

**PREVENTION OF HYPOTENSION AFTER SPINAL ANESTHESIA FOR CESAREAN SECTION  
6% hydroxyethyl starch 130/0.4 (Voluven®) versus lactated Ringer's solution**

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Madi-Jebara S, Ghosn A, Sleilaty G, Richa F, Churfane A, Haddad F, Yazigi A, Antakly MC. Prevention of hypotension after spinal anesthesia for cesarean section : 6% hydroxyethyl starch 130/0.4 (Voluven®) versus lactated Ringer's solution. *J Med Liban* 2008 ; 56 (4) : 203-207.

**ABSTRACT • GOALS :** The aim of this study is to compare the efficacy of HES 130/0.4, a new hydroxyethyl starch, to lactated Ringer's solution (LR) in the prevention of hypotension after spinal anesthesia for cesarean section (CS).

**MATERIAL AND METHODS :** One hundred and twenty nonlaboring ASA I and II women having non urgent CS were enrolled in this prospective and randomized study. Subjects were randomly assigned to receive prior to anesthesia either 1 liter of LR (Gr I : n = 59) or 500 ml of HES 130/0.4 (Gr II : n = 61). Blood pressure was measured until discharge from the post anesthesia care unit. Hypotension was treated with IV boluses of 3 mg of ephedrine. The nausea scale was recorded. Arterial and venous umbilical blood gases were obtained. Data were compared using Mann-Whitney U-test and Student's t-test ( $p < 0.05$  was significant).

**RESULTS :** Thirty-nine patients in Gr II while 48 pts in Gr I experienced hypotension ( $p = .033$ ). The total dose of ephedrine was statistically smaller in Gr II compared with Gr I ( $p = .001$ ). Nausea after induction of spinal anesthesia occurred with similar frequency in both groups. Neonatal outcome was excellent and similar in both groups.

**CONCLUSION :** HES 130/0.4 is more effective than LR to prevent hypotension following spinal anesthesia for CS ; its routine use in this purpose should be considered.

Madi-Jebara S, Ghosn A, Sleilaty G, Richa F, Churfane A, Haddad F, Yazigi A, Antakly MC. Prévention de l'hypotension artérielle après une rachianesthésie pour césarienne : 6% hydroxyéthylamidon 130/0.4 versus Ringer Lactate solution. *J Med Liban* 2008 ; 56 (4) : 203-207.

**RÉSUMÉ • BUT :** Le but de cette étude est de comparer l'efficacité de HES 130/0.4, un nouvel hydroxyéthylamidon, au Ringer Lactate (LR) dans la prévention de l'hypotension après une rachianesthésie pour césarienne.

**MATÉRIEL ET MÉTHODES :** Cent vingt parturientes ASA I et II programmées pour une césarienne ont été incluses dans cette étude prospective et randomisée. Les parturientes ont été tirées au sort pour recevoir 1 litre de LR (Gr I : n = 59) ou 500 ml de HES 130/0.4 (Gr II : n = 61) avant la rachianesthésie. La tension artérielle a été mesurée jusqu'à la décharge de la salle de réveil. L'hypotension a été traitée avec des bolus IV de 3 mg d'éphédrine. Le score de nausée a été noté. Des gaz du sang ombilical artériel et veineux ont été prélevés. L'étude statistique a utilisé le test de Mann-Whitney et le t-test de Student ( $p < 0.05$  significatif).

**RÉSULTATS :** Trente-neuf patientes du Gr II et 48 du Gr I ont présenté une hypotension ( $p = .033$ ). La dose d'éphédrine utilisée était statistiquement plus faible dans le Gr II comparée au Gr I ( $p = .001$ ). Le score de nausée est identique dans les deux groupes. Les gaz du sang du nouveau-né étaient excellents et semblables dans les deux groupes.

**CONCLUSION :** HES 130/0.4 est plus efficace que LR pour prévenir l'hypotension après une rachianesthésie pour césarienne ; son utilisation courante dans ce but devrait être considérée.

## INTRODUCTION

Hypotension after spinal anesthesia for cesarean section remains a common and potentially serious complication [1]. Techniques currently in use for preventing hypotension include intravenous fluid prehydration [2],

sympathomimetic drugs [3], and physical methods such as leg bindings, left uterine displacement devices and compression stocking [4]. Comparisons have mainly been made between differences in volumes of crystalloid solutions and between crystalloid and colloid solutions. Crystalloid prehydration has poor efficacy for preventing hypotension [5-8], probably because it undergoes rapid distribution [9].

