COMPARATIVE STUDY OF 6% HYDROXYETHYL STARCH (450/0.7) AND RINGER’S LACTATE AS PRELOADING FLUID FOR PREVENTION OF HYPOTENSION DURING SPINAL ANESTHESIA IN ELECTIVE CESAREAN DELIVERY

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ABSTRACT: We compared the efficacy of volume preloading with Ringer’s Lactate and Hydroxyethyl starch (HEAS) 6% 450/0.7 on the onset and incidence of spinal-induced hypotension in elective cesarean delivery. 60 healthy parturients scheduled for elective cesarean section under spinal anesthesia were selected for the study. Group A was preloaded with 1000ml of RL while as group B preloaded with 500ml of 6% HEAS (450/0.7) over a period of 10 minutes just prior to the administration of spinal anaesthesia. Immediately after the preloading period, subarachnoid block was instituted with 2.5ml of Bupivacaine 0.5% (heavy) at L3-L4 or L4-L5 interspace using 26 Gauge Quinke’s spinal needle in sitting position. The patient were then positioned supine with left lateral tilt. Adequate block was obtained and height of block was tested by pinprick method using blunt needle. Hypotension following spinal anaesthesia was treated with 6 mg bolus doses of Ephedrine and additional rapid infusion of Ringer’s lactate solution. All were administered supplemental oxygen 5L/min by venturi mask throughout the period of surgery. Intraoperatively, heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were monitored every 2 minutes for the first 20 minutes and every 5 minutes thereafter till the end of surgery. Spo2 and ECG were monitored continuously throughout the period of surgery. In addition, height of the block, amount of blood loss, amount of vasopressor required, and amount of i.v fluids used intraoperatively and any allergic reactions to i.v fluids were noted. All parturients received 10 IU of oxytocin i.v infusion after delivery of baby. These observations were analyzed to get information on the onset and incidence of hypotension, intraoperative requirements of Ephedrine, and i.v fluids, and incidence of adverse effects like nausea and/or vomiting. The incidence of hypotension in group A was 60% and that in group B 23.3%. The mean time period of onset of hypotension in group A was 6.3±2.09 (range 4-10 min) and that in group B was 12.9±2.27 (Range 10-16 min). The lowest systolic pressure noted in group A was 109. 8mmHg and in group was 113.9mmHg. None of the patients in group A and group B had bradycardia. The mean amount of Ephedrine required in group A and group B was 13 and 9.4 mg respectively. The average amount of i.v fluid used intra-operatively in group A was 1200±152.56 (Range 1000-1500 ml) and in group B was 1191.70±130.70 (Range 1000-1450 ml). The average intraoperative blood loss in group A was 837.50±65.90 (Range 750-1000 ml) and in group B was 819.20±64.56 (Range 750-950 ml). 4 patients in group A and 3 patients in group B
developed vomiting. The neonatal Apgar scores were good and similar in both groups.

CONCLUSION: It is concluded that: Among preloading agents, colloids are superior to crystalloids in reducing the onset and incidence of spinal-induced hypotension. Hydroxyethyl starch 6% is an ideal preloading agent. High molecular weight HEAS (e. g. 450/0.7) seems to be better option than Ringer’s anaesthesia in parturients scheduled for elective cesarean section. It is suggested to use 500 ml of high molecular weight 6% HEAS 450/0.7 as an effective prophylactic measure to reduce the incidence of spinal-induced hypotension in parturients planned for elective cesarean section. Also no allergic reaction with 6% HEAS 450/0.7 were observed in our study.

KEYWORDS: Hypotension, Preloading, HEAS, and Ringer lactate Elective LSCS.

INTRODUCTION: Cesarean delivery is most commonly performed under spinal or epidural anaesthesia.1 In 2002 in the UK, 95% of elective sections and 87% of emergency operative deliveries were performed under Regional anaesthesia.2 Van Houwe et al performed a survey in Flanders and reported that regional anesthesia was used in 95% of patients undergoing cesarean section.3 Spinal anaesthesia is popular because it is a simple technique which produces fast and highly effective anesthesia whilst avoiding general anaesthesia. The most common indications for cesarean delivery include arrest of cervical dilatation, non-reassuring fetal status, cephalopelvic disproportion, malpresentation, prematurity, prior cesarean delivery, and prior surgery involving the corpus.4

General anesthesia is associated with significantly more maternal morbidity and mortality.5 Regional anesthesia for cesarean section has several advantages: It is associated with less maternal morbidity and mortality which is largely due to a reduction in the incidence of pulmonary aspiration and failed intubation,6 avoids neonatal exposure to depressant anaesthetic drugs, and allows the mother to remain awake during delivery. In addition operative blood loss may also be reduced compared with general anaesthesia. However, spinal anaesthesia is associated with a high incidence of maternal hypotension which can result in fetal distress and maternal discomfort.

