Original Article

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A Comparison of A Crystalloid Co-Load, with or without A Phenylephrine Infusion, for Prevention of Hypotension Following Subarachnoid Block for Caesarean Section

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Abstract

Hypotension produced by the sympathetic blockade associated with spinal anesthesia has maternal and foetal adverse effects. Intravenous fluid expansion and vasopressors are used to prevent this hypotension. In this study we compared the effect of a combination of crystalloid co-load of lactated Ringer's solution and a prophylactic phenylephrine infusion versus crystalloid co-load alone in preventing pre-delivery hypotension in the mother following subarachnoid block for lower segment caesarean section. 100 ASA I or II term parturients posted for caesarean delivery were enrolled. They were randomly divided in to two groups: Group 1) a co-load of lactated Ringer's solution at a volume of 15ml/kg body weight given over 10 minutes and a prophylactic phenylephrine infusion at rate of 50mcg/min. Group 2) a co-load of lactated Ringer's solution at a volume of 15ml/kg body weight given over 10 minutes alone. Subarachanoid block was performed with 2 ml hyperbaric 0.5% bupivacaine (10 mg) at L3-4 interspace. Immediately after the injection of the intrathecal medication, the co-load with or without infusion of phenylephrine was started depending on the group allocated. NIBP, heart rate and SpO_2 were recorded every 1 minute until delivery, and thereafter every 3 minutes until the end of study. The incidence of pre-delivery hypotension was 2 % and 68 % respectively in group 1 and group 2. The lower incidence of pre-delivery hypotension in the group 1 was found to be statistically significant with a p value less than 0.01. The side effect profile of the two regimens was also comparable. In conclusion we found that prophylactic phenylephrine infusion at rate of 50mcg/min with a co-load of lactated Ringer's solution at a volume of 15ml/kg body over 10 minutes significantly lowered pre-delivery hypotension in the mother.

Keywords: Ringer Lactate Co-Load; Phenyephrine Infusion; Sub-Arachnoid Block; Hypotension.

Introduction

Caesarean deliveries have increased in incidence over the past several decades and have become a commonly performed surgical procedure [1]. Providing anaesthesia for caesarean delivery is a challenging task for the anaesthesiologist

The most commonly used anaesthetic technique for caesarean delivery is spinal anesthesia [2,3]. This simple and reliable technique provides rapid onset of dense neuroblockade. The risk of systemic local anaesthetic toxicity is negligible with spinal anaesthesia. The transfer of drug to the foetus is minimal. The danger of aspiration and neonatal depression associated with general anaesthesia is also avoided.

Hypotension produced by the sympathetic blockade associated with this technique is a concern as it has maternal and foetal adverse effects. Anaesthesiologists should aim to actively prevent hypotension. Among several ways to prevent hypotension are intravenous fluid expansion and use of vasopressors.

Phenylephrine infusion is a safe and effective way to reduce incidence and frequency of hypotension during subarachnoid block for caesarean delivery [4]. A rapid administration of crystalloid after the induction of spinal anaesthesia (co-load) rather than before (preload) has been shown to be of advantage in preventing maternal hypotension prior to delivery [5]. However, the optimal administration regimen is undetermined.

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Hypotension was virtually eliminated by use of high-dose prophylactic phenylephrine infusion at a rate of 100mcg/min and rapid crystalloid co-load up to two litres. However, incidence of reactive hypertension was up to 47% [6]. This is of concern in patients in whom increase of blood pressure might be detrimental, like in the presence chronic hypertension or a compromised uteroplacental blood flow. Phenylephrine 25 and 50 mcg/min administered as a prophylactic fixed rate infusion provided greater maternal hemodynamic stability than phenylephrine 75 and 100 μg/min [7].

There is a paucity of studies comparing crystalloid co-loading versus phenylephrine infusion with crystalloid co-loading in parturients undergoing caesarean section under spinal anaesthesia. This study compared incidence of hypotension in mothers who received a co-load of lactated Ringers solution at a volume of 15ml/kg body weight over ten minutes, with or without a phenylephrine infusion at the rate of 50mcg/min.

