ORIGINAL ARTICLE

# Comparison of intravenous colloid and colloid-crystalloid combination in hypotension prophylaxis during spinal anesthesia for cesarean section

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## Abstract

**Context:** Many studies comparing different intravenous fluid types usually do not use equipotent volumes of three to one crystalloid to colloid ratio in such comparisons. Conflicting results emanate from such studies.

**Aim:** This study was designed to compare the efficacy of equipotent volumes of colloid and crystalloid-colloid combination in spinal anesthesia-induced hypotension prophylaxis during cesarean section.

**Settings and Design:** A prospective randomized double blinded experimental study carried out in a tertiary hospital in Nigeria.

**Materials and Methods:** Pregnant women scheduled for elective cesarean section were prospectively randomized into two groups to receive either 1000 ml of crystalloid/colloid (750/250 ml) combination or 500 ml colloid intravenous fluid preload, before spinal anesthesia. Hemodynamic variables were monitored till the end of surgery. The results were collated, analyzed, and rational conclusions deduced.

**Statistical Analysis Used:** Data collected and analyzed with Statistical Package for Social Sciences (SPSS) version 16 and rational deductions derived.

**Results:** In the first 10 min, the crystalloid-colloid combination showed better efficacy in hypotension prophylaxis over the colloid only regimen. In the next 30 min; however, there was no significant difference between both groups in hemodynamic parameters.

**Conclusion:** Beyond 10 min the crystalloid-colloid combination has no advantage over colloid alone in hypotension prophylaxis, as used in this study.

**Key words:** Cesarean section, hypotension, intravenous fluids, spinal anesthesia

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## Introduction

Hypotension is a prominent side effect of spinal anesthesia.

Prophylactic methods include fluid preloading, prophylactic ephedrine, Trendelenburg positioning, relieving aorto-caval compression, etc., For effective prevention, fluid preloading must be sufficient to significantly increase cardiac output[1]

Crystalloid have a short intravascular half-life, large volumes are therefore needed. Colloids stay longer in the circulation and smaller amounts are required. Both fluid types have their implications and side effects[2,3]

Colloid and crystalloid combination tend to reduce the disadvantages of either agent alone and synergize their advantages. Comparison of the fluid regimens in equipotent volumes may alter current opinion on the phenomenon[4-7]

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## Materials and Methods

This study seeks to evaluate which intravenous fluid: Colloid or their combination preload in equipotent volumes is more efficacious in preventing spinal anesthesia-induced hypotension in parturient for cesarean section. It is a prospective, randomized, double-blinded, experimental design. The study population was drawn from parturient scheduled for elective cesarean section in a Tertiary Hospital in Nigeria. Non-laboring American Society of Anesthesiologist (ASA) I or II women, having non-urgent cesarean section were enrolled in the study.

Multiple pregnancy, weight over 115 kg, height less than 150 cm, diabetes mellitus, hypertensive diseases in pregnancy, intra-uterine death, age less than 18 years or more than 40 years, patients on diuretic therapy, and contraindication to central neural blockade (patients refusal, raised intracranial pressure, hypovolemic states, abnormal coagulopathy) were excluded from the study. Approval of the Institutional Ethics Committee, and informed patient consent were obtained. Seventy non-laboring ASA I or II women, having non-urgent cesarean section were enrolled in the study.

Patients were fasted over-night for at least 6-8 h. The patients did not receive intravenous fluid prior to entering the study. In addition, all the patients received 50 mg of intravenous ranitidine, 1 h prior to anesthesia, for gastric acid aspiration prophylaxis. The subjects were randomly assigned by blind balloting into one of two groups of 35 patients each. Group PS received 500 ml of 6% pentastarch (PS, $n = 35$) and Group PRC received a combination of 250 ml 6% pentastarch and 750 ml of Ringer's lactate (PRC, $n = 35$).

On arrival in the operating theatre suite, multi-parameter monitor was attached to the patients and baseline vital signs including blood pressure (systolic, diastolic, and mean), pulse rate, and $SpO_2$ were recorded. Intravenous access was established with an 18 gauge cannula. Each patient was preloaded with the wrapped designated preloading fluid over 15 min. The investigator was absent during the period of preload. All data were collected by the investigator.

