Comparison between Preload with Colloid versus Preload with Crystalloid before Spinal Anesthesia

Prof. Dr. Mohammed Saeed Abd El-Aziz[1], Ass. Prof. Dina Salaah El-Deen[1], Dr. Alaa Abd El-Aziz niazy[2] and Moustafa Tarek Nabieh Ghazal[2]

[1]Anesthesiology, Intensive Care & Pain Management Department, Faculty of Medicine, Ain Shams University, Egypt.
[2]Anesthesiology, Intensive Care & Pain Management Department, Faculty of Medicine, Misr University for Science and Technology, Egypt.
moustafaghazal69@gmail.com

Abstract: Background: Hypotension following spinal anaesthesia is mainly occurs due to sympathetic blockade leading to peripheral vasodilatation and venous pooling of blood. As a result, there is decreased venous return and cardiac output leading to hypotension. **Objectives:** To aid in making appropriate therapeutic decisions in the prophylaxis and management of post spinal hypotension and decreasing hazards of hypotension and the use of vasopressor. **Patients and Methods:** Type of study: Prospective randomized controlled Study. The study was performed in the teaching hospitals of Misr university of Science and Technology. Study period: 5 months from March to July 2018. Study population: 20-50 years old patients undergoing elective surgery with spinal anesthesia. **Results:** To aid in making appropriate therapeutic decisions in the prophylaxis and management of post spinal hypotension and decreasing hazards of hypotension and the use of vasopressor. **Conclusion:** In conclusion, colloid appears to be more effective than crystalloid in maintaining the blood pressure after spinal anesthesia. Nevertheless, further large-scale trials are still needed to confirm our findings.

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1. Introduction

Hypotension following spinal anaesthesia is mainly occurs due to sympathetic blockade leading to peripheral vasodilatation and venous pooling of blood. As a result, there is decreased venous return and cardiac output leading to hypotension ***(Williamson et al., 2009).***

The spectrum of morbidity associated with hypotension may include but is not limited to a higher incidence of nausea, vomiting, dizziness, aspiration, syncope and cardiac arrhythmias ***(NganKee et al., 2005).***

One of the most commonly used methods to reduce spinal anaesthesia induced hypotension is administration of fluids before implementation of spinal anaesthesia, a technique named 'pre-loading' first described by Wollman and Marx. This preloading with intravenous fluids offset the vasodilating effects of sympathetectomy caused by spinal anaesthesia thereby maintaining the venous return and thus the drop in blood pressure is prevented. Crystalloids have shorter half-life in the intravascular compartment and generally exit the intravascular space within 1 hour so that their ability to expand the intravascular volume is limited due to shorter duration of action. Pre-loading with crystalloids has been found to be less effective due to the shorter half-life as they are less successful in maintaining the intravascular volume during the dynamic establishment of spinal anaesthesia effect and the resulting vasodilatation ***(Bajwa et al., 2013).***

Colloids, on the other hand, have a longer half-life in the intravascular compartment and are able to maintain the increase in intravascular volume for longer durations ***(Tamilselvan et al., 2009).***

Aim of the Work

To aid in making appropriate therapeutic decisions in the prophylaxis and management of post spinal hypotension and decreasing hazards of hypotension and the use of vasopressor.

2. Patients and Methods

- **Type of study:**

Prospective randomized controlled Study.

The study was performed in the teaching hospitals of Misr university of Science and Technology.

- **Study period:**

5 months from March to July 2018.

- **Study population:**

20-50 years old patients undergoing elective surgery with spinal anesthesia.

Inclusion criteria:

The study included adult patients medically free, of either sex, with ages ranging from 20 to 50 years.

No special consideration was given to race, geographic region or marital status.

Exclusion criteria:

1. Patient refusal.
2. Patient younger than 20 years old or older than 50 years old.
3. Allergy to any of study medications.
4. Emergency procedures.
5. Patients on any antihypertensive treatment.
6. Patients with history of heart rhythm abnormality and heart failure.
7. Patients with anomalies in the vertebral column.
8. Patients receiving anticoagulants such as warfarin or heparin or with coagulopathies and blood diseases.
9. Infection of skin around the lumbar area in the back.
10. Patients with kidney, liver, or central nervous system disease.