SPINAL-INDUCED HYPOTESION: THE SCOPE OF THE PROBLEM: Hypotension is the most common side effect seen with the spinal anaesthesia.7 The severity depends on the height of the block, the position of the parturient, and whether prophylactic measures were taken to prevent the hypotension. The pathophysiology of hypotension following spinal anaesthesia is well described. Sympathetic block causes arterial and arteriolar venodilation, resulting in hypotension. Also venodilation is present, which results in decreased cardiac preload, reduced cardiac output and maternal hypotension. In pregnancy, this is further aggravated by the effects of the gravid uterus and subsequent aortocaval compression. As a result of sympatholysis, maternal bradycardia accentuates the observed hemodynamic effects. The reported incidence of maternal hypotension is high with most trials reporting an incidence well over 50%.8 Also the incidence is much higher than that reported following general and epidural anaesthetic techniques.9 Hypotension causes maternal nausea and vomiting and as a result treatment of hypotension can induce iatrogenic pulmonary edema or severe maternal hypertension. Because of hypotension,
patients may also fail to cooperate, complicating surgery. Also the fetus is affected by hypotension. If hypotension is severe enough and/or prolonged enough, fetal acidosis is a distinct possibility. Roberts et al. compared general, epidural, spinal and CSE anaesthesia techniques in over 1600 patients undergoing elective cesarean section in a single centre.\(^\text{10}\) Significantly more patients treated with either CSE or single shot spinal anaesthesia experienced fetal umbilical artery acidosis. Mueller and co-workers published a large epidemiologic study evaluating the incidence of fetal acidosis in a Swiss population of 5806 patients undergoing elective cesarean section.\(^\text{11}\) Significantly more patients receiving spinal anaesthesia experienced serious fetal acidosis (Umbilical artery pH <7.10) as compared to patients treated with either epidural or general anaesthesia. In a recent metaanalysis, Reynolds and Seed confirmed that spinal anaesthesia produces more neonatal acidosis as compared to epidural and general anaesthetic.\(^\text{12}\)

Techniques to prevent maternal hypotension include intravenous volume expansion using i. v. fluids ("preload") immediately before spinal injection,\(^\text{13}\) use of left lateral tilt or manual uterine displacement, or both,\(^\text{14}\) and administration of i.v. fluids and vasopressor drugs both prophylactically and in response to cardiovascular changes subsequent to neural block.\(^\text{15,16}\) The rate of administration, total volume and type of fluid remain controversial.

Fluid preloading was routinely used in up to 87% of cases in spinal anaesthesia for cesarean section.\(^\text{17}\) Rout et al noted that the incidence of hypotension was reduced from 71% in patients without prehydration to 55% in patients who received crystalloid 20 ml/kg.\(^\text{18}\) However, some trials showed that using 10-30 ml/kg Ringer's lactate for acute volume expansion before induction of spinal anaesthesia, no differences in the indices of maternal hypotension or dosage of ephedrine were observed.\(^\text{19}\) Both the rate\(^\text{20}\) and volume\(^\text{21}\) of crystalloid preloading have also been shown to be unimportant. The studies of this kind have led to a reappraisal of the role of fluid preloading.\(^\text{22,23}\) It is still reasonable to administer a modest amount of crystalloid preload before spinal injection, as patients for elective surgery are often relatively dehydrated. However, there is no need to delay emergency surgery in order to preload.

A recent systematic review found that crystalloid was inconsistent in preventing hypotension and that colloid was significantly better.\(^\text{24}\) Dahlgren et al studied crystalloid compared with colloid for preloading.\(^\text{25}\) Hypotension was significantly reduced after larger volumes of colloid. It is postulated that parturient preoperatively susceptible to the supine position would benefit the most from colloid preloading. In another study of preloading comparing pentastarch with crystalloid, French et al demonstrated a reduction in the incidence of hypotension in the colloid group (12.5% versus 47.5%).\(^\text{26}\) In contrast to these studies which all found colloid preload of benefit, Karinen et al failed to find any reduction in the incidence of hypotension when colloid was used.\(^\text{27}\) Moreover, disadvantages of colloid include the additional cost, possibility of anaphylactoid reactions and excessive volume expansion, which may lead to pulmonary edema.\(^\text{28}\)

**MATERIAL & METHODS: Methods of Collection of Data:** 60 parturients admitted in government Lalla Ded Hospital., which is an associated hospital of government medical college Srinagar, scheduled for elective cesarean section during the study period meeting the inclusion and exclusion criteria were taken up for the study.
Approval and Consent: The study was approved by the Hospital Ethics committee and written informed consent from the patients was obtained.

Inclusion Criteria:
- The parturients belonging to ASA physical status class 1 and 2.
- Age group of 18-40 years.
- Only elective cesarean section cases.

Exclusion Criteria: All contraindications for spinal anaesthesia like:
- a. Patient’s refusal.
- b. Local infections.
- c. Concomitant disease.
- d. Spinal deformities.
- e. Bleeding disorders.
- f. Increased intracranial tension (ICT).
- g. Systolic blood pressure <100 mmHg.
- h. Age <18 years or >40 years.
- i. Obesity, Diabetes mellitus, Pregnancy-induced hypertension.
- j. Short stature.
- k. Multiple gestations, Placenta previa, Placental abruption.
- l. Other than ASA class 1 and 2.

Sample Size:
- Total 60 parturients.
- 30 parturients in each group.
- Group A: Crystalloid Preload.
- Group B: Colloid Preload.

Study Design: This is a prospective, randomized comparative study.

Premedication: After overnight fasting, all parturients were premedicated with Inj. Rantidine 50 mg and inj. Metoclopramide 10mg intravenously one hour before surgery.

PROCEDURE: The Patients were randomly allocated in of two groups before transfer to the theatre, where baseline measurements of heart rate, blood pressure and oxygen saturation were recorded in the modified supine position with at least 15° of left lateral tilt. A 16-guage i.v. cannula was inserted into a peripheral vein. Group A 1000 ml preload of Ringer’s lactate solution and Group B received a 500 ml preload of 6% Hydroxyethyl starch (450/0.7) solution over a period of 10 minutes just before induction of spinal anaesthesia.