Spinal anesthesia was performed by the investigator under aseptic condition at $L_2/L_3$ or $L_3/L_4$ interspaces, with the patients in sitting position. All the patients received 2.5 ml of 0.5% heavy bupivacaine through a 25G Whitarce needle over a period of 12 s. Immediately after injection, the patients were positioned supine with left lateral uterine displacement. The blood pressure, pulse rate, $SpO_2$ were monitored using a multi-parameter monitor, every minute for the first 10 min and then every 3 min for the next 10 min, there-after 5 min till the end of surgery. Hypotension was taken as systolic blood pressure less than 80% of baseline values and the number of patients that were hypotensive was taken to represent the incidence of hypotension for each group. Hypotension when it occurred was treated with 3 mg of aliquots of ephedrine hydrochloride and rapid infusion of fluids.

The severity of hypotension was determined by the number of patients that required ephedrine, total amount of ephedrine used to treat hypotension, and the total amount of infusion used nausea and or vomiting. Apgar score were also used to determine the severity of hypotension, this was done by educating patients to report any nausea and also encouraged to rate it with the nausea score of 0-3 (0-no nausea, 1-mild, 2-moderate, and 3-severe nausea) while retching/vomiting was observed by the investigator and documented. This was done before and after volume preloading and after spinal anesthesia. A nausea score was recorded anytime the patient complained of nausea or noticed to have vomited intra-operatively and if related to any hypotensive episode. Neonatal outcome was assessed using Apgar score at 1 and 5 min, any value less than 7 in 1 min needed resuscitation and the number noted. Other complications like birth asphyxia, meconium aspiration were noted and managed appropriately. Other variables that were recorded are medications and their doses, maximum block height assessed using pinprick test. Parameters such as blood loss, urine output were monitored and managed appropriately for safe anesthesia till end of surgery.

The two groups were compared using Student's *t*-test, represented as mean ± standard deviation (SD) (continuous data) and Chi-square for categorical data. The null hypothesis was rejected at $P < 0.05$. Data collected was analyzed with Statistical Package for Social Sciences (SPSS) version 16 and rational deductions derived.

## Results

The mean age, height, and weight of patients in both groups were similar. There were no differences in the upper levels of spinal blockade; the maximum block height was between T8 and T4 for each group [Table 1].

There were no differences in the pre-induction values of the systolic and diastolic blood pressures; heart rates and $SpO_2$ [Table 2]. After spinal anesthesia, mean and minimum systolic blood pressures, diastolic blood pressures, heart rates, $SpO_2$ were lowest in the colloid group. These were however not statistically significant [Table 2]. In the two groups, all hemodynamic parameters were reduced with

**Table 1: Demographic data/clinical characteristics**

| | Colloid group | Combination group | *P* value |
|---|---|---|---|
| Age (years) | 34.03±4.82 | 32.74±5.09 | 0.285 |
| Height (m) | 1.59±0.09 | 1.63±0.06 | 0.027 |
| Weight (kg) | 79.51±12.55 | 80.13±12.01 | 0.836 |
| Level of block | T8-T4 | T8-T4 | |

time. The combination group had less reduction in the mean arterial blood pressure [Figure 1].

Comparison of ephedrine requirements showed that the number of patients that required ephedrine and the mean ephedrine dose were highest in the colloid group. The mean duration of surgery and estimated blood loss were similar in both groups [Table 3].

Incidence of hypotension in the first 10 min after spinal anesthesia was highest in the colloid group with (91%), versus 68% in the combination group. These differences were statistically significant. The incidence of hypotension in the latter 30 min, that is, between 10 and 40 min after spinal showed that, colloid had 76% and combination group had 62%. These differences were not statistically significant, [Table 4].