HES 130/0.4 (Voluven®) is a new hydroxyethyl starch, with a relatively low incidence of side effects. HES 130/0.4 has an average molecular weight of 130,000 Dalton and a degree of substitution of 6% (HES 130/0.4). Its molecular weight distribution is the narrowest of all available HES types and it has a volume effect of approximately 100% and 4 to 6 h duration.

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No clinical data on exposed pregnancies are currently available concerning the use of HES 130/0.4 in this indication.

The aim of this study is to compare the efficacy of HES 130/0.4 compared to LR in the prevention of hypotension after spinal anesthesia for cesarean section.

## METHODS

### Patients' selection

After obtaining institutional review board approval and written informed consent, 120 nonlaboring ASA class I women having non urgent cesarean sections were enrolled in the study. Exclusion criteria included obesity (weight over 115 kg), height less than 152 cm, diabetes, pregnancy induced hypertension, chronic hypertension, heart disease, multiple gestation, and age less than 18 or more than 40 yr. Patients did not receive intravenous fluids prior to entering the study. Subjects were randomly assigned to receive either 1 liter of LR (Group I ; n = 59) or 500 ml of HES 6%, 130/0.4 (Group II ; n = 61).

### Interventions

Spinal anesthesia was performed at the L2-3 or L3-4 interspaces with the patient in the sitting position with the side-port of the needle pointing cephalad. All subjects received 10 mg of 0.5% hyperbaric bupivacaine, morphine 0.1 mg and sufentanil 2.5 µg delivered through a 25-gauge pencil-point needle. Immediately after injection, the patient was positioned supine with left uterus displacement. Blood pressure was measured with an automated blood device (Dinamap ; Critikon, Inc, Tampa, FL) before performing the spinal anesthesia and then every 2 min until the umbilical clamp, then every 3 min until discharge from the post anesthesia care unit. Hypotension was defined as a systolic pressure less than 100 mmHg or a decrease of 20% of the baseline and was treated with IV boluses of 3 mg of ephedrine. Ephedrine treatment was repeated every 2 min if hypotension persisted or recurred.

Patients rated their nausea on scale of 0 to 3 (0 = no nausea, 1 = minimal nausea, 2 = moderate nausea, 3 = severe nausea or vomiting) any time they complained of nausea or vomited. Other variables recorded included the maximum height of the block as assessed by pin-prick, other drugs used and their doses, and the amount of additional IV fluid given prior to delivery. Neonatal outcome was assessed using Apgar scores and umbilical arterial and venous blood gases obtained from a doubly clamped segment of umbilical cord.

## STATISTICAL ANALYSIS

Statistical power was calculated on the following assumptions : prevalence of hypotension during spinal anesthesia for cesarean section varies between 55 and 85%. Assuming an incidence of 80% with the intention to detect a decrease in the rate of hypotension by half

**TABLE I**  
DEMOGRAPHIC DATA

FACTOR	LR	6% HES	p value
MATERNAL			
• Weight (kg)	75.5 ± 9.6	73.7 ± 10.8	.32
• Height (cm)	162.7 ± 5.6	163.2 ± 5.4	.66
• Age (y)	30 ± 3	30 ± 4	.32
GESTATIONALWEEK	38.0 ± 1.6	37.9 ± 1.4	.76
LR : lactated Ringer's solution HES : hydroxyethyl starch			

(from 80% to 40%) in patients treated with 6% HES 130/0.4, 55 patients per group are needed to reach statistical significance, with 99% power and 5% type I error. Continuous data were compared using the Mann-Whitney U-test or Student's t-test depending on normality of data distribution. Proportionate data were compared with chi-square test. A p value less than .05 was considered significant. All tests were two-sided. Values are reported as mean ± standard deviation, 95% confidence intervals (95% CI), unless specified otherwise. The 95% CI were calculated by the software and controlled with the fleiss quadratic method.

Shapiro-Wilk and Kolmogorov-Smirnov tests were used to assess data normality. Data that deviated from normality were analyzed using non parametric methods, and summaries were reported as medians, except for Apgar Score.

SPSS v 13.0 (Chicago, Illinois) was used.

