

The impact of colloid infusion prior to spinal anaesthesia for caesarean section on the condition of a newborn — a comparison of balanced and unbalanced hydroxyethyl starch 130/0.4

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Abstract

Background. Fluid therapy is the most commonly used treatment to prevent hypotension associated with spinal anaesthesia. The aim of this study was to test the hypothesis that a balanced solution of 6% hydroxyethyl starch will have a more beneficial impact on the condition of newborns at birth than an unbalanced 6% solution of HES.

Methods. The study participants included 51 healthy parturients undergoing elective caesarean section with spinal anaesthesia. Patients received a transfusion of 500 mL of unbalanced 6% HES (Voluven) or balanced 6% HES (Tetraspan) prior to anaesthesia. The condition of the newborn was assessed using the Apgar score, and the acid-base balances of venous and arterial umbilical cord blood were also measured.

Results. The incidence of hypotension after spinal anaesthesia was 80% in Group A and 76.9% in Group B ($P = 1.0$). There were no differences between the two groups in the total doses of ephedrine and no differences between treatment groups in Apgar scores. Also, no differences in acid-base balance parameters (pH, H^+ , pCO_2 , pO_2 , HCO_3^- , BE) were found.

Conclusion. A balanced 6% solution of hydroxyethyl starch (HES 130/0.42) did not significantly influence the condition of the newborns at birth or the acid-base and electrolyte concentration of newborns compared to an unbalanced solution of 6% hydroxyethyl starch (HES 130/0.4).

Key words: caesarean section, spinal anaesthesia; caesarean section, newborn condition; spinal anaesthesia, hypotension; balanced colloid solutions, hydroxyethyl starch

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Spinal anaesthesia is the commonest pain management system used during caesarean section. However, the extensive blockade of the sympathetic system that occurs during spinal anaesthesia frequently triggers a sharp reduction in maternal blood pressure. This may cause nausea, vomiting or shortness of breath. Hypotension may also lead to reduced bloodflow through the vascular bed of the uterus, which reduces perfusion and leads to hypoxia, acidosis and the poor health of the newborn [1, 2].

In 1968, Marx et al. [1] were the first to show that hypotension could be prevented by the transfusion of crystalloids. Since then, fluid therapy has become the most commonly used method of preventing falls in blood pressure

during spinal anaesthesia for caesarean section. Although 40 years have passed since the technique was first introduced, the most effective scheme for fluid administration remains unknown. Three major changes have been made to the fluid administration protocol: the type of fluid (i.e. crystalloids or colloids), the time of administration i.e. prior to anaesthesia (pre-load) or during anaesthesia (co-load), and the volume of transfused fluids.

Until recently, the most widely used fluids were crystalloids at doses of up to 30 mL kg^{-1} . Disappointing results, and the side effects from the rapid transfusion of crystalloids, led to the wider use of colloids, especially hydroxyethyl starch (HES) preparations. Many studies have demonstrated the

superior efficacy of the preventive infusion of colloid solutions for this purpose; the third-generation preparations of hydroxyethyl starch (HES) are generally used today. A risk of hyperchloraemia is associated with HES transfusions due to the use of 0.9% NaCl as a dispersion solution. To prevent hyperchloraemia, HES preparations have been produced in which the starch particles are suspended in a crystalloid solution balanced with an electrolyte composition that is similar to that of plasma i.e. chloride ions partially replaced by acetate or malate anions.

The aim of this study was to test the hypothesis that a balanced 6% hydroxyethyl starch solution would have a more positive effect on the health of the newborn than an unbalanced solution.

METHODS

The research protocols were approved by the Independent Bioethics Committee for Scientific Research at the Medical University of Gdansk. Study participants were in anaesthesia risk classes I and II as stratified by the American Society of Anesthesiologists (ASA) and underwent elective caesarean sections. We excluded patients who did not agree to participate in the study, had contraindications to perineural anaesthesia, or had one or more of the following exclusion criteria: multiple pregnancies, body mass greater than 115 kg, height less than 152 cm, age less than 18 years or more than 40 years, diabetes, pregnancy-induced hypertension, chronic hypertension and heart disease.

The study included 60 patients who were randomly divided into two groups. Patients in Group A received a 500 mL transfusion of 6% HES 130/0.4 with 0.9% NaCl used as the dispersal agent (Voluven, Fresenius Kabi Polska, Kutno, Poland) prior to anaesthesia; patients in Group B received 500 mL of 6% HES 130/0.42 in a physiological electrolyte solution (Tetraspan, B Braun, Melsungen, Germany) before anaesthesia. All patients were given an oral dose of 150 mg ranitidine 90 minutes before the anaesthetic, and 30 mL of 0.3 M sodium citrate solution 30 minutes before the anaesthetic.