Neonatal outcome with Apgar score less than 7 in 1 min, (those that require active resuscitation) occurred most in the combination group, with six neonates, versus four neonates in the combination group. In the colloid group one patient vomited and two others had mild nausea

**Table 2: Pre-and intraoperative values after spinal**

| Hemodynamic parameters | Colloid | Combination | *P* value |
|---|---|---|---|
| Pre-induction Values | 138.47±14.84 | 137.14±18.00 | 0.740 |
| Systolic (mmHg) | 80.97±8.93 | 78.97±8.96 | 0.357 |
| Diastolic (mmHg) | 97.09±12.23 | 97.14±10.75 | 0.984 |
| Heart rate (/min) | 97.97±0.72 | 97.97±1.07 | 0.997 |
| $SpO_2$ | | | |
| Mean intraoperative values | | | |
| Systolic (mmHg) | 114.18±15.61 | 116.97±17.71 | 0.490 |
| Diastolic (mmHg) | 60.47±9.81 | 63.06±11.12 | 0.310 |
| Heart rate (/min) | 97.65±12.24 | 99.91±15.36 | 0.501 |
| $SpO_2$ | 97.82±0.94 | 97.94±1.41 | 0.681 |
| Minimum values after spinal (10 min after spinal) | | | |
| Systolic (mmHg) | 95.44±15.35 | 97.94±20.58 | 0.570 |
| Diastolic (mmHg) | 47.00±9.17 | 50.43±12.45 | 0.198 |
| Heart Rate (/min) | 81.62±15.27 | 86.51±15.17 | 0.186 |
| $SpO_2$ | 96.74±1.24 | 96.00±3.66 | 0.271 |

**Table 3: Intraoperative clinical values**

| | Colloid | Combination | *P* value |
|---|---|---|---|
| Level of sensory block | T8-T4 | T8-T4 | |
| Mean duration of surgery (min) | 52.82±17.99 | 57.37±22.06 | 0.352 |
| Mean blood loss (ml) | 625.15±300.81 | 607.14±202.61 | 0.771 |
| Mean ephedrine dose (mg) | 5.76±9.61 | 3.66±7.23 | 0.306 |
| No. of patient requiring ephedrine | 13.00 | 10.00 | |
| Total amount of ephedrine (mg) | 166 | 128 | |

**Table 4: Incidence of hypotension**

| Incidence of hypotension | Identification | | *P* value |
|---|---|---|---|
| | Colloid (%) *n*=34 | Combination (%) *n*=35 | |
| First 10 min | 31 (91) | 24 (68) | 0.0419 |
| 10-40 min | 26 (76) | 22 (62) | 0.3335 |

