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CLINICAL STUDY

Caesarean section in isobaric spinal anesthesia with and without direct preoperative hydration with crystalloids

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Abstract: *Background:* Because the direct preoperative hydration with crystalloids (20 ml/kg) does not adequately prevent spinal hypotension during cesarean section, the authors investigated whether a continuous intravenous infusion of ephedrine (50 mg/500 ml of Ringer solution) without preoperative hydration would prevent the spinal hypotension more effectively.
Methods: Forty parturients with ASA status I were randomized either to receive a preoperative hydration with 20 ml/kg of Ringer solution, or to receive continuous ephedrine infusion, simultaneously with spinal anesthesia. The infusion rate was adjusted according to systolic blood pressure. Significant hypotension was defined as a systolic blood pressure below 100 mmHg. Rescue boluses consisted of ephedrine 10 mg in parturients with prehydration and ephedrine 5 mg in parturients with ephedrine infusion.
Results: Significant hypotension occurred less frequently in the ephedrine group than in the volume group: 40 % versus 60 % ($p<0.05$). Nausea and vomiting occurred less frequently in the ephedrine group than in the volume group: 40 % and 30 % versus 60 % and 50 %, respectively ($p<0.05$). The mean quantity of infused Ringer solution was 370 ml ± 31 in the ephedrine group, i.e. significantly lower than 1,640 ml ± 192 in the volume group ($p<0.05$). The mean quantity of ephedrine given in the ephedrine group was 30 mg ± 4.1. The mean quantity of ephedrine given in the volume group was 25 mg ± 2. The difference was not significant. Apgar scores were similarly good in both groups.
Conclusion: The continuous infusion of ephedrine simultaneously with spinal anesthesia is superior to direct preoperative hydration with crystalloids in preventing the spinal hypotension and its clinical manifestations in parturients delivered with C-section *(Tab. 3, Ref. 20).* Full Text in free PDF *www.bmj.sk.*
Key words: spinal anesthesia, Caesarean section, spinal hypotension, ephedrine, crystalloids.

Spinal anesthesia (SA) for cesarean section (C-section) is gradually substituting the general anesthesia. International goal for protection of future mothers is 80–90 % of all C-sections to be done in SA. It is because 1:250 parturients have difficult intubation (1). SA for C-section is a simple and reliable anesthesiological technique. It provides a high-quality sensory and motor block, which begins quickly after the intrathecal injection with local anesthetic (2). The fetal exposure to medicaments is minimal, while the parturient is conscious with preserved protective reflexes. The latter properties avoid the risk of aspiration. The most importanat advantage of SA over the general anesthesia is that the preoperative mortality of parturients during SA is reduced seven-fold (3).

The extensive sympathycolysis causes arteriolar dilatation, venodilatation and suppression of the inotropy and chronotropy of the heart. This in combination with the aorto-caval compression leads rapidly to hypotension, bradycardia and low cardiac output. Arterial hypotension is a dangerous complication for the parturient as well as for the fetus. The arterial hypotension manifests itself with clinical signs on the parturient´s side, namely nausea, vomiting and yawning. The long-lasting profound hypotension causes fetal acidosis and neonatal depression (4).

In the clinical practice, the methods used to prevent hypotension include direct preoperative hydration with crystalloids and/or colloids, use of vasopressor medicaments such as ephedrine, phenylephrine, and their combination, leg compression, use of small intrathecal doses of local anesthetics together with opioids and positioning of the parturient on the operative table.

Tab. 1. Demographic characteristics.

	V n=20	E n=20
Age (years)	23.6±2.4	24.3±2.8
Body weight (kg)	73.2±8.3	72.3±8.9
Syst. art. pressure (mmHg))	123±14.3	131±14.9
SaO2 (%)	98 ±1	98±1

The numbers are arithmetical mean values ± SD. No significant difference between the groups.