Objectives

To compare the effect of a combination of crystalloid co-load of lactated Ringer's solution at a volume of 15ml/kg body weight given over 10 minutes and a prophylactic phenylephrine infusion at rate of 50mcg/min versus crystalloid co-load alone in preventing pre-delivery hypotension in the mother following subarachnoid block for lower segment caesarean section.

Materials and Methods

The study was a prospective cohort study conducted over a period of 18 months after obtaining approval of Institutional Technical Committee and Human Ethical Committee of Government Medical College, Thrissur. Based on similar studies in the past a total sample size of 100 in two groups of 50 each was found sufficient for a two sided confidence level (1-alpha) of 95% and power (1-beta) of 80 %.

Inclusion Criteria

1. ASA physical status 1 and 2 pregnant women posted for caesarean delivery under spinal anaesthesia.
2. Singleton gestation at a gestational age of > 36 weeks

Exclusion Criteria

1. ASA physical status 3 or more,
2. Age < 20yrs or >40yrs
3. Height <145 cm or >165 cm,
4. Body weight <45 kg or >75 kg
5. Presence of foetal distress

Patients were assessed for eligibility for the study during pre-anaesthetic evaluation. A total of 100 patients who were found eligible and were willing to be part of the study, were enrolled after obtaining informed written consent in the patients mother tongue.

Group 1 consisted of 50 patients who received a co-load of lactated Ringer's solution at a volume of 15ml/kg body weight given over 10 minutes and a prophylactic phenylephrine infusion at a rate of 50mcg/min.

Group 2 consisted of 50 patients who received a co-load of lactated Ringer's solution at a volume of 15ml/kg body weight given over 10 minutes.

All patients were premedicated with intravenous ranitidine 50 mg; on the night before and on the morning of day of the surgery and intravenous metoclopramide 10 mg on the morning of day of the surgery. Baseline systolic blood pressure and heart rate (mean of 3 consecutive measurements taken 5 minutes apart with patient left undisturbed in supine position with left uterine displacement) was recorded. Phenylephrine infusion with concentration of 50mcg/ml in measured volume infusion devices was prepared. Rescue syringes of Phenylephrine (50mcg/ml), and atropine (0.6mg/ml) were also prepared and labelled. Patient was transferred on to a levelled operating table and pulse-oximetry , electrocardiography, and non-invasive blood pressure monitoring established. Oxygen at a rate of 5 L/min was given by a facemask. Intravenous cannulas of 16G and 18G were inserted on the forearm and connected to a bottle of warmed lactated Ringer's solution and a measured volume infusion device respectively. 2 ml hyperbaric 0.5% bupivacaine (10 mg) was given intrathecally with a 25-gauge Quincke's spinal needle at L3–L4 vertebral interspace by aseptic technique with the patient in right lateral position. Immediately after the injection of the intrathecal medication, the co-load of Ringer Lactate 15ml/kg was started. Infusion from the measured volume infusion device was started at a rate of 60ml/h, group 1 patients were given phenlyephrine 50mcg/min. Patients were returned to the supine position with a 15-degree wedge under

the right hip. The upper dermatomes blocked to light touch and cold sensation was recorded. NIBP, heart rate and SpO_2 were recorded every 1 minute until delivery, and thereafter every 3 minutes until the end of study. Systolic blood pressure was maintained above the lower limit of acceptable range with phenylephrine 50mcg boluses when needed

After delivery oxytocin 10 IU was administered intravenously as an infusion, phenylephrine infusion if administered was stopped . On completion of the co load, lactated Ringer's solution was administered at a maintenance rate. Completion of surgery marked the end of the study. All patients were subsequently followed up until they were discharged from the hospital.

The primary outcome was the incidence of pre-delivery hypotension in the mother. Secondary outcomes were the total number of episodes of hypotension during the study period, maternal bradycardia, the incidence of nausea and vomiting, the total dose of phenylephrine used, Apgar scores at 1 and 5 minutes Side effects were defined as following

1. Hypotension - Systolic BP < 20% of baseline, or <100 mm of Hg whichever is higher.
2. Hypertension- Systolic BP> 20% of baseline.
3. Bradycardia- Heart rate < 50 beats per minute.

