THE EFFICACY OF INTRATHECAL DEXAMETHASONE TO PREVENT EARLY COMPLICATIONS OF SPINAL ANAESTHESIA FOR ELECTIVE CAESAREAN SECTION

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Abstract: Spinal anaesthesia is commonly used for elective caesarean section. But it has some disadvantages and complications in intra- and postoperative period.

The aim of this study was to explore the efficacy of intrathecal or intravenous dexamethasone to prevent some early complications of spinal anaesthesia such as arterial hypotonia, nausea, vomiting, bradycardia, shivering etc.

Material and methods: there were examined 154 healthy, not obese women, ASA I–II, 18–36 years old, 36–40 weeks of gestation, undergoing elective caesarean section under spinal anaesthesia. All patients were divided into three equal groups for randomized, prospective, double-blinded, placebo-controlled clinical trial.

The women of each group received intrathecal hyperbaric bupivacaine 0.5 % 10 mg. Group B (n=51) additionally received intrathecal 1 ml of normal saline=placebo; Group BD (n=52) additionally received 4 mg (1 ml) intrathecal dexamethasone, and Group D (n=51) received 8 mg intravenous dexamethasone directly after spinal puncture. The patients were evaluated for blood pressure, heart rate, nausea, vomiting, shivering or other complications during intra- or postoperative period (24 h). The complications that required medicines correction were recorded and cured.

Results: the addition of intrathecal dexamethasone in Group BD vs Group B significantly decreased frequency and manifestations of arterial hypotonia and nausea (Pearson's χ^2=0.486 and χ^2=0.479, p<0.05) in intra- and postoperative period after the spinal anaesthesia in elective caesarean section. Intrathecal dexamethasone in Group BD vs Group B significantly reduced shivering (Pearson's χ^2=0.316, p<0.05) in intra- and postoperative period, and significantly didn`t impact on vomiting and bradycardia.

Conclusions: the addition of 4 mg intrathecal dexamethasone as an adjuvant for spinal anaesthesia can significantly decrease frequency and manifestations of arterial hypotonia and nausea, reduce shivering during perioperative period. The addition of 8 mg intravenous dexamethasone has not the same quality.

Keywords: dexamethasone, spinal anaesthesia, caesarean section, adjuvant, arterial hypotension, complications.

1. Introduction

Spinal anaesthesia is commonly used for elective caesarean section, and has a lot of advantages. It is easier and quicker than epidural anaesthesia and it exposes the fetus to fewer drugs than general anaesthesia. But the best benefit of spinal anaesthesia for elective caesarean section is the mother`s ability to be conscious when her baby is delivered.

However, spinal anaesthesia has some disadvantages and complications in intra- and postoperative period. Maternal hypotension is the most frequent complication of spinal anaesthesia for caesarean section, thus can affect 90 % of women and can be associated with nausea and vomiting, fetal acidosis and in severe cases fetal bradycardia. It can be the source of serious risks to the mother (pulmonary aspiration, unconsciousness) and baby (hypoxia, acidosis, neurological injury, etc) [1, 2].

Maternal hypotension, nausea and vomiting are significantly more frequent during spinal anaesthesia for caesarean section than during non-obstetric surgery. The aetiology of this is multifactorial (the sympathetic vasomotor block caused by spinal anaesthesia, inferior vena cava compression, acute hypotension reduces cerebral perfusion, induces transient brainstem ischaemia and activates the vomiting centre [3], secondary low systemic vascular resistance and artery vasodilation due to progesterone action, hormonally caused hypersensitivity of nerve fibres of local anaesthetics and opioids, etc).

Intrathecal opioids are frequently administered to patients undergoing elective caesarean section under spinal anaesthesia for postoperative analgesia. The incidence of postoperative nausea and vomiting (PONV) in patients who have received an intrathecal opiate is 60–80 % [4]. The reported incidence of intrathecal opioid-induced pruritus is 20–90 % [5]. Although the prophylactic and therapeutic effects of several antiemetic and antipruritic drugs have been extensively studied, a decrease in the incidence of PONV and pruritus after intrathecal opioids remains a major therapeutic challenge.

