Hydroxyethyl starch should not be used for cesarean section to prevent maternal hypotension following spinal anesthesia

Spinal anesthesia is typically administered to women undergoing cesarean section. A common side effect after onset of spinal anesthesia is maternal hypotension caused by sympathectomy. Maternal hypotension is associated with adverse effects in the mother, such as nausea and vomiting, dyspnoea, loss of consciousness, and pulmonary aspiration in case of prolonged hypotension, and in the baby, including hypoxia, acidosis, and lower Apgar scores.[1,2] According to a recent international consensus statement, maternal hypotension following spinal anesthesia should be treated or prevented routinely with vasopressors (preferentially phenylephrine); other measures such as intravascular fluid loading (colloid preloading, crystalloid coloading) have also been investigated but should only be used in addition to vasopressors.[2,3] Importantly, however, the pre-emptive use of synthetic colloids such as hydroxyethyl starch (HES) in parturients is concerning since HES may increase the risk of bleeding, renal injury, and mortality.[4,5]

A recent Cochrane systematic review of randomized controlled trials comparing different treatments for preventing maternal hypotension following spinal anesthesia reported that the incidence of maternal hypotension was lower with colloids than crystalloids (average risk ratio 0.68, 95% confidence interval 0.58–0.80; 2,105 women; 28 studies).[1] However, the evidence was of very low quality and a high degree of heterogeneity was detected among studies; furthermore, some of the studies evaluated were considered to be at high risk of bias, for instance, the CAESAR trial.[6] The authors of the Cochrane review concluded that owing to the serious potential adverse effects of HES the use of colloids in this setting should be questioned. Furthermore, since crystalloids appear to be more effective at higher coloading doses[1,3] and 1,000 ml crystalloid coloading seems as effective as 500 ml colloid preloading,[7] there is no cost, safety, or efficacy justification for using HES to prevent maternal hypotension following spinal anesthesia. Additionally, most studies assessing volume therapy in obstetrics have focused on short-term (hypotension, haemodynamic instability, Apgar score) rather than on long-term postoperative outcomes (mortality, kidney injury).[8]

Guidelines on intravascular volume therapy in adults from the Association of the Scientific Medical Societies in Germany make an open recommendation on the use of HES for preloading prior to spinal anesthesia, whereby synthetic colloids may be used to optimize intraoperative hemodynamic values.[9] This recommendation was not supported by the German Sepsis Society and the weakness of the available data was highlighted.[9] Furthermore, due to a lack of data on child safety, these guidelines recommend that antepartum administration of colloids to pregnant and breastfeeding women must be limited to emergency cases only. Interestingly, due to insufficient evidence also, no consensus was reached regarding the specific case of colloid preloading during secondary cesarean section under epidural anesthesia.[9]

The recent international consensus statement on the management of hypotension during cesarean section under spinal anesthesia stated that both colloid and crystalloid fluid-loading techniques can be recommended to improve the hemodynamic stability provided by vasopressor prophylaxis.[2] However, known HES safety concerns were not adequately addressed. In particular, the increased risk of bleeding, renal injury, and mortality with HES coloading is not considered and should preclude any recommendation for the use of HES in pregnant women.

Regulatory bodies and some HES manufacturers now stipulate that HES should only be used to treat hypovolemia following acute blood loss, and only when crystalloids alone are not considered sufficient.[10] Furthermore, due to the lack of well-controlled studies in pregnant women, the FDA states that HES should only be used during pregnancy if the potential benefits justify the potential risks to the fetus, and only during labor if clearly needed.[10]

Therefore, the use of HES to improve the hemodynamic stability provided by vasopressor prophylaxis is not only unsupported by guidelines, but also off-label use and contrary to directives from regulatory bodies. Given that HES is not the first-line-treatment for maternal hypotension and that the benefits of HES preloading compared with crystalloid coloading are not clearly proven while the risks are widely acknowledged, HES should not be used for cesarean section to prevent maternal hypotension following spinal anesthesia.