- **Sampling Method:**

- Patients were randomly allocated to one of two groups according to a computer-generated list of random numbers and concealed in closed envelopes; Group A (Crystalloid Group), and Group B (Colloid Group).
- Each of group (A) received10 ml/kg normal saline 0.9%.
- Each of group (B) received10 ml/kg hydroxyethyl starch (MW 130,000/0.4%, 6%) (Voluven, Fresenius Kabi, Germany).

- **Sample Size:**

30 patients in each group

- **Ethical consideration:**

After obtaining approval from the medical ethical committee in Misr University of Science and Technology, this study was conducted in Misr University of Science and Technology operating rooms.

- **Study Procedures:**

Preoperative assessment including history, preoperative examination and all routine investigations were done as CBC, Coagulation Profile, Liver Function Tests, Kidney Function Tests and Blood Grouping. After patient arrival to the preanesthetic room 18G venous cannula were inserted in both groups then, preload was given within 15 min as following: (group A) received 10 ml/kg normal saline 0.9% and (group B) received 10ml/kg hydroxyethyl starch and BP was measured.

- **Induction and maintenance of anesthesia:**

After preload, patients entered the operative room and monitors (noninvasive blood pressure, pulse oximeter and electro cardiography) were applied the patients received spinal anesthesia in setting position with 25G spinal needle in L3-4 or L4-5 vertebral spaces then measuring of blood pressure every 5 minutes in the first. Hour, if mean blood pressure were decreased less than 60 mmHg ephedrine increments 3mg were given until satisfactory Blood Pressure (BP) within 20% decrease or increase of preoperative level. We maintained fluid volume as 4-6ml/kg of lactated ringer solution during the operation.

- **Recovery:**

At the end of surgery, all patients of both groups were transferred to the recovery room where all hemodynamic parameters (blood pressure, heart rate & oxygen saturation), especially blood pressure were measured every 30 minutes for 2 to 3 hours after the end of the surgery. The patients were discharged to the ward after they started regaining sensation by pin-prick test.

- **Measurement tools:**

Brachial artery blood pressure was checked with the patient in supine position using calibrated mercury sphygmomanometer and appropriate cuff size.

The blood pressure were monitored as follow

1) Every 5 minutes in first hour.
2) Every half an hour in second and third hours.

- **Primary outcome:**

- Blood pressure (Systolic, Diastolic and Mean)

- **Secondary outcome**:

- Pulse rate
- Oxygen saturation
- Level of conscious
- Complications [nausea, vomiting, chest pain]

3. Results

Table (1): Comparison of age between colloid and crystalloid groups

	Colloid (n=30)	Crystalloid (n=30)	p-value
Age (Years)	34.40± 8.66	33.57± 7.02	0.68

P-value calculated by independent t-test

Table (2): Comparison of Systolic blood pressure between colloid & crystalloid groups

Time	Colloid	Crystalloid	p-value
Baseline	112.03 ± 5.11	109.77 ± 4.17	0.07
After taking the preload	120.37 ± 4.90	115.27 ± 3.96	<0.0001*
After 5 mins	120.37 ± 4.90	115.27 ± 3.96	<0.0001*
After 10 mins	100.67 ± 2.58	93.63 ± 1.73	<0.0001*
After 15 mins	112.93 ± 54.85	97.20 ± 2.25	0.12
After 20 mins	112.93 ± 54.85	97.20 ± 2.25	0.12
After 25 mins	106.33 ± 6.54	102.80 ± 3.19	0.01*
After 30 mins	106.33 ± 8.89	104.83 ± 4.64	0.42
After 35 mins	107.47 ± 10.15	106.77 ± 7.31	0.76
After 40 mins	109.80 ± 10.37	108.20 ± 10.27	0.55
After 45 mins	112.07 ± 9.42	110.73 ± 10.45	0.61
After 50 mins	114.60 ± 8.61	113.87 ± 9.12	0.75
After 55 mins	117.07 ± 8.20	116.10 ± 7.48	0.64
After 60 mins	120.1 ± 6.24	118.10 ± 5.48	0.26
After 90 mins	1**22.50** ± 7.**29**	1**20.90** ± **6.21**	0.**36**
After 120 mins	1**24.37** ± **6.13**	1**22.33** ± **5.73**	0.**19**
After 150 mins	1**26.13** ± **5.27**	1**24.21** ± **5.49**	0.**19**
After 180 mins	1**2**6.87 ± 4.26	124.72 ± 5.15	0.09