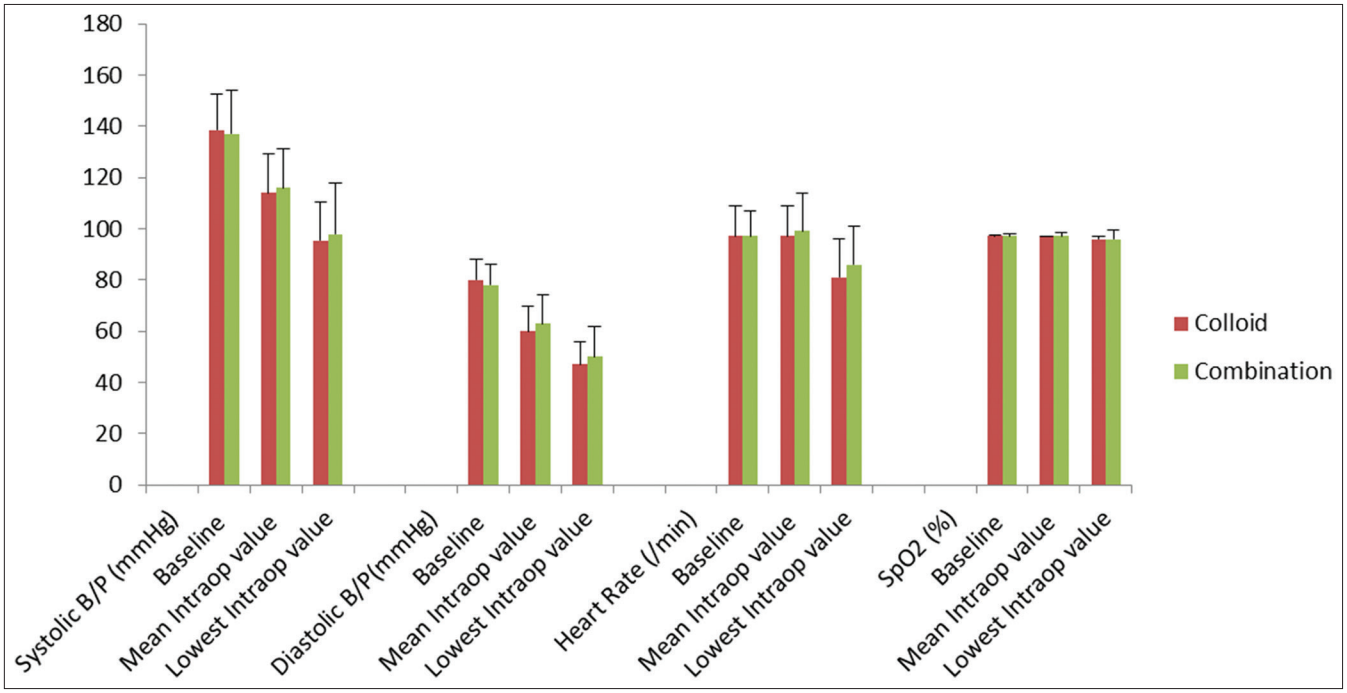


**Figure 1:** Mean arterial pressure v time (min)

against one patient that vomited in the combination group. Nausea and/or vomiting coincided with episodes of maternal hypotension and were successfully treated by correcting the hypotension with IV ephedrine and rapid fluid infusion.

Hypotension occurred earliest in the combination group with mean time of 2.39 min, while the colloid group was delayed till 3.85 min [Figure 2].

## Discussion

In this study, combination of intravenous fluids reduced the incidence of hypotension better than the colloid alone within the outcome measurement time frame of 10 min (average uterine delivery time and optimal effect of pharmacological sympathectomy). Within a 15 min period of preload before establishment of spinal anesthesia, volumetric effect is more important than osmotic effect. Combination group had better efficacy in preventing hypotension because a larger amount of fluid 1000 ml (750 ml of crystalloid and 250 ml of colloid) was infused compared to 500 ml of colloid in the other group, though they were given in equipotent volumes.

Our result is similar to that of Vercauteren *et al.*,[8] who had better hypotension prophylaxis after subarachnoid blockade with the combination of crystalloid-colloid compared to colloid. Though there was a reduced incidence of hypotension in the combination group when compared to the colloid group in both our studies. Their study compared 1000 ml of 6% hydroxylethylstarch (HES) and 1000 ml of Ringer's lactate to 1000 ml of HES, these volumes were not equipotent, it should have been 1000 ml of Ringer's and 660 ml of HES in the combination group rather than the 1000 ml they used. This could have accounted for the much reduced incidence of hypotension of 10%, compared to the 68% in this study. Another study also showed the superiority of combination therapy, but was compared against crystalloid; interestingly they were not in equipotent volumes[4]

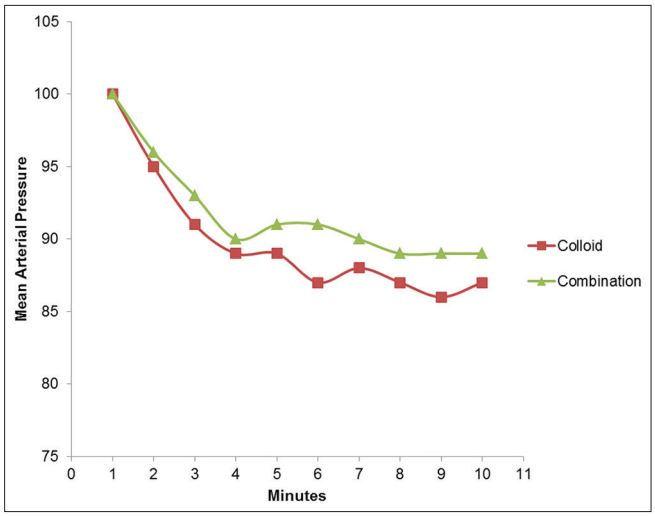


**Figure 2:** Bar chart showing intraoperative values

Another reason that can be attributed for the reduced incidence of hypotension in the combination group compared to the colloid group in our study could be the acute hydration in about 15 min before spinal anesthesia was established. The time to establishment of spinal anesthesia should be less than the intravascular half-life of the crystalloid in other to prevent redistribution to interstitial space. The time for preload did not seem to affect Vercauteren's result; they had preloading from the ward before proceeding to the operating theater for the anesthetic technique. Although the exact interval between preload and spinal anesthesia was not stated, the increased total volume could have been responsible for better results in the Vercauteren study compared to that obtained in this study.