Immediately after preloading, spinal block was given with 2.5ml of 0.5%heavy Bupivacaine at L3-L4 interspace or L4-L5 using 26-guage Quincke spinal needle in sitting position. The women were then turned rapidly to left modified supine position. All blocks extended to T6 or
above before surgery was allowed start. Both groups were then managed identically. Hypotension following spinal anaesthesia was treated with 6 mg i. v. bolus doses of ephedrine and additional rapid infusion of Ringer's lactate solution. Both groups received supplemental oxygen 5L/min by venture mask throughout the period of surgery. After delivery of the baby, all mothers received Oxytocin 10U i.v. as infusion.

**Following observations were made intraoperatively in each group:**
- Heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were monitored every 2 minutes for the first 20 minutes and then every 5 minutes till the end of surgery using a Mindray Beneview Multiparameter Monitor.
- Oxygen saturation and ECG were monitored continuously during the intraoperative period using same monitor.
- In addition, the height of spinal block, amount of blood loss, amount of vasopressor required, amount of i.v. fluid used intraoperatively and reaction(s) to i.v. fluids were noted.

**These observations were analyzed to get information on:**
1. Degree and duration of hypotension which was defined as decrease in the systolic blood pressure by 30% or more below baseline values or <90mmHg.
2. Bradycardia which was defined as heart rate <60 beats/min.
3. Requirement of vasopressor.
4. Incidence of nausea and vomiting.
5. Incidence of allergic reactions.
6. Cardiovascular collapse, if any.

**STATISTICAL ANALYSIS:** Data was analysed with the help of means and standard deviations. Parametric data was analysed with the help of Student’s t-test and for non-parametric data Chi-square test or Fischer’s exact test was used. P-value <0.05 was considered to be statistically significant.

**STATISTICS & RESULTS:**

| Age | Mean | Range | P-value | Significance |
|-----|------|-------|---------|--------------|
| Group A | 26.6 | 18-40 | 0.547 | SNSD |
| Group B | 25.8 | 18-39 |       |              |

Table 1: Age Distribution (years)

SNSD = statistically non-significant difference (P>0.05).
The age of the patients ranged from 18-40 years. The mean age in group A and group B was 26.6 and 25.8 years respectively. Hence, the age was comparable in both groups and was found to be statistically insignificant (Table 1 and Fig. 1).

| Age | Mean | SD  | Range    | P-Value | Significance |
|-----|------|-----|----------|---------|--------------|
| Group A | 151.2 | 5.17 | 143-169  | 0.579   | SNSD         |
| Group B | 150.4 | 5.42 | 144-167  |         |              |

Table 2: Distribution of Height (cm)

SNSD = Statistically non-significant difference (P>0.05).
The height of the patients ranged from 143-167cm. The mean height in group A and group B was 151.2±5.17 cm and 150.4±5.42 cm respectively. Hence, the height was comparable in both groups and was found to be statistically insignificant (Table 2 and Fig. 2).

| Age   | Mean  | SD | Range | P-value | Significance |
|-------|-------|----|-------|---------|--------------|
| Group A | 53.2  | 3.71| 48-67 | 0.491   | SNSD         |
| Group B | 53.9  | 4.13| 47-65 |         |              |

Table 3: distribution of Weight (kg)

SNSD = statistically non-significant difference (P>0.05).

The weight of the patient's ranged from 47-67kg. The mean weight in group A and group B was 53.2±3.71kg and 53.9±4.13 kg respectively. Hence, the weight was comparable in both groups and was found to be statistically insignificant (Table 3 and Fig. 3).

**Level of blockade:** The level of sensory block obtained was also comparable in both the groups and most of the patients had average blockade level of T6. (Table 4 and Fig. 4).

| HSL   | Group             | p-value     |
|-------|-------------------|-------------|
|       | Group A (n=30)    | Group B (n=30) |         |
| T4    | 5 (16.7%)         | 6 (20%)     | 0.809 (SNSD) |
| T5    | 8 (26.7%)         | 7 (23.3%)   |           |
| T6    | 15 (50%)          | 16 (53.4%)  |           |
| T7    | 2 (6.6%)          | 1 (3.3%)    |           |
| Median(Range) | T6 (T4-T6) | T6 (T4-T6) |           |

Table 4: Comparison of Sensory Levels

SNSD = statistically non-significant difference (P>0.05).
The duration of surgery was also comparable in both groups. The duration of surgery ranged from 45-60 minutes in both groups. The mean duration of surgery in group A and group B was 52.3±5.26 minutes and 53.4±4.63 minutes respectively and statistically insignificant. (Table 5 and Fig.5).

Table 5: Duration of surgery (minutes)

| Age     | Mean | SD   | Range | P-Value | Significance |
|---------|------|------|-------|---------|--------------|
| Group A | 52.3 | 5.26 | 45-60 | 0.422   | SNSD         |
| Group B | 53.4 | 4.63 | 45-60 |         |              |

SNSD = statistically non-significant difference (P>0.05).
**Maternal Heart Rate Variations:** The ranges of mean maternal heart rate in group A and group B were 82.9-98.0 and 81.0-98.9 respectively and were found to be comparable (table 6 and Fig. 6).

