Acta Anaesth. Bel., 2023, 74 (2): *113-121*

Review

Fluid co-loading or preloading for the prevention of hypotension during spinal anesthesia for C-section: a narrative review

N. Decuyper[1], M. Van De Velde[1]

[1]*Departement of Cardiovascular Sciences Catholic University Leuven and Department of Anesthesiology. University Hospital Leuven (UZL), Leuven, Belgium.*

Corresponding author: Decuyper N., Department of Anesthesiology, University hospital Leuven, Herestraat 49, 3000 Leuven. E-mail: nathalie.decuyper@uzleuven.be

Abstract

Background: **Fluid management strategies are one of the potential strategies to prevent spinal induced hypotension in parturients scheduled for caesarean section.**
Objectives: **This review will assess the current evidence on fluid strategies as a prophylactic measure for spinal induced hypotension.**
Methods: **A narrative review was conducted where Pubmed, Embase and the Cochrane library were searched in November 2021 for RCTs, meta-analyses and systematic reviews, that compared different fluid regimen in ASA classification one or two women scheduled for elective caesarean section.**
Results: **77 studies were selected from initial screening, based on titles and abstracts. Out of the 77 initial studies, 37 were considered eligible for inclusion. Crystalloid preloading seemed ineffective in the prevention of spinal hypotension. Crystalloid co-loading, colloid pre- and co-loading all proved to reduce the incidence of spinal hypotension, as well as the incidence of nausea and vomiting and vasopressor use. There was no significant difference in neonatal outcome, regardless of the fluid regimen.**
Conclusion: **Crystalloid co-loading, colloid co-loading and colloid preloading all have been shown to be effective in the prevention of spinal hypotension.**

Introduction

Spinal anesthesia is considered to be the anesthetic technique of choice in healthy pregnant women undergoing a routine caesarean section. Unfortunately associated hypotension is a common side effect, that can lead to undesirable maternal and fetal effects[1-4]. This is mainly due to a pharmacological sympathectomy, induced by spinal anesthesia resulting in arterial vasodilation and decreased systemic vascular resistance[5,6]. Parturients are more prone to hypotension due to the required high level of block and the pregnancy related physiological and anatomical changes. There is limited autoregulation in the uteroplacental circulation and therefore flow is almost directly related to the mean uterine perfusion pressure. When maternal hypotension occurs, blood flow in the uteroplacental circulation consequently is reduced and this can lead to fetal distress[6]. In addition to fetal distress, spinal hypotension can also cause maternal adverse outcomes like nausea and vomiting. Treating and particularly preventing spinal hypotension is therefore a very important part of the anesthetic management of a caesarean section. A range of strategies have been identified, including physical interventions such as left lateral tilt or compression stockings, the prophylactic use of vasopressors, low dose-spinal anesthesia, fluid management and recently the use of ondansetron has also been found to be effective[7]. This review will focus on fluid loading strategies during spinal anesthesia in order to prevent spinal anesthesia-induced hypotension, by increasing the venous return[8]. Different types and timings of fluids have been studied. Intravascular volume expansion can be achieved by either fluid preloading (before spinal anesthesia) or co-loading (after spinal anesthesia). Therefore, this review is divided into two parts: preloading and co-loading.

Methods

PubMed, Embase and the Cochrane library were searched in November 2021 and the following keywords were used: colloid, crystalloid, preload, co-load, spinal anesthesia, caesarean section, spinal hypotension. Also synonyms like: succinylated gelatin, albumin, hydroxyethyl starch, HES, 2-hydroxyethyl starches, hydroxyethyl starch 130-0.4, hydrocolloids, volulyte, Ringer's lactate, plasmalyte, preloading, co-loading, caesarean delivery, abdominal delivery, C-section, and post-caesarean section, were included in our search. Only RCTs, meta-analyses, systematic reviews, which compared different fluid regimen in ASA classification one or two women scheduled for elective caesarean section, without a complicated pregnancy, were eligible for inclusion. Exclusion criteria consisted of language (only studies in Dutch, French or English were included), retracted studies, studies where only the abstract was available, studies without a p-value or an exact volume description, studies without an obstetric population, studies older than 30 years and studies that included urgent caesarean sections. Additionally, guidelines concerning fluid regimen during elective caesarean section were also searched. Our primary outcome was the incidence of hypotension, as defined by individual authors, and our secondary outcomes were the incidence of nausea and vomiting, vasopressor use and neonatal outcome. This narrative review was written with the aid of guidelines[9]. Initially titles and abstracts were screened on their relevance to this review. Full-text manuscripts of all remaining articles were then obtained, read and assessed qualitatively. In addition, the reference lists of the relevant articles were studied for additional relevant articles.

Results

Seventy-seven studies were selected from initial screening, based on titles and abstracts. Out of the 77 initial studies, 37 studies were considered eligible for inclusion consisting out of 32 RCT's and five systematic reviews. Results were divided into two parts: studies regarding preload and studies regarding co-load. Hypotension was defined by individual authors, but the most common definition of hypotension used in research studies are either a decrease to 80% of the baseline blood pressure value or a drop of the systolic pressure below 100 mmHg.

