SPINAL ANAESTHESIA FOR CESAREAN SECTION WITH REDUCED DOSE OF INTRATHECAL BUPIVACAINE PLUS FENTANYL

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Abstract: Background and Objectives: The hypotension following spinal anesthesia remains common place in cesarean delivery. The combination of reduced dose of local anesthetics with intrathecal opioids makes it possible to achieve adequate spinal anesthesia with minimum hypotension. We investigate whether this synergistic phenomenon could be used to provide less frequent hypotension while incurring adequate spinal anesthesia for cesarean section.

Methods: Forty women scheduled for cesarean delivery (twenty in each group) were divided into two groups of patients who received a spinal injection of either 13.5 mg of standardized isobaric 0.5% bupivacaine or 9 mg of isobaric bupivacaine with 20 µg fentanyl added. Each measurement of a systolic blood pressure less than 95 mm Hg or a decrease in systolic pressure of greater than 25% from baseline was considered as hypotension and treated with a bolus of 5 to 10 mg of intravenous ephedrine. The quality of surgical anesthesia was evaluated also.

Results: Spinal block provided excellent surgical anesthesia in almost all patients. Peak sensory level was higher (Th 2–3 vs. Th 4–5) and motor block was more intense in the plain bupivacaine group; the patients from standardized bupivacaine group were more likely to require treatment for hypotension (75% vs 15%) and had more persistent hypotension (4.6 vs. 1.0 hypotensive measurements per patient) than patients in the reduced bupivacaine-fentanyl group. Mean ephedrine requirements were 22.0 mg and 3.5 mg, respectively. Patients in the bupivacaine group also complained of emetic effects more frequently than patients in the reduced dose bupivacaine-fentanyl group.
Conclusions: Bupivacaine 9 mg plus fentanyl 20 µgr provided spinal anesthesia for cesarean delivery with less hypotension and vasopressor requirements while ensuring excellent peripoperative surgical anesthesia.

Key words: Cesarean delivery; spinal anesthesia; bupivacain, fentanyl.

Introduction

A spinal anesthesia for cesarean section has become increasingly popular and the recent decade has been the preferred technique for the majority of aesthesiologist. This is primarily due to increased maternal mortality with general anesthesia and benefits conveyed to the mother. But, spinal anesthesia is associated with major or minor complications in the pregnant patient, the commonest being maternal hypotension. It is believed to occur in up to 95% of the patients and may lead to a reduction in utero-placental perfusion resulting in fetal acid-base abnormalities [3].

How important is this and what should we be doing to prevent it?

Local anesthetics plus opioids administered together intrathecally have been shown to have a synergistic analgesic effect [4, 5, 9]. Intrathecal opioids increase the quality of analgesia and reduces local anesthetic requirements, with some studies showing favourable effects on haemodinamics stability [6, 7, 9, 10]. Therefore, it may be possible to achieve spinal anesthesia with less hypotension, by using a reduced (low) dose of local anesthetic in combination with fentanyl.

The aim of this study was to test a reduced dose intrathecall bupivacaine in combination with intrathecal fentanyl for cesarean delivery both in terms of its feasibility as an anesthetic and as its potential to minimize maternal hypotension.

Methods

The study included 40 ASA I healthy parturients between 19 and 38 years of age with similar demographic characteristics, scheduled for elective, semiurgent or urgent cesarean section. Complicated pregnancies such as multiple pregnancy, serious pregnancy-induced hypertension, and placenta previa patients were excluded; patients with cardiac, renal, or other organ-system disease were also excluded from the study. Each patient received 10 mg metoclopramide intravenously before spinal block and a rapid intravenous infusion of 500 mL of saline solution were given in the operating room via a 16-gauge intravenous catheter. In addition to the loading dose of iv fluids, patients
received a further saline solutions during the remainder of the operation. Only minimal sedative medications were administered during the operation (midazolam 1–2 mg). Standard continuous electrocardiogram monitoring and pulse oximetry was included. Baseline maternal heartbeat and blood pressure values were established before the lumbar puncture. The lumbar puncture was performed at the L2–3 (mostly patients with bupivacaine-fentanyl injection) or L3–4 interspace, with a 26-gauge Braun needle, with the parturients in the sitting position. After confirming the correct placement of the spinal needle by aspiration of the cerebrospinal fluid (CSF) and after completion of the injection (the spinal volume was injected over 20–25 seconds) the patients were immediately returned to the supine position with 15 to 20 degrees of left uterine displacement breathing oxygen via face mask.