The side effects were managed as mentioned below.

Hypotension- 50 mcg intravenous boluses of phenylephrine

Hypertension - Stopping of infusions. Infusion was restarted only when SBP decreases to below the upper limit of the target range.

Bradycardia - Stopping of drug infusion and, if associated with hypotension intravenous Atropine 0.6 mg.

Intraoperative nausea or vomiting was treated with Ondansetron 4 mg IV.

Observations and Results

The observations made were tabulated and analysed using computer software, Statistical Package for Social Sciences. The mean and standard deviation for various parameters were calculated. Independent t-test, Chi-square tests, and Mann-Whitney U test were used to compare variables

Table 1: Comparison of maternal characteristics

Variable	Group 1 Mean ± SD, (range)	Group 2 Mean ± SD, (range)	p value
Age (years)	27.2 ± 4.2, (20-39)	27.8 ± 4.7, (20-38)	0.501
Height (cms)	152.0 ± 5.2, (145-165)	154.0± 5.3, (145-165)	0.050
Weight (kg)	63.0 ± 8.2, (49-75)	65.5 ± 7.4, (49-75)	0.109
BMI	27.2 ± 2.5, (21.7-30)	27.5 ± 2.8, (21.7-30.4)	0.45
Gestational age (days)	270.3 ± 5.8, (254-283)	269.8 ± 6.7, (253-285)	0.727

The patients in both groups were comparable with respect to their age, height, weight, body mass index, and period of gestation.

Table 5.2: Comparison of parity

Gravidity	Group 1		Group 2		χ^2	P
	Count	Percent	Count	Percent		
Nullipara	12	24.0	7	14	2.3	0.129
Multipara	38	76.0	43	86		

The differences between the groups were not statistically significant.

Table 5.3: Comparison of baseline hemodynamic parameters

	Group 1 Mean ± SD, (range)	Group 2 Mean ± SD (range)	p value
Baseline Heart rate	84.3 ± 6.7, (75-95)	83.1 ± 6.1, (76 -95)	0.376
Baseline Systolic BP	119.6 ± 10.3, (100 -132)	119.5 ± 8.4, (103-132)	0.966

The patients in both groups were comparable with respect to their baseline heart rate and systolic blood pressure.

Table 5.4: Comparison of sensory block level at beginning of surgery

Sensory block level at beginning of surgery	Group 1		Group 2		χ^2	P
	Count	Percent	Count	Percent		
T5	2	4.0	21	42.0	27.7**	0.000
T6	22	44.0	22	44.0		
T7	21	42.0	7	14.0		
T8	5	10.0	0	0.0		

** Significant at 0.01 level

The level of sensory blockade at the beginning of surgery was analysed using the Chi-Square test. There was a significant difference between the two groups with respect to the level of sensory blockade at the beginning of surgery with a p value of < 0.01.

Table 5.5: Comparison of operative data

Variable	Group 1 Mean ± SD, (range)	Group 2 Mean ± SD, (range)	p value
Spinal induction – Delivery interval (minutes)	14.3 ± 1.6, (11-18)	14.3 ± 1.9, (11- 18)	0.955
Skin incision – Delivery interval (minutes)	10.3 ± 1.4, (8- 13)	10.3 ± 1.6, (8- 13)	0.842
Uterine incision – Delivery interval (minutes)	1.4 ± 0.5, (1-2)	1.6 ± 0.5, (1-2)	0.073
Duration of surgery (minutes)	43.2 ± 2.9, (37- 49)	43.3 ± 2.9, (38- 49)	0.863
Volume of RL (ml)	1006.8 ± 127.9, (800 - 1200)	1046.0 ± 115.9, (780 - 1220)	0.112
Intraoperative Blood loss (ml)	412.8 ± 62.3, (250 - 540)	391.8 ± 67.4, (270 - 550)	0.109

The two groups were comparable with respect to operative data like Spinal induction – Delivery interval, Skin incision – Delivery interval, Uterine incision – Delivery interval, Duration of surgery, Volume of Ringer Lactate infused, and Intraoperative Blood loss

Table 5.6: Comparison of incidence of pre delivery hypotension

Pre delivery hypotension	Group 1		Group 2		χ^2	P
	Count	Percent	Count	Percent		
No	49	98.0	16	32.0	47.87**	0.000
Yes	1	2.0	34	68.0		

** Significant at 0.01 level

The difference in incidence of pre delivery hypotension was found to be of statistical significance with a p value <0.01.