| Study Period | Group A | | Group B | | P-value | Significance |
|--------------|---------|---|---------|---|----------|----------------|
|              | Mean    | SD | Mean    | SD |          |                |
| Baseline     | 85.3 | 3.52 | 86.1 | 4.16 | 0.388   | SNSD           |
| 2 min        | 92.8 | 3.63 | 94.1 | 4.70 | 0.255   | SNSD           |
| 4 min        | 93.1 | 4.84 | 94.6 | 3.25 | 0.164   | SNSD           |
| 6 min        | 93.4 | 4.09 | 96.8 | 4.16 | 0.093   | SNSD           |
| 8 min        | 95.9 | 3.78 | 98.9 | 2.69 | 0.075   | SNSD           |
| 10 min       | 97.9 | 1.78 | 98.5 | 2.53 | 0.357   | SNSD           |
| 12 min       | 98.0 | 2.25 | 98.3 | 1.73 | 0.579   | SNSD           |
| 14 min       | 96.2 | 3.48 | 98.1 | 3.41 | 0.112   | SNSD           |
| 16 min       | 94.6 | 3.81 | 96.7 | 2.73 | 0.154   | SNSD           |
| 18 min       | 93.7 | 2.98 | 94.7 | 3.23 | 0.201   | SNSD           |
| 20 min       | 91.9 | 4.70 | 93.2 | 3.06 | 0.184   | SNSD           |
| 25 min       | 89.5 | 2.99 | 91.3 | 3.71 | 0.167   | SNSD           |
| 30 min       | 88.8 | 2.43 | 89.4 | 2.02 | 0.345   | SNSD           |
| 35 min       | 87.6 | 3.29 | 88.7 | 3.38 | 0.194   | SNSD           |
| 40 min       | 86.5 | 3.86 | 85.8 | 3.6  | 0.468   | SNSD           |
| 45 min       | 85.1 | 4.22 | 84.2 | 3.66 | 0.332   | SNSD           |
| 50 min       | 82.9 | 4.39 | 82.2 | 2.63 | 0.540   | SNSD           |
| 55 min       | 83.3 | 4.42 | 82.2 | 1.72 | 0.390   | SNSD           |
| 60 min       | 83.3 | 3.30 | 81.0 | 2.00 | 0.349   | SNSD           |

Table 6: Comparison of Maternal Heart Rate

SNSD=statistically non-significant difference (P>0.05).

The maternal heart rate variations between Group A and Group B were comparable before spinal anaesthesia and throughout the period of surgery.
Onset of Hypotension: The onset of hypotension was early in group A than group B. The mean time period of onset of hypotension in group A was 6.3±2.09 minutes (Range 4-10 minutes) and in group B was 12.9±2.27 minutes (Range 10-16 minutes). The difference was statistically significant between the two groups (Table 7 and Fig. 7).

| Onset of Hypotension | No. | Mean | SD  | Range | P-value | Significance |
|----------------------|-----|------|-----|-------|---------|--------------|
| Group A              | 18  | 6.3  | 2.09| 4-10  | <0.001  | SSD          |
| Group B              | 7   | 12.9 | 2.27| 10-16 |         |              |
| Inference            |     |      |     |       |         | Onset of hypotension is early in Group A than in Group B |

Table 7: Onset of Hypotension

SSD = statistically significant difference (P<0.05).
Incidence of Hypotension: The incidence of hypotension in group A and Group B was 60% and 23.3% respectively. The difference in the incidence of hypotension was found to be statistically significant among two groups (Table 8 & Fig. 8).

| Hypotension | Group A (n=30) | Group B (n= 30) | P-Value       |
|-------------|----------------|-----------------|---------------|
| Absent      | 12 (40%)       | 23 (76.7%)      | 0.004 (SSD)   |
| Present     | 18 (60%)       | 7 (23.3%)       |               |

Table 8: Incidence of Hypotension

SSD = statistically significant difference (P<0.05).
Systolic Blood Pressure Variations: The variations in mean systolic blood pressure (SBP) in group A and group B after spinal anaesthesia were in the range of 109.8-129.3 mm Hg and 113.9-131.0 mm Hg respectively. (Table 9 and Fig. 9).

| Study Period | Group A Mean | Group A SD | Group B Mean | Group B SD | P-value | Significance |
|--------------|--------------|------------|--------------|------------|---------|--------------|
| Baseline     | 129.7        | 9.91       | 131.0        | 7.5        | 0.569   | SNSD         |
| 2 min        | 120.8        | 9.10       | 128.4        | 4.62       | <0.001  | SSD          |
| 4 min        | 112.7        | 10.24      | 125.2        | 5.39       | <0.001  | SSD          |
| 6 min        | 109.9        | 10.94      | 122.1        | 6.46       | <0.001  | SSD          |
| 8 min        | 109.8        | 10.90      | 118.9        | 5.32       | <0.001  | SSD          |
| 10 min       | 110.7        | 9.71       | 116.2        | 6.09       | 0.011   | SSD          |
| 12 min       | 113.2        | 6.68       | 114.4        | 6.66       | 0.489   | SNSD         |
| 14 min       | 118.6        | 5.04       | 113.9        | 6.90       | 0.004   | SSD          |
| 16 min       | 122.2        | 4.79       | 117.1        | 7.20       | 0.002   | SSD          |
| 18 min       | 121.9        | 3.66       | 120.9        | 5.54       | 0.397   | SNSD         |
| 20 min       | 124.8        | 4.04       | 123.6        | 3.69       | 0.222   | SNSD         |
| 25 min       | 126.2        | 5.41       | 125.4        | 4.87       | 0.533   | SNSD         |
| 30 min       | 125.4        | 5.57       | 125.6        | 4.17       | 0.896   | SNSD         |
| 35 min       | 127.2        | 4.73       | 126.6        | 3.74       | 0.588   | SNSD         |
| 40 min       | 125.0        | 4.11       | 126.0        | 3.44       | 0.295   | SNSD         |
| 45 min       | 125.4        | 4.15       | 125.0        | 3.94       | 0.657   | SNSD         |
| 50 min       | 122.6        | 2.17       | 123.6        | 2.19       | 0.149   | SNSD         |
| 55 min       | 121.3        | 2.77       | 121.6        | 2.50       | 0.820   | SNSD         |
| 60 min       | 121.0        | 3.56       | 121.3        | 2.08       | 0.892   | SNSD         |