The patients were randomly assigned into two groups defined by the spinal injection. They received either 13.5 mg (2.7 ml) of isobaric 0.5% bupivacaine in the first group or 9 mg of isobaric bupivacaine plus fentanyl 20 µg (2.2 mL) of volume in the second group. Blood pressures was measured via the noninvasive blood pressure (NIBP) monitor at 3 minute interval during the first 15 minutes after the spinal injection and every 5 minutes thereafter. Whenever systolic blood pressure was lower than 95 mm Hg or 20% below the preinduction level (defined as hypotension), ephedrine 5 mg intravenously dosage was administered. The number of hypotensive measurements and total ephedrine use for each patient were recorded. Patients who complained of pain were given 50 µg increments of iv fentanyl. Pain scores were summed across the following sequential intervals during the procedure: skin incision, delivery until uterine exteriorization, uterine replacement and start of facial closure and skin closure. The visual analogue scale (VAS) was used if pain (analgesia) persists. The protocol allowed for conversion to general anesthesia as deemed necessary.

The degree of motor block was assessed using Bromage Scale (BS): BS 0, full flexion of knees and feet; 1, just able to move knees; 2, able to move feet only; 3, unable to move feet and knees, and complete motor block was defined as BS 3. The level of sensory block was tested with method of touch sensation. All of these time variables were measured from the beginning of the spinal injection.

The newborns’ Apgar scores at 1 and 5 minutes and umbilical pH values were recorded immediately after delivery.

Emethic effects- nausea or vomiting were registered; other side effects were evaluated if needed.

Statistical analysis was performed using statistical tests included Student’s t-test, Fisher exact test and contingency table analysis. Results were considered significant at a p value of 0.05.
Results

There were 20 patients in each group of total 40 patients, and were similar with respect to age, weight, and height among the groups (Table 1).

Table 1 – Таблица 1

<table>
<thead>
<tr>
<th></th>
<th>Plain bupivacaine</th>
<th>Reduced bupivacaine + fentanyl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Previous cesarean s.</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>26.0 ± 7.5</td>
<td>27.2 ± 4.7</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>74.5 ± 10</td>
<td>76.0 ± 8</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>164 ± 7</td>
<td>165 ± 5</td>
</tr>
<tr>
<td>Initial systolic BP</td>
<td>132 ± 15.2</td>
<td>129.4 ± 12.5</td>
</tr>
<tr>
<td>Initial diastolic BP</td>
<td>79.4 ± 12.0</td>
<td>82.4 ± 9.9</td>
</tr>
<tr>
<td>Length of the operation</td>
<td>82.5 ± 9.5</td>
<td>79.0 ± 15.0</td>
</tr>
</tbody>
</table>

Block onset times of sensory block (to Th 5) was slightly faster in the plain bupivacaine group (6.5 min versus 8 min), but it was not significantly different from bupivacaine plus fentanyl group. Peak median cephalad sensory block to touch sensation was significantly higher (by at least 2 dermatome) in the plain bupivacaine group with the highest level of anesthesia occurred at the fifth cervical dermatome in the same group (Table 2). Sensory block was sufficiently intense in both groups to provide surgical anesthesia for all patients although one patient from bupivacaine plus fentanyl group required conversion to general anesthesia (GA) because of inadequate surgical anesthesia.

Pain: Two of the 20 patients (2/20) in each group, noted transient pressure or stretching or mild operative pain at the time of delivery; but all patients from bupivacaine-fentanyl group reported a high level of satisfaction with their anesthetic at the end of the procedure. There was the sole exception of one patient needed general anesthesia, which was at the time of the delivery until uterine exteriorization. No patient in plain bupivacaine group required conversion to general anesthesia. Dissatisfaction because of nausea, not from anesthesia, was noted by 3 women in the bupivacaine group.

