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Research Article

Dexamethasone for Management of Nausea and Vomiting during and after Spinal Anaesthesia for Elective Caesarean Section

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Abstract

Spinal anesthesia is widely performed for elective caesarean section. But some early complications of spinal anesthesia, especially arterial hypotonia, shivering, nausea and vomiting, pruritus can nullify all the benefits of this anesthesia.

This randomized, prospective, clinical experimental, placebo-controlled study was undertaken to compare the efficiency of intrathecal introduction of dexamethasone or intravenous introduction combination of dexamethasone and ondansetron for prevention nausea and vomiting, arterial hypotonia, shivering during and after spinal anesthesia for elective caesarean section. All 124 healthy patients were randomized by age (18 - 38 years), weight and BMI (65 - 95 kg, BMI = 20 - 29), gestational period (36 - 40 weeks), ASA grade (I-II), indications for surgery (not urgent), total blood loss volume (500 - 800 ml), duration of surgery (20 - 40 min), and postoperative period in PACU (6 - 10 hours).

Base combination for intrathecal administration for each patient were hyperbaric bupivacaine 0.5% 11 mg, intrathecal 10 mcg fentanyl and intrathecal 100 mcg morphine.

Group KONTR (n = 41) additionally received intrathecal 1ml of normal saline like placebo.

Group ITD (n = 42) additionally received 4mg (1ml) intrathecal dexamethasone, and Group IVDO (n = 41) received intravenous combination of 8mg dexamethasone and 4mg ondansetron directly after spinal punction.

All data of patient`s monitoring during operation, all the complications during and after spinal anesthesia for elective caesarean section were entered into the individual observation card of the patient. The occurrence of nausea, vomiting, arterial hypotension and shivering were a point of special interest in this study.

Software SPSS 22.0 and methods of variational statistics used to analyze data base.

Induced by spinal anesthesia for elective caesarean section arterial hypotensia and nausea in Group ITD (intrathecal dexamethasone) vs KONTR Group significantly decreased (Pearson's $\chi^2 = 0.487$ and $\chi^2 = 0.479$, $p = 0.002$ in both cases). Mean arterial pressure (MAP) was significantly higher at ($p \leq 0.014$ and $p \leq 0.026$) at 5 minutes and 10 minutes after spinal punction in Group ITD. Cases of nausea the most common in KONTR Group (intrathecal base combination bupivacaine with opioids and placebo). Nausea occurred with equal frequency ($p = 0.539$) in Group ITD (intrathecal dexamethasone) and IVDO (intravenous dexamethasone plus ondansetron combination), but intrathecal dexamethasone additionally prevented the occurrence of arterial hypotensia ($p = 0.002$). There was no significant difference between the groups in occurrence of vomiting (a small number of casas for reliable statistical analysis). Induced by spinal anesthesia for elective caesarean section shivering in Group ITD (intrathecal dexamethasone) vs Group KONTR was significantly lower frequency (Pearson's $\chi^2 = 0.325$, $p < 0.05$) in intra- and postoperative period.

Keywords: Dexamethasone; Ondansetron; Spinal Anesthesia; Adjuvant; Caesarean Section; Nausea; Vomiting; Arterial Hypotension

Abbreviations

IONP: Intraoperative Nausea and Vomiting; PONV: Postoperative Nausea and Vomiting; SAT: Systolic Arterial Pressure; MAP: Mean Arterial Pressure; MAP0: Mean Arterial Pressure Before Operation; MAPF: Mean Arterial Pressure at the End of Operation; MAP1: Mean Arterial Pressure After Spinal Anesthesia; MAP5, MAP10, MAP20: Mean Arterial Pressure at 5, 10, 20 Min of Operation; PACU: Postanesthesia Care Unit; KONTR: Group Received Intrathecal 1 ml of Normal Saline Like Placebo; ITD: Group Received 4 mg (1 ml) Intrathecal Dexamethasone; IVDO: Group Received Intravenous Combination of 8 mg Dexamethasone and 4 mg Ondansetron Directly After Spinal Punction

Introduction

Spinal anesthesia is widely performed for elective caesarean section. The best benefit of spinal anesthesia for elective caesarean section is the mother`s ability to be conscious when her child is delivered. Despite its simplicity and wide implementation, some early complications of spinal anesthesia, especially arterial hypotonia, shivering, pruritus, nausea, vomiting can nullify all the benefits of this anesthesia.