Table (3): Comparison of Diastolic blood pressure between colloid & crystalloid groups

Time	Colloid	Crystalloid	p-value
Baseline	86.57 ± 3.70	86.13 ± 4.81	0.70
After taking the preload	74.23 ± 3.91	71.90 ± 4.77	0.04*
After 5 mins	74.23 ± 3.91	71.90 ± 4.77	0.04*
After 10 mins	59.40 ± 2.69	57.10 ± 6.27	0.07
After 15 mins	61.00 ± 3.28	59.83 ± 2.02	0.11
After 20 mins	61.60 ± 3.20	61.37 ± 2.80	0.77
After 25 mins	62.87 ± 2.96	62.03 ± 4.95	0.43
After 30 mins	63.97 ± 3.48	62.30 ± 5.57	0.17
After 35 mins	65.20 ± 5.07	63.87 ± 5.87	0.35
After 40 mins	66.63 ± 7.15	63.80 ± 5.06	0.08
After 45 mins	68.23 ± 7.10	65.17 ± 5.53	0.07
After 50 mins	70.73 ± 5.55	66.93 ± 4.88	0.007*
After 55 mins	72.13 ± 5.00	67.23 ± 5.32	0.001*
After 60 mins	74.13 ± 3.12	69.32 ± 4.35	0.001*
After 90 mins	7**5.67** ± 4.**04**	70.83 ± 4.**48**	<0.0001*
After 120 mins	7**6.93** ± **3.95**	7**2.70** ± 4.**32**	<0.0001*
After 150 mins	7**8.07** ± **3.16**	7**4.21** ± 4.**36**	<0.0001*
After 180 mins	7**8**.37 ± 2.19	7**5**.07 ± 4.28	<0.0001*

Table (4): Comparison of Mean blood pressure between colloid & crystalloid groups

Time	Colloid	Crystalloid	p-value
Baseline	82.93 ± 3.45	81.93 ± 4.08	0.26
After taking the preload	89.59 ± 3.57	86.30 ± 4.19	0.001*
After 5 mins	70.80 ± 3.57	67.60 ± 4.19	0.001*
After 10 mins	73.17 ± 2.07	70.20 ± 6.63	0.02*
After 15 mins	78.40 ± 18.41	72.27 ± 1.87	0.08
After 20 mins	76.13 ± 2.62	74.33 ± 2.37	0.007*
After 25 mins	76.83 ± 4.96	76.23 ± 2.81	0.57
After 30 mins	77.60 ± 3.97	76.97 ± 6.25	0.64
After 35 mins	79.07 ± 5.64	78.33 ± 6.81	0.65
After 40 mins	80.53 ± 8.17	79.13 ± 6.43	0.46
After 45 mins	82.43 ± 7.96	80.80 ± 6.29	0.38
After 50 mins	85.13 ± 6.44	82.83 ± 5.58	0.15
After 55 mins	87.10 ± 6.01	83.53 ± 5.24	0.02*
After 60 mins	87.10 ± 6.01	83.53 ± 5.24	0.02*
After 90 mins	91.37 ± 4.94	87.43 ± 4.56	0.002*
After 120 mins	92.73 ± 4.27	89.20 ± 4.20	0.002*
After 150 mins	94.07 ± 3.55	90.97 ± 4.08	0.002*
After 180 mins	94.53 ± 2.53	91.66 ± 4.11	0.002*

