|| Print ISSN: 2589-7837 || Online ISSN: 2581-3935 ||

International Journal of Medical Science and Diagnosis Research (IJMSDR)

Available Online at www.ijmsdr.com

Volume 3, Issue 2; February: 2019; Page No. 201-205

PHENYLEPHRINE DOSES FOR THE PREVENTION OF OXYTOCIN-INDUCED HYPOTENSION IN CAESAREAN SECTION: EFFECT OF PRELOAD

Dr. Atul Kumar Agrawal[1], Dr. Ravindra Kumar Bhasker[2]

[1&2]Assistant Professor Dept. of Anesthesiology Rohilkhand Medical College and Hospital, Bareilly (UP).

Conflicts of Interest: Nil

ABSTRACT:

INTRODUCTION: Approximately 80% of the patients suffers Spinal-induced hypotension (SIH) for cesarean delivery (CD) and is a frequently encountered problem. Phenylephrine is a short-acting alpha agonist, can be administered by bolus as well as by infusion to treat oxytocin induced hypotension. Phenylephrine has been associated with a decreased incidence of hypotension and maternal nausea and vomiting and improved umbilical artery pH.

MATERIAL AND METHODS: Via computer-generated blocked randomization patients were randomized to be in the colloid or crystalloid infusion groups. 18-gauge intravenous (IV) catheter was inserted into a forearm vein, and vein patency was maintained with Lactated Ringer's solution (LR) at a rate of 5 ml/h before administering the preload. Colloid preload was 500 ml hydroxyethyl starch in 0.9% normal saline and crystalloid preload was LR (1500 ml). Volume of crystalloid and colloid preload was 1:3 colloid to crystalloid ratio to achieve a similar degree of volume expansion. Spinal anaesthesia was given with a 25-gauge pencil point needle at the L2-L3 or L3-L4 vertebral interspace. A mixture of hyperbaric bupivacaine 0.75%, 12 mg with morphine, 200 mcg was injected intrathecally. All patients were given a phenylephrine infusion (10 mg phenylephrine in 100 ml 0.9% NS). Just after intrathecal injection at a rate of 100 mcg/min. Phenylephrine infusion protocol was continued until the time of uterine incision. The infusion was stopped if the HR decreased below 60 beats per minute (bpm), or if the SBP increased to >20% above baseline, and was again restarted when the BP decreased to <20% below baseline (defined as hypotension). The total dose of phenylephrine used during the study period was recorded.

RESULTS: A total of 92 patients were included in the study, 56 in each group. 2 patients from crystalloid preload group were excluded because of the high sensory levels and 2 patients from colloid group was excluded because of significant hypertension prior to starting the phenylephrine infusion. Finally 54 patients in each group were included in the study. Mean age in lacteted ringer solution group was 27.21±6.24 years while in hydroxyethyl starch group it was 28.14±5.49. Mean Spinal uterine incision time was 16.58±4.21 and 18.28±3.39 in lacteted ringer solution group and hydroxyethyl starch group respectively. Estimated blood loss in ml(mean±SD) was 446±60.89 and 498±59.45 in lacteted ringer solution group and hydroxyethyl starch group respectively. Systolic blood pressure baseline (mean±SD) 128.88±10.28 and 131.31±9.54 in lacteted ringer solution group and hydroxyethyl starch group respectively. Heart rate (mean±SD) was 90.87±10.25 and 88.56±11.56 in lacteted ringer solution group and hydroxyethyl starch group respectively. Significantly less phenylephrine was used in the colloid group (1068 ± 554 mcg) compared to the crystalloid group (1401 ± 527 mcg) (P = 0.003) . There was no significant difference in the incidence of maternal nausea and vomiting, as well as APGAR scores at 1 and 5 min. Emergency rescue medications were administered to a total of 4 patients. 3 in crystalloid group and 1 in colloid group for supraventricular tachycardia.

CONCLUSION: In prevention of SIH and treatment Phenylephrine with colloids are shown to be superior to crystalloids because of the phenylephrine sparing effect.