Induced by spinal anesthesia maternal arterial hypotensia can affect 85% of women undergoing elective caesarean section. It can be trigger for nausea, vomiting, shivering in perioperative period. All these factors can be a source of complications for mother (pulmonary aspiration, unconsciousness) and child (hypoxia, fetal acidosis, neurological injury etc) [1,2]. All these complications are also caused significantly longer stay in the postanesthesia care unit (PACU) and increased the total duration of hospitalization and medical care outgoings [13-15].

Thus, all these complications can be a significant negative experience, increase dissatisfaction of medical care and can compromise this method of anesthesia.

Young nonsmoking women with perioperative nausea and vomiting, motion sickness in anamnesis is the most vulnerable to occurrence of IONV or PONV during and after spinal anesthesia for caesarean section (evidence B1) [16]. Obstetric and gynecological surgery are also associated with an increased risk of IONV and PONV (evidence B1) [16]. The aetiology of IONV and PONV in obstetric surgery is multifactorial. Spinal anaesthesia caused the sympathetic vasomotor block and low systemic vascular resistance. Increased size of the uterus with the baby during pregnancy in supine position caused vena cava inferior compression and as resulting maternal arterial hypotension. Acute arterial hypotension reduces cerebral perfusion and causes transient brainstem ischaemia and activates the vomiting centre [3]. Progesterone background affects the development of secondary low systemic vascular resistance and artery vasodilatation during pregnancy. There is also hormonally caused hypersensitivity of nerve fibers of local anesthetics and opioids. Intraoperative pain and medication, especially uterotonics and antibiotics are associated with an increased risk of IONV and PONV. Uterine exteriorization and peritoneal irrigation are associated with surgical techniques that increase risks of intra- or postoperative nausea, vomiting and shivering. The frequency of perioperative nausea and vomiting, pruritus are significantly higher in patients who have such medication as intrathecal opiate during spinal anesthesia (till 60% - 80%) [5,6].

Accordingly, the many important risk factors and their relative contribution are summarized in patients with spinal anesthesia for elective caesarean section. Thus, just extended multimodal strategy should be used to prevent arterial hypotension, nausea, vomiting, shivering and pruritus during and after spinal anesthesia with a patient undergoing elective cesarean section [13,14,16].

The systematic reviews and network meta-analysis allow specialists to compare and choose appropriate impact strategies for maternal hypotension, IONV and PONV, shivering, pruritus for women undergoing spinal anaesthesia for caesarean section [1-3]. Such interventions as crystalloids or colloids infusion; vasopressor infusion, ondansetron, left lateral position or lower leg compression, etc. can reduce the incidence of maternal hypotension but only in combinations of influences. The main purpose should be to keep the level of systolic arterial pressure (SAP) at ≥ 90% of baseline measured before spinal anaesthesia and avoid a decrease it more than 20% from baseline. Vasopressors are the first line to prevention hypotension during spinal anaesthesia for cesarean section (Gr. high to moderate) [2,4]. Variable rate prophylactic infusion of phenylephrine (from 25 - 50 $\mu g.min^{-1}$ immediately after the intrathecal local anaesthetic injection and continuous infusion at the same rate with the correction due to blood pressure and pulse level) are widely recommended [3,4]. Mean arterial pressure (MAP) is a determinant of organ perfusion and more important variable for prevention early complications of spinal anaesthesia for cesarean section. But in routine clinical practice MAP determination needs further implementation.