Table 9: Comparison of Systolic Blood Pressure (mm Hg)

SSD = statistically significant difference (P<0.05); SNSD = statistically non-significant difference (P>0.05).
The two groups had similar pre-induction mean systolic blood pressure; however, after spinal anaesthesia lowest mean SBP was lower in group A compared to group B. The lowest mean SBP in group A and group B was 109.8 and 113.9 mmHg respectively.

**Requirement of Ephedrine:** The requirement of ephedrine was more in group A when compared to group B. In group A, the mean requirement of ephedrine was 13.0 mg and in group B was 9.4 mg. The difference was found to be statistically significant (Table 10 and Fig. 10).

| Use of Ephedrine(mg) | Group A (n=30) | Group B (n=30) | P-value |
|----------------------|----------------|----------------|---------|
| No                   | 12(40%)        | 23(76.7%)      | 0.004(SSD) |
| Yes                  | 18(60%)        | 7(23.3%)       |         |
| Mean±SD              | 13.0±3.71      | 9.4±3.21       | 0.035(SSD) |

Table 10: comparison of use of Ephedrine (mg) in two groups

SSD = statistically significant difference (P<0.05).

**IV Fluids:** The mean volume of fluid used intraoperatively in group A and group B was 1200±152.56 and 1191.7±130.70 respectively, and was found to be comparable and statistically in significant (Table 11 and Fig. 11).

| Group     | Mean  | SD    | Range      | P-value | Significance |
|-----------|-------|-------|------------|---------|--------------|
| Group A   | 1200.0| 152.56| 1000-1500  | 0.821   | SNSD         |
| Group B   | 1191.7| 130.70| 1000-1450  |         |              |

Table 11: Comparison of intraoperative fluid (ml) used among two groups

SNSD = statistically non-significant difference (P>0.05).
Blood Loss: The average amount of intraoperative blood loss in group A and group B was 837.5±65.90 ml and 819.2±64.56 ml respectively, and was found to be comparable and statistically insignificant (Table 12 and Fig. 12).

| Group | Mean  | SD    | Range      | P-value | Significance |
|-------|-------|-------|------------|---------|--------------|
| Group A | 837.5 | 65.90 | 750-1000   | 0.281   | SNSD         |
| Group B | 819.2 | 64.56 | 700-950    |         |              |

Table 12: Comparison of intraoperative blood loss (ml) among two groups

SNSD = statistically non-significant difference (P>0.05).
Complications: The complications such as nausea and vomiting after induction of spinal anaesthesia were a minor problem and occurred in similar frequency in both the groups (Table 13 and Fig. 13).

| Nausea/Vomiting | Group A | Group B | P-value  |
|-----------------|---------|---------|----------|
| Yes             | 4(13.3%) | 3(10%)  | 0.688 (SNSD) |
| No              | 26(86.7%) | 27(90%) |          |

Table 13: Comparison of complications in two groups

SNSD = statistically non-significant difference (P>0.05).

DISCUSSION: Hypotension is the commonest serious problem following spinal anaesthesia for cesarean section with an incidence reported in the literature of upto 85%. This is in spite of pregnant patients having 40-45% of more blood volume at term compared to non-pregnant patients. Pregnant patients at term are more prone to develop hypotension due to the occurrence of aortocaval compression by the fetal head and higher level of sympathetic blockade owing to increased spread of local anaesthetic in the cerebrospinal fluid. Hypotension, hazardous to the mother and more so, to the fetus, is better prevented than treated. Blood pressure is usually maintained in the face of vasodilation, caused due to factors other than central neural blockade, by a reflexive increase in cardiac output. However, in the presence of spinal induced venodilation, venous return is reduced to an extent that cardiac output cannot increase and is often reduced. The result is severe hypotension with reduced uteroplacental perfusion and decreased Apgar score. Therefore, efforts were made to increase cardiac preload before instituting spinal blockade in the hope of preventing subsequent hypotension; the concept of intravenous ‘preload’ was born. 37
Various fluids, including crystalloids and colloids have been used for preloading before spinal anaesthesia for cesarean section. Many studies have been reported regarding the effects of volume preload, using various fluid regimens, on the incidence and severity of hypotension induced by spinal anaesthesia. Initial recommendations for prehydration of healthy women about to undergo cesarean section under regional anaesthesia recommended 1000 ml of balanced electrolyte solution. Although prehydration with 1000 ml of crystalloid decreased the incidence of hypotension, hypotension remained a frequent event. Investigators attempted to further decrease the frequency through more aggressive fluid administration. Some investigators increased the volume of crystalloid to 2000 ml, whereas others continued with about 1000 ml of fluid but included some colloid in that volume. Since colloid remain in the vascular compartment for a much longer time period than do crystalloids, it is said to require only one-third to one-fourth as much colloid as crystalloid for an equivalent amount of venous expansion. However colloid solution is considerably more expensive than crystalloids and, depending on the product, has other significant disadvantages, including anaphylaxis.

