Original Article

Role of Ephedrine and Epinephrine in the Management of Hypotension after Sub-Arachnoid Block (SAB) in Caesarean Section

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Abstract

Introduction*: Caesarean section is a common operation in obstetrics and usually performed by sub-arachnoid block (spinal anaesthesia). The principal advantages of spinal anaesthesia for caesarean delivery are its simplicity, speed, reliability, & minimal foetal exposure to depressant drugs. The parturient remains awake, & the hazards of aspiration are minimized.[1]*

Hypotension remains the most common complication associated with spinal anaesthesia for caesarean delivery. It can have detrimental effect on both mother & neonate ; these effects include impaired foetal oxygenation with asphyxial stress & foetal acidosis, & maternal symptoms of low cardiac output , such as nausea, vomiting, dizziness, & impaired consciousness .[2] Excessive hypotension may potentially produce myocardial and cerebral ischaemia, and is associated with neonatal acidaemia.[3] Maternal hypotension lasting more than 2 minutes should be avoided , as it may be associated with lower Apgar scores.[1]

Hypotension after spinal anaesthesia for caesarean section has an incidence up to 80% without prophylactic management.[4] Recommended measures to decrease the incidence of hypotension include pre-hydration with 1000-1500 ml of lactated Ringer's solution & maintaining left uterine displacement during anaesthesia.[1]

Despite these conservative measures, a vasopressor drug is often required. The drug usually recommended in this context is ephedrine, which is effective in restoring maternal arterial pressure after hypotension.[2] Despite the wide acceptance of ephedrine as the vasopressor of choice for obstetric anaesthesia[5], its superiority over other vasopressors has not been clearly defined and its position has been challenged because of potential complications that include supraventricular tachycardia, tachyphylaxis and foetal acidosis.[6,7]

Moreover, when the fall of blood pressure is much greater, ephedrine does not exhibit prompt effect; in that case, epinephrine would be the better option as a vasopressor agent in restoring maternal arterial pressure as because it is very quick on onset & very potent on action and does not exhibit tachyphylaxis.

This study assesses whether the use of Ephedrine and Epinephrine are different in their efficacy for managing maternal hypotension and their effects on neonatal outcome in women having spinal anaesthesia for caesarean delivery.

Summary: *One hundred and sixty-seven (167) healthy patients, aged between 20 to 40 years, undergoing elective caesarean section under subarachnoid block (SAB) were assessed to determine maternal haemodynamic changes and neonatal Apgar score. Among the 167 patients, sixty (60) patients developed hypotension; These 60 patients were divided into two groups.*

In Group A *(n=26), Systolic blood pressure (SBP) decreased 83.56 (±4.84) mm Hg and Ephedrine was given in 5 mg increments to maintain SBP > 90 mm Hg. Diastolic blood pressure (DBP) also reduced to*

61.26 (±4.94) mm Hg from its baseline value of 76.24 (±7.35) mm Hg and following Ephedrine therapy it restored toward baseline value, 70.32 (±5.67). In Group B *(n=27), Systolic blood pressure (SBP) decreased 84.12 (±4.36) mm Hg and Epinephrine was given in 20 µgm increments to maintain SBP > 90 mm Hg. Diastolic blood pressure (DBP) also reduced to 62.19 (±4.78) mm Hg from its baseline value of 74.94 (±7.05) mm Hg and following Epinephrine therapy it remained close to the value obtained during hypotension, 63.06 (±3.59). Both the vasopressors restored the heart rate (HR) towards normal like 78.43 (±7.35), & 82.85 (±5.68) from 108.24 (±8.45) & 109.34 (±11.04) beats/min, during hypotension by intravenous ephedrine and epinephrine respectively.*

Conclusion: *Use of Ephedrine and Epinephrine for the management of maternal hypotension doesn't affect the neonatal outcome; neonatal Apgar score remains satisfactory. Epinephrine causes prompt restoration of systolic blood pressure towards baseline but doesn't increase the diastolic blood pressure, thus may compromise the coronary perfusion. On the other hand, Ephedrine increases both systolic & diastolic blood pressure and to be used routinely for the management of hypotension during caesarean section under subarachnoid block.*

(JBSA 2017; 30(1): 53-65)

Introduction:

The incidence of caesarean section has increased dramatically over the last 20 years. In 1980, caesarean sections accounted for 16.5% of all deliveries in the USA. This figure rose to 24.7% in 1988.[1]

The selection of an anaesthetic technique for caesarean delivery depends on several surgical, anaesthetic, and maternal factors. Surgical factors include the indication for, and therefore the degree of urgency of, delivery. Anaesthetic considerations include anticipated ease to intubation, presence of a lobour epidural catheter, contraindications to regional techniques, and potential for technical difficulties (obesity, spinal deformities). Maternal factors include consent and cooperation. When feasible, regional is preferred to general anaesthesia because of its better safety profile.[1]