## RESULTS

The groups were similar with respect to maternal height and weight and gestational age (Table I). Both groups had similar pre induction systolic blood pressure (SBP) and heart rates (HR). Time to hypotension was similar in both groups. Thirty-nine patients (63.9%, 95% CI 50.6%-75.8%) in group HES while 48 patients (81.4%, 95% CI 69.1%-90.3%) in group LR experienced hypotension (p = .033). Compared with group HES 130/0.4, patients in group LR had greater minimum recorded SBP and greater

**TABLE III**  
PERCENTAGE OF PATIENTS WITH NAUSEA AND VOMITING

	Group I (LR)	Group II (HES 130/0.4)
Score 0	60.8 %	63.9 %
Score 1	15.3 %	19.7 %
Score 2	15.3 %	11.5 %
Score 3	11.9 %	4.9 %
p value	.293	
LR : lactated Ringer's solution HES : hydroxyethyl starch		

**TABLE II**  
HEMODYNAMIC VARIABLES, FLUID AND VASOPRESSOR REQUIREMENTS

	<b>Group I (LR)</b>	<b>Group II (HES 130/0.4)</b>	<b>p value</b>
BLOCK LEVEL AT 10 MIN	6.2 ± 1.9	6.4 ± 2.1	.63
BASELINE SYSTOLIC BLOOD PRESSURE (mmHg)	116 ± 15	115 ± 13	.29
BASELINE HEART RATE (bpm)	81 ± 8	80 ± 9	.53
TIME TO HYPOTENSION (min)	6.6 ± 7.4	5.02 ± 7.33	.25
MINIMUM SYSTOLIC BLOOD PRESSURE (mmHg)	84 ± 11	93 ± 12	.001*
MAXIMUM HEART RATE (bpm)	118 ± 15	105 ± 16	.001*
PERCENT OF PATIENTS WITH HYPOTENSION	81.4%	63.9%	.033*
DOSES OF EPHEDRINE (mg)	15.9 ± 14.1	5.84 ± 11.72	.001*
EXTRA-LR'S SOLUTION BEFORE DELIVERY (ml)		215 ± 256	.053

LR : lactated Ringer's solution    HES : hydroxyethyl starch    \* p < 0.05

maximum recorded HR. The total dose of ephedrine was statistically smaller ( $p = .001$ ) in group HES ( $5.83 \pm 11.62$  mg) compared with group LR ( $15.86 \pm 14.18$  mg). There was also a trend for group LR to receive a larger volume of additional fluid IV before delivery, but this difference was not significant (Table II).

Nausea after induction of spinal anesthesia was a minor problem and occurred with similar frequency in both groups. Only 4.9% in group Voluven and 11.9% in group LR had nausea score of 3 at any time (Table III).

Neonatal outcome was excellent and similar in both groups (Table IV).

#### DISCUSSION

In this study, patients receiving HES 130/0.4 had a significantly lower incidence of hypotension after spinal anesthesia than those receiving LR. This is consistent with the findings of others who have compared colloid and crystalloids fluid administration prior to spinal anesthesia. Riley et al. compared Hetastarch 6% with LR to LR alone [10], Siddik et al. compared Pentastarch 10% to LR [11], Mathru et al. compared 5% albumin to 5% dextrose in LR [12], all these authors found less hypotension in colloid groups compared to LR groups.

The more stable hemodynamic status observed after colloid administration is probably related to their longer intravascular persistence than crystalloids [13] and the

significant increase in cardiac output after HES preload compared to LR [9]. The advantage of HES 130/0.4 over other colloid is that it has not any potential risk of allergic reactions described till now.

The incidence of hypotension in both groups in the current study was higher than in other studies of spinal anesthesia for cesarean section. For example Maltru et al. [12] reported no hypotension after colloid infusion, whereas we had an incidence of 63.9%. Rout et al. reported a 43% incidence of hypotension in patients preloaded with crystalloids [13], whereas our LR group had an 81.4% incidence of hypotension. There may be several reasons for the higher incidence of hypotension in the current study. First, opioids were not added to the local anesthetic in either of the two studies above. We added both morphine and sufentanil, which may increase the incidence of hypotension. Second, we used a larger dose of local anesthetic (hyperbaric bupivacaine 10 mg) than did Rout et al. (isobaric bupivacaine 7.5 mg) or Maltru et al. (hyperbaric tetracaine 6-8 mg). The larger local anesthetic dose might be expected to cause a higher block and a more extensive sympathectomy than smaller doses. However, Rout et al. and Mathru et al. reported similar sensory block levels to ours.

A third hypothesis to explain our higher incidence of hypotension is that the relatively large preload given to our LR group may, paradoxically, have caused more hypotension. Carvalho et al. found a greater hypotension

**TABLE IV**  
NEONATAL OUTCOMES

<b>FACTOR</b>	<b>Group I (LR)</b>	<b>Group II (HES 130/0.4)</b>	<b>p value</b>
APGAR SCORE (5')	9.84 ± .62	9.48 ± 1.43	.25
UMBILICAL PH VENOUS	7.37 ± .048	7.37 ± .03	.93
UMBILICAL PH ARTERIAL	7.28 ± .05	7.26 ± .05	.93

LR : lactated Ringer's solution    HES : hydroxyethyl starch

after volume loading with a 20 ml/kg vs. 10 ml/kg preload LR. They postulated that the larger fluid load diluted plasma proteins, lowering colloid oncotic pressure (COP) to a greater extent than the smaller volume, resulting in greater extravasation of fluid into the extra cellular fluid compartment [14]. HES 130/0.4 infused does not affect the COP [15].