1. Preload

The use of fluid preloading in the prevention of spinal hypotension can be divided into two categories: preloading with crystalloids or preloading with colloids.

A. Crystalloid preload

Twenty studies were included looking at crystalloid preloading as a prophylactic measurement for spinal hypotension. A subcategorization was made comparing crystalloid preload with a control group (three studies), with a colloid preload group (16 studies) and with a crystalloid co-load group (one study). Details can be found in Table I to III. Table I shows the results of three studies that compared crystalloid preloading with a control group (no preload or different volumes of preloading). Efficacy of preloading was poor[10-12]. There was no difference in vasopressor use or the incidence of nausea and vomiting between both groups and neonatal outcome was also similar. The details of the comparison between crystalloid and colloid preloading are summarized in table two. Colloid preloading appears to be preferable in preventing spinal hypotension. In eight studies[13,14,19,21-24,28] where hetastarch 6% was given as a preload, there was a significant reduction in the incidence of spinal hypotension or in the percentage of reduction in systolic blood pressure. In three other studies [14,25,26], preloading with hetastarch 6% demonstrated a better hemodynamic stability (higher overall

Table I. — Comparison of crystalloid preload with a control group.

	Study design	Comparison	Year	Number of patients	Results
(1)	RCT[10]	Plasmalyte 20 ml/kg preload vs control	1993	140	*Incidence of hypotension: significant difference of 16% * No significant difference in dose of vasopressor (ephedrine) * No significant difference in neonatal outcome
(2)	RCT, single blinded [11]	Hartmann 200 ml vs Hartmann 1000 ml preload. Prophylactic ephedrine infusion	1995	60	*Incidence of hypotension: no significant difference * No significant difference in dose of vasopressor (ephedrine) * No significant difference in the incidence of nausea and vomiting * No significant difference in neonatal outcome
(3)	RCT, double blinded [12]	Ringer's lactate 10 mg/kg vs 20 ml/kg vs 30 ml/kg	1996	55	*Incidence of hypotension: no significant difference * No significant difference in the dose of vasopressor (ephedrine) * No significant difference in neonatal outcome

Table II. — Comparison of colloid preload with crystalloid preload 1/2.

	Study design	Comparison	Year	Number of patients	Results
(4)	RCT, blinded[13]	6% hetastarch 500 ml (+1L RL) vs RL 2L. Prophylactic 10 mg ephedrine.	1995	40	*Incidence of hypotension: 45% vs 85% (p<0.05) * Ephedrine use: 0mg vs 2mg (p <0.05) * No significant difference in nausea and vomiting * No significant difference in neonatal outcome
(5)	RCT[14]	6% HES 500 ml vs RL 1l	1995	26	* Incidence of hypotension: 38% vs 62% => no statistical analysis *Decrease systolic BP: 27.6 (95 %CI 20.5-34.7)% in the crystalloid group and 21.3(16.0-26.6)% in the colloid group (p=0.15) * Neonatal outcomes were similar
(6)	RCT[15]	RL 1.5l vs 6% HES 500 ml vs 6% HES 1000 ml + a 500 ml RL co-load in all the groups	1999	36	*Incidence of hypotension: 75% vs 58% vs 17% (p<0.05)
(7)	RCT, double blinded[16]	Hartmann 15 ml/kg vs 15 ml/kg pentastarch	1999	160	*Incidence of hypotension: 47.5 vs 12.5% (p=0<0.0001) * Ephedrine use: 8.35 mg (12.56) [0–57] vs 1.35 mg (3.93) [0–18], P < 0.05 * Neonatal outcomes were similar
(8)	RCT[17]	HES 10% 500 ml vs RL 1l	2000	40	*Incidence of hypotension: 40% vs 80% (p<0.05) * Ephedrine use: 10.6 mg ± 8.6 vs 35.3 mg ± 18.4 (p<0.05) * Nausea and vomiting: 20% vs 50% (p<0.05) * Neonatal outcomes were similar
(9)	RCT, double blinded[18]	RL 1l vs dextran 3% 1l	2005	110	*Incidence of hypotension: 85% vs 66% (p= 0.03) * Ephedrine use: 8.5-9.7 mg (SD) vs 15.0-11.9 mg (SD), (p<0.05) * Neonatal outcomes were similar
(10)	RCT, Blinded[19]	HES 6% 500 ml vs RL 20 ml/kg	2007	200	*Incidence of hypotension: when both under spinal: 44% vs 18% (p = 0.023), crystalloid under spinal vs colloid under CSE: 24% vs 18% (p = 0.047) * Ephedrine use: no statistical difference * Nausea: significant lower incidence in colloid preloading (p<0.05)
(11)	RCT, double blinded[20]	Hartmann 1.5 L vs HES 6% 0.5l vs HES 6% 1l	2009	60	*Incidence of hypotension: 70% vs 35% vs 65% P= 0.069 * Ephedrine use: no significant difference * Nausea and vomiting: no significant difference * Neonatal outcomes were similar
(12)	RCT[21]	HES 130/0.4 500 ml vs NaCl 0.9% 1L	2012	60	*Incidence of hypotension: 40% vs 66% (P=0.03) * Ephedrine: 7.6 - 13 mg vs 16.4 - 15 mg (p<0.05) * Nausea: no significant difference * Neonatal outcomes were similar
(13)	RCT, double blinded[22]	HES 6% 7.5 ml/kg vs RL 1L vs NaCl 0.9% 1l	2014	90	*Incidence of hypotension: 13.3% vs. 46.6% vs 40% (p<0.05) * Ephedrine: 13.3% vs. 46.6% and 40%, (P<0.05) * Neonatal outcomes were similar
(14)	RCT[23]	HES 6% 500 ml vs NaCl 0.9% 1.5L	2014	105	*Incidence of hypotension: 69% vs 87 (p= 0.028) * No significant difference in ephedrine dose, incidence of nausea nor neonatal outcome
(15)	RCT, double blinded, multi-centered[24]	500 ml of 6% HES + 500 ml of RL vs RL 1l	2014	167	*Incidence of hypotension: 36.6% vs 55.3% (P<0.025) * No significant difference between total phenylephrine use * Neonatal outcomes were similar
(16)	RCT[25]	RL 1L vs HES 6% 0.5l L	2015	32	*Incidence of hypotension: 73.3 % vs 46.7 %, p= 0.26 *A significant difference in usage of ephedrine and phenylephrine (p = 0.015 and p = 0.029, respectively) * Neonatal outcomes were similar