Caesarean section is a common operation in our country and usually performed by subarachnoid block (spinal anaesthesia). The principal advantages of spinal anaesthesia for caesarean delivery are its simplicity, speed, reliability, & minimal foetal exposure to depressant drugs.[1] The parturient remains awake, & the hazards of aspiration are minimized.[1] Furthermore, the neurobehavioral assessment of neonates born following spinal anaesthesia is better than after general anaesthesia with either thiopental or ketamine inductions.[42]

In spite of lot many advantages, there are some major disadvantages of this technique of which the most commonest one is sudden and dramatic onset of systemic hypotension.[43] It can have detrimental effect on both mother & neonate ; these effects include impaired foetal oxygenation with asphyxial stress & foetal acidosis, & maternal symptoms of low cardiac output, such as nausea, vomiting, dizziness, & impaired consciousness .[2] Excessive hypotension may potentially produce myocardial and cerebral ischaemia, and is associated with neonatal acidaemia.[3] Maternal hypotension lasting more than 2 minutes should be avoided, as it may be associated with lower Apgar scores .[1]

Deciding when to treat haemodynamic derangements during spinal anaesthesia is perhaps more difficult than deciding how to treat them. There are currently no studies that clearly define the lower limit of acceptable blood pressure or heart rate for any group of patients.

In the absence of such data, several authors have recommended treating blood pressure if it decreases more than 25% to 30% below baseline or in normotensive patients, if systolic pressure falls below 90 mm Hg. Recommendations regarding bradycardia suggest initiating treatment if heart rate falls below 50 to 60 beats/minute. These recommendation are reasonable, although not universally applicable.[12]

Recommended measures to decrease the incidence of hypotension include pre-hydration with 1000–1500 ml of lactated Ringer's solution & maintaining left uterine displacement during anaesthesia.[1]

Despite these conservative measures, a vasopressor drug is often required. The drug usually recommended in this context is ephedrine, which is effective in restoring maternal arterial pressure after hypotension.[2] Despite the wide acceptance of ephedrine as the vasopressor of choice for obstetric anaesthesia[5], its superiority over other vasopressors has not been clearly defined and its position has been challenged because of potential complications that include supraventricular tachycardia, tachyphylaxis and foetal acidosis.[6,7]

Moreover, when the fall of blood pressure is much greater, ephedrine does not exhibit prompt effect; in that case, epinephrine would be the better option as a vasopressor agent in restoring maternal arterial pressure as because it is very quick on onset & very potent on action and does not exhibit tachyphylaxis. Epinephrine has both alpha- and beta- adrenergic effects with the predominant effect being determined by the dose.

Foetal well being depends on an adequate placental flow.[44] At term uterine blood flow is approximately 500 ml/min, of which 70–90% is distributed to the placenta. Placental blood flow depends on the balance between the perfusion pressure across the intervillous space and the resistance of the spiral arteries. Perfusion pressure on the other hand depends on mean arterial pressure as well as venous pressure. Thus perfusion pressure is therefore reduced by changes in cardiac output and blood pressure. So, during hypotension there will be great decrease in placental perfusion.

Use of vasopressor for the management of hypotension also decreases placental perfusion. As placental blood vessels contain $á_1$ receptor, use of Ephedrine causes very minimum interference in placental circulation but not so effective for increasing blood pressure. Epinephrine, on the other hand, causes effective increase in blood pressure but theoretically it decreases placental blood flow.

As normal foetus can tolerate a 50% reduction of uteroplacental blood flow because there is good circulatory reserve [45], so effective increase in blood pressure is the prime concern in spite of mild decrease in placental blood flow during hypotension after subarachnoid block.

Aim and objective of the study is to find out the effects of ephedrine and epinephrine in the management of hypotension following subarachnoid block (SAB) for elective caesarean section.

Methods and materials:

After obtaining approval from the local ethical clearance committee and written informed patient consent, 60 ASA physical status I and II women with term singleton pregnancies, aged between 20 – 40 years, who developed hypotension after subarachnoid block for elective caesarean section were randomized into two groups : **Group A** and **Group B**.

Hypotension was defined as a 30% decrease in systolic blood pressure from pre-anaesthetic baseline value or reduction of systolic blood pressure below 90 mm Hg. Patients with preexisting or pregnancy-induced hypertension, cardiovascular or cerebrovascular disease, known foetal abnormalities, or contraindication to subarachnoid block were excluded.