Most of the patients in the plain bupivacaine group developed and vanished significantly faster and more intense motor block (Bromage score 2, 3, p < 0.05) compared with patients from bupivacaine–fentanyl group, (Table 2).
Table 2 – Таблица 2

**Intervertebral space used for spinal punction; characteristics of sensory and motor spinal block and number of patients required additional analgesia or GA; patient comfort satisfaction.**

Интервертебрален простор за спиналина функција; карактеристики на сензорниот и моторниот блок; број на пациентки кои бараа дополнилна аналгезија или ОЕТ; сатисфакција од анестезијата

<table>
<thead>
<tr>
<th>Intervertebral space for punction</th>
<th>Plain bupivacaine (n = 20)</th>
<th>Reduced bupivacaine + fentanyl (n =20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L2–3</td>
<td>1</td>
<td>16</td>
</tr>
<tr>
<td>L3–4</td>
<td>18</td>
<td>4</td>
</tr>
<tr>
<td>L4–5</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Peak sensory level</td>
<td>Th 2, 3 (C5–Th5)</td>
<td>Th 4, 5 (2–6)</td>
</tr>
<tr>
<td>median, range</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motor block (Bromage scale 0–1–2–3)</td>
<td>0–0–4–16</td>
<td>0–6–12–2</td>
</tr>
<tr>
<td>Pain during surgery,</td>
<td>2/20</td>
<td>2/20</td>
</tr>
<tr>
<td>(requiring fentanyl)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain during surgery,</td>
<td>0/20</td>
<td>1/20</td>
</tr>
<tr>
<td>(requiring GA)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>8/20</td>
<td>0/20</td>
</tr>
<tr>
<td>Satisfaction with anesthesia</td>
<td>3–0–17</td>
<td>1–0–19</td>
</tr>
<tr>
<td>(1–4, 5–7, 8–10)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Haemodinamic effects and neonatal outcomes:

With regard to hypotension, there were pronounced and significant differences between the groups. 12/20 patients developed hypotension in the bupivacaine group compared with only 2/20 patients in the bupivacaine-fentanyl group; further more, other 2/20 patients with bupivacaine injection developed severe hypotension with transient respiratory or conscience disturbances. In the bupivacaine-fentanyl group, only 3 patient required treatment for hypotension versus 15/20 patients (75%) of the patients in the plain bupivacaine group. There was a difference between groups in the frequency, severity, and persistence of the hypotension also. No patient in the bupivacaine-fentanyl group required more than 10 mg of ephedrine, whereas in the plain bupivacaine group the median dose was 22.0 (range 0–65 mg) (Table 3).

Nausea and vomiting were more pronounced in the plain bupivacaine group, occurring in 40% of patients as opposed to none of patients in the bupivacaine-fentanyl group. As noted, mostly patients express dissatisfaction.
with their anesthesia in the plain bupivacaine group. Interestingly, patient dissatisfaction stemmed from the unpleasant sensation (nausea) rather than from pain. Nausea and unpleasant feeling occurred mostly at the end of exteriorization of the uterus and manipulation of the peritoneum.

Table 3 – Таблица 3

<table>
<thead>
<tr>
<th></th>
<th>Plain bupivacaine (n = 20)</th>
<th>Reduced bupivacaine + fentanyl (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension &lt; 95 mmHg, &gt; 25%</td>
<td>12/20</td>
<td>2/20</td>
</tr>
<tr>
<td>Severe hypotension &lt; 80 mmHg</td>
<td>2/20</td>
<td>0/20</td>
</tr>
<tr>
<td>Number of measurements of</td>
<td>4.6 ± 3</td>
<td>1.0 ± 1.2</td>
</tr>
<tr>
<td>hypotension (mean ± sd)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Required treatment of hypotension</td>
<td>15/20</td>
<td>3/20</td>
</tr>
<tr>
<td>Ephedrine total dose</td>
<td>22.0 ± 18.4</td>
<td>3.5 ± 3.4</td>
</tr>
<tr>
<td>(mean ± sd), range</td>
<td>(0–65)</td>
<td>(0–10)</td>
</tr>
<tr>
<td>Apgar score, 1 min</td>
<td>8.5 ± 0.5</td>
<td>8.8 ± 0.8</td>
</tr>
<tr>
<td>Umbilical pH</td>
<td>7.26 ± 0.6</td>
<td>7.28 ± 0.2</td>
</tr>
</tbody>
</table>

Neonatal outcome parameters Apgar scores and umbilical pH values, were similarly excellent in both groups, and there were no significant differences between the groups. Two newborns from bupivacaine spinal anesthesia had umbilical pH under 7.20, which not happened in bupivacaine-fentanyl group.