A lot of systematic reviews and network meta-analysis allow us to compare methods of prevention maternal hypotension, nausea and vomiting, pruritus in women receiving spinal anaesthesia for caesarean section [1–3, 6].

Vasopressors should be given to healthy women to prevent hypotension during caesarean section with spinal anaesthesia (Gr. high to moderate) [2, 7].

The aim should be to maintain systolic arterial pressure (SAP) at ≥90 % of an accurate baseline obtained before spinal anaesthesia and avoid a decrease to <80 % baseline. It is recommended variable rate prophylactic infusion of phenylephrine using a syringe pump (started at 25–50 $\mu g.min^{-1}$ immediately after the intrathecal local anaesthetic injection, and titrated to blood pressure and pulse rate) [3, 7]. The SAP is a less important variable than mean arterial pressure (MAP) as a determinant of organ perfusion; however, because methods used to measure blood pressure in routine clinical practice did not include the mean until recent decades.

But while interventions such as crystalloids, colloids, ephedrine, phenylephrine, ondansetron, left lateral position, or lower leg compression can reduce the incidence of hypotension, none have been shown to eliminate the need to treat maternal hypotension in some women. That is why it is important to find new, simple and safe methods of improvement spinal anaesthesia for elective caesarean section.

Dexamethasone is a potent anti-inflammatory agent which has been investigated in the last decade for its role as an adjuvant to local anaesthetics in neuraxial as well as peripheral nerve blocks.

The mechanisms by which steroids potentiate the analgesic effects seem to be different from its intrinsic anti-inflammatory mechanism [4]. There is also evidence to show that the local action on nerve fibres and systemic effects, both potentiate dexamethasone's analgesic properties [8, 9]. Both perineural and intravenous dexamethasone may prolong duration of sensory block and are effective in reducing postoperative pain intensity and opioid consumption [5]. Local wound infiltration of dexamethasone is more effective than systemic administration to decrease postoperative pain with weaker antiemetic effect [10]. But combination of dexamethasone and ondansetron administered prophylactically significantly reduced the incidence of PONV in pregnant women on intrathecal morphine for caesarean section. Addition of dexa-

methasone to bupivacaine in spinal anaesthesia significantly improved the duration of sensory block/surgical analgesia as well as post-operative analgesia/pain free period without any complications [11].

The aim of this study was to evaluate the efficacy of intrathecal or intravenous dexamethasone to prevent some early complications of spinal anaesthesia such as arterial hypotonia, nausea, vomiting, bradycardia, shivering etc.

2. Materials and methods

During 2019–2020 a randomized, prospective, double-blinded, placebo-controlled clinical trial were performed in Kyiv City Center of Reproductive and Perinatal Medicine. Study design was approved by Ethics committee of Shupik National medical Academy of Postgraduate education (No. 1, 04.02.2019). According to Helsinki declaration, all the patients were informed regarding aim and methods of the current study and had provided the written informed consent.

A total of 154 healthy, not obese women, ASA I–II, 18–36 years old, 36–40 weeks of gestation undergoing elective caesarean section under spinal anaesthesia were randomly divided into *three equal groups*. All patients were randomized by age, weight and growth rates, BMI, gestational period, assessment of somatic status, indications for surgery, duration of surgery, and postoperative period in ICU.

The women of each group received intrathecal hyperbaric bupivacaine 0.5 % 10 mg.

Group B (n=51) additionally received intrathecal 1 ml of normal saline like placebo.

Group BD (n=52) additionally received 4mg (1 ml) intrathecal dexamethasone.

Group D (n=51) received 8 mg *intravenous dexamethasone* directly after spinal puncture.

All data of patient`s monitoring were recorded before spinal puncture at 1, 5, 10, 20, 30 minutes of operation, at the end of operation, every hour during post-operative period (24 h). The patients were evaluated for blood pressure (including mean arterial pressure (MAP)), heart rate, nausea, vomiting, shivering or other complications during intra- or postoperative period. The complications that required medicines correction were recorded and cured.