Table (5): Comparison of Pulse rate between colloid & crystalloid groups

Time	Colloid	Crystalloid	p-value
Baseline	80.90 ± 5.19	82.41 ± 3.66	0.15
After taking the preload	85.79 ± 5.14	90.47 ± 4.31	<0.0001*
After 5 mins	86.23 ± 5.14	89.27 ± 4.31	<0.0001*
After 10 mins	85.80 ± 5.45	88.73 ± 3.87	0.02*
After 15 mins	85.40 ± 4.93	87.57 ± 3.96	0.07
After 20 mins	84.13 ± 4.49	86.77 ± 3.46	0.01*
After 25 mins	84.27 ± 7.03	86.53 ± 4.06	0.13
After 30 mins	84.30 ± 8.35	86.37 ± 5.76	0.27
After 35 mins	84.53 ± 9.35	86.27 ± 8.00	0.44
After 40 mins	84.10 ± 9.73	86.17 ± 9.88	0.42
After 45 mins	82.97 ± 8.58	84.77 ± 9.65	0.45
After 50 mins	81.90 ± 7.72	83.23 ± 8.34	0.52
After 55 mins	80.67 ± 7.42	81.60 ± 7.77	0.64
After 60 mins	80.67 ± 7.42	81.60 ± 7.77	0.64
After 90 mins	**77.20** ± 6.4**2**	7**7**.20 ± 7.1**6**	**1.00**
After 120 mins	**75.87 ± 5.79**	7**6.00 ± 6.86**	**0.94**
After 150 mins	74.55 ± **5.28**	7**4.53 ± 6.28**	**0.94**
After 180 mins	73.24 ± 5.08	7**3**.37 ± 6.48	1.00

Table (6): Comparison of induction of vasopressor agent (Ephedrine in mg) between colloid and crystalloid groups

	Colloid	Crystalloid	p-value
Yes	6 (20%)	18 (60%)	0.003*
No	24 (80%)	12 (40%)	

p-value calculated by Fisher's exact test

4. Discussion

Hypotension is the most common side effect associated with spinal anesthesia. The incidence of hypotension following spinal anesthesia has been reported as 53% to 80%. The possible mechanism of spinal anesthesia-induced hypotension is associated with spinal nerve sympathectomy, vasodilation of peripheral arteries, decrease of venous return, and consequently decreasing the cardiac output. Loss of the circulating fluid decreases venous return and leads to decreased stretch of ventricular muscle, reducing cardiac output, which ultimately results in hypotension and poor perfusion. To prevent such hypotension, there are two main types of intravenous solutions, crystalloids and colloids, which are used preoperatively ***(Melchor et al., 2015).***

Over the past few decades, different approaches were developed to prevent the spinal anesthesia induced hypotension such as leg wrapping, elastic stockings, optimizing patient's position, intravenous fluids, and vasopressors from time to time to offset these hypotensive effects of spinal anaesthesia with varying degree of success. One of the foremost methods includes prophylactic administration of intravenous fluids before implementation of subarachnoid block to offset the hypotensive effects of sympathectomy by maintaining intravascular volume which is commonly called as pre-loading. This preloading with intravenous fluids offset the vasodilating effects of sympathetectomy caused by spinal anaesthesia thereby maintaining the venous return and thus the drop in blood pressure is prevented. Studies have shown that pre-loading decreases the incidence of hypotension after spinal anaesthesia in the first 5 minutes following subarachnoid injection as compared to the patients who did not receive any pre-loading ***(Bajwa et al., 2013).***

Crystalloid and colloids are one of the most commonly used solutions for maintaining intravascular volume during spinal anesthesia. Crystalloid solutions are released freely within intravascular spaces and interstitial tissues. The crystalloid solutions could be used in the isotonic, hypertonic, and hypotonic forms and include normal saline, ringer, balanced salt solution, hypertonic sodium chloride, and dextrose (5%). The main drawback of the crystalloid solutions is that excessive use of these agents causes peripheral and pulmonary edema through decreasing the colloid oncotic pressure of the plasma ***(Orbegozo et al., 2016).***

On the other hands, colloids are generally better than crystalloids at expanding the circulatory volume, since their larger molecules are retained more easily in the intravascular space and increase osmotic pressure. Colloids are also more effective in preventing the hypotension following spinal anesthesia than the crystalloids. However, administration of colloid solutions can cause pulmonary edema as well as anaphylactic shock, resulting in a higher rate of death. Colloids, compared with crystalloids, have longer half-life in blood circulation; therefore, these agents stabilize hemodynamic changes more efficiently ***(Loubert et al., 2017).***

Nevertheless, selection of the right solution for fluid therapy to prevent hypotension is still controversial. Meanwhile, there is the lack of consensus on using appropriate volume expanders for fluid therapy to prevent hypotension following spinal anesthesia. Therefore, the current study aimed to compare the efficacy and safety of preload application of crystalloid versus colloid solutions in maintaining the blood pressure after spinal anesthesia.