All patients were transferred to the operation theatre without any pre-medication. Standard monitoring included noninvasive blood pressure, electrocardiogram (ECG), and pulse oximetry. Baseline measurements of heart rate (HR), blood pressure (BP) and oxygen saturation (SpO_2) were recorded. Baseline blood pressure and heart rate were calculated as the mean of three successive measurements, 1 minute apart.

A large-bore IV cannula (18 G) was then inserted into a forearm vein and intravenous (IV) preload of 20 ml/kg lactated Ringer's solution was given for 10–15 minutes. Lumbar subarachnoid block (SAB) was then induced with the patient in the sitting position. After skin infiltration with 2% lignocaine, a 25-gauge Quincke needle was inserted at the L3-L4 vertebral interspace and hyperbaric 0.5% bupivacaine 2.5 ml was injected intrathecally. The patient was then immediately turned supine with left lateral tilt. Oxygen 4 L/min was given by clear face mask until delivery. Maternal systolic & diastolic blood pressure were recorded every minute and heart rate (HR) was recorded continuously with an automatic instrument. ECG

and oxygen saturation (SpO_2) were monitored continuously.

Total of one hundred and sixty seven (167) patients were studied. One hundred and seven (107) patients received no vasopressor therapy because their systolic blood pressure (SBP) remained above 90 mm of Hg after subarachnoid block. Sixty (60) patients whose systolic blood pressure (SBP) decreased below 90 mm of Hg or decreased 30% from the pre-induction SBP were randomly allocated into two groups of equal size; **Group A** and **Group B**.

Patients in **Group A** were given 5 mg intravenous injection of ephedrine and in **Group B** 20 μgm intravenous injection of epinephrine as soon as systolic hypotension was detected.

Since systolic blood pressure (SBP) was measured every minute, the hypotensive episode did not last longer than 60 seconds before therapy was instituted. Additional injections of ephedrine and epinephrine were used if systolic hypotension recurred.

In **Group A** seven (7) patients required injection ephedrine for once, eleven (11) patients required twice and eight (8) patients required injection ephedrine for three times. In **Group B** five (5) patients required injection epinephrine for once, seven (7) patients required twice, eleven (11) patients required thrice and four (4) patients required injection epinephrine for four times.

In both groups, haemodynamic measurements were made prior to the injection of local anaesthetic, when the first episode of hypotension occurred and following correction of the first episode of hypotension with ephedrine or epinephrine. Haemodynamic measurements during subsequent hypotensive episodes and following vasopressor therapy in both groups were recorded.

Times from skin incision to delivery (I-D interval) and from uterine incision to delivery (U-D interval) were recorded by using a stopwatch. After delivery, neonatal Apgar scores were assessed at 1 and 5 min. Every patient received intravenous oxytocin, 10 units slowly after delivery of the baby. Per-operative maintenance fluid requirement (1.5 ml/kg/hr) together with the fluid replacement for blood loss were continued as usually in both groups. Maternal blood pressure was recorded every 15 minutes for the first two hours following operation.

Four patients in **Group A** & three patients in **Group B** were omitted from the study because of adverse effects and poor control of blood pressure. The results of remaining patients (Group A, n=26; Group B, n=27) were expressed as (mean ± SD). Student's Paired '*t*' test was used to compare the values of different groups.

In both groups, pre-anaesthetic baseline haemodynamic parameters were compared with values in the same group obtained during hypotension and after vasopressor therapy using a Paired '*t*' test.

A value of $P < 0.05$ were considered statistically significant.

Result:

Demographic data of the Group A, Group B and non-hypotensive group are shown in **Table-I**. There are no significant differences in *Age, Body weight, Height, Gestational period, and Foetal weight* among the three groups.

In Table-II, pre-anaesthetic maternal haemodynamic parameters *(heart rate, systolic blood pressure*, *diastolic blood pressure, & mean arterial pressure*) of Group A & Group B are shown. There are no significant differences in pre-anaesthetic baseline heart rate & blood pressures among the both groups.

In Table-III, Comparison of the skin incision to delivery interval (I-D interval), uterine incision to delivery interval (U-D interval) and last recorded foetal heart rate (FHR) before delivery are shown.

The I-D interval were 12.87 (±2.84) & 11.98 (±3.32) min in group A & B respectively. The corresponding U-D intervals were 72.22 (±22.84) & 70.87 (±20.35) seconds. The last recorded foetal heart rate (FHR) before delivery were 146.43 (±10.34) & 145.56 (±11.87) beats/min in Group A & B respectively.

The maternal heart rate (HR) increased significantly during hypotension after subarachnoid block (SAB) in both groups but it decreased

following vasopressor therapy (Table-IV, VIII & XII).