Corresponding author: Dr. Ravindra Kumar Bhasker

Introduction

Approximately 80% of the patients suffers Spinal-induced hypotension (SIH) for cesarean delivery (CD) and is a frequently encountered problem[i].Postpartum haemorrhage (PPH) is one of the leading causes of maternal mortality with uterine atony in about 50% cases[ii]. Prophylactic use of oxytocin has been shown to reduce the PPH by up to 40%[iii].as oxytocin receptors found in the heart and large vessels it causes hypotension and reflex tachycardia as an adverse effect[iv]. If hypotension is prolonged, impairment in placental blood flow and fetal acidosis can occur[v].to prevent this prophylactic phenylephrine infusion can be given. There are many approaches to prevent hypotension but no single approach has been shown as the gold standard, and each prophylactic treatment comes with accompanying risks. Crystalloid preload can prevent hypotension has a poor efficacy in preventing hypotension, due to rapid redistribution into the extracellular space[vi].

To prevent oxytocin induced hypotension , many approaches have been recommended, commonly used, synthetic colloids such as hydroxyethyl starch are more expensive than crystalloid and side effects include pruritis, anaphylactoid reactions, association with kidney injury, and coagulopathy[vii],[viii].

Phenylephrine is a short-acting alpha agonist, can be administered by bolus as well as by infusion to treat oxytocin induced hypotension[ix]. Phenylephrine obtunds oxytocin-induced decrease in systemic vascular resistance (SVR) and increase in heart rate and cardiac output[x]. Phenylephrine has been associated with a decreased incidence of hypotension and maternal nausea and vomiting and improved umbilical artery pH[xi],[xii]. In *ex vivo* studies, phenylephrine has been shown to improve fetal arterial perfusion than ephedrine[xiii].

In this prospective, comparative study, we formulated two groups of patients receiving prophylactic phenylephrine infusions which was combined with either a colloid or crystalloid preload. We assume that patients receiving prophylaxis with a phenylephrine infusion and colloid preload would show a reduced incidence of hypotension i.e. <20% below baseline as compared to patients receiving a phenylephrine infusion with crystalloid preload. We selected our secondary outcomes to reflect the clinical evidence of reduced cardiac output; these included the total dose of phenylephrine, incidence of bradycardia, nausea, and vomiting, as well as APGAR scores at 1 and 5 min.

MATERIAL AND METHODS

Via computer-generated blocked randomization patients were randomized to be in the colloid or crystalloid infusion groups. Normal singleton pregnancy, beyond 36 weeks gestation, between 18 and 35 years of age, , weight between 50 and 120 kg, and height ranging from 150-180 cm. Exclusion criteria were: Contraindications to spinal anesthesia, pregnancy-induced hypertension, preeclampsia, known uteroplacental insufficiency, multiple gestation, fetal abnormalities, congenital heart abnormalities, prematurity, or clinical evidence of fetal distress, signs of onset of labor, or history of adverse reactions to hydroxyethyl starch.

Pre-anaesthetic evaluation of all the parturients was done and an informed written consent was taken. 18-gauge intravenous (IV) catheter was inserted into a forearm vein, and vein patency was maintained with Lactated Ringer's solution (LR) at a rate of 5 ml/h before administering the preload. Colloid preload was 500 ml hydroxyethyl starch in 0.9% normal saline and crystalloid preload was LR (1500 ml). Volume of crystalloid and colloid preload was 1:3 colloid to crystalloid ratio to achieve a similar degree of volume expansion[xiv]. Intravenous administration of preload was delivered for 30 min, prior to spinal anaesthesia and when the fluid load was complete, IV patency was maintained at a rate of 5 ml/hour and medications were flushed with LR. Standard monitoring for all patients was done through use of non-invasive blood pressure (NIBP) measurement, electrocardiography, and pulse oximetry. Oxygen (2 l/min) was administered via nasal cannula. The average

Systolic BP and accompanying heart rate (HR) of these 3 measurements were recorded as mean baseline values.

Spinal anaesthesia was given with a 25-gauge pencil point needle at the L2-L3 or L3-L4 vertebral interspace. A mixture of hyperbaric bupivacaine 0.75%, 12 mg with morphine, 200 mcg was injected intrathecally. Patients were then kept in supine position with 15° left lateral tilt. BP and HR were measured and recorded at 1-min intervals starting 1-min after intrathecal injection until uterine incision. BP measurements were then taken as per instructions of anaesthesia team.

All patients were given a phenylephrine infusion (10 mg phenylephrine in 100 ml 0.9% NS). Just after intrathecal injection at a rate of 100 mcg/min. Phenylephrine infusion protocol was continued until the time of uterine incision. The infusion was stopped if the HR decreased below 60 beats per minute (bpm), or if the SBP increased to >20% above baseline , and was againrestarted when the BP decreased to <20% below baseline (defined as hypotension). The total dose of phenylephrine used during the study period was recorded.

