Lower incidence of hypotension following spinal Anesthesia with 6% hydroxyethyl starch preload Compared to 9 ‰ saline solution in caesarean Delivery.

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Incidence de l'hypotension après une anesthésie rachidienne avec 6% d'amidon hydroxyéthyle comparé au sérum salé à 9‰ dans les césariennes.

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R É S U M É

Pré-requis : L'hypotension artérielle (hTA) consécutive à la rachianesthésie pour césarienne reste une complication fréquente et potentiellement grave pour la mère et le nouveau-né. Le remplissage vasculaire est un moyen de prévention de cette hypotension maternelle.
But : Le but de notre étude était de comparer l'efficacité de HES 130/0,4 (Voluven®), à celle du sérum physiologique (SP) dans la prévention de l'hTA après une rachianesthésie pour césarienne.
Méthodes : Étude prospective randomisée en simple aveugle mono-centrique, entre février 2009 et juillet 2010. Critère de jugement principal : incidence de l' hTA définie par une baisse de la PAS supérieure à 20% de sa valeur de base. Randomisation en 2 groupes en fonction du soluté de pré remplissage: Groupe SP 1500 ml de Sérum physiologique (SP) et Groupe V 500 ml de HES 130/0.4. Des gaz du sang ombilical artériel ont été prélevés, et le score d'Apgar a été calculé aux première et cinquième minutes. p<0,05 était considéré comme significatif.
Résultats : 105 patientes ont été incluses. Les caractéristiques démographiques étaient similaires dans les deux groupes. L'incidence de l'hypotension a été plus élevée dans le Gr SP. 46 parturientes du Gr SP (87 %) et 33 parturientes du Gr V (69 %) ont présenté une hypotension (p = 0.025). Aucune différence significative n'est mise en évidence pour la variation de la PAM au cours du temps. Par contre, la PAS était significativement plus élevée (p = 0.047) dans le Gr V uniquement à la 13ème min (108 ± 14 versus 113 ± 13).
Conclusions : Un pré remplissage par 500 ml d'HES 130/0.4 est plus efficace que celui réalisé par 1500 ml de SP pour prévenir l'hypotension après une rachianesthésie pour césarienne.

M o t s - c l é s
Rachianesthésie, hypotension, hydroxyethyl amidons.

C. Romdhani, W. Trabelsi, A. Lebbi, I. Naas, H. Elaskri, H. Gharsallah, R. Rachdi, M. Ferjani

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S U M M A R Y

Background: Hypotension is a common complication following spinal anesthesia for cesarean delivery. Techniques to prevent hypotension include preloading intravenous fluid.
Aim : To compare the effect of two preloading regimens: 6% hydroxyethyl starch (HES) and 9‰ saline solution, to prevent hypotension after spinal anesthesia in cesarean delivery.
Methods: 105 patients undergoing intrathecal anesthesia for elective cesarean delivery were randomized and allocated to receive a preload of 500 ml HES 130/0.4 (HES Group) or a preload of 1500 ml 9‰ saline solution (CR group). Blood pressure and heart rate were recorded at baseline and after spinal anesthesia (every minute for the first 10 min, every 3 min for the next 10 min, and then every 5 min for the last 20 min). The primary outcome was to compare the incidence of hypotension (defined as a 20% reduction in systolic arterial pressure from baseline) between the two preloading regimens. Vasopressor requirements (i.v. bolus of 6 mg ephedrine) were also compared.
Results: The incidence of hypotension was 87% in the CR group and 69% in the HES group (p= 0.028). Ephedrine requirement, incidence of nausea, and/or vomiting and neonatal outcome did not significantly differ between the two groups.
Conclusion: The incidence of hypotension was lower after preloading of 500 mL of HES 130/0.4 than preloading with 1500 mL of 9‰ saline solution.

K e y - w o r d s
spinal anesthesia, hypotension, hydroxyethyl starch.