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Motive

In our everyday practice we frequently encounter the problem of hypotension despite meticulously performed direct preoperative hydration with crystalloids. This hydration in the majority of parturients was not effective in preventing the hypotension. We have to intervene with intravenous boluses of ephedrine to correct the hypotension. This prompted us to assume that a continuous infusion of ephedrine could be a good method to prevent hypotension. The design of this study aims to check this hypothesis.

The purpose of the study

The purpose of this study was: a) to examine and compare the success rate in preventing the hypotension with the conventional, standard method with direct preoperative hydration with crystalloids compared with the method of continuous intravenous infusion of ephedrine without direct preoperative hydration in young and healthy parturients with normal pregnancy delivering with C-section, b) frequency of significant arterial hypotension (systolic pressure < 100 mmHg), c) quantity of crystalloids (ml) infused till the moment of clamping the umbilical cord d) quantity of ephedrine (mg) given intravenously till the moment of clamping the umbilical cord, e) presence of nausea and vomiting from the beginning of SA till the moment of clamping the umbilical cord, f) neonatal Apgar score in the immediate postdelivery period, g) time (min) from the beginning of SA till the moment of clamping the umbilical cord.

Patients and examined groups

This prospective and randomized study was carried out in the Clinical hospital Bitola. After receiving a written consent, 40 parturients with normal pregnancy were examined. C-section was elective and performed because of: breech presentation of the fetus, cefalo-pelvic disproportion and reoperation. The parturients were 21–28 years old and classified in the first group according to ASA classification. Parturients with body weigh > 90 kg and parturients who refused C-section were not included in this study. The parturients were distributed in two groups. Each group consisted of 20 parturients. The first group was designated as volume (V) and served as a control group, while the second group was designated as ephedrine (E) and represented the examined group.

Methods and analyzed parameters

The parturients were canulated with G-18 intravenous canula.

The parturients from group V received 20 ml/kg Ringer solution, warmed to room temperature 20–30 min before the beginning of SA. SA was performed in a sitting position in the vertebral interspace L3–L4. Spinal needle G-27 was used. After the identification of intrathecal position of the needle, 2.5ml of 0.5% isobaric bupivacine with 6.25 μg fentanyl ($^1/_8$ volume of the tuberculine syringe) were injected. After that the parturients were placed in a moderate left tilt position and moderate anti Trendelenburg position. They received 8 L/min O_2 via face mask. The arterial blood pressure was measured every 2 min with noninvasive method till the moment of clamping the umbilical cord, and every 5 min thereafter. EKG and pulse oxymetry were measured continuously with the "Nihon – Kohden life scope 8" monitor. Till the moment of clamping the umbilical cord, the parturients of this group continuosly received Ringer solution and ephedrine intravenous boluses of 10 mg if needed (when the systolic blood pressure was < 100 mmHg). After clamping the umbilical cord, the Ringer solution was replaced with a new one of 500 ml with 20 international units (i.u.) of oxytocine added.

In the parturients of group E, the direct preoperative hydration was not done. Immediately after the venous canulation, they received 500 ml of Ringer solution with 50 mg of ephedrine added. This infusion was a continuous fast-drop infusion. The spinal anesthesia in this group was performed in exactly the same way as in group V. The arterial blood pressure had been measured every 2 min with noninvasive method till the moment of clamping the umbilical cord, and every 5 min thereafter. EKG and pulse oxymetry were measured continuously with the "Nihon–Kohden life scope 8" monitor. Till the moment of clamping of the umbilical cord, the parturients of this group received Ringer solution with ephedrine added and intravenous boluses of 5 mg ephedrine if needed (when the systolic blood pressure was < 100 mmHg). After clamping the umbilical cord, this Ringer solution was replaced with a new one of 500 ml with 20 i.u. of oxytocine added.

During the study, the monitored and analyzed parameters included significant hypotension, nausea, vomiting, quantity of infused Ringer,s solution, quantity of given ephedrine, time from the moment of completing SA till the moment of clamping the umbilical cord, and the Apgar score of the newborn immediately after birth.