Table II. — Comparison of colloid preload with crystalloid preload 2/2.

	Study design	Comparison	Year	Number of patients	Results
(17)	RCT[26]	RL 1.5l vs HES 6% 0.5l + prophylactic phenylephrine infusion	2016	82	*Incidence of hypotension: 27% Vs 0.8% (P = 0.12) *No significant difference in the incidence of nausea nor neonatal outcomes. * Significantly less phenylephrine (1077.5 ± 514 mcg) was used in the colloid group than the crystalloid group (1477 ± 591 mcg, P = 0.003).
(18)	RCT[27]	HES 6% 7 ml/kg vs NaCl 0.9% 15ml/kg	2017	120	*Incidence of hypotension: 60% vs 65% (P > 0.05) * No significant difference in total ephedrine uses or neonatal outcomes
(19)	RCT, double blinded[28]	6% HES 500 ml vs RL 500 ml	2018	96	*Decrease systolic BP: -4.501 ± 8.120 vset al.-2.008 ± 8.041 (p= 0.008) * Ephedrine: 8.979 +/- 6.045 mg vs 14.63 +/- 7.27 mg (p<0.05) * Nausea: no significant difference * Neonatal outcomes were similar

blood pressure and less usage of vasopressors) compared to preloading with crystalloids, despite a nonsignificant reduction in hypotension.

In two studies[20,27] no significant reduction in hypotension was seen when hetastarch 6% as preload was given. One study compared crystalloid and colloid preloading when giving a prophylactic phenylephrine infusion and concluded no significant difference in the incidence of hypotension, nevertheless a lower dose of the vasopressor was needed in the colloid group[26]. Ueyama et al[15] compared two doses of HES 6% and discovered a dose-dependent effect, but this result was not repeated in a study from 2007[19]. Siddik et al[17] used a higher concentration, hetastarch 10%, and also found a significant lower incidence of spinal hypotension. Studies using other colloids, including pentastarch 10% 15 ml/kg[16] and 3% dextran 1l[18], both confirmed a significant decrease in spinal hypotension, in comparison with crystalloid preloading. The incidence of nausea and vomiting differed between studies with similar results between both groups in six studies[13,20,21,23,26,28] and with a decrease in incidence in the colloid group in two studies[17,19]. Vasopressor use was overall higher in het crystalloid group compared to a colloid group[13,16-18,21,22,25,26,28], although in some studies a statistical significance was not reached[19,20,23,24,27]. Neonatal outcome was consistently similar in all of the studies. One study[29], as seen in table three, demonstrated that crystalloid co-loading is more efficient in the prevention of maternal hypotension then administering crystalloids before the spinal anesthesia. There also was a lower incidence of nausea and vomiting and of the administration of ephedrine in het co-load group. Neonatal outcome was similar.

B. Colloid preload

Twenty-four studies were included looking at colloid preloading. A subcategorization was made comparing colloid preloading with a control group (two studies), with a crystalloid preload group (16 studies), with a colloid co-load group (five studies) and with a crystalloid co-load group (one study). Details can be found in Table II + IV to VI. The comparison between colloid preloading and crystalloid preloading has already been mentioned above. A significant difference in the incidence of hypotension was found when comparing a colloid preload (gelofusine 15 ml/kg) with giving no preload30. When comparing two doses of colloid preloading (pentastarch 10 ml/kg vs pentastarch 5 ml/kg), a dose-dependent significant reduction in hypotension was seen[31]. Nausea was less frequent in the colloid group[30] and there was a reduction in vasopressor use. Neonatal outcome was similar in

Table III. — Comparison of crystalloid preload with crystalloid co-load.