Due to important influence and multifactorial causes of arterial hypotension, nausea and vomiting during and after spinal anesthesia for elective cesarean section the search of new direction and methods of prevention these complications is always relevant.

Dexamethasone is a long-acting synthetic corticosteroid with pronounced anti-inflammatory, anti-allergic and antipruritic effects without mineralocorticoid properties. It modulates all stages of inflammatory process, reduces the permeability of blood vessels, the release of kinins and other biologically active substances. Dexamethasone effects on selective μ-receptors (opioid-like effect), has direct stabilizing effect on nerve fibers (nociceptive C-fibers) and causes local vasoconstriction [19,20]. Due to these properties dexamethasone has potentiate analgesic effect, not only intrinsic anti-inflammatory. Thus, over the last decade dexamethasone has been explored as an adjuvant to local anesthetics for neuraxial anesthesia and peripheral nerve blocks [7,8,10,19,20]. Due to systemic and local anti-inflammatory and analgetic influences perineural and intravenous dexamethasone may prolong duration of sensory block. These properties make dexamethasone effective adjuvant for postoperative pain management, and it may reduce postoperative opioid consumption without any complications [9,12].

For perioperative nausea and vomiting management corticosteroids are widely used for many years. Currently, the recommended dose of dexamethasone for prevention IONV, PONV is determined between 4 and 10 mg. Additionally, the early dosing of dexamethasone at the beginning of a surgical intervention better than at the end of operation for the prevention of PONV according to recent studies [16]. The question of safety perineural, intrathecal and intravenous introduction dexamethasone has been raised in numerous studies. A recent Cochrane Database analysis of 37 trials and additional review of 56 trials concluded that dexamethasone especially single dose, did not increase wound infection rates, systemic infection rates, anastomotic leak, wound healing, bleeding, or clinically significant hyperglycemia, but with wide confidence interval [1].

Ondansetron is widely recommended and studied 5-HT_3 receptor antagonist in perioperative nausea and vomiting management (evidence A1) [16-18]. Single dose of ondansetron (4 - 8 mg intravenous) or the same with combination of medication have strong antivomiting and antinausea effects [16]. Ondansetron has better antivomiting and antinausea effects than 10 mg metoclopramide intravenous and similar antivomiting and antinausea effects compared to dexamethasone 4 - 8 mg intravenous [16]. Preemptive combination of dexamethasone and ondansetron intravenous significantly reduced the incidence of perioperative nausea and vomiting for parturients after intrathecal morphine for caesarean section [13].

Thus, just extended multimodal strategy should be used to prevent arterial hypotension, nausea, vomiting, shivering and pruritus during and after spinal anesthesia with a patient undergoing elective cesarean section [13,14,16].

Aim of the Study

The aim of this study was to compare the efficiency of intrathecal dexamethasone or intravenous combination of dexamethasone and ondansetron for prevention nausea and vomiting, arterial hypotonia, shivering during and after spinal anesthesia for elective caesarean section.

Materials and Methods

This clinical trial were conducted in Kyiv City Center of Reproductive and Perinatal Medicine during 2018 - 2020.

The study is randomized, prospective, placebo-controlled experimental clinical trial for eexpansion of indications for use already known medicines. Research design was certified by Ethics committee of Shupik National Healthcare University of Ukraine. This clinical trial was complied with international regulations and with the current legislation of Ukraine. All the patients were informed regarding aim and methods of the trial and had provided the written informed consent due to current legislation of Ukraine.

All 124 healthy parturients were randomized by age (18 - 38 years), weight and BMI (65 - 95 kg, BMI = 20 - 29), gestational period (36 - 40 weeks), ASA grade (I-II), indications for surgery (not urgent), total blood loss volume (500 - 800 ml), duration of surgery (20 - 40 min), and postoperative period in PACU (6 - 10 hours).