Upon arrival in the operating room, the patient's systolic, diastolic and mean arterial pressures (SAP –15, DAP –15 and MAP –15 respectively) were measured using an automatic sphygmomanometer; these values constituted the baseline blood pressure. A drop in systolic pressure of 20% below the baseline pressure (or below 100 mm Hg) was adopted as the definition of hypotension requiring the administration of ephedrine.

A cannula was inserted into a peripheral vein, and transfusion of the randomly selected fluid was carried out over 15 minutes. After the transfusion, the spinal anaesthesia was delivered to the patient, who was placed in a seated position, using a 27G pencil-point needle. The puncture

was made in the L3–L4 or L4–L5 space. The dosage of bupivacaine hyperbaric solution was selected based on the mother's height (from 152 to 160 cm: 1.8 mL, 161 to 170 cm: 2.0 mL, above 170 cm: 2.2 mL). A 25- μ g dose of fentanyl was given with a local anaesthetic. The patient was then immediately placed on her back in a 15° counter-clockwise position. The scope of the block was determined based on patient feedback (report of feeling cold). Treatment was started after the patient achieved anaesthesia at the T4 level. Until the birth of the child, the patient did not receive any further fluid transfusions. Any decreases in blood pressure were adjusted by fractional (5–10 mg) doses of ephedrine administered intravenously. During the delivery, the patient received oxygen through a mask (40%). After delivery, 10 U of oxytocin was administered intravenously. The duration of hypotension was defined as the time elapsed from the onset of hypotension to the birth of the child (T-Hyp). The time elapsed from the time of anaesthesia to delivery (ADT), the time from the beginning of surgery to delivery (IDT), the time from the uterine incision to delivery (UDT), and the total dose of ephedrine given to the patient were also recorded.

The patient's blood pressure was checked every two minutes after administration of the anaesthetic and at the time of delivery. The patient's heart rate (HR) and the haemoglobin oxygen saturation of arterial blood were monitored continuously and non-invasively. The newborn's Apgar score was evaluated one, three, five and ten minutes after birth, and the newborn was weighed. The acid-base balance of the venous and arterial cord blood was also determined. Immediately after the umbilical cord was clamped and cut, one blood vessel of the umbilical cord was punctured. The blood was collected into heparinised syringes in 2-mL aliquots, and the acid-base balance was measured immediately after collection. The parameters analysed were pH, concentration of hydrogen ions (H^+), pCO_2 , pO_2 , the concentration of bicarbonate ions (HCO_3^-) and base excess (BE). Blood from the umbilical vein was also collected to determine the concentrations of sodium and chlorine ions.

STATISTICAL ANALYSIS

A minimal sample size of 25 per group was calculated assuming an α level = 0.05 and β level = 0.8. A significant change of pH was recognised when there was a difference between groups equal to 0.05, assuming a mean value of blood pH 7.43 ± 0.05 among newborns delivered by caesarean section under regional anaesthesia according to Petropoulos et al. [3].

The statistical analyses were conducted with Statistica 7.1 PL (Statsoft, Tulsa, OK, USA) as follows:

1. Continuous variables with normal distributions (verified by the Shapiro and Wilk tests) were compared us-

ing a Student's t-test for independent variables (after verification of homogeneity of variance by Levene's test) with an independent estimation of variance. ANOVA was used for comparisons between more than two groups. When ANOVA demonstrated intra- or inter-group differences, the data was subjected to detailed analysis with a post-hoc HSD (honest significant difference) Tukey test.

2. The U Mann-Whitney test was used to compare ordinal scale data and non-normally distributed continuous data.
3. Nominal scale data was compared using the chi-square test (Fisher's) or the Fisher-Snedecor test, as appropriate. The significance threshold was set at a *P* value of 0.05.

RESULTS

The study group was initially composed of 60 patients. Over the course of the study, five patients from Group A and four patients from Group B were removed from the study due to problems with cord blood collection for gasometric tests (e.g. inability to perform dual collection of blood samples from the same vessel or no collection). Successful tests were conducted in the remaining 51 patients (25 in Group A and 26 in Group B). The two groups did not differ with respect to age, weight, height, or gestational age. There were no significant differences in time from the ADT, IDT and UDT between the two groups (Tab. 1).