Maternal hypotension is a common side effect after spinal anesthesia for cesarean delivery (1). This complication leads to maternal side effects (2) and worsens the clinical and biochemical outcomes of neonates (3). A survey has shown that crystalloid-fluid therapy remains a popular methodology to prevent maternal hypotension (4). Traditionally, crystalloid intravenous fluids have been administered before inducing spinal anesthesia for cesarean delivery (preload) (5). However, recently, volume preloading has been reported with the latest generation of hydroxyethyl starch (HES 130/0.4), although a recent meta-analysis was unable to conclude that the time of fluid loading, either before or during induction of spinal anesthesia, affected the incidence of hypotension (6). According to this meta-analysis and the practice guidelines for obstetric anesthesia (7), intravenous-fluid preloading could be used to decrease the frequency of maternal hypotension after spinal anesthesia for non-urgent cesarean deliveries.

Our randomized study compared the effect of preloading with 1500 mL of 9‰ saline solution versus 500 mL of HES 130/0.4 on the incidence of hypotension after spinal anesthesia for non-urgent cesarean sections.

METHODS

We obtained ethics-committee approval and written informed consent from each patients. This study enrolled healthy parturient women with term singleton pregnancies who were not in labor and were undergoing elective cesarean delivery under spinal anesthesia. We did not include women with pre-eclampsia, those who weighed >110 kg, were <150 cm tall, had an allergy to HES, had known fetal abnormalities, and/or had contraindications for spinal anesthesia. Exclusion criteria also included a sensitive block height that exceeded T4, hemodynamic instability caused by a surgical complication, and a failed spinal anesthesia.

In the operating room, oxygen at 3 L/min was administered by nasal cannula. We measured non-invasive blood pressure, heart rate, and oxygen saturation. A vein in the antecubital fossa was cannulated with a 16-gauge catheter to administer the i.v. fluid. Using random allocation software (8), parturients were randomized into two groups based on their preload protocol. A computer program randomly selected the number and size of each block. The HES group and the crystalloid group (CR group), respectively, received 500 mL of 6% HES 130/0.4 (Voluven®, Fresenius Kabi, Germany) and 1500 mL of 9‰ saline solution at 30 min prior to spinal anesthesia. One of the authors (C.R.) assessed eligibility of the patients for enrollment into the study.

We performed spinal anesthesia, with patients in a sitting position, through a 25-gauge pencil-point needle through L2–3 or L3–4 interspaces. All parturients received 10 mg of 0.5% hyperbaric bupivacaine, 2.5 μg of sufentanyl, and 100 μg of morphine within 90 s (left uterine displacement were employed in all cases). After preload, a continuous saline infusion at a rate of 10 ml/Kg was established.

The maximum height of the sensory block was assessed using an ice pack. Systolic blood pressure (SAP), diastolic blood pressure, mean arterial-blood pressure (MAP), and heart rate were recorded every minute for the first 10 min following spinal anesthesia, and then at 3-min intervals for the next 10 min. These hemodynamic measurements were further monitored every 5 min until the end of surgery.

Hypotension episodes, defined as a reduction in systolic blood pressure that exceeded 20% of the baseline value (just before subarachnoid block), were treated with a 6-mg IU bolus of ephedrine. This treatment was repeated if hypotension persisted or recurred. Presence of nausea and/or vomiting was noted. A 5-IU bolus of oxytocin over 2 min was administered immediately after delivery plus intravenous infusion of 10 IU of oxytocin diluted in a 500-mL

saline solution. Neonatal outcome was assessed using Apgar scores at 1 and 10 min.

Blood-gas samples from double-clamped umbilical veins were obtained immediately after delivery.

Statistical analysis

The primary outcome was incidence of hypotension. Assuming an α-risk of 0.05 and a β-error of 0.20, to show a 30% difference in the HES group (9), we needed at least 48 patients per group. The number needed to treat hypotension was calculated using web-based software (Statistics for Health, GraphPad Quick Calcs online calculator) (10).