	Study design	Comparison	Year	Number of patients	Results
(20)	RCT[29]	Hartmann 15 ml/kg preload vs co-load	2014	60	*Incidence of hypotension: 53% vs. 83%, P = 0.026 * Smaller dose of ephedrine in the co-load group compared to the preload group (7.5% vs 15%, p=0.015) * The incidence of nausea was lower in the co-load group (27% vs. 60%, P = 0.019). *Neonatal outcome measures were comparable between two groups.

Table IV. — Comparison of colloid preload with a control group.

	Study design	Comparison	Year	Number of patients	Results
(21)	RCT, not blinded[30]	Gelofusine 15ml/kg vs no preload	2001	68	*Incidence of hypotension: 31% vs 64%, (P = 0.01) * Incidence of nausea: 6% vs 24% (P = 0.04) * Vasopressor use: metaraminol: 1.7 mg vs 1.4 mg, 0.5 vs 0.25 mg/min infusion rate (P <0.05) * Neonatal outcome similar
(22)	RCT, blinded[31]	Pentastarch 10 ml/kg vs pentastarch 5 ml/kg	2006	70	*Incidence of hypotension: 20% vs 42.8%, p<0.05 * Vasopressor use: ephedrine: 114 mg vs 198 mg (P<0.05) * Neonatal outcome similar

Table V. — Comparison of colloid preload with colloid co-load.

	Study design	Comparison	Year	Number of patients	Results
(23)	RCT, double blinded[32]	6% HES 15 ml/kg preload vs co-load vs control group	2007	54	*Incidence of hypotension: 11% (preload), 16% (co-load), 56% (control). Only significant difference with control group. * No significant difference in dose of ephedrine. * No significant difference in neonatal outcome
(24)	RCT, double blinded[33]	6% HES 500 ml preload vs co-load	2009	178	*Incidence of hypotension: 68% (preload) vs 75% (co-load) , P = 0.28 * No significant difference in dose of ephedrine or phenylephrine * No significant difference in nausea or vomiting *No significant difference in neonatal outcome
(25)	RCT, Not blinded[34]	6% HES 500 ml preload vs co-load	2009	46	*Incidence of hypotension: 48% (preload), 30% (co-load). P= 0.2 * No significant difference in dose of vasopressor (ephedrine + phenylephrine) * No significant difference in nausea or vomiting *No significant difference in neonatal outcome
(26)	RCT, single blinded[35]	6% HES 15 ml/kg preload vs co-load	2009	40	*Incidence of hypotension: no significant differenceet al. * No significant difference in dose of vasopressor (phenylephrine) * No significant difference in nausea or vomiting *No significant difference in neonatal outcome
(27)	RCT, double blinded[36]	6 % HES 10 ml/kg preload vs co-load	2013	42	*Incidence of hypotension: 10% (preload), 25% (co-load), p=0.21 * No significant difference in dose of vasopressor (phenylephrine) * No significant difference in nausea or vomiting *No significant difference in neonatal outcome

both groups. Colloid co-loading and preloading seem equally effective in preventing spinal induced hypotension, following five studies where HES 6% was used in different volumes as a colloid[32-36]. One study[35] however showed a significant increase in cardiac output during the first five minutes after colloid preloading and not after colloid co-loading. Nausea and vomiting, the use of a vasopressor and neonatal outcome were similar in all groups [32-36]. One study compared the use of colloid preloading with crystalloid co-loading, but showed no significant difference in the prevention of spinal hypotension, nor the vasopressor use, the incidence of nausea and vomiting or neonatal outcome[37].

2. Co-load

The use of fluid co-loading in the prevention of spinal hypotension can be divided into two categories: co-loading with crystalloids or co-loading with colloids.

A. Crystalloid co-load

The difference in hemodynamic profile between crystalloid co-loading and crystalloid or colloid preloading has already been discussed in the previous sections. Comparing crystalloid co-loading with a control group[40], showed a significant reduction in hypotension when using crystalloid co-loading in combination with a

Table VI. — Comparison of colloid preload with crystalloid co-load.

	Study design	Comparison	Year	Number of patients	Results
(28)	RCT, double blinded	6% HES 500 ml preload vs Ringer's lactate 1l co-load. Prophylactic phenylephrine infusion. [37]	2014	205	*Incidence of hypotension: 52.4% vset al.42.2% (P=0.18) * No significant difference in dose of vasopressor (ephedrine) *No significant difference in nausea or vomiting *No significant difference in neonatal outcome

Table VII. — Comparison of colloid co-load with crystalloid co-load.

	Study design	Comparison	Year	Number of patients	Results
(29)	RCT, double blinded	1l Ringer lactate vs HES 6% 1l + prophylactic phenylephrine infusion[38]	2011	60	*No significant difference in CO, episodes of hypotension * No significant difference in the incidence of nausea and vomiting * No significant difference in the use of a vasopressor (phenylephrine) * Neonatal outcomes were similar
(30)	RCT	15 ml/kg Ringer lactate vs 8 ml/kg HES 6%[39]	2016	70	*Incidence of hypotension: 57.14% vs 54.2%, with a more significant fall in diastolic blood pressure and mean arterial pressure in the crystalloid co-loading group. * There is no statistically significant difference between systolic blood pressure and heart rate among the two groups. *The number of vasopressor units required to treat hypotension among groups were comparable statistically. * Neonatal outcomes and the incidence of nausea and vomiting were similar.