The degree of hypotension that requires treatment is controversial. Differing definitions of ‘significant’ hypotension are at least partly responsible for the wide variation in the incidences of hypotension reported in the literature. Although the degree of reduction in uteroplacental blood flow associated with hypotension is proportional to the degree of reduction in blood pressure, much may depend upon the starting blood pressure. For example, a 20% reduction in systolic blood pressure, from 130 to 104 mmHg, does not have same implication as a reduction from 100 down to 80 mmHg. The more commonly used definitions; therefore, include elements of both relative and absolute decreases in blood pressure. Our current working definition is a reduction in systolic blood pressure by 30% from baseline and to below 90 mmHg.

Many studies, continues to emphasize the role of intravenous volume loading as a prophylactic measure in reducing the incidence of hypotension. In 1968, Wollman and Marx demonstrated that rapid infusion of 1000 ml of 5% dextrose in lactated Ringer’s solution is safe and effective method of reducing the incidence of hypotension in parturients. In 1976, Clark et al viewed spinal hypotension as a persistent problem and investigated the interaction of fluid loading and uterine displacement. They found that the incidence of spinal induced hypotension could be greatly reduced by combination of fluid loading and left uterine displacement. One major flaw in the Clark et al study was the failure to include a group that had uterine displacement alone.

The persistence of hypotension despite uterine displacement and preloading led to increasing volumes of preload being used, perhaps in the belief that enough preload had not been used in earlier studies. This view is supported in a study by Ueyama H et al, who showed that the augmentation of blood volume with preloading, regardless of the fluid used, must be large enough to result in a significant increase in cardiac output for effective prevention of hypotension. Lewis et al in 1983 found that the incidence of hypotension with epidural anaesthesia for cesarean section could be substantially reduced by increasing crystalloid prehydration to 2000 ml. However, in a study by Park GE et al in 1996 to assess the effect of varying volumes of crystalloid administration before cesarean delivery on maternal hemodynamics, it was found that increasing the volume of i.v. crystalloid administered to 30ml/kg
in the healthy parturient did not significantly alter the maternal hemodynamics or Ephedrine requirements after spinal anaesthesia and has no apparent benefit.

Moreover, unbridled use of large volumes of crystalloid fluid risks acute hemodilution with decreased oxygen-carrying capacity, and pulmonary edema. It has been suggested that term parturients may be at greater risk of pulmonary edema, with a reduced pulmonary interstitial safety margin due to a fall in oncotic pressure and increase in plasma volume.

Other than increasing the volume of preload used, there are two ways of tackling this problem, first by administering the solution over a much shorter period and second by preloading with colloid solution with a longer intravascular half-life. More rapid administration of preload before spinal anaesthesia has been studied by Rout et al in 1992. In this study investigators failed to demonstrate a reduction in the incidence of hypotension in the rapidly preload group. Also Jackson et al in a study found that a preload of 1L of crystalloid solution infused during the 10 min preceding the administration of spinal anaesthesia for cesarean section in combination with a prophylactic infusion of Ephedrine did not reduce the incidence, severity or duration of hypotension. The crystalloid solutions used for preloading the patients usually remains in the vascular compartment for 20min at the most because crystalloid solutions, such as Ringer's lactate have a short intravascular half-life because of their rapid distribution into the interstitial space. They do not thus expand the volume in the real sense. Evidence is accumulating that colloid preloading offsets hypotension and hypovolemia more effectively than the crystalloids solutions. This is because colloid solutions contain large molecules that do not immediately redistribute throughout the extracellular fluid compartment. Therefore, they should not decrease plasma colloid oncotic pressure (COP) as much as crystalloid solutions and intravascular volume should be better maintained. Colloid solutions, due to their longer stay in the vascular compartments, maintain a sustained hemodynamics whereas crystalloid solutions, in large doses, dilute plasma proteins resulting in greater extravasation of fluid into the extracellular fluid compartment secondary to lowering of plasma colloid oncotic pressure.

Wennberger et al (1990) reported that COP decreased by only 1.7 mmHg after preloading with 3% dextran 70 before epidural anaesthesia for cesarean section, compared with a 5.6 mmHg decrease after preload with Ringer's lactate.

Mathru et al in 1980 demonstrated a 0% incidence of hypotension when parturients, undergoing cesarean section under spinal anaesthesia, received prophylactic infusion of 15 ml/kg of 5% albumin in D5RL within 15-20 min before the administration of spinal anaesthesia. The disadvantages of albumin use are that it is more expensive, not universally available and carries a small but definitive risk of infection transmission and histamine release.

In our study, the incidence of hypotension was found to be low in patients who received 6% Hydroxyethyl starch solution (23.3%) as compared to patients prehydrated with Ringer's Lactate solution (60%). In colloid group (group B), 76.7% had no hypotension when compared to crystalloid group (group A) in which only 40% had no hypotension. This difference was found to be statistically significant. The results in our study correlated well with other various studies conducted to know the efficacy of crystalloid and colloids in preventing hypotension following spinal anaesthesia.

Hallworth et al in 1982 compared the effect of preloading of 1L of Hartman's solution with that of 1L of preparation containing 500ml each of Hartman's solution and polygelatin on the
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incidence of hypotension in parturients undergoing cesarean section under spinal anaesthesia. They found that hypotension occurred in 45% of Hartman’s group and 5% of polygelatin group and Hartman’s group. In our study, the incidence of hypotension in crystalloid group was 60% and in colloid group the incidence of hypotension was 23.3%. This may be due to the difference in the amount and composition of the preload.