In the present trail, we included 60 patients who underwent different types of surgeries with spinal anesthesia. The patients were randomly divided them into 2 groups; 30 patients in each, group 1 (colloid group) and group 2 (crystalloid group).

Regarding the demographic and clinical characteristics, our analysis showed that there were no significant differences between study groups in terms of age, gender, types of the surgeries performed, baseline blood pressure, pulse rate, and oxygen saturation at base line.

In term of our primary outcomes, we found that the preload application of colloid solution was more effective in maintaining the systolic, diastolic, and mean blood pressures than crystalloid solution. The results showed that the colloid group had statistically significant higher systolic, diastolic, and mean blood pressures than crystalloid solution. However, there was no significant change in oxygen saturation between both groups.

In concordance with our findings, Xie and colleagues (2011) performed a randomized, double-blinded study including 47 elderly patients underwent scheduled total hip replacement to compare the effects of colloid and crystalloid preload on cardiac output and incidence of hypotension in elderly patients under spinal anesthesia. They found that cardiac output and change of systolic blood pressure were increased significantly after fluid preloading in both crystalloid and colloid groups as compared with baseline. Intravascular volume preload with colloid is more effective than crystalloid solution in maintaining cardiac output, which may be improved the hemodynamic stability in elderly patients during spinal anesthesia. In contrast, there was a no significant trend toward decrease in the heart rate after spinal anesthesia in each group.

Moreover, ***Dahlgren and colleagues (2005)*** colleagues performed a randomized double-blinded study on a total 110 patients presenting for elective cesarean ml acetated Ringer's solution (crystalloid group) section received either 1000 ml 3% dextran 60 solution (colloid group) intravenously immediately or 1000 before spinal anesthesia. They concluded that there was reduction in the incidence of overall hypotension and the incidence of clinically significant hypotension in colloid group compared to crystalloid group.

In contrary to our findings, ***Gousheh and colleagues (2018)*** conducted a randomized, controlled, double-blind study on 96 females candidate of elective cesarean section to compare the effects of crystalloid and colloid solutions used as the preload on the post-spinal hypotension and its complications. They found that there was a significant higher change in systolic blood pressure in crystalloid group and there was significant higher decrease in diastolic blood pressure in the crystalloid group. While there was no statistical significant difference in heart rate between the 2 groups.

Similarly, ***Tawfik and colleagues (2014)*** performed a randomized double-blind study in order to compare colloid preload and crystalloid co-load in reducing the incidence of severity of hypotension patients scheduled for elective cesarean section under spinal anesthesia. A total of 210 patients were randomly allocated to receive either 6% hydroxyethyl starch 130/0.4 500 mL before spinal anesthesia (colloid preload) or Ringer's acetate solution 1000 mL administered rapidly starting with intrathecal injection (crystalloid co-load). The results showed that were no significant differences in the incidence of hypotension (52.4% vs. 42.2%; P=0.18) or severe hypotension (15.5% vs. 9.8%; P=0.31) between colloid preload and crystalloid co-load groups, respectively.

The exact causes of such discrepancies between our findings and the abovementioned studies are unclear. However, it can be attributed to many methodological differences. For example, ***Tawfik and colleagues (2014)*** compared colloid preload and crystalloid co-load in reducing the incidence of severity of hypotension; while we compared the preload applications of both solutions. Moreover, patients' characteristics were apparently different in which some studies included only patients scheduled for CS and excluded other indications of spinal anaesthesia. The notable difference in sample size may be another factor. This inconsistency may also be partly due to the inability to control for history of chronic diseases, and to inadequate adjustment for

several other confounders such as socioeconomic status or previous surgery.

As regard to the required dose of ephedrine (mg), our results showed that there was statistically significant difference between crystalloid and colloid groups. Patients in colloid group required lower dose of ephedrine (mg) than crystalloid group.