Spinal anesthesia was conducted in the sitting or lying position at the L2/3 interspace with 25G Pencil point needle. For prevention arterial hypotension were used co-load infusion of crystalloids, 15° left lateral tilt position with using an special shaped wedge for reducing aortocaval compression and prophylactic infusion of phenylephrine (from 25 - 50 $\mu g.min^{-1}$ immediately after the spinal punction).

Base combination for intrathecal administration for each patient were hyperbaric bupivacaine 0.5% 11 mg, intrathecal 10 mcg fentanyl and intrathecal 100 mcg morphine:

- Group KONTR (n = 41) additionally received intrathecal 1 ml of normal saline like placebo.
- Group ITD (n = 42) additionally received 4 mg (1 ml) intrathecal dexamethasone, and

- Group IVDO (n = 41) received intravenous combination of 8 mg dexamethasone and 4mg ondansetron directly after spinal punction.

During cesarean section we fixed all data of patient`s monitoring before spinal punction, on 1, 5, 10, 20, 30 minutes of surgical intervention, at the end of operation. Patient`s monitoring data were recorded every hour during 24 hours of postoperative period. Blood pressure rate (including mean arterial pressure (MAP)), heart rate, pulse rate, breath rate, saturation, temperature, Apgar score of the newborn at 1 and 5 minutes of life were entered into the individual observation card of the patient. In case of complications, such as arterial hypotonia, nausea, vomiting, shivering or other complications during intra- or postoperative period - the time of occurrence, mode of manifestation and required medicines for correction were entered into the individual observation card of the patient.

Software SPSS 22.0 and methods of variational statistics used to analyze data base. Continuous variables were presented as mean ± standard deviation when they were normally distributed, or median and interquartile range if otherwise. Categorical variables were studied as frequencies and percentages. Mann-Whitney criteria were used for intergroup differences and quantitative values. The qualitative variables were analyzed by the χ^2 test and exact Fisher test. All differences were considered statistically significant with $p \leq 0.05$.

Results and Discussion

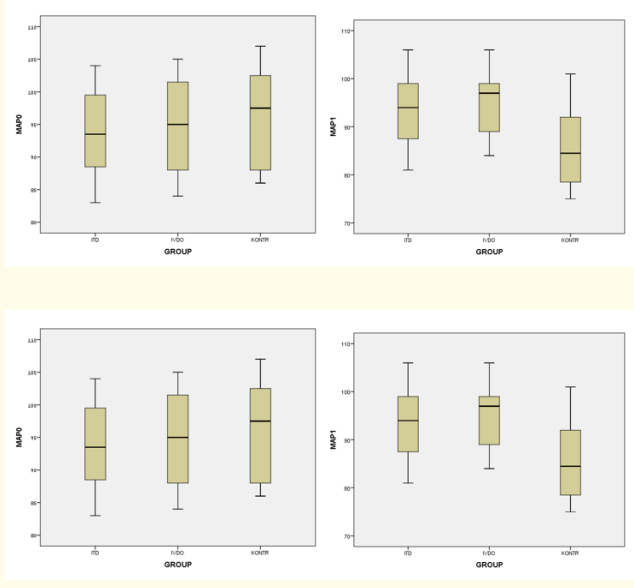
Organ perfusion is best assessed by mean arterial pressure (MAP), than by systolic or diastolic arterial pressure. It is important variable for detection and prognosis of early complications of spinal anaesthesia for cesarean section. Due to abnormally distributed variables in nonparametric analysis mean arterial pressure (MAP) were presented as median and interquartile range in table 1.

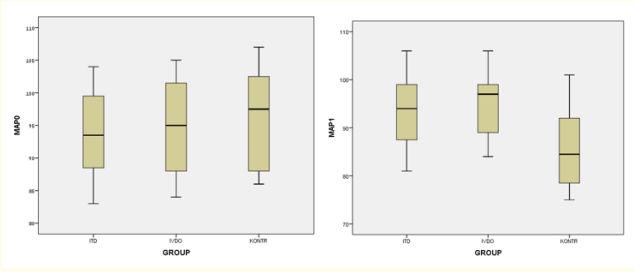
Mean arterial pressure (MAP) was significantly higher at ($p \leq 0.014$ and $p \leq 0.026$) at 5 minutes and 10 minutes after spinal punction in Group ITD vs KONTR Group after pairwise group comparisons. There was no significant difference between the groups at 0 minute, 1 minute, 30 minutes after spinal punction. The mean arterial pressure (MAP) variables were presented as box plot diagrams at picture 1 for better visibility.