Table VIII. — Comparison of crystalloid co-load with a control group.

	Study design	Comparison	Year	Number of patients	Results
(31)	RCT	Ringer's lactate rapidly (max 2l) vs at a minimal maintenance rate. Both receiving prophylactic IV phenylephrine.[40]	2005	106	*Incidence of hypotension: 1.9% vs 28.3% (P=0.0001). * Nausea, vomiting, neonatal outcomes: similar between both groups

phenylephrine prophylactic infusion. Looking further into the difference between crystalloid co-loading and colloid co-loading, there are conflicting results. Neither one proved to result in a superior hemodynamic profile in one study[38], whilst another study showed a small but significant better profile in the colloid co-loading group[39]. An important sidenote in the difference between both studies is the prophylactic use of a phenylephrine infusion in the first study. Neonatal outcome and the incidence of nausea and vomiting were comparable between both groups. When using a combination of colloid preloading and crystalloid co-loading in comparison to only crystalloid co-loading, no benefit on spinal hypotension was seen[41]. Details can be found in Table III + VI to IX.

B. Colloid co-load

A comparison of colloid co-loading with colloid and crystalloid co-loading and preloading has already been mentioned before.

Discussion

Different fluid regimens have been studied, fluid preloading and co-loading. Both fluid management strategies can occur with either a colloid solution or a crystalloid solution.

Crystalloid preloading showed to be ineffective in preventing hypotension despite high infusing volumes. Studies suggested the role of ANP release with its diuretic and vasodilating effects[42] as a cause of its ineffectiveness, but also the fact that crystalloids immediately redistribute[11], with only 28% of the infused crystalloids remaining

intravascular[15]. The rapid administration of a crystalloid preload (10 min instead of 20 min) also failed to reduce the incidence of hypotension[40].

Colloid preloading on the other hand, demonstrated to be an adequate prophylactic measure in the prevention of spinal hypotension. When comparing colloid preloading with a lower dose of the same colloid, the incidence of hypotension was reduced. This suggests a dose dependent effect and the importance that the volume of fluid must be large enough to result in a significant increase in cardiac output. A systematic review from 200244 where the two types of preloading were investigated, supported the efficacy of colloid preloading in reducing spinal hypotension whereas crystalloid preloading seemed uniformly ineffective. Another systematic review and meta-analysis from 2015[45], including 990 patients,et al.also noted the difference between crystalloids and colloids (where most of the included trials involved preloading) and showed that colloids reduced the incidence of hypotension more than crystalloids. The most recent systematic review and meta-analysis from 2021[46], which included 2566 patients, again confirmed the superiority of colloid preloading to crystalloid preloading in reduction of spinal hypotension and nausea and vomiting. HES 6% in a dose of 7-10 ml/kg or 500 ml, was the fluid regimen of choice according to a subgroup analysis in this review.et al.The fact that colloid preloading is more effective then crystalloid preloading probably is because colloids have a longer intravascular life then crystalloids. They consist of larger molecules that do not immediately redistribute through the interstitial space. Therefore, they do not decrease plasma colloid oncotic pressure so much and intravascular volume is better maintained[15], with less occurrence of tissue edema and electrolyte abnormalities[13]. One study also found that the protective effect of the colloid solution was more pronounced for severe than for less severe hypotension18.et al.Hetastarch, pentastarch, dextran and albumin are all considered effective in the prevention of hypotension. Pentastarch may be slightly preferable because of its shorter plasma expansion effect (12h vs 36h)[16].

Crystalloid and colloid co-loading both showed to be effective in the prevention of spinal hypotension. When both were compared with each other, no significant difference was seen. Unlike crystalloid preloading, crystalloid co-loading achieves its maximum effect during the time of spinal anesthesia, when the vasodilationet al.evolves, plus it results in a rapid circulation of the vasopressor.

No fluid regimen alone has proven to be effective enough in eliminating spinal hypotension following neuraxial anesthesia for caesarean delivery. A combination of prophylactic measurements is therefore the golden standard[47]. The simultaneous use of vasopressors, like the alfa-agonist phenylephrine which directly counteracts the decrease in arterial resistance, or noradrenaline have been proven to be effective[7]. Left lateral tilt, low dose spinal anesthesia and the use of 5-HT3 antagonists like ondansetron are other potential strategies to prevent hypotension[7]. Ondansetron has shown to reduce spinal hypotension by blocking the Bezold-Jarisch reflex, induced by a reduced venous return[55].et al.In this narrative review colloid preloading, co-loading and crystalloid co-loading showed to be effective as a part of the prophylactic management. In a meta-analysis from 2020[48] where a forest plot was created, the effectiveness was showed in descending order, with colloid co-load more effective than colloid preload and crystalloid co-load more than crystalloid preload. A systematic review from 2020[7] where 125 studies involving 9469 women were included, supported the use of crystalloids co-loading in higher volumes, as well as colloid pre- or co-loading. NICE guidelines on caesarean section from 2021[47] recommend the use of crystalloid co-loading, in addition to the prophylactic use of vasopressors as the golden standard. Colloids were not supported because of cost and risk of side-effects such as anaphylaxis, hemostatic impairment and renal impairment. However, in none of the obstetric studies any serious side-effects were noted. The use of colloids therefore seems safe especially in this healthy pregnant population receiving low volumes of colloids (up to maximum 15 ml/kg or 1000 mL)[49-52].