These findings were in parallel with ***Gousheh and colleagues (2018)*** findings as they found that the average amount of injected ephedrine was significantly lower in the colloid group than crystalloid group. Similarly, ***Dahlgren and colleagues (2005)*** who reported that ephedrine consumption in the colloid group was lower than crystalloid group.

Concerning complications of spinal anesthesia, our analysis showed that there was no difference between the study groups in terms of the incidence of nausea and vomiting. This finding was in concordance with ***Gousheh and colleagues (2018)*** results. As they reported that there was no significant difference observed between the study groups in terms of nausea and vomiting. Moreover, ***Tawfik and colleagues (2014)*** reported that there were no significant differences in maternal nausea or vomiting between the colloid preload and crystalloid co-load groups ***(Tawfik et al., 2014)***.

In contrary to these findings, ***Dahlgren and colleagues (2005)*** found that nausea and vomiting were reported to higher in the crystalloid group compared to colloid group.

The differences between these findings may be attributed to the difference in simple size and characteristics of the included patients.

5. Conclusion

In conclusion, colloid appears to be more effective than crystalloid in maintaining the blood pressure after spinal anesthesia. Nevertheless, further large-scale trials are still needed to confirm our findings.

Corresponding author:
Name: Moustafa Tarek Nabieh Ghazal
Address: Anesthesiology, Intensive Care & Pain Management Department, Faculty of Medicine, Misr University for Science and Technology, Egypt.
E-mail: moustafaghazal69@gmail.com

References

1. Bajwa, S. J., Jindal, R. and Kulshrestha, A. 'Co-loading or pre-loading for prevention of hypotension after spinal anaesthesia! a therapeutic dilemma', Anesthesia: Essays and Researches, 2013; 7:, 155.
2. Dahlgren, G., Granath, F., Pregner, K., Rösblad, P. G., Wessel, H. and Irestedt, L.L. 'Colloid vs. crystalloid preloading to prevent maternal hypotension during spinal anesthesia for elective cesarean section', Acta Anaesthesiologica Scandinavica, 2005; 49:, 1200–1206.
3. Gousheh, M. R., Akhondzade, R., Asl Aghahoseini, H., Olapour, A. and Rashidi, M. 'The Effects of Pre-Spinal Anesthesia Administration of Crystalloid and Colloid Solutions on Hypotension in Elective Cesarean Section', Anesthesiology and Pain Medicine, 2018; 8:, e69446.
4. Loubert, C., Gagnon, P. O. and Fernando, R. 'Minimum effective fluid volume of colloid to prevent hypotension during caesarean section under spinal anesthesia using a prophylactic phenylephrine infusion: An up-down sequential allocation study', Journal of Clinical Anesthesia, 2017; 36:, 194–200.
5. Melchor, J.R., Espinosa, Á., Hurtado, E.M., Frances, R.C., Perez, R.N., Gurumeta, A.A., Vecino, J.C. Colloids versus crystalloids in the prevention of hypotension induced by spinal anesthesia in elective cesarean section. A systematic review and meta-analysis. Minerva Anestesiol. 2015; 81(9):1019-30.
6. NganKee WD. Prevention of maternal hypotension after regional anaesthesia for caesarean section. Curr Opin Anaesthesiol. 2010;23:304–9.
7. Orbegozo, D., Su, F., Santacruz, C., He, X., Hosokawa, K., Creteur, J., De Backer, D. and Vincent, J. L. 'Effects of Different Crystalloid Solutions on Hemodynamics, Peripheral Perfusion, and the Microcirculation in Experimental Abdominal Sepsis', Anesthesiology, 2016; 125:, 744–754.
8. 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;109:1916–21.
9. Tawfik, M. M., Hayes, S. M., Jacoub, F. Y., Badran, B. A., Gohar, F. M., Shabana, A. M., Abdelkhalek, M. and Emara, M. M. 'Comparison between colloid preload and crystalloid co-load in cesarean section under spinal anesthesia: A randomized controlled trial', International Journal of Obstetric Anesthesia, 2014; 23:, 317–323.
10. Williamson W, Burks D, Pipkin J, Burkard JF, Osborne LA, Pellegrini JE. Effect of timing of fluid bolus on reduction of spinal-induced hypotension in patients undergoing elective cesarean delivery. AANA J. 2009;77:130–6.

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