The database presented on box plot diagrams allowed us to conclude that mean arterial pressure (MAP) was significantly higher at ($p \leq 0.014$ and $p \leq 0.026$) at 5 minutes and 10 minutes after spinal

MAP	Group	Q_1	Me	Q_3
0 min	KONTR	92,48	97,50	99,22
	ITD	90,45	93,50	96,65
	IVDO	91,10	95,00	97,95
1 min	KONTR	85,98	87,50	91,92
	ITD	90,38	94,00	97,42
	IVDO	91,88	96,50	98,12
5 min	KONTR	60,42	62,00	64,18
	ITD	68,22	70,00	72,98
	IVDO	65,79	67,00	69,37
10 min	KONTR	65,52	69,00	69,28
	ITD	74,41	78,00	79,29
	IVDO	70,51	75,00	75,39
20 min	KONTR	68,23	69,50	71,71
	ITD	81,54	83,50	85,60
	IVDO	74,27	76,00	79,52
30 min	KONTR	80,40	83,00	84,60
	ITD	83,03	85,50	88,07
	IVDO	82,46	85,00	87,01

Table 1: The mean arterial pressure (MAP) variables in the trial groups.





Picture 1: The mean arterial pressure (MAP) variables in the trial groups.

MAP0- Mean arterial pressure before operation; MAP1- Mean arterial pressure after spinal anesthesia: MAP5, MAP10, MAP20- Mean arterial pressure at 5, 10, 20 min of operation; MAPF- Mean arterial pressure at the end of operation; KONTR- Group with intrathecal placebo; ITD - Group with intrathecal dexamethasone; IVDO - Group with intravenous complex dexamethasone+ondansetron.

punction in Group ITD vs KONTR Group. There was no significant difference between the groups at 0 minute, 1 minute, 30 minutes after spinal punction.

Only in group ITD (intrathecal dexamethasone) arterial pressure kept at the level + 10% of baseline measured before spinal anaesthesia and avoided fluctuations more than 20% from baseline.

Despite its simplicity and wide implementation, some early complications of spinal anesthesia, especially arterial hypotonia, shivering, pruritus, nausea, vomiting can nullify all the benefits of this anesthesia. The review of complications rate was presented in table 2.

Induced by spinal anesthesia arterial hypotensia and nausea in Group ITD (intrathecal dexamethasone) vs KONTR Group significantly decreased (Pearson's $\chi^2 = 0.487$ and $\chi^2 = 0.479$, $p = 0.002$ and $p = 0.013$ in accordance). Cases of nausea the most common in KONTR Group (intrathecal base combination bupivacaine with opioids and placebo). Nausea occurred with equal frequency ($p = 0.539$) in Group ITD (intrathecal dexamethasone) and IVDO (intravenous dexamethasone plus ondansetron combination), but intrathecal dexamethasone additionally prevented the occurrence of arterial hypotensia ($p = 0.002$). There was no significant difference between the groups in occurrence of vomiting (a small number of casas for reliable statistical analysis). Induced by spinal anesthesia for elective caesarean section shivering in Group ITD (intrathecal dexamethasone) vs Group KONTR was significantly lower frequency (Pearson's $\chi^2 = 0.325$, $p < 0.05$) in intra- and postoperative period.