In a recent study Yokoyama et al. showed that volume preloading has little effect on maternal hemodynamics and neonatal outcomes, suggesting that stable perioperative management is possible with or without volume preload before spinal anesthesia. Limitations of this paper are the small number of patients and the Japanese language [16]. Mercier et al. randomly assigned parturients to receive 1 liter crystalloid before or after induction, they found no difference in vasopressor requirements between groups [17]. However, vasopressor requirement was inversely correlated with the speed of crystalloid administration in patients who received fluid after induction; therefore, they concluded that fluid should be given as quickly as possible.

Dyer et al. randomly assigned patients to receive 20 ml/kg modified LR solution either before or immediately after induction of spinal anesthesia for elective cesarean delivery. They found that patients who received fluid after induction had a smaller requirement for ephedrine [18].

Ngan Kee et al. described the use of high-dose phenylephrine infusions in maintaining maternal blood pressure. They found that, despite using liberal phenylephrine infusion regimens, approximately one fourth of patients still experienced one or more episodes of hypotension [19-20].

In a more recent study, the same authors investigated the combination of rapid crystalloid cohydration with a high-dose phenylephrine infusion [21]. Although they found that hypotension was virtually eliminated, a large proportion of patients had transient episodes of reactive hypertension with decreases in maternal heart rate. The authors advised that caution is necessary when applying this technique particularly in patients in whom an increase in blood pressure could be detrimental. The use of direct intraarterial pressure could facilitate very accurate maintenance of blood pressure, but this is difficult to justify in routine clinical cases.

Despite a significant difference in the incidence and severity of hypotension in the LR group, neonatal outcome was uniformly good in both groups. This reflects the experience that transient decreases in blood pressure, rapidly treated with ephedrine, do not usually affect fetal acid-base status [22-23]. However, current knowledge of the effect of vasoconstrictors on the feto-utero-placental unit is incomplete and prevention of hypotension must be preferable to its correction. There is no specific data with HES 130/0.4 concerning placental transfer but many studies showed that there is no significant transplacental transfer of HES 10% [24]. No adverse reactions to HES 130/0.4 occurred in this study.

## CONCLUSION

HES 130/0.4 is the most advanced HES product with respect to the observed clinical effects, pharmacology and safety.

HES 130/0.4 is more effective than LR to prevent hypotension following spinal anesthesia for cesarean section; its use in this purpose should be considered.

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## الوقاية من هبوط الضغط بعد التخدير الشوكي للعملية القيصرية : هيدروكسي أثيل النشا (فوليفن) مقابل محلول لكتات رينغر

موجز : هدف الدراسة مقارنة مفعول HES 130/0.4 مقابل محلول رنغر وقاية من هبوط الضغط بعد إجراء التخدير الشوكي لعملية قيصرية.

الأدوات والطرق : 120 حامل في مجموعتين بعد تخدير شوكي (1) و (2) تقرر لهن قيصرية ادخلن في هذه الدراسة الأستقبالية وعشوائياً.

أختير من الحوامل لتناول لتر رنغر (مجموعة أولى 59) و 500 مليلتر HES 130/0.4 (مجموعة ثانية 61) قبل التخدير الشوكي. روقب الضغط الشرياني حتى الخروج من غرفة الاستيقاظ. عولج هبوط الضغط ببلعة افدرين مقدارها 3 ملغ. روقب حرز الغثيان وغازات دم الحبل السريّ الشرياني والوريدي . الدراسة الإحصائية المستعملة كانت باختباري (من هويتني) و (ستودانتس)، احتمال أقل من 0.05

النتائج : 39 من المجموعة 2 و 48 من المجموعة 1 أديتا هبوط ضغط (إحتمال 0.033) الأفدرين المستعمل كان إحصائياً أقل في المجموعة 2 مما هو عليه في المجموعة 1 (إحتمال 0.001). حرز الغثيان مشابه في المجموعتين، غازات دم الوليد كانت جيدة ومتشابهة في المجموعتين.

الخلاصة - HES 130/0.4 أكثر فعالية من رنغر للوقاية من هبوط الضغط بعد التخدير الشوكي لعملية قيصرية وإستعماله دائماً لهذه الغاية يجب أن يؤخذ في الاعتبار.