Significant hypotension was defined as systolic blood pressure of < 100 mmHg. Its frequency was registered.

The frequencies of nausea and vomiting were registered from the beginning of SA till the moment of clamping the umbilical cord.

The quantity of infused Ringer,s solution was registered from the beginning of infusion till the moment of clamping the umbilical cord.

In the parturients of group V, the quantity of injected ephedrine was registered from the beginning of SA till the moment of clamping the umbilical cord. The total dose of ephedrine was the sum of single ephedrine boluses of 10 mg.

In the parturients of group E, the quantity of given ephedrine was registered from the beginning of infusion of Ringer,s solution with ephedrine added till the moment of clamping the umbilical cord. The total dose of ephedrine was the sum of infused ephedrine (1mg /10ml) and single ephedrine boluses of 5 mg.

Statistical analysis

The demographic data, quantity of infused Ringer,s solution, quantity of given ephedrine, and the time from the beginning of SA till the moment of clamping the umbilical cord were expressed with the arithmetical mean value ± standard deviation (SD). They were analyzed with the method of comparison of arithmetical mean values for small non-dependant variables ($p < 0.05$). The numerical values for Apgar score were expressed with median value and analyzed with median test ($p < 0.05$).

Tab. 2. Results: significant hypotension, nausea and vomiting.

	V n=20	E n=20
Significant hypotension	12/20	8/20
Nausea	12/20	8/20
Vomiting	10/20	6/20

The numbers are quality frequencies. There is a significant difference between groups ($p<0.05$)

Tab. 3. Results: Ringer`s solution, ephedrine, time SA–UC[§] clamping and Apgar score.

	V n=20	E n=20
Ringer`s sol. (ml)	1640±192	370±3 1
Ephedrine (mg)	25±2	30±4.1
time SA–UC (min)	9.7±2.9	10.3±3.1
Apgar	9	9

[§]SA=spinal anesthesia; UC=umbilical cord
The numbers are arithmetical mean values ± SD. The numbers for Apgar score are median values..There is a significant difference for Ringer`s solution between the groups ($p<0.05$). Other parameters are not significant.

Results

The study was done on 40 parturients. No one was excluded from the study.

The demographic data of parturients were similar in both groups.

The parturients from control group had a statistically significant difference in frequency of appearance of significant hypotension, nausea and vomiting when compared with the partutients from analyzed group (Tab. 2).

The quantity of infused Ringer,s solution was greater in parturients of the control group when compared with those of the analyzed group. Noticeable is the smaller volume of Ringer,s solution infused in parturients of the analyzed group. The difference was statistically significant.

The quantity of ephedrine given to parturients of the analyzed group was greater compared to the control group. The difference was not significant.

The time from the beginning of SA till the moment of clamping the umbilical cord, and the Apgar score were similar for both groups (Tab. 3).

Discussion

The prevention of hypotension with preoperative hydration is an established method in clinical practice but studies of several authors showed that this method was not reliable (5, 6). This is because of fast redistribution of the infused solute as a consequence of vasodilatation and liberation of the atrial natriuretic peptide and endotheline-$_1$. These factors decrease the vascular tone and attenuate the effect of hydration (7). In the intravascular space only 20–25 % of the infused solute remains. The rest of the solute migrates to the already edematous interstitial space, and loads it in addition (8). The preoperative hydration is time-dependant and can provoke hypothermia should the solutes be not warm enough. The colloids are a better choice for this purpose than are crystalloids (9). In spite of hydration, the need for additional "rescue" intravenous boluses of vasoconstrictor medicaments to maintain a stable blood pressure is great (10). In our study, even 60 % of the parturients of group V needed ephedrine as a supplement.

As the cause of the hypotension during SA is the dilatation of blood vessels, the need to treat it with the use of medicaments causing vasoconstriction is logical.