Both groups had similar baseline SAPs and HRs. Serial SAP and HR values taken ten minutes after the onset of spinal anaesthesia were not significantly different between the two groups (Figs. 1, 2). The incidence of hypotension after spinal anaesthesia was 80% in Group A and 76.9% in Group B (*P* = 1.0). The analysis revealed no significant differences between the groups with respect to the duration of hypotension from the beginning of anaesthesia to delivery (T-Hyp, *P* = 0.107). There were no differences between the two groups in the total doses of ephedrine. Data is shown in Table 2.

There were no differences between treatment groups in Apgar scores. All infants in both groups had Apgar scores greater than 7. Neonatal acidosis (pH in umbilical artery < 7.10 or umbilical vein < 7.20) was not recorded in either group. No differences in other acid-base balance parameters (H^+ , pCO_2 , pO_2 , HCO_3^- , BE) were found (Tab. 3).

DISCUSSION

Currently, there are no effective methods for preventing hypotension resulting from perineural anaesthesia in obstetric patients. Initial vascular filling (pre-loading) with crystalloids became a routine clinical practice after Marx et al. reported the procedure in 1969 [1, 2]. Subsequent publications have shown that the traditional pre-loading by crystalloids is not very effective, and its utility in preventing hypotension has been questioned [4, 5, 6, 7]. For the past several years, discussions regarding the appropriateness and efficacy of the procedure, as well as the most effective fluid, have been common in the literature. Different types of fluid therapy are currently used, but different studies investigating the most effective volume, type and rate of transfusion have reported inconsistent results [8, 9, 10]. In many centres, crystalloids remain the primary fluid transfused to patients before central blocking, despite many studies that have demonstrated a greater efficacy of prophylactic colloid transfusion.

The absence of satisfactory effects of the rapid transfusion of crystalloids and the associated side effects (risk of hyperchloraemic acidosis, increased secretion of atrial natriuretic peptide (ANP) and haemodilution leading to reduction of colloid-osmotic pressure) [11, 12, 13] has led to the wider use of colloids, especially the formulations of hydroxyethyl starch (HES). A 0.9% sodium chloride solution is used as the dispersive compound in the vast majority of hydroxyethyl starch formulations. Similar to other saline transfusions, this sodium chloride solution carries a risk of electrolyte imbalance. Balanced HES preparations, in which an isotonic solution with a plasma-like electrolyte

Table 1. Demographic, obstetric, anaesthetic and surgical data. Data is presented as the mean \pm SD or the median (IQR)

	Group A n = 25	Group B n = 26	<i>P</i> -value
Age (years)	30.8 \pm 4.5	29.4 \pm 4.1	0.247
Body mass (kg)	79.3 \pm 12.8	80.3 \pm 12.1	0.770
Height (cm)	167 (160–170)	166 (164–172)	0.434
Gestational age (weeks)	39 (39–40)	39 (39–40)	0.685
Nullipara/multipara (%)	32/68	42/58	1.0
Time from anaesthesia to delivery (min)	9 (7–11)	9.5 (9–12)	0.149
Time from skin incision to delivery (min)	4 (3–5)	4 (3–6)	0.932
Time from uterine incision to delivery (sec)	45 (35–90)	50 (30–65)	0.434