Complications*	Group KONTR, n = 41	Group ITD, n = 42	Group IVDO, n = 41	Fisher`s F- test		p-value		Pearson's χ^2		Efficacy
				KONTR-ITD	KONTR-IVDO	KONTR-ITD	KONTR-IVDO	KONTR-ITD	KONTR-IVDO	KONTR-ITD
Arterial hypo-tension	27	12	18	0.0191	0.0751	p≤0.05	p≥0.05	0.487	0.215	Strong
Nausea	21	7	12	0.0127	0.0476	p≤0.05	p≤0.05	0.479	0.309	Strong
Vomiting	4	1	1	0.202	0.202	p≥0.05	p≥0.05	0.217	0.217	Weak
Shivering	19	10	14	0.039	0.276	p≤0.05	p≥0.05	0.325	0.175	Middle

Table 2: The complications rate in the trial groups.

*Complications in which medicines correction was applied.

The systematic reviews and network meta-analysis allow specialists to compare and choose appropriate impact strategies for maternal hypotension, IONV and PONV, shivering, pruritus for women undergoing spinal anaesthesia for caesarean section [1-3]. Different directions of appointment of dexamethasone or ondansetron for this purpose are explored [5,7]. But only a small number of studies about intrathecal appointment of dexamethasone for prevention early complications of spinal anaesthesia for elective caesarean section have been identified. Therefore, the study of intrathecal dexamethasone as an adjuvant for spinal anaesthesia for elective caesarean section is considered a promised direction.

In our opinion, it would be appropriate to combine intrathecal dexamethasone and intravenous combination of dexamethasone plus ondansetron at the beginning of the elective caesarean section. Also, we will explore patient's blood glucose level, serum insulin level and noradrenaline level, cortisol level in the patient's daily urine, Apgar score of the newborn at 1 and 5 minutes of life, the pH level of the umbilical cord blood of the newborn, the level and duration of sensory and motor block during spinal anaesthesia, pain assessment on the VAS and NPRS scale, time to first analgesic request, total opioids consumption in the postoperative period. It will be a further direction of our research.

Conclusion

Spinal anesthesia is widely performed for elective caesarean section. Despite its simplicity and wide implementation, some early complications of spinal anesthesia, especially arterial hypotonia, shivering, pruritus, nausea, vomiting can nullify all the benefits of this anesthesia. All these complications can be a significant negative experience, increase dissatisfaction of medical care and can compromise this method of anesthesia. All these factors can be a source of complications for mother and child. They are also caused significantly longer stay in the postanesthesia care unit and increased the total duration of hospitalization and medical care outgoings [13-15].

Such interventions as crystalloids infusion; vasopressor infusion, ondansetron, left lateral tilt position or lower leg compression can reduce the incidence of maternal hypotension and other early complications but only in combinations of influences.

Intrathecal dexamethasone as an adjuvant of spinal anaesthesia for elective caesarean section is considered a perspective direction for early complication management. Spinal anesthesia induced arterial hypotensia and nausea significantly decreases after intrathecal dexamethasone appointment (Pearson's $\chi^2 = 0.487$ and $\chi^2 = 0.479$, $p = 0.002$ and $p = 0.013$ in accordance). Mean arterial pressure (MAP) was significantly higher at ($p \leq 0.014$ and $p \leq 0.026$) at 5 minutes and 10 minutes after spinal punction in intrathecal group. Nausea decreases with equal frequency ($p = 0.539$) with appointment of intrathecal dexamethasone and intravenous dexamethasone plus ondansetron combination, but intrathecal dexamethasone additionally prevented the occurrence of arterial hypotensia ($p = 0.002$). Induced by spinal anesthesia for elective caesarean section shivering has significantly lower frequency with intrathecal dexamethasone (Pearson's $\chi^2 = 0.325$, $p < 0.05$).

Therefore, just extended multimodal strategy with different influencing factors should be used to prevent arterial hypotension, nausea, vomiting, shivering and pruritus during and after spinal anesthesia for a woman undergoing elective cesarean section. It will improve the patient's satisfaction during and after operation, will promote early activation and socialization of the patient, and will save health care funds.

Conflict of Interests

No conflict of interest.

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