Rout *et al.*, rapidly administered crystalloid, but did not decrease the incidence of hypotension after spinal anesthesia for elective cesarean section[9] They compared 20 ml/kg of crystalloid infused over 10 and 20 min, and found no difference. It is possible that the 20 min infusion time which is the upper border before redistribution into interstitial space occurs, may be responsible for no difference in the incidence of hypotension in their study.

In this study, the incidence of hypotension was 91% when 500 ml of 6% HES was used as a preloading agent. Ueyema *et al.*, had 58% incidence when same volume of colloid was used[1] It could be that there was more time for the osmotic effect of colloid in Ueyema's study, with 30 min as preloading time, as against 15 min preloading time in our study. A 6% HES is said to have no initial plasma increase unlike other colloids like 10% HES which are hyper-osmotic when first infused[10]

The osmotic effect of colloid came more into play after the spinal was established. The incidence of hypotension between the groups which was statistically significant in the first 10 min was not significant after this. This may be due to the combination fluid initially exerting its volumetric effect, while the osmotic effect of colloid was negligible, but between the 10 and 40 min time frame, they were no longer statistically significant. The reason for this may be because colloid osmotic effect was appreciating, while the volumetric effect of the combination fluid was waning. Colloid osmotic effect of the colloid group could predominate over combination group if the period of monitoring extended over hours after spinal anesthesia.

Although Sharma *et al.*, rapidly infused 500 ml of 6% HES over 15 min, as in this study, they recorded a lower incidence of hypotension of 52% was observed[11] This lower incidence would have been possible because their study group were non-parturients. So also were Buggy

*et al.*, who rapidly infused 500ml of colloid (Haemaccel) in elderly patients over 5-8 min and had 39% incidence of hypotension[12] Pregnant patients at term are more prone to develop hypotension due to the occurrence of aorto-caval compression by the fetal head and higher sympathetic blockade owing to increased spread of local anesthetic agent in the cerebrospinal fluid.

The observation that preloading does not eliminate hypotension after spinal anesthesia was further established by our study. Although some workers[13,14] at various times reported no hypotension in their studies, the agents and quantity used could have been responsible for this observation. Mathru *et al.*,[14] for example, used 15 ml/kg of 5% albumin in 5% dextrose Ringer's lactate (D5RL) which is a combination of colloid and crystalloid. This result could only be possible because of albumin used, is a principal natural colloid comprising of 50-60% of all plasma proteins. It contributes to 80% of normal oncotic pressure[15] Wollman and Marx also used 1000 ml of D5RL, though not a colloid, there was no incidence of hypotension[13] These results have not been replicated by other workers because the quality may be responsible for this.

Vasopressors like ephedrine are used in the management of spinal induced-hypotension, among others. In this study, total rescue ephedrine used was lowest in the combination group because the numbers of hypotensive patients were least in the group. This reveals the superior effect of combination in preventing spinal induced maternal hypotension, within the time frame of 10 min outcome study. Nausea and vomiting also occurred more in the colloid group because they had a higher incidence of hypotension.

No adverse reaction to crystalloid or colloid occurred in this study, although the incidences of allergic reaction with artificial colloid are high[15] Severe anaphylactic or anaphylactoid reaction did not occur with HES in this study.

Common complications that occurred were headache, chest pain, shivering, and dizziness. These complications are due mainly to spinal anesthesia or exteriorization of the uterus. Complications were unrelated to the type of fluid used for preload. It is however, not expected that significant pulmonary pathology would have occurred after 1000 ml fluid load, considering the fact that they were healthy parturients with ASA I and II fitness.

## Conclusion

The incidence of hypotension was better reduced by crystalloid/colloid fluid combination, compared to colloid only over a 15 min hydration period. This could be due to the fact that the comparison was in equipotent volumes and not equal volumes or in ratios other than 3:1. It could also be due to outcome measures determination over a 10 min time frame. When outcome measures extend beyond 10 min, there was no statistical significance between the groups.

As there are no methods that totally prevent spinal hypotension in these groups of patients, vigilant monitoring of maternal blood pressure every minute after spinal injection, with immediate treatment of hypotension by bolus ephedrine is advocated.

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