Karinen et al\textsuperscript{27} in 1995 conducted a comparative study to investigate the effect of 1L of crystalloid and 500 ml of colloid preloading on uteroplacental and maternal hemodynamic state during spinal anaesthesia for cesarean section. They found that the incidence of maternal hypotension in the crystalloid group was 62% whereas that in the colloid group was 38%. In our study, the incidence of hypotension is almost similar in crystalloid group (60%) but lower in colloid group (23.3% versus 38%).

Riley et al\textsuperscript{25} in 1995 also compared the effect of preloading of 2L of RL with that of a preloading preparation containing 500ml of 6% hetastarch mixed in 1500ml of RL. In spite of higher preloading volume, they found 85% of hypotension in crystalloid group, which is about 15% higher than that seen in the crystalloid group of our study. The reason for this difference is not clearly known. The incidence of hypotension in the 6% Hetastarch containing group was 45%, which is also about 21.7% higher than that seen in the colloid group of our study (23.3%).

During the study, hypotension was treated with additional intravenous fluids. Later on vasopressor (Ephedrine 6mg i.v. boluses) was used aggressively if above measures failed to bring up the blood pressure. The amount of vasopressor (Ephedrine 6mg boluses) required to treat hypotension was found to be more in group A (13.0±3.71mg) compared with group B (9.4±3.21 mg). Because factors like amount of intraoperative blood loss, amount of intraoperative fluids used and amount of Oxytocin required also influence the incidence of hypotension, they were also studied and were found to be comparable in all groups in our study. The other parameters like the age of the patient, height of the patient, weight of the patient, the dosage of local anaesthetic used for the spinal block and the level of sensory blockade obtained were intentionally kept comparable in all the groups as much as possible so as to avoid these factors influencing our study and to know more appropriately the true characteristics of the fluids used on our study. Neonatal outcome, as determined by Apgar score, was found to be good and similar in all groups. All neonates in the study group had Apgar score of >7 at 1 min and none had Apgar score <7 at 5min.

The dose of Bupivacaine 0.5% (heavy) used was 2.5ml in all patients and the sensory block obtained was around T6 segment in most of the cases. These steps were taken because it is well known that the severity and incidence of hypotension depends on the level of block obtained. There were no significant difference in heart rate and lowest systolic blood pressure recorded in all groups. In our study no patient in both groups had bradycardia. Incidence of nausea/vomiting and was comparable in all the groups as well. In present study, hydroxystarch 6% did not produced any allergic reactions.

Jackson et al\textsuperscript{31} (1995) compared the protective effective of 1L preload with 200ml preload of crystalloid solution, administered 10min before spinal anaesthesia for cesarean section. Investigators did not find significant differences in Ephedrine requirement between the two groups or in the incidence, severity or duration of hypotension. Similarly, Husainiet al\textsuperscript{38} in a study
found that the group that received 1L RL preloading had similar incidence and severity of hypotension as that of control group, which received no preload. However, we feel that the results of current study suggest that there may still be a place for preloading using colloid. Further investigations using starches are warranted before we abandon the practice of preloading on favour of the aggressive use of vasoconstrictors.