Table 5.7: Comparison of number of episodes of pre delivery hypotension

Number of episodes of pre delivery hypotension	Group 1		Group 2		Z#	P
	Count	Percent	Count	Percent		
0	49	98.0	16	32.0	6.82**	0.000
1	1	2.0	5	10.0		
2	0	0.0	14	28.0		
3	0	0.0	12	24.0		
4	0	0.0	3	6.0		

Mann-Whitney U Test
** Significant at 0.01 level

A comparison of number of episodes of hypotension using the Mann-Whitney U Test showed a statistically significant difference between the groups with a p value < 0.01.

Table 5.8: Comparison of total dose of phenylephrine used based on group

	Group1	Group 2
Mean	718.0	92.0
SD	81.9	82.9
Median	725.0	100.0
Minimum	550	0
Maximum	900	300

The difference in mean of total dose of phenylephrine between the groups was statistically significant with a p value < 0.01.

Table 5.9: comparison of number of physician intervention based on group

	Group1	Group 2
Mean	0.1	1.8
SD	0.2	1.7
Median	0.0	2.0
Minimum	0	0
Maximum	1	6

t = 7.51**, p = 0.000
The difference in mean number of physician interventions between the groups was statistically significant with a p value < 0.01.

Table 5.10: Distribution of APGAR scores of new borns

APGAR score		Group 1		Group 2	
		Count	Percentage	Count	Percentage
1 minute	9	50	100.0	50	100
5 minutes	9	50	100.0	50	100

All new-borns born to mothers in both groups had APGAR scores of nine at one and five minutes after delivery.

There were no episodes of maternal bradycardia, nausea, vomiting, or any other side effects in either group.

Discussion

Single-shot spinal anaesthesia has emerged as the technique of choice for routine scheduled caesarean delivery. It is a simple, fast, reliable, and cost-effective technique. Hypotension following subarachnoid blockade for caesarean delivery remains a common clinical problem with a reported incidence of up to 85 %.

Pregnant patients at term are more prone to develop hypotension due to the occurrence of aortocaval compression and due to the higher level of sympathectomy owing to increased spread of local anaesthetic in the cerebrospinal fluid. Hypotension is hazardous to the mother and foetus and is associated with morbidity for both the mother (nausea and vomiting) and the foetus (foetal acidosis). The aim of anaesthesiologists should be to actively prevent maternal hypotension and to treat it quickly and efficaciously.

Hypotension has been variously defined as a reduction in arterial pressure of 30 mm of Hg, a reduction to less than 100 mm of Hg or as a reduction of 20% below baseline pressure. For the purpose of this study, hypotension was defined as a reduction of systolic blood pressure to less than 100 mm of Hg or to 20% of the baseline pressure whichever was higher.

Strategies that have been used to minimize hypotension include maternal left tilt, leg wrappings, sympathomimetic drugs, and intravenous fluid loading before or with induction of spinal anaesthesia. The combination of vasopressors with a rapid crystalloid loading at the time of spinal injection is an interesting strategy. Recent work suggests that prophylactic continuous infusion of the alpha-adrenergic agonist phenylephrine is superior to ephedrine in prevention of spinal anaesthesia induced hypotension. Although some studies showed that phenylephrine was not associated with maternal or foetal morbidity, the high incidence of maternal bradycardia is of concern.

This study aimed to compare the effect of a combination of crystalloid co-load of lactated Ringer's solution at a volume of 15ml/kg body weight given over 10 minutes and a prophylactic phenylephrine infusion at rate of 50mcg/min versus crystalloid co-load alone in preventing pre-delivery hypotension in the mother following subarachnoid block for lower segment caesarean section. In this study 100 term parturients posted for caesarean delivery were allocated to two groups.