Günther Putz, Christian J. Wiedermann[1]

Department of Anesthesiology and Intensive Care, Innsbruck Medical University, Innsbruck, [1]Institute of Public Health, Medical Decision Making and HTA, UMIT - University of Health Sciences, Medical Informatics and Technology, Hall in Tyrol, Austria

Address for correspondence: Prof. Christian J. Wiedermann, University of Health Sciences, Medical Informatics and Technology, Eduard-Wallnöfer-Platz 1, 6060, Hall in Tyrol, Austria.
E-mail: christian.wiedermann@ext.umit.at

References

1. Chooi C, Cox JJ, Lumb RS, Middleton P, Chemali M, Emmett RS, *et al.* Techniques for preventing hypotension during spinal anaesthesia for caesarean section. Cochrane Database Syst Rev 2017;8:CD002251.
2. Kinsella SM, Carvalho B, Dyer RA, Fernando R, McDonnell N, Mercier FJ, *et al.* International consensus statement on the management of hypotension with vasopressors during caesarean section under spinal anaesthesia. Anaesthesia 2018;73:71-92.
3. Bottiger BA, Bezinover DS, Mets B, Dalal PG, Prozesky J, Ural S, *et al.* Phenylephrine infusion for spinal-induced hypotension in elective caesarean delivery: Does preload make a difference? J Anaesthesiol Clin Pharmacol 2016;32:319-24.
4. Mutter TC, Ruth CA, Dart AB. Hydroxyethyl starch (HES) versus other fluid therapies: Effects on kidney function. Cochrane Database Syst Rev 2013;7:CD007594.
5. Zarychanski R, Abou-Setta AM, Turgeon AF, Houston BL, McIntyre L, Marshall JC, *et al.* Association of hydroxyethyl starch administration with mortality and acute kidney injury in critically ill patients requiring volume resuscitation: A systematic review and meta-analysis. JAMA 2013;309:678-88.
6. Mercier FJ, Diemunsch P, Ducloy-Bouthors AS, Mignon A, Fischler M, Malinovsky JM, *et al.* 6% Hydroxyethyl starch (130/0.4) vs Ringer's lactate preloading before spinal anaesthesia for Caesarean delivery: The randomized, double-blind, multicentre CAESAR trial. Br J Anaesth 2014;113:459-67.
7. Tawfik MM, Hayes SM, Jacoub FY, Badran BA, Gohar FM, Shabana AM, *et al.* Comparison between colloid preload and crystalloid co-load in cesarean section under spinal anesthesia: A randomized controlled trial. Int J Obstet Anesth 2014;23:317-23.
8. Kaufner L, Karekla A, Henkelmann A, Welfle S, von Weizsäcker K, Hellmeyer L, *et al.* Crystalloid coloading vs. colloid coloading in elective Caesarean section: Postspinal hypotension and vasopressor consumption, a prospective, observational clinical trial. J Anesth 2019;33:40-9.
9. Marx G, Schindler AW, Mosch C, Albers J, Bauer M, Gnass I, *et al.* Intravascular volume therapy in adults: Guidelines from the association of the scientific medical societies in Germany. Eur J Anaesthesiol 2016;33:488-521.
10. Wiedermann CJ, Eisendle K. Comparison of hydroxyethyl starch regulatory summaries from the food and drug administration and the European medicines agency. J Pharm Policy Pract 2017;10:12.

Access this article online	
Quick Response Code:	Website: www.joacp.org
	DOI: 10.4103/joacp.JOACP_59_19

How to cite this article: Putz G, Wiedermann CJ. Hydroxyethyl starch should not be used for cesarean section to prevent maternal hypotension following spinal anesthesia. J Anaesthesiol Clin Pharmacol 2020;36:102-3.

Submitted: 04-Mar-2019 **Accepted:** 13-Sep-2019 **Published:** 18-Feb-2020