Ephedrine is a directly acting β_1 and indirectly acting α_1 adrenergic agonist. One part of its vasoconstricting capacity is a result of elevated production of angiotensin-$_2$ (β_1 – renin effect of the juxtaglomerular apparatus). The continuous ephedrine use that parallels the vasodilatation is a simple and fast method for maintaining stable blood pressure (11).

The fact that only 7 parturients of E group needed additional ephedrine intravenous boluses of 5 mg speaks for the small number of parturients who manifested significant hypotension in this group.

The continuous ephedrine infusion that starts during SA performance, and the changing of its rate according to the level of blood pressure are more effective in maintaining a stable blood pressure than the preoperative hydration with crystalloids and supplemental intravenous ephedrine boluses. It provides a constant ephedrine plasma concentration (12). Our study confirmed this finding too.

Morgan showed that ephedrine in doses > 3–4 mg/min caused neonatal acidosis, as well as that the degree of acidosis was proportional to ephedrine doses (13). In our study, the doses of ephedrine in the control group and analyzed group were ≈2.6 mg/min (25±2 / 9.7±2.9), and ≈2.9 mg/min (30±4.1 / 10.3±3.1) respectively and were lower than the Morgan's dose (Tab. 3).

There is a proportional dependence between the severity of neonatal acidosis and the concentration of noradrenaline (ephedrine) in neonatal blood. The increased β_1-adrenergic fetal activity when O_2 utilization is maximal, leads to anaerobic glycolysis and metabolic acidosis (14). Regretfully, in our study, we could not determine the neonatal acidosis because of objective and technical reasons, which is a disadvantage of this study.

The paradoxical conclusion that ephedrine corrects the hypotension but at the same time causes neonatal acidosis, imposes the need for ephedrine to be substituted or combined with other vasoactive medicaments. Experiments showed that the pregnant uterus tolerates the vasoconstrictive effect of phenylephrine (15). Intravenous phenylephrine in a dose of 40–100 μg is effective and reliable for both parturient and fetus. It causes bradycardia in parturients. The parturients tolerate the bradycardia well unless associated with hypotension. The medicament of choice for the treatment of bradycardia is glycopirrolate (16). Therefore, phenylephrine which had been formerly contraindicated because of its pure α_1–adrenergic effect, began to find its place in obstetrics. The combined use of ephedrine and phenylephrine (combined α_1 and β_1 effect) is more effective in the prevention of hypotension, bradycardia, tachycardia, nausea, vomiting and fetal acidosis than the

ephedrine alone. This combination reduces the ephedrine dose for more than half. The cardiac output increases, the blood pressure keeps stable, and the fetal acidosis disappears (17). Regretfully, phenylephrine in R. Macedonia is still not registered.

The nausea and vomiting were more frequent in group V compared with group E. They were in close connection with the frequency of significant hypotension. These symptoms could be interpreted as clinical manifestations of parturient's hypotension. The increased vagal tone and decreased preload (decreased end-diastolic pressure in the heart) could explain the occurrence of these symptoms (18). One possible explanation for the reduced frequency of these symptoms in group E, could be the antiemetic effect of ephedrine alone (19).

The Apgar score immediately after the delivery was equally high in both groups. It spoke for the good condition of newborns. Apgar score is a better index for evaluating the well-being of newborns than acidosis (20).

The time from the beginning of SA (operative intervention) till the moment of clamping the umbilical cord was similar in both groups. The mean value of 10±3 min speaks for the good operative technique of gynecologists in our hospital

Conclusion

Our study showed that the maternal hypotension is a very frequent complication during C-section in SA.

The direct preoperative hydration with crystalloids is less effective in preventing the hypotension and its clinical manifestations compared to the continuous ephedrine infusion without preoperative hydration.

The parturients who were hydrated, needed supplemental "rescue" intravenous boluses of ephedrine in a great percentage.

The continuous infusion of ephedrine is a fast and effective method for preventing the hypotension and its clinical manifestations.

The results of this study investigate thoroughly the effect of preoperative hydration of parturients with crystalloids as a method for preventing the arterial hypotension during SA for C-section.

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