An important note is that none of the included studies were able to demonstrate any adverse fetal outcome (based on Apgar scores and fetal pH), this is probably due to the rapid treatment of hypotension, with preservation of cardiac output andet al.uteroplacental perfusion[53].

Limitations of the studies are the use of ephedrine as a vasopressor in the treatment of hypotension in most studies, which is no longer relevant to current recommended practice, with phenylephrine or noradrenaline now established as a first line vasopressor treatment. Also almost no study compared fluid regimen in women under prophylactic vasopressor administration, which is now recommended and as recent literature underscores: the most important fundament in the prevention. Following this limitation, other studies need to be set up to assess the impact of a fluid regimen as a adjuvants to a prophylactic vasopressor for the prevention of spinal induced hypotension.

Conclusion

No fluid regimen alone has proven to be effective enough in the elimination of spinal hypotension following neuraxial anesthesia for caesarean delivery. Crystalloid preloading is ineffective for prevention of hypotension despite high infusing volumes. Crystalloid co-loading, colloid co-loading and colloid preloading all have been shown to be effective looking at individual RCT's, as well as systematic reviews and meta-analyses. NICE guidelines support the use of crystalloid co-loading because of the better safety profile, however no adverse effects were reported in previous studies regarding colloid administration.et al.

Acknowledgment statements relating to this article:
1. Assistance with this article: None.
2. Financial support and sponsorship: None.
3. Conflict of interest: Dr. Hendrickx has received lecture support, travel reimbursements,equipment loans, consulting fees, and/or meeting organizational support from AbbVie (North Chicago, Illinois, USA), Acertys (Aartselaar, Belgium), Air Liquide (Paris,France), Allied Healthcare (St. Louis, Missouri, USA), ArmstrongMedical (Coleraine, United Kingdom), Baxter (Deerfield, Illinois, USA), Dräger (Lübeck, Germany), General ElectricHealthcare (Madison, Wisconsin, USA), Getinge (Gothenburg, Sweden), Hospithera (Anderlecht, Belgium), Heinen und Lowenstein (Bad Ems, Germany),Intersurgical (Wokingham, United Kingdom), MDoloris Medical Systems (Loos, France),MEDEC (Aalst, Belgium), Micropore (Elkton, Maryland, USA), Molecular Products (Harlow, United Kingdom), Philips (Brussels, Belgium), Piramal (Mumbai, India), and Quantium Medical (Barcelona, Spain). Dr. Hendrickx is the current chair of the Industry Liaison Task Force of the European Society of Anaesthesiology and Intensive Care (Brussels,Belgium). The other authors declare no competing interests.