**Discussion**

The principal finding of this study was that the combination of reduced (low) dose of bupivacaine -9 mg with opioid (fentanyl) provides excellent spinal anesthesia for cesarean delivery with significantly less hypotension than standard dosage of bupivacaine alone. Nowadays, textbooks of anesthesia recommend large (standard) doses of bupivacaine still, even though clinical experience favor small doses combined with opioids. Often, dosages between 12–15 mg of either is or hyperbaric bupivacaine are recommended, but hypo-
tension could be very often complication with such dosages. Further, unaccep-
table high spinal anesthesia has been reported with doses larger than 12 mg
of bupivacaine in patients undergoing cesarean section, although the problem
seems not to be often [8, 21]. Thus, the appropriate dosage of bupivacaine
seems to be under reevaluation [8].

Hyptension is the perhaps the most common complication of stan-
dardized bupivacaine spinal anesthesia. If no preventive measures are taken
during this maneuver, the incidence of hyptension is reported as 92% and 94%
[15, 18]. The variety of ways have been tried to minimize the hyptension
during this anesthetic procedure. Measures to prevent hyptension include the
administration of fluids (colloids or crystalloids) before the regional anesthesia,
left uterine displacement and administration of a prophylactic vasopresor. But,
adding colloids as preloading protocol may counteract hyptension; the infusion
of prophylactic efedrine may be associated with umbilical pH values under 7.20
in some newborns [4, 11, 22].

The concept of using a reduced (low) dose of local anesthetic with
opioid to minimaize hyptension has received an attention [1, 5]. The combina-
tion of reduced (low) dose of local anesthetic plus lipophilic opioid, over
traditional higher-dose local anesthetic spinal anesthesia, has increased in recent
years, producing clear benefits: less hyptension and better peripoperative anal-
gesia. Vercauteren et al. used a combination of sufentanil with low-dose
bupivacaine (6.6 mg) for spinal anesthesia in cesarean section and found a
lower incidence of hyptension [26]; spinal administration of fentanyl, may
potentiate the local anesthetics analgesia and be associated with a decreased
incidence of hyptension also, faster onset of block and motor recovery, and
shorter time to micturition [7]. Bruce Ben-David et al. concluded that spinal
anesthesia using very low doses (as 5 mg) of isobaric bupivacaine plus 25 µgr
fentanyl, is associated with significantly less hyptension and vasopressor
requirements than 10 mg of isobaric plain bupivacaine, but they have evaluated
no representative number of patients [3]. Other clinical experiences with doses
between 5–10 mg bupivacaine are valuable and report about similar findings [5,
10, 13, 17]. Definitely, the reduced local anesthetic doses (bupivacaine) play
role in getting less severe hyptension together with the mechanism by which
intrathecall opioids decrease hyptension.

Intrathecall fentanyl have a very selective spinal cord site of action; it
acts synergistically with bupivacaine to enhance the effect on the efferent
pathways but without an effect on sympatetic patways, thus producing no hyptension [20, 25]. Even more, it appears that the addition of intrathecall fentanyl
to bupivacaine spinal anesthesia, potentials the surgical analgesia for somatic
and visceral pain, thus making the patients from bupavaicaine-fentanyl anest-
hesia more satisfied with their anesthetic (Table 2). It is likely that complex
mechanisms along with potency, lipophilicity, and drug concentration all play a role in the local anesthetic actions of spinal opioids [16]. Furthermore, studies in gravid animal models suggest hormonal milieu may also contribute to opioid effectiveness. Jayaram and Carp found that spinal progesterone potentiated the analgesic effect of spinal opioids in rats [19]. Adequate spinal anesthesia for caesarean section which provides sympathetic blockade up to Th 4 causes a minimal reaction of hypotension compounded with reflex increase in heart rate and cardiac rate. Most patients in the bupivacaine-fentanyl group reached lower median peak sensory level (Th 4), compared with patients from other group, but it seems this sensory level was quite enough to reach adequate surgical anesthesia. The normal blood pressure compounded with this median peak sensory level, was associated with a reduction in the mean ephedrine requirement; in fact, most patients in the bupivacaine – fentanyl group required no ephedrine. It seems, that peak sensory level above those segment, affects the cardiac sympathetic intervention, thereby attenuating the compensatory mechanism and so high spinal block may further reduce the heart rate and produce a hypotension with more ephedrine requirement (Table 2).

Maintenance of normal maternal blood pressure during spinal cesarean section is key factor for adequate neonatal outcome, too. The mature placenta is high capacitance organ with no autoregulatory ability, so uteroplacental perfusion pressure is dependent on systemic blood pressure. Spinal anesthesia with adequate blood pressure results in better neonatal blood gas and acid-base measurements at cesarean delivery. Two newborns from bupivacaine spinal anesthesia had umbilical pH under 7.20, which not happened in bupivacaine-fentanyl group, where no hypotension occurred.