Group 1 consisted of 50 patients who received a co-load of lactated Ringer's solution at a volume of 15ml/kg body weight given over 10 minutes and a prophylactic phenylephrine infusion at rate of 50mcg/min

Group 2 consisted of 50 patients who received a co-load of lactated Ringer's solution at a volume of 15ml/kg body weight given over 10 minutes The two groups were comparable with respect to age, height, weight, body mass index, and period of gestation and parity. The baseline heart rate and systolic blood pressure were also comparable between the groups

In this study, there was a statistically significant difference between the groups with respect to the level

of sensory blockade at the beginning of the surgery.

2 patients (4%) in group 1 had T5 sensory blockade, while 22 patients (42%) in group 2 had T5 sensory blockade at the beginning of the surgery. 22 patients (44%) in both groups had a T6 sensory blockade, 21 patients (42%) in group 1 and 7 patients (14%) in group 2 had a T7 sensory blockade. 5 patients (10%) in group 1 had a T8 sensory blockade; while none of patients in group 2 had a T8 sensory blockade at the beginning of the surgery. Thus the level of sensory blockade was found to be significantly lower in the group 1 (Chi-square test, $p < 0.01$).

Cooper et al [8] in 2004 reported that intravenous administration of phenylephrine, to prevent maternal hypotension during combined spinal epidural anaesthesia for caesarean section decreases the rostral spread of spinal anaesthesia. A possible mechanism is by reduction of epidural pressure as a result of epidural vein constriction produced by phenylephrine.

The two groups were comparable with respect to operative data like Spinal induction – Delivery interval, Skin incision – Delivery interval, Uterine incision – Delivery interval, Duration of surgery, Volume of Ringer Lactate infused, and Intra operative blood loss

The primary outcome studied was the incidence of pre-delivery hypotension in the mother. Only 1 patient (2%) in group 1 developed pre-delivery hypotension while 34 patients (68%) had pre-delivery hypotension in group 2. The lower incidence of pre-delivery hypotension in the group of patients who received a co-load of lactated Ringer's solution at a volume of 15ml/kg body weight given over 10 minutes and a prophylactic phenylephrine infusion at rate of 50mcg/min was found to be of statistical significance with a p value less than 0.01

Secondary outcomes studied were the total number of episodes of pre-delivery hypotension, maternal bradycardia, incidence of nausea and vomiting, total dose of phenylephrine used, number of physician interventions, Apgar scores at 1 and 5 minutes

There was only one episode of pre-delivery hypotension among all of the group 1 patients, while among group 2 patients, 5, 14, 12 and 3 patients had 1,2,3,4 episodes of pre-delivery hypotension. The lower number of episodes of pre-delivery hypotension in the group 1 was found to be of statistical significance (Mann-Whitney U test, $p < 0.01$)

There were no episodes of maternal bradycardia, nausea, vomiting, or other side effects in both groups.

The mean of total dose of phenylephrine used in group 1 and group 2 were 718 and 92 micrograms respectively. The higher total dose of phenylephrine in group 1 was found to be of statistical significance with a p value less than 0.01. However, this higher dose did not produce any side effects in those patients.

There was a statistically significant decrease in the number of physician interventions in the group 1 (p value less than 0.01).

All new-borns born to mothers in both groups had Apgar scores of nine at one and five minutes. Thus in this study there was no difference in neonatal outcomes as assessed clinically by using Apgar score.

Conclusion

According to the results of this study prophylactic phenylephrine infusion at rate of 50mcg/min with a co-load of lactated Ringer's solution at a volume of 15ml/kg body over 10 minutes significantly lowered pre-delivery hypotension in the mother. This prophylactic phenylephrine infusion also reduced the number of physician interventions needed to maintain hemodynamic stability during caesarean section under subarachnoid block. However, in this study, the prophylactic phenylephrine infusion resulted in a significantly higher total dose of phenylephrine when compared to a lone co-load of lactated Ringer's solution at a volume of 15ml/kg body over 10 minutes. But this higher dose did not produce any side effects in those patients. No significant difference in neonatal outcomes clinically assessed by Apgar score was however evident between the groups. The side effect profile of the two regimens was also comparable in this study.

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