References

1. Hollmen AI, Jouppila R, Koivisto M, et al. Neurologic activity of infants following anesthesia for cesarean section. Anesthesiology 1978;48:350-6.
2. Mueller MD, Bruhwiller H, Schupfer GK, Lusher KP. Higher rate of fetal acidemia after regional anesthesia for elective cesarean delivery. Obstet Gynecol 1997;90:131–4.
3. Roberts SW, Leveno KJ, Sidawi JE, Lucas MJ, Kelly MA. Fetal acidemia associated with regional anesthesia for elective cesarean delivery. Obstet Gynecol 1995;85:79–83
4. Reynolds F, Seed PT. Anaesthesia for Caesarean section and neonatal acid–base status: a meta-analysis. Anaesthesia 2005; 60:636–53
5. McCrae AF, Wildsmith JAW. Prevention and treatment of hypotension during central neural block. Br J Anaesth 1993;70(6):672–680.
6. Langesæter E, Dyer RA. Maternal haemodynamic changes during spinal anaesthesia for caesarean section. Curr Opin Anaesthesiol. 2011 Jun;24(3):242-248.
7. Chooi C, Cox JJ, Lumb RS, et al. Techniques for preventing hypotension during spinal anaesthesia for caesarean section. Cochrane database of systematic reviews 2017; 8: CD002251.
8. Wollman SB, Marx GF. Acute hydration for prevention of hypotension of spinal anesthesia in parturients. Anesthesiology 1968;29:374-380.
9. Green BN, Johnson CD, Adams A. Writing narrative literature reviews for peer-reviewed journals: secrets of the trade. J Chiropr Med. 2006 Autumn;5(3):101-17.
10. Rout CC, Rocke DA, Levin J, et al. A reevaluation of the role of crystalloid preload in the prevention of hypotension associated with spinal anesthesia for elective cesarean section. Anesthesiology 1993;79(2):262-9.
11. Jackson R, Reid JA, Thorburn J. Volume preloading is not essential to prevent spinal-induced hypotension at Caesarean section. Br J Anaesth 1995;75(3):262-5.
12. Park GE, Hauch MA, Curlin F, Datta S, Bader AM. The effects of varying volumes of crystalloid administration before Cesarean delivery on maternal hemodynamics and colloid osmotic pressure. Anesth Analg 1996; 83(2): 299–303
13. Riley ET, Cohen SE, Rubenstein AJ, et al. Prevention of hypotension after spinal anesthesia for cesarean section: six percent hetastarch versus lactated Ringer's solution. Anesth Analg; 1995 Oct;81(4):838-42.
14. Karinen J, Alahuhta RJS, Jouppila JRP. Effect of crystalloid and colloid preloading on uteroplacental and maternal haemodynamic state during spinal anesthesia for cesarean section. Br J Anaesth; 1995 Nov;75(5):531-5
15. Ueyama H, He YL, Tanigami H, et al. Effects of crystalloid and colloid preload on blood volume in the parturient undergoing spinal anesthesia for elective Cesarean section. Anesthesiology; 1999 Dec;91(6):1571-6.
16. French GW, White JB, Howell SJ, Popat M. Comparison of pentastarch and Hartmann's solution for volume preloading in spinal anaesthesia for elective caesarean section. Br J Anaesth 1999;83(4):475–7.
17. Siddik SM, Aouad MT, Kai GE, et al. Hydroxyethylstarch 10% is superior to Ringer's solution for preloading before spinal anesthesia for Cesarean section. Can J Anaesth. 2000 Jul;47(7):616-21.
18. Dahlgren G, Granath F, Pregner K, Rosblad PG, Wessel H, Irestedt L. Colloid vs. crystalloid preloading to prevent maternal hypotension during spinal anesthesia for elective cesarean section. Acta Anaesthesiol Scand 2005;49(11):1200–6.
19. Ko JS, Kim CS, Cho HS, Choi DH. A randomized trial of crystalloid versus colloid solution for prevention of hypotension during spinal or low-dose combined spinal-epidural anesthesia for elective cesarean delivery. Int J Obstetr Anesth 2007;16(1):8-12.
20. Tamilselvan P, Fernando R, Bray J, Sodhi M, Columb M. The effects of crystalloid and colloid preload on cardiac output in the parturient undergoing planned cesarean delivery under spinal anesthesia: A randomized trial. Anesth Analg 2009;109(6):1916-21.
21. Bouchnak M, Magouri M, Abassi S, et al. Preloading with HES 130/0.4 versus normal saline solution to prevent hypotension during spinal anaesthesia for elective caesarean section. Ann Fr Anesth Reanim. 2012 Jun;31(6):523-7.
22. Alimian M, Mohseni M, Safaeian R, et al. Comparison of hydroxyethyl starch 6% and crystalloids for preloading in elective caesarean section under spinal anesthesia. Med Arch. 2014 Aug;68(4):279-81.
23. Romdhani C, Trabelsi W, Lebbi A, et al. Lower incidence of hypotension following spinal anesthesia with 6% hydroxyethyl starch preload compared to 9 ‰ saline solution in caesarean delivery. Tunis Med. 2014 Jun;92(6):406-10.
24. Mercier FJ, Diemunsch P, Ducloy-Bouthors AS, 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 Sep;113(3):459-67.
25. Matsota P, Karakosta A, Pandazi A, et al. The effect of 0.5 L 6% hydroxyethyl starch 130/0.42 versus 1 L Ringer's lactate preload on the hemodynamic status of parturients undergoing spinal anesthesia for elective cesarean delivery using arterial pulse contour analysis. J Anesth. 2015 Jun;29(3):352-359.
26. Bottiger BA, Bezinover DS, Mets B, et al. Phenylephrine infusion for spinal-induced hypotension in elective cesarean delivery: does preload make a difference. Anaesthesiol Clin Pharmacol. 2016 Jul-Sep;32(3):319-24.
27. Saghafinia M, Jalali A, Eskandari M, Eskandari N, Lak M. The effects of hydroxyethyl starch 6% and crystalloid on volume preloading changes following spinal anesthesia. Adv Biomed Res. 2017 Sep 21;6:115.
