعمليات الولادة القيصرية.

طرق البحث: في التجربة السريرية المزدوجة التعمية الحالية، تم تعيين 90 امرأة حامل في المرضى المقرر اخضاعها لعملية الولادة القيصرية عشوائياً وتم تقسيمهم إلى ثلاث مجموعات بعد إعطاء التخدير. المرضى الذين تم تعيينهم إلى المجموعة A (ن = 30) تلقوا 12.5 مل من 0.5٪ بوبيفاكائيين عالي الضغط وتم تخفيفه بالنورمال سلاین (0.5 مل)، المجموعة B (n = 30): تلقى 12.5 مل من 0.5٪ بوبيفاكائيين عالي الضغط و2 مل دكساميثازون خالي من المواد الحافظة، عموماً 3.5 مل حجم داخل القراب، ومجموعة C (n = 30): تلقى 12.5 مل (0.5٪ بوبيفاكائيين عالي الضغط و 4 مل من الدكساميثازون خالي من المواد الحافظة، عموماً 3.5 مل حجم داخل القراب.

النتائج: في الوقت الحاضر كان متوسط العمر للمرضي 26.49 ± 5.49 سنة (ال مدى: 18-40 سنة) وكان عمر المرضى 12.5 ± 6.85 سنة (ال مدى: 18-24 سنة). وأظهرت الدراسة أن مدة الأحصار الحسي (الدقيقة) في المرضى كانت أعلى ب 165.33 ± 44.95 دقيقة بالمقارنة مع المجموعة A. وحول الأمر، المرضى المعطين المجموعات C و B لم يكن بإمكانهم ان يقلل احصار الحسية والحركي (0.05). ولم يكن لدى المرضى من ثلاث مجموعات فرقاً أساسيًا في تواتر الآثار الجانبية أثناء وبعد العملية الجراحية، والتي تتضمن الغثيان والقيء، انخفاض ضغط الدم، بطء نبضات القلب، الأرتجاف البدني، نوبات الصداع.

الاستنتاجات: أظهرت الدراسة أن إعطاء 2 و 4 مل من الدكساميثازون مع البوبيفاكائيين في التخدير داخل القراب يزيد من مدة الأحصار الحسية والحركي بصورة واضحة أثناء عملية الولادة القيصرية تحت التخدير الشعبي. وان إضافة 2 مل من الدكساميثازون تزيد مدة الأحصار الحسية والحركي بنفس تأثير اضافة 4 ملغم.