All obtained data from the study were processed using SPSS software by methods of variational statistics. As for statistical data analysis, continuous variables were presented as mean ± standard deviation when they were normally distributed, or median and interquartile range if otherwise. Categorical variables were presented as frequencies and percentages. Mann-Whitney criteria were used for intergroup differences and quantitative values. The qualitative variables were expressed as percentages and were analyzed by the χ^2 test and exact Fisher test. All differences were considered statistically significant with $p \leq 0.05$.

3. Results

Mean arterial pressure (MAP) more than SAP is a determinant of organ perfusion. Continuous variables of MAP are presented as median and interquartile range in **Table 1**.

Pairwise group comparisons of mean arterial pressure (MAP) were performed statistically significant differences in Group BD vs Group B ($p \leq 0.012$ and $p \leq 0.023$) at 5 min and 10 min after spinal puncture. In addition, no significant differences were found in the comparative characteristics of groups at 0 min, 1 min, 30 min after spinal puncture.

The same trends of arterial pressure were performed in **Fig. 1.** There were presented statistically significant differences in Group BD vs Group B ($p \leq 0.014$ and $p \leq 0.026$) at 5 min and 10 min after spinal puncture. Only in Group BD arterial pressure was holding on accurate baseline obtained before spinal anaesthesia and avoid a decrease to < 80 % baseline.

Table 1

The review of mean arterial pressure (MAP) in the research groups

MAP	Group	Quartile		
		Q_1	Me	Q_3
0 min	BD	85	95	98
	B	87	96	99
	D	85	94	97
1 min	BD	88	97	103
	B	94	95	102
	D	90	98	100
5 min	BD	69	70	75
	B	54	57	60
	D	63	65	69
10 min	BD	74	77	80
	B	65	66	69
	D	71	74	80
20 min	BD	83	85	87
	B	88	81	83
	D	82	83	85

Arterial hypotension, nausea, vomiting, bradycardia, shivering are the most frequent complications of spinal anaesthesia for caesarean section (**Table 2**).

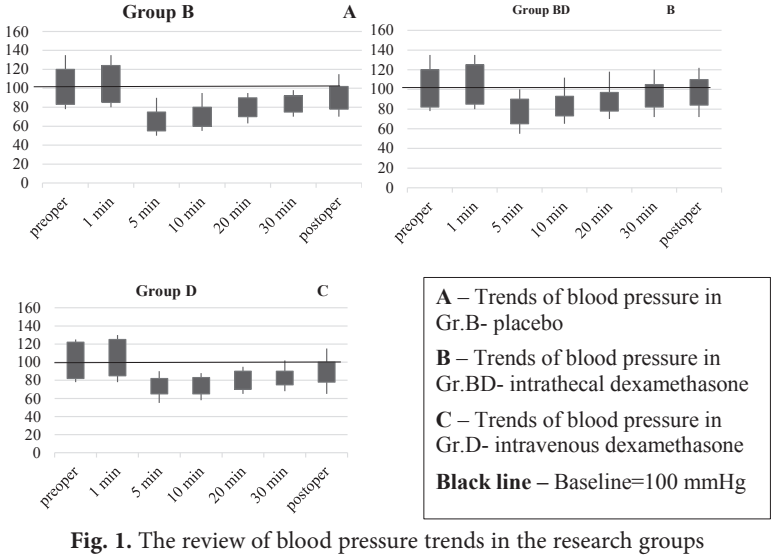

Fig. 1. The review of blood pressure trends in the research groups

Table 2
The review of complications in the research groups

Complications*	Group			Fisher`s F- test		p-value		Pearson's χ^2		Efficacy
	B, n=51	BD, n=52	B, n=51	B-BD	B-D	B-BD	B-D	B-BD	B-D	B-BD
Arterial hypoten-sion	33	15	27	0.004	0.236	p≤0.05	p≥0.05	0.479	0.169	strong
Nausea	26	9	24	0.003	0.843	p≤0.05	p≥0.05	0.474	0.056	strong
Vomi-ting	5	1	2	0.269	0.274	p≥0.05	p≥0.05	0.166	0.158	weak
Brady-cardia	15	6	11	0.029	0.376	p≤0.05	p≥0.05	0.306	0.127	middle
Shive-ring	23	12	19	0.023	0.546	p≤0.05	p≥0.05	0.321	0.124	middle

Note: complication that required medicines correction

4. Discussion

The addition of intrathecal dexamethasone in Group BD vs Group B significantly decreased frequency and manifestations of arterial hypotension and nausea (Pearson's χ^2=0.486 and χ^2=0.479, p=0.002 in both cases) in intra- and postoperative period after the spinal anaesthesia in elective caesarean section.