Continuous data were expressed as means ± standard deviations (SD), and categorical data were reported as numbers (percentages), unless otherwise specified. A P-value of <0.05 was considered significant.

RESULTS

We recruited 105 patients between February 2009 and July 2010. Four patients were excluded: two parturients failed spinal anesthesia, one had a low birth weight, and the fourth suffered surgical complications. There were no significant differences between the two groups concerning demographic data and baseline hemodynamic parameters (Table 1).

There were no differences in maximum heights of the sensory blockades (T5 [T4–T6] in the CR group vs. T4 [T4–T6] the HES group, P = 0.14). No significant differences were noted between the two groups in the amount of perioperative saline infusion administered during cesarean delivery (Table 2).

The incidence of hypotension was higher in the CR group (46 patients, 87%) vs. the HES group (33 patients, 69%; P = 0.028) (Figure 1). Preloading with HES 130/0.4 resulted in a 20.8% absolute risk reduction (95% CI: from 1.8–33.6%). The number-needed-to-treat was six (95% CI: 3, 55). There were no significant differences between the groups regarding the incidence of SAP <80 mmHg (Table 2), or the percentage decrease of SAP and MAP (Table 2). The minimum recorded SAP and MAP data were not significantly different (Table 2).

SAP (Figure 2) was only significantly increased in the HES group in the 13th minute (113 ± 13 in SAP vs. 108 ± 14 mmHg in CR; P = 0.047).

Table 1: Demographic data and baseline hemodynamic measurements

	CR group (n=53)	HES group (n=48)	P
Age (years)	32 ± 4	33 ± 6	0.5
Weight (kg)	77 ± 12	76 ± 13	0.8
Height (cm)	163 ± 5	163 ± 5	0.2
BMI (kg/m2)	29 ± 4	29 ± 5	0.3
Gestational age (weeks)	37.9 ± 0.4	38 ± 0.4	0.6
Baseline SBP (mmHg)	124 ± 13	123 ± 13	0.7
Baseline DBP (mmHg)	78 ± 11	80 ± 12	0.97
Baseline MBP (mmHg)	91 ± 12	92 ± 12	0.8
Baseline HR (bpm)	91 ± 15	92 ± 13	0.7
SBP after preload (mmHg)	123 ± 11	125 ± 11	0.3
DBP after preload (mmHg)	72 ± 9	73 ± 11	0.8
MBP after preload (mmHg)	89 ± 8	90 ± 10	0.6
HR after preload (bpm)	84 ± 11	84 ± 8	0.6

Data are mean ± SD.
SBP: systolic blood pressure; DBP: diastolic blood pressure; MBP: mean blood pressure; HR: heart rate; CR: crystalloid; HES: hydroxyethyl starch; BMI: body-mass index

There were no significant differences between the groups in MAP at any point within the first 40 min after lumber puncture (Figure 3). Time intervals from spinal anesthesia until the end of surgery are shown in Table 2: no significant time differences were noted between the groups.

Table 2: Maternal hemodynamic anesthesia data and neonatal outcomes

Factor	CR group (n=53)	HES group (n=48)	P
Incidence of hypotension[a]	46 (87 %)	33 (69 %)	0.028
Incidence of SBP <80 mmHg[a]	12 (23 %)	13 (27 %)	0.39
Minimal SBP (mmHg)	87 ± 12	88 ± 15	0.7
Percent decrease in SBP	29 ± 11	28 ± 12	0.5
Minimal MBP (mmHg)	54 ± 10	56 ± 12	0.4
Percent decrease in MBP	40 ± 12	38 ± 12	0.5
Minimal HR (bpm)	69 ± 14	72 ± 13	0.1
Dose of ephedrine (mg)	16 ± 18	13 ± 14	0.4
SA to delivery time (min)	15 ± 6	17 ± 5	0.1
SA to operative end time (min)	44 ± 12	46 ± 11	0.5
Peroperative saline infusion (mL)	871 ± 294	978 ± 257	0.09
Umbilical venous pH	7.36 ± 0.04	7.36 ± 0.06	0.8
Apgar at 1 min	9 ± 1	9 ± 1	0.7
Apgar at 5 min	10	10	0.9
Nausea or vomiting [n (%)]	18 (34 %)	16 (33 %)	0.8

CR: crystalloid; HES: hydroxyethyl starch; SA: spinal anesthesia; SBP: systolic blood pressure; DBP: diastolic blood pressure; MBP: mean blood pressure; HR: heart rate. [a]We defined hypotension as a >20% reduction in systolic arterial pressure compared to baseline, and severe hypotension as SAP <80 mmHg.