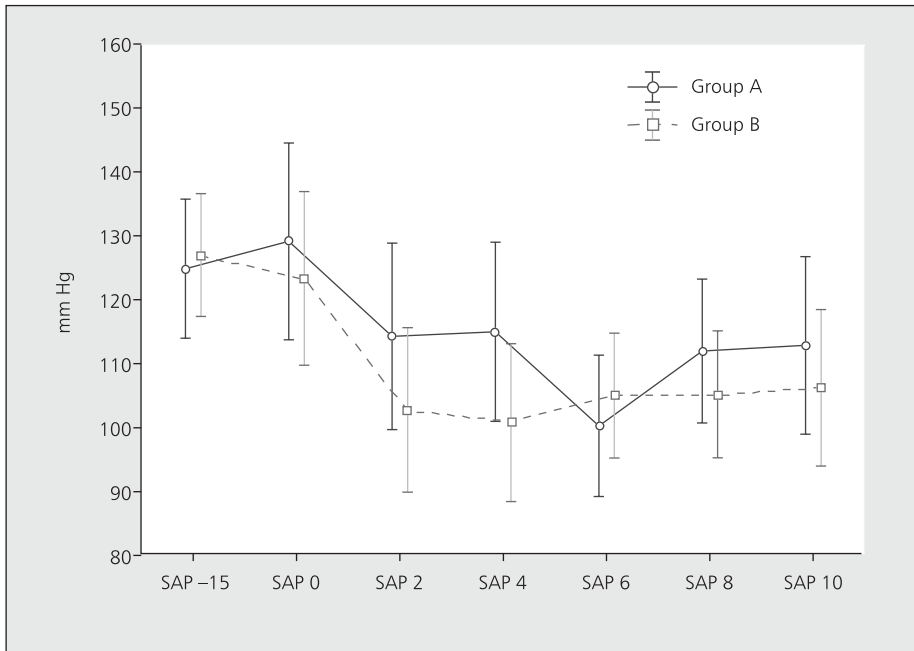


Figure 1. Systolic arterial pressure over time. Time course of maternal systolic pressures for ten minutes following spinal anaesthesia in Groups A and B. Data is presented as mean values with 95% confidence intervals (CI)

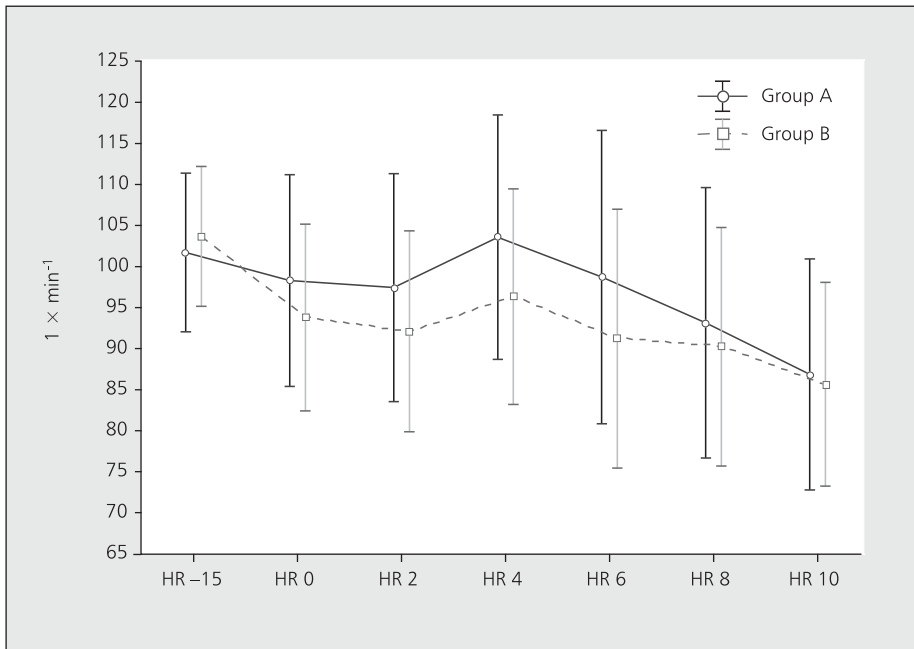


Figure 2. Heart rate over time. Time course of maternal heart rate for ten minutes following spinal anaesthesia in Groups A and B. Data is presented as mean values with 95% confidence intervals (CI)

composition is used as a dispersant, are used to prevent electrolyte imbalance.

This study compared third-generation preparations of hydroxyethyl starch to identical concentrations, molecular weights, degrees of DS substitution and C2/C6 ratios (6% HES 130/0.4) suspended in 0.9% NaCl (Voluven) or

a balanced electrolyte solution (Tetraspan). The aim of this study was to test the hypothesis that a balanced 6% hydroxyethyl starch solution would improve the acid-base and electrolyte economy and the general health condition of the newborn (assessed with the Apgar scale) relative to an unbalanced 6% hydroxyethyl starch solu-

Table 2. Haemodynamic variables and dose of ephedrine. Data is presented as the mean \pm SD or the median (IQR)

	Group A n = 25	Group B n = 26	P-value
Baseline systolic pressure (mm Hg)	123 \pm 11	126 \pm 11	0.414
Baseline heart rate (beats min ⁻¹)	103 \pm 12	97 \pm 13	0.066
Incidence of hypotension (%)	80	76.9	1.0
Dose of ephedrine (mg)	10 (5–15)	10 (0–20)	0.88
Duration of hypotension (min)	2 (1–3)	3 (1–6)	0.107

Table 3. Neonatal outcome data. Data is presented as the mean \pm SD or the median (IQR)