After intrathecal dexamethasone addition mean arterial pressure (MAP) will be significantly higher (p≤0.012 and p≤0.023) at 5 min and 10 min after spinal puncture.

The addition of intrathecal dexamethasone in Group BD vs Group B significantly reduced shivering (Pearson's χ^2=0.316, p<0.05) in intra- and postoperative period, and significantly didn`t affected on vomiting and bradycardia.

Intravenous and intrathecal dexamethasone has the same impact factor for nausea (no significant difference, p=0.539) during spinal anaesthesia for elective caesarean section, but intrathecal dexamethasone is better for prevention arterial hypotension (p=0.002).

Only whole complex of intervention, including different impact factors, can prevent or reduce some early complications of spinal anaesthesia, such as arterial hypotonia, nausea, vomiting, bradycardia, shivering etc.

A lot of systematic reviews and network meta-analysis allow us to compare methods of prevention maternal hypotension, nausea and vomiting, pruritus in women receiving spinal anaesthesia for caesarean section [1–3]. There are a lot of information about intravenous dexamethasone for this purpose [4, 12]. But there are absent large, high-quality evidence studies about intrathecal dexamethasone for prevention early complications of spinal anaesthesia for elective caesarean section, such as arterial hypotonia, nausea, vomiting, bradycardia, shivering etc.

The advantage of the studied method of spinal anaesthesia for elective caesarean section is availability to reduce the incidence and manifestations of early complications of spinal anaesthesia by using one single-shot injection of complex medicines (local anaesthetic bupivacaine 0.5 % 10 mg and additionally 4 mg intrathecal dexamethasone as adjuvant).

The disadvantages of this method are unclear mechanism of the actions for intrathecal dexamethasone, insufficient data about optimal dose and long-term effects of intrathecal dexamethasone, the need for legal support and implementation of new spinal anesthesia protocols and drug instructions for using intrathecal dexamethasone, introduction of new preservative-free forms of drugs, etc. Implementation of this method in patients with preeclampsia has certain limitations (due to the blood pressure increasing effect).

That is why there is still a need for large randomised multicentral clinical trials to research intrathecal dexamethasone as an adjuvant for spinal anaesthesia for elective caesarean section.

As a result, it will be able to obtain and implement a new methodology for spinal anaesthesia of elective caesarean section, which will improve the patient's well-being during cesarean section and in the postoperative period, will promote early activation and socialization of the patient.

Study limitations. The small number of patients in the sample groups and the limited time period were certain limitations for this study.

Prospects for further research. The addition of intrathecal dexamethasone as an adjuvant for spinal anaesthesia of elective caesarean section improve the patient's well-being during cesarean section and in the postoperative period and facilitate early activation and socialization of the patient.

There is still a need for large randomised multicentral clinical trials to research intrathecal dexamethasone as an adjuvant for spinal anaesthesia for elective caesarean section (for clarification and study of new properties, mechanism of action, optimal dose, long-term effects of this medicine and method of anaesthesia).

5. Conclusions

Maternal hypotension is the most frequent complication of spinal anaesthesia for caesarean section and can be associated with nausea and vomiting. But while interventions such as crystalloids, colloids, ephedrine, phenylephrine, ondansetron, left lateral position, or lower leg compression can reduce the incidence of hypotension, none have been shown to eliminate the need to treat maternal hypotension in some women.

The addition of 4 mg intrathecal dexamethasone as an adjuvant for spinal anaesthesia can significantly decrease frequency and manifestations of arterial hypotonia and nausea, reduce shivering during perioperative period. The addition of 8 mg intravenous dexamethasone has not the same quality.

Conflict of interests

The authors declare that they have no conflicts of interest.

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