28. Gousheh MR, Akhondzade R, Asl Aghahoseini H, Olapour A, Rashidi M. The Effects of Pre-Spinal Anesthesia Administration of Crystalloid and Colloid Solutions on Hypotension in Elective Cesarean Section. Anesth Pain Med. 2018 Aug 8;8(4).
29. Oh AY, Hwang JW, Song IA, Kim MH, Ryu JH, et al. Influence of the timing of administration of crystalloid on maternal hypotension during spinal anesthesia for cesarean delivery: preload versus coload. BMC Anesthesiology 2014 14:36.
30. Ngan Kee WD, Khaw KS, Lee BB, Ng FF, Wong MM. Randomized controlled study of colloid preload before spinal anaesthesia for caesarean section. Br J Anaesth 2001;87(6):772-774.
31. Davies P, French GW. A randomised trial comparing 5 mL/kg and 10 mL/kg of pentastarch as a volume preload before spinal anaesthesia for elective caesarean section. Int J Obstet Anesth 2006; 15(4): 279-83.
32. Nishikawa K, Yokoyama N, Saito S, Goto F. Comparison of effects of rapid colloid loading before and after spinal anesthesia on maternal hemodynamics and neonatal outcomes in cesarean section. J Clin Monit Comput 2007; 21:125-9.
33. Siddik-Sayyid SM, Nasr VG, Taha SK, et al. A randomized trial comparing colloid preload to oload during spinal anesthesia for elective cesarean delivery. Anesth Analg 2009; 109:1219-24.
34. Carvalho B, Mercier FJ, Riley ET, Brummel C, Cohen SE. Hetastarch co-loading is as effective as pre-loading for the prevention of hypotension following spinal anesthesia for cesarean delivery. Int J Obstet Anesth 2009; 18:150-5.
35. Teoh WHL, Sia AT. Colloid preload versus coload for spinal anesthesia for cesarean delivery: the effects on maternal cardiac output. Anesth Analg 2009; 108:1592-8.
36. Varshney, R. and Jain, G. (2013). Comparison of colloid preload versus coload under low dose spinal anesthesia for cesarean delivery. Anesthesia: Essays and Researches, 7(3), p.376.
37. Tawfik MM, Hayes SM, Jacoub FY, Badran BA, Gohar FM, Shabana AM, Abdelkhalek M, Emara MM. Comparison between colloid preload and crystalloid coload in caesarean section under spinal anesthesia: a randomized controlled trial. Int J Obstet Anesth 2014; 23(4):317-23.
38. McDonald S, Fernando R, Ashpole K, Columb M. Maternal cardiac output changes after crystalloid or colloid coload following spinal anesthesia for elective delivery: a randomized controlled trial. Anesth Analg 2011; 113:803-10.
39. Sushma, K. S., Jyoti, B., & Shaikh, S. I. A randomized controlled trial to compare crystalloid and colloid co-loading in preventing spinal hypotension in parturients undergoing caesarean section. Journal of Clinical Anesthesia 2016, 34, 557-560.
40. NganKee WD, Khaw KS, Ng FF. Prevention of hypotension during spinal anesthesia for cesarean delivery. An effective technique using combination phenylephrine infusion and crystal-loid cohydration. Anesthesiology 2005;103:744-50.
41. Tawfik, M.M., Tarbay, A.I., Elaidy, A.M., Awad, K.A., Ezz, H.M. and Tolba, M.A. (2019). Combined Colloid Preload and Crystalloid Coload Versus Crystalloid Coload During Spinal Anesthesia for Cesarean Delivery. Anesthesia & Analgesia, 128(2), pp.304–312.
42. Pouta A, Karinen J, Vuolteenaho O, Laatikainen T. Preeclampsia: the effect of intravenous fluid preload on atrial natriuretic peptide secretion during caesarean section under spinal anaesthesia. Acta Anaesthesiol Scand 1996;40:1203–9.
43. Rout CC, Akoojee SS, Rocke DA, Gouws E: Rapid administration of crystalloid preload does not decrease the incidence of hypotension after spinal anaesthesia for elective caesarean section. Br J Anaesth 1992;68:394-397.
44. Emmett RS, Cyna AM, Andrew M, Simmons SW. The effects of an increase of central blood volume before spinal anesthesia for cesarean delivery: a qualitative systematic review.
45. Ripollés Melchor J, Espinosa Á, Martínez Hurtado E, et al. Colloids versus crystalloids in the prevention of hypotension induced by spinal anesthesia in elective cesarean section. A systematic review and meta-analysis.
46. Shang Y, Li H, Ma J, Tan L, Li S, Li P, Sheng B, Wang R. Colloid preloading versus crystalloid preloading to prevent hypotension after spinal anesthesia for cesarean delivery: A protocol for systematic review and meta-analysis.
47. National Institute for Health and Clinical Excellence. Caesarean section (update). 2021
48. Rijs K, Mercier FJ, Lucas D, Rossaint R, Klimek M, Heesen M. Fluid loading therapy to prevent spinal hypotension in women undergoing elective caesarean section: Network meta-analysis, trial sequential analysis and meta-regression.
49. Laxenaire MC, Charpentier C, Feldman L. Anaphylactoid reactions to colloid plasma substitutes: frequency, risk factors, mechanisms. Ann Fr Anesth Reanim 1994; 13: 301–310.
50. Westphal M, James MF, Kozek-Langenecker S, Stocker R, Guidet B, Van Aken H. Hydroxyethyl starches: Different products — different effects. Anesthesiology 2009; 111:187-202.
51. Datta R, Nair R, Pandey A, Kumar N, Sahoo T. Hydroxyeyhyl starch: Controversies revisited. J Anaesthesiol Clin Pharmacol 2014; 30:472-80.
52. Weeks S. Reflections on hypotension during Cesarean section under spinal anesthesia: do we need to use colloid? Can J Anaesth 2000; 47: 607±10.
53. Corke BC, Datta S, Ostheimer GW, et al. Spinal anaesthesia for caesarean section. The influence of hypotension on neonatal outcome. Anaesthesia 1982;37:658-62.

doi.org/10.56126/74.1.09