	Group A n = 25	Group B n = 26	P-value
Body mass (g)	3,449 \pm 488	3,480 \pm 412	0.808
Apgar score at 1 min	9 (9–9)	9 (8–9)	0.763
Apgar score at 3 mins	10 (9–10)	9 (9–10)	0.181
Apgar score at 5 mins	10 (10–10)	10 (10–10)	0.920
Apgar score at 10 mins	10 (10–10)	10 (10–10)	0.624
Umbilical vein			
pH	7.38 (7.36–7.39)	7.37 (7.35–7.40)	0.992
H ⁺ (nmol L ⁻¹)	43 (41–45)	43 (40–45)	0.776
pCO ₂ (mm Hg)	39.7 \pm 6	40.5 \pm 7.2	0.664
pO ₂ (mm Hg)	27.7 \pm 6.4	27.4 \pm 7.9	0.899
HCO ₃ ⁻ (mmol L ⁻¹)	22.4 \pm 1.9	22.8 \pm 1.7	0.429
Base excess (mmol L ⁻¹)	-2.1 \pm 1.3	-1.8 \pm 1.1	0.384
Umbilical artery			
pH	7.33 (7.30–7.33)	7.33 (7.33–7.36)	0.412
H ⁺ (nmol L ⁻¹)	47 (47–50)	47 (44–50)	0.412
pCO ₂ (mmol L ⁻¹)	49 \pm 6	47.7 \pm 10.9	0.6
pO ₂ (mm Hg)	17.5 \pm 4.6	17.9 \pm 4.1	0.743
HCO ₃ ⁻ (mmol L ⁻¹)	24.8 \pm 2	25.0 \pm 1.8	0.718
Base excess (mmol L ⁻¹)	-1.3 \pm 1.3	-1.1 \pm 1.3	0.548
UV Na ⁺ (mmol L ⁻¹)	136.9 \pm 2.7	137.1 \pm 2	0.726
UV Cl ⁻ (mmol L ⁻¹)	109.1 \pm 2.4	109.2 \pm 2	0.957

UA — umbilical artery; UV — umbilical vein

tion. Other parameters that may affect the birth condition of a newborn were also measured.

Ephedrine is the drug of choice for preventing and treating hypotension in obstetric patients because it does not shrink the arterial vascular bed of the uterus and does not reduce bloodflow through the uterus or placenta. However, many studies have shown that ephedrine can cause bradycardia and acidosis in the foetus [14, 15, 16, 17] especially if used in large doses (>15 mg) [9]. In this study, there were no significant differences between groups with respect to the total dose of ephedrine used to treat hypotension. Six patients in Group A and eight patients in Group B received a dose of more than 15 mg.

In the group of patients receiving Voluven, all of the infants had Apgar scores of at least 7 (two infants had scores of 7 at the first minute and all newborns had scores of at least 8 at the fifth minute). Similarly, in the group of patients receiving Tetraspan, all infants had Apgar scores of at least 7 (one infant had a score of 7 at the first minute and all newborns had scores of 8 or higher at the fifth minute). No cases of acidosis, defined as lactic venous cord blood with a pH below 7.2 and arterial cord blood with a pH below 7.1 [18], were identified in either group. Furthermore, no statistically significant differences were observed among other parameters associated with the acid-base balance including pCO₂, pO₂, SO₂, bicarbonate concentration (HCO₃⁻) and the

BE, which are rarely taken into account when assessing the condition of a newborn.

The type of fluid transfused had no effect on the condition of the newborn. The volume of 500 mL (doses of 5.0 to 9.3 mL kg⁻¹ in Group A and 4.4 to 8.1 mL kg⁻¹ in Group B) proved ineffective in the prevention of hypotension associated with subarachnoid anaesthesia. It is possible that the application of HES 130/0.4 in doses greater than 500 mL might improve the safety profile of the preparation. As a final note, phenylephrine, which is commonly recommended for use in obstetrics [19], is not registered in Poland; therefore, our actions should aim to limit the doses of ephedrine.

CONCLUSIONS

1. A balanced solution of 6% hydroxyethyl starch (HES 130/0.42) delivered in a dose of 500 mL before subarachnoid anaesthesia for caesarean section did not improve the condition of the newborns as evaluated by the Apgar scale compared to an unbalanced solution (HES 130/0.4).
2. A balanced solution of 6% hydroxyethyl starch (HES 130/0.42) did not improve the acid-base or electrolyte economy of the newborns compared to an unbalanced solution (HES 130/0.4).
3. Neither the balanced (HES 130/0.42) nor unbalanced (HES 130/0.4) 6% hydroxyethyl starch solution transfused in a volume of 500 mL prior to anaesthesia effectively prevented hypotension associated with subarachnoid anaesthesia for elective caesarean section.

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