There was no significant difference in total ephedrine dose (Table 2), the incidence of nausea and/or vomiting (Table 2), or differences in neonatal outcomes between the two groups.

Umbilical vein pH and Apgar scores at 1 and 5 min were also not significantly different between the groups (Table 2).

Figure 1: Incidence of hypotension in parturients receiving hydroxyethyl starch or crystalloids. *Chi-squared test to compare groups.

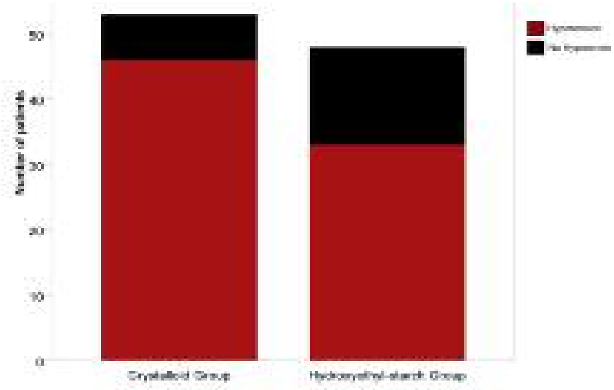


Figure 2: Serial changes in systolic blood pressure (SBP) for the first 40 min. HES: Hydroxyethyl starch, B: baseline, *P = 0.047.

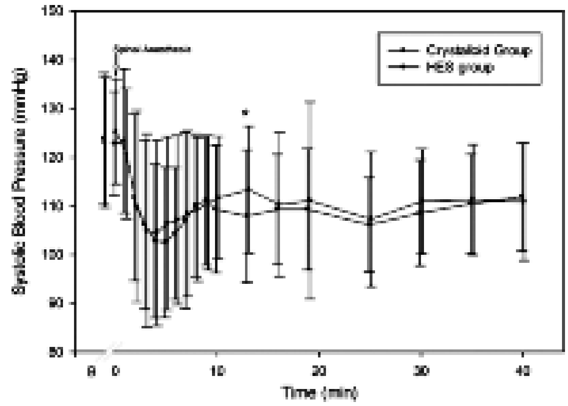
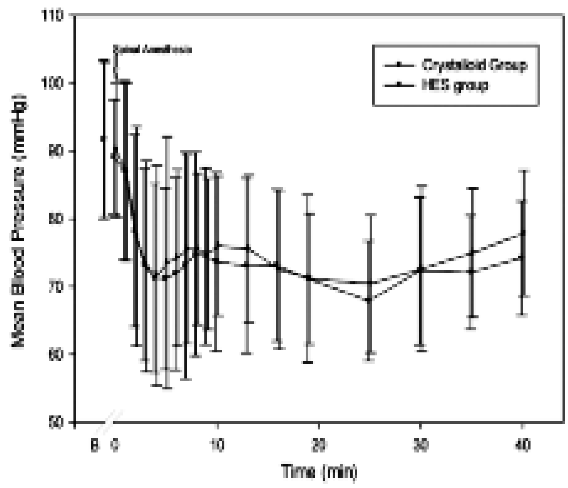


Figure 3: Serial changes in mean blood pressure (MBP) for the first 40 min. HES: Hydroxyethyl starch, B: baseline



DISCUSSION

This prospective, randomized, but not blinded study, which used equipotent doses, showed that a preload of 500 mL of 6% HES was efficacious at reducing the incidence of hypotension when compared to a preload of 1500 mL of saline solution (even the dose was one third of saline). This result corresponds to the findings of Madi Jebara et al. (11) and Ko et al.(12).