REFERENCES:
1. Bucklin BA, Hawkins JL, Anderson JR, Ullrich FA: Obstetric anaesthesia workforce survey: twenty-year update. Anaesthesiology 2005; 103: 645.
2. Jenkins JG, Khan MM: Anaesthesia for cesarean section: A survey in a UK Region From 1992 to 2002. Anaesthesia 2003; 58 1114-1118.
3. Van Houwe P, Heytens L, Vercruysse P: A survey of obstetric anaesthesia practice in Flanders, ActaAnaesthBelg 2006; 57: 29-37.
4. Landon MB, HauthJC, Leveno KJ, et al: Mateernal and prenatal outcomes associated with a trial of labour after prior cesarean delivery. N Engl J Med 2004; 351: 2581.
5. Hawkins JL, Koonin LM, Palmer SK, Gibbs CP: Anaesthesia-related deaths during obstetric delivery in the United States, 1979-1990; Anaesthesiology 1997; 86; 277-284.
6. Djabatey EA, Barclay PM: Difficult and failed intubation in 3430 obstetric general anaesthetics. Anaesthesia 2009; 64: 1168.
7. Carpenter RL, Caplan RA, Brown DL et al: Incidence and risk factors for side effects of spinal anaesthesia. Anaesthesiology 1992; 76: 906.
8. NganKee WD, Khaw Ks, Lee BB, Lau TK, Gin T: A dose-response study of prophylactic intravenous ephedrine for the prevention of hypotension during spinal anaesthesia for cesarean delivery. Anaesthesia and Analgesia 2000; 90: 1390-1395.
9. Dyer RA, Els L, Farbas J, Torr GJ, Schoeman LK, James MF: Prospective, randomized trial comparing general with spinal anaesthesia for cesarean delivery in preeclamptic patients with a nonreassuring fetal heart trace. Anaesthesiology 2003; 99: 561-569.
10. Roberts SW, Leveno KJ, Sidawi JE, Lucas MJ, Kelly MA: Fetal academia associated with regional anaesthesia for cesarean section. ObstetGynecol 1995; 85: 79-83.
11. Mueller MD, Bruhwiler H, Schupfer G, Luscher KP; Higher rate of fetal academia after regional anaesthesia for elective cesarean delivery. ObstetGynecol 1997; 90: 131-134.
12. Reynolds F, Seed PT: Anaesthesia for cesarean section and neonatal acid-base status: a meta–analysis. Anaesthesia 2005; 60: 636-653.
13. Wollman SG, Marx GF: Acute Hydration for the prevention of hypotension of spinal anaesthesia in parturients. Anaesthesiology 1968; 79: 347-379.
14. Clark RB, Thompson DS, Thompson CH: prevention of spinal hypotension associated with cesarean section. Anaesthesiology 1976; 45: 670-674.
15. Datta S, Alper MH, Osteimer GW, Weiss JB. Method of ephedrine and nausea and vomiting during spinal anaesthesia fo cesarean section. Anaesthesiology 1962; 29: 68-70.
16. Marx GF, Cosmi EV, Wollman SG: Biochemical status and clinical condition of mother and infant and cesarean section. Anaesthesia and analgesia 1969; 48: 986-993.
17. Burns SM, Cowan CM, Wolkes RG: prevention and management of hypotension during spinal anaesthesia for elective cesarean section: A Survey of practice. Anaesthesia 2001; 56: 794-798.
18. Rout CC, Rocke DA, Levin J, Gouws E, Reddy D: A re-evaluation of the role of crystalloid preload in the prevention of hypotension associated with spinal anaesthesia for elective cesarean section. Anaesthesiology 1993; 79: 262-269.
19. Park GE, Hauch MA, Curlin F, Datta S, Bader A: Effects of varying volume preload before cesarean delivery on maternal haemodynamics and colloid osmotic pressure. Anaesthesia and analgesia 1996; 83: 299.
20. Rout CC, Akoojee SS, Rocke DA, Gouws: Rapid administration of crystalloid preload does not decrease the incidence of hypotension after spinal anaesthesia for elective cesarean section. Br J Anaesth 1992; 68: 394-397.
21. McKinlay J, Lyons G: Obstetric neuraxial anaesthesia: which pressor agents should we be using? Int J Obstet Anaesth 2002; 11: 117-121.
22. Riley ET: Spinal Anaesthesia for cesarean delivery: Keep the pressure up and don’t spare the vasoconstrictors. Br J Anaesth 2004; 92: 459-461.
23. Morgan PJ, Halpern SH, Tarshis J: The effect of an increase of central blood volume before spinal anaesthesia for cesarean delivery: A qualitative systematic review. Anaesthesia and Analgesia 2001; 92: 997-1005.
24. Dahlgren G, Granath F, Wessel H, Irestedt L: Prediction of hypotension during spinal anaesthesia for cesarean section and its relation to the effect of crystalloid or colloid preload. Int J Obstet Anaesth 2007; 16: 128-134.
25. Riley ET, Cohen SE, Rubenstein AJ, Flanagan B: Prevention of hypotension after spinal anaesthesia for cesarean section: 6% hetastarch versus lactated Ringer’s solution. Anaesthesia and analgesia 1995; 81: 838-842.
26. French GWG, White JB, Howell SJ, Popat M: comparison of pentastarch and Hartmann’s solution for volume preloading in spinal anaesthesia for elective cesarean section. Br J Anaesth 2002; 89: 475-477.
27. Karinen J, Rasanen J, Alahuhta S, Jouppila R, Jouppila P: Effect of crystalloid and colloid preloading on uteroplacental and maternal haemodynamic state during spinal anaesthesia for cesarean section. Br J Anaesth 1995; 75: 531-535.
28. Weeks S: Reflections on hypotension during cesarean section under spinal anaesthesia: Do we need to use colloid? Can J Anaesth 2000; 47: 607-610.
29. Ueyama H, He YL, Tanigami H, Mashimo T, Yoshia I: Effects of crystalloid and colloid preload on blood volume in the parturient undergoing spinal anaesthesia for elective cesarean section. Anaesthesiology 1999; 91: 1571-1576.
30. Lewis M, Thomas P, Wilkes RG: Hypotension during epidural anaesthesia for cesarean section. Anaesthesia 1983; 38: 250-253.
31. Jackson R, Reid JA, Thorburn J: Volume preloading is not essential to prevent spinal-induced hypotension at cesarean section. Br J Anaesth 1995; 75: 262-265.
32. Mathru M, Rao TLK, Kartha RK, Shanmugham M, Jacobs HK: Intravenous albumin administration for prevention of spinal hypotension during cesarean section. Anaesthesia and Analgesia 1980; 59: 655-658.

33. Hallworth D, Jelliceo JA, Wilkes RG: Hypotension during epidural anaesthesia for cesarean section: A comparison of intravenous loading with crystalloid and colloid solutions. Anaesthesia 1982; 37: 53-56.

34. Wennberg E, Frid I, Haljamae H, Wennergren M, Kjellmer I: Comparison of Ringer’s acetate with 3%dextran 70 for volume loading before extradural cesarean section. Br J Anaesth 1999; 85: 654-660.

35. Lin CS, Lin TY, Huang CH, Lin YH, Lin CR, Chan WH, Tsai SK: Prevention of hypotension after spinal anaesthesia for cesarean section: Dextran 40 versus Lactated Ringer’s Solution. Acta Anaesthesiology Scand 1999; 37: 55-59.

36. Siddik SM, Aouad MT, Kai GE, Sfeir MM, Baraka AS: Hydroxyethyl starch 10% is superior to Ringer’s solution for preloading before spinal anaesthesia for cesarean section. Can J Anaesth 2000; 47: 616-621.

37. Kaye AD, Grogona AW: Fluid and electrolyte physiology, Chapter 45, Anaesthesia, 4th ed, Miller RD, Philadelphia, Churchill Livingstone, 2000: 1586-161.

38. Hussaini SW, Russell IF: Volume Preloading: Lack of effect in prevention of spinal induced hypotension at cesarean section Int J Obstet Anesth 1998,7,76-81.

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