After baby extraction, test drug solutions (10 mL) were administered based on group allocation over a period of 5 min using a syringe infusion pump. Patients idea about nauseating feeling was recorded from start of anaesthesia at every 5 minutes interval.

All normally distributed data were expressed as mean ± standard deviation. The data for the incidence of hypotension and occurrence of nausea and/or vomiting were compared using the Chi-squared test or Fisher's exact test as appropriate.

RESULTS OF STUDY

A total of 92 patients were included in the study, 56 in each group. 2 patients from crystalloid preload group were excluded because of the high sensory levels and 2 patients from colloid group was excluded because of significant hypertension prior to starting the phenylephrine infusion. Finally 54 patients in each group were included in the study.

TABLE 1: Patients characteristics in each group

Characteristics	Lacteted ringer solution group (n=54)	Hydroxyethyl starch group (n=54)	P value
Age (mean±SD)	27.21±6.24	28.14±5.49	P = 0.4128
Height(mean±SD)	160.27±6.44	161±5.22	P = 0.519
Spinal uterine incision time(mean±SD)	16.58±4.21	18.28±3.39	P = 0.023
Estimated blood loss in ml(mean±SD)	446±60.89	498±59.45	P <o.oo1
Systolic blood pressure baseline (mean±SD)	128.88±10.28	131.31±9.54	P = 0.206
Heart rate (mean±SD)	90.87±10.25	88.56±11.56	P = 0.274

Mean age in lacteted ringer solution group was 27.21±6.24 years while in hydroxyethyl starch group it was 28.14±5.49. Mean Spinal uterine incision time was 16.58±4.21 and 18.28±3.39 in lacteted ringer solution group and hydroxyethyl starch group respectively. Estimated blood loss in ml (mean±SD) was 446±60.89 and 498±59.45 in lacteted ringer solution group and hydroxyethyl starch group respectively. Systolic blood pressure baseline (mean±SD) 128.88±10.28 and 131.31±9.54 in lacteted ringer solution group and hydroxyethyl starch group respectively. Heart rate (mean±SD) was 90.87±10.25 and 88.56±11.56in lacteted ringer solution group and hydroxyethyl starch group respectively.

Significantly less phenylephrine was used in the colloid group (1068 ± 554 mcg) compared to the crystalloid group (1401 ± 527 mcg) (*P* = 0.003) . There was no significant difference in the

incidence of maternal nausea and vomiting, as well as APGAR scores at 1 and 5 min.

Emergency rescue medications were administered to a total of 4 patients. 3 in crystalloid group and 1 in colloid group for supraventricular tachycardia.

DISCUSSION AND CONCLUSION

The benefits of prophylactic phenylephrine infusion are still controversial. However, it has been associated with a decreased incidence of hypotension and maternal nausea and vomiting and improved umbilical artery pHxv,xvi. In our study there was lower incidence of hypotension with colloid preload when compared with the crystalloid group this results were comparable with the study by Bottiger BA et al[xvii] observed that here was a lower incidence of hypotension with colloid preload (10.8%) when compared with the crystalloid group (27.0%).in a study by Gangadharaiah R [xviii]et al it has been observed that co-administration of 75 µg phenylephrine with oxytocin reduced the incidence and the number of episodes of oxytocin-induced hypotension whereas 50 µg of phenylephrine did not reduce the incidence of hypotension but reduced the number of episodes of hypotension and rescue vasopressor requirement compared to control. Some studies have compared the efficacy of different doses of phenylephrine i.e. 100 µg, 125 µg and 150 µg to treat post-spinal hypotension in elective caesarean section and concluded that there was no significant difference in all groups[xix].

There was a gradual decrease in HR in both groups, despite the different dose required, may be attributed to the effect of the spinal anesthetic as well as the phenylephrine infusion. Phenylephrine has been associated with decreased cardiac output and dysrhythmias, including ventricular tachycardia, supraventricular tachycardia, coronary artery spasm, and myocardial infarction, although these side effects seem to be reduced when compared with ephedrine[xx].in our study 3 in crystalloid group and I in colloid group experienced supraventricular tachycardia. In our study no significant difference was observed in relation to clinical evidence of reduced cardiac output; nausea, and vomiting, as well as APGAR scores at 1 and 5 min.

In prevention of SIH and treatment Phenylephrine with collids are shown to be superior than crystelloids because of the phenylephrine sparing effect associated with preloading colloids. Further studies are required to confirm the results.

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