The patients in the bupivacaine-fentanyl group experienced significantly less nausea than patients in the plain bupivacaine group. The decreased incidence of emetic effects after supplementation of spinal anesthesia with intrathecal fentanyl in our study has also been reported by other investigators [27]. The finding of less nausea in the bupivacaine-fentanyl group may be surprising in that nausea is generally considered a side effect of intrathecal opioids. Palmer et al. found a lower incidence of perioperative nausea and vomiting when 15 µgr fentanyl was added to lidocaine spinal anesthesia for cesarean delivery [16]; Dahlgren et al. found that either fentanyl or sufentanil added to the spinal anesthetic for cesarean delivery led to reduced need for intraoperative antiemetics [7]. The increased emetic effects in the bupivacaine group may be secondary to the increased incidence of hypotension, because effects were relieved when the blood pressure was increased after the administration of ephedrine. It has been our observation that rare hypotension in bupivacaine-fentanyl group occurs in the absence of nausea and vice versa. These findings and observations suggest about a protective effect of the intrathecal fentanyl, rather than from the more stable hemodynamics.
In summary, the findings of this study suggest that spinal anesthesia for cesarean delivery using 9 mg isobaric bupivacaine plus 20 µg fentanyl is associated with significantly less hypotension, vasopressor requirements and nausea than spinal anesthesia with 13.5 mg of isobaric bupivacaine, without untoward effects. This combination has been shown to improve the quality of spinal anesthesia for cesarean delivery and makes possible the use of otherwise inadequate doses of bupivacaine. But, further large study is warranted to verify a reliable minimum dose of bupivacaine-fentanyl for spinal anesthesia in cesarean delivery.

REFERENCES


**Резиме**

**СПИНАЛНА АНЕСТЕЗИЈА ЗА ЦАРСКИ РЕЗ СО РЕДУЦИРАНА ДОЗА БУПИВАКАИН ПЛУС ФЕНТАНИЛ**

**Сивевски А.**

*Клиника за анестезиолошти, реанимации и интензивно лекување (КАРИЛ), Гинеколошко-акушерска клиника, Клинички центар, Универзитет ,,Св. Кирил и Методиј“, Скопје, Р. Македонија*

Хипотензијата за време на спиналната анестезија за царски рез претставува чест проблем. Со комбинирањето редуцирана дози од локален анестетик и интратекално даден опиоид може да се постигне адекватна спинална анестезија со минимална појава на хипотензија. Во трудот испитуваме дали овој синергистички феномен може да обезбеди поретка појава на хипотензија, но во услови на ефикасна спинална анестезија за царски рез.

**Методи и пациенти:** Четириесет родилки поделени во две групи (по двесет во секоја група) примаа 13,5 мг (2,7 мл) 0,5% стандарден изobarен бупивакаин или 9 мг изobarен бупивакаин плус 20 µг фентанил интратекално. Хипотензијата се дефинирала како намалување на крвниот притисок под 95 mmHg или намалување на систоличниот притисок за 25% од почетната вредност и се третираше со додатоци од 5–10 µg интранзивно даден ефедрин. Исто така беше оценена и квалитетот на хируршката анестезија.

**Резултати:** Спиналниот блок овозможил одлична хируршка анестезија скоро кај сите пациентки од двете групи. Највисоките сензорни нивоа, како и моторниот блок беа повисоки и поинтензивни кај пациентките од стандардната бупивакаинска група (Th 2–3 vs. Th 4–5). Кај пациентките од истата група, хипотензијата беше значително почеста и со почет хипотензивин третман (75% на спротив 15%); исто така беше со подолгораѓно време траење (4,6 на спротив едно хипотензивно мерење) во спротив со пациентките од бупивакаин-фентанилската група. Просечните употребени дози ефедрин за корекција на хипотензијата беше 22,0 мг во бупивакаинската

группа на против 3,5 мг. Пациентките од бупивакаинската grupa почасцо се жалеа на еметички тегоби во споредба со останатите.

Заклучок: Спиналната анестезија за царски рез со 9 мг бупивакаин плус 20 µг фентанил, обезбедува можносет за помала и поретка појава на хипотензис и вазопресорни побарувања, а во услови на одлична периоперативна хируршки аналгезија.

Ключни зборови: царски рез, спинална анестезија, бупивакаин, фентанил.

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