Although we used 1500 mL of saline (20 mL/kg) as a preload in the crystalloid group, the incidence of hypotension remained high (87%). This was probably caused by preloading of crystalloids, which were ineffective at increasing or maintaining intravascular volume at the time of maximum vasodilation.

Tamilselvan et al. (13) measured cardiac output and corrected flow time (a measure of intravascular volume) with a suprasternal Doppler ultrasound after prehydration with either 0.5 or 1 L of 6% HES solution, or with 1.5 L of lactated Ringer's solution. They showed that preloading with crystalloid solution failed to maintain corrected flow time and cardiac output after the initiation of spinal anesthesia.

In our study, ephedrine boluses were used to treat hypotension. There was a trend towards decreased requirement for vasopressors in the HES group, but the difference between the groups was not statistically significant. However, our study was not powered for this outcome. Madi-Jabara et al. (11) and Siddik et al. (14) reported giving smaller doses of ephedrine to colloidal groups, although the total dose of vasopressor was not statistically different to that reported in Ko et al.'s (12) study.

In spite of the significant difference in the incidence of hypotension between our two groups, neonatal outcome was uniformly good as measured by cord-blood gases and Apgar scores. Transient decreases in blood pressure, rapidly treated with vasopressors, usually do not have an impact on fetal acid–base status (15,16).

The incidence of hypotension was increased in our study, but was similar to that reported in the literature (11, 14, 17). Hypotension can be caused by multiple factors: the fluid volume (1.5 L) used in our CR group probably played an important role in the high incidence of hypotension. Elevated hypotension could also have been caused by increased atrial natriuretic peptide secretion. In response to intravascular volume load, significantly increased release of atrial natriuretic peptide can decrease vascular tone, which may antagonize the effect of volume load on arterial blood pressure (18).

Despite preloading with HES 130/0.4, we still had a 69% incidence of hypotension. Sensitivity to local anesthetics and susceptibility to the effects of sympathetic block increased during pregnancy (1). Sharwood-Smith and Drummond assumed that the main mechanism of hypotension following regional anesthesia relates to increased dependence on sympathetic vascular tone (8). This hypothesis is supported by the pathophysiology of pre-eclampsia, in which persistent vasoconstriction, secondary to the effect of placental-derived mediators, leads to relative resistance to sudden decreases in sympathetic vascular tone and, thus, to less hypotension during spinal anesthesia (1).

Smiley et al. (19) reported that titrated infusions of phenylephrine in the range of 25–100 μg/min, to prevent hypotension after spinal anesthesia, were highly effective at maintaining maternal blood pressure. Thus, the association between fluid load and the prophylactic use of vasopressors may decrease the incidence of hypotension.

Several recent studies have compared prehydration versus co-hydration of colloids, and have shown that hemodynamic changes and vasopressor requirements are similar (16,20,22). Thus, surgery does not need to be delayed when administering a predetermined volume of fluid before proceeding with spinal anesthesia, particularly in urgent cases (7). Banerjee et al.(6) compared preload and co-load and found that the incidence of hypotension was similar, whether the fluid used was crystalloid or colloidal. No studies seem to have compared co-loading with colloids versus with crystalloids (23). Although crystalloids are ineffective at preloading, they are cost-effective and may have a place in co-loading. Thus, further studies are needed to determine the best fluid for co-loading regimens.

In summary, a preload of 0.5 L of hydroxyethyl starch 130/0.4 was more effective than 1.5 L of 9‰ saline solution in preventing hypotension after spinal anesthesia for cesarean delivery. However, the incidence of hypotension remained relatively high in the colloid group. Thus, the use of a vasopressor to prevent hypotension may be necessary. Further studies are required to establish optimal strategies to prevent hypotension during spinal anesthesia for cesarean section.

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