In both groups (Group A & B), systolic blood pressure (SBP) decreased significantly following lumbar subarachnoid block (SAB). Treatment of hypotension with both the vasopressors (ephedrine & epinephrine) restored the systolic blood pressure (SBP) towards pre-anaesthetic baseline values; but in case of epinephrine, post treatment values did not differ significantly from pre-anaesthetic baseline values (Table-V, IX & XIII).

In both groups, diastolic blood pressure (DBP) decreased following subarachnoid block. Treatment of hypotension with Ephedrine restored the diastolic blood pressure (DBP) towards pre-anaesthetic baseline values; but in case of epinephrine, post treatment values remained close to the values obtained during hypotension (Table-VI, X & XIV).

In both groups, mean arterial pressure (MAP) decreased significantly following subarachnoid block (SAB). Treatment of hypotension with both the vasopressors (ephedrine & epinephrine) restored the mean arterial pressure (MAP) towards pre-anaesthetic baseline values; but Ephedrine restored the MAP better than Epinephrine (Table-VII, XI & XV).

Changes of systolic blood pressure (SBP) 1 min after vasopressor therapy in both groups were also analyzed and Table-XVI showed that epinephrine restored systolic blood pressure (SBP) more effectively towards baseline within 1 min. (statistically significant)

In Table-XVII, frequency of both vasopressors therapy for the management of hypotension after subarachnoid block (SAB) are shown; epinephrine needed to be used more frequently than Ephedrine in order to restore baseline blood pressure, thereby managing hypotension.

Two neonates in group A & three neonates in Group B had an Apgar score of 7 at 1 minute, whereas no other Apgar score at 1 minute was <8 and no Apgar core at 5 minutes was <9 (Table-XVIII).

Table I *Demographic characteristics of patients in the Group A (n=26), Group B (n=27) and non-hypotensive (n=107) subjects.*

Demographic parameters	Patients with no significant hypotension n=107	Patients with significant hypotension (SBP below 90 mm Hg or 30% reduction from baseline) Group A n=26	Group B n=27
Age (years)	28.82 (±4.8)	29.78 (±3.5)	28.94 (±2.6)
Weight (Kg)	54.75 (±6.2)	56.23 (±3.8)	55.64 (±4.2)
Height (cm)	155.43 (±5.3)	156.45 (±4.2)	156.27 (±3.8)
Gestational period (weeks)	39 (±1)	40 (±1)	40 (±1)
Foetal weight (Kg)	2.86 (±3.8)	2.91 (±3.2)	2.92 (±3.8)

Data are presented as mean values (x) with standard deviation (SD)

Group A (n=26) : Patients received **Ephedrine** following hypotension.

Group B (n=27) : Patients received **Epinephrine** following hypotension.

SBP–systolic blood pressure

Table-II *Pre-anaesthetic maternal haemodynamic status in Group A (n=26) and Group B (n=27) :*

Haemodynamic Parameters	Group A n=26	Group B n=27
Heart rate (HR)	86.55	87.19
(Beats/min)	(±10.82)	(±11.24)
Systolic blood pressure (SBP)	118.23	116.78
(mm Hg)	(±8.20)	(±8.06)
Diastolic blood pressure (DBP)	76.24	74.94
(mm Hg)	(±7.35)	(±7.05)
Mean arterial pressure (MAP)	89.02	88.24
(mm Hg)	(±4.47)	(±4.12)

Data are presented as mean values (x) with standard deviation (SD).

Group A (n=26) : Patients received **Ephedrine** following hypotension.

Group B (n=27) : Patients received **Epinephrine** following hypotension.

Table-III *Comparison of the skin incision to delivery interval (I-D interval), uterine incision to delivery interval (U-D interval) and neonatal Apgar score in Group A (n=26) & Group B (n=27).*

Parameters	Group A n=26	Group B n=27
I-D interval	12.87	11.98
(minutes)	(±2.84)	(±3.32)
U-D interval	72.22	70.87
(seconds)	(±22.84)	(±20.35)
Last recorded foetal heart rate	146.43	145.56
(FHR) before delivery	(±10.34)	(±11.87)

Data are presented as mean values (x) with standard deviation (SD).

The differences are not significant.

Group A (n=26) : Patients received **Ephedrine** following hypotension.

Group B (n=27) : Patients received **Epinephrine** following hypotension.

Table-IV *Haemodynamic parameter in Group A (n=26)*

Changes in heart rate (HR) during hypotension after SAB and following Ephedrine therapy:

Haemodynamic parameter	Heart rate (HR) (Beats/min)	Student's *'t'* test
Pre-anaesthetic	86.55	
Base line value	(±10.82)	P < .001
During hypotension	108.24	
following SAB	(±8.45)	
Following Ephedrine	78.43	
therapy	(±7.35)	

Data are presented as mean values (x) with standard deviation (±SD).

Group A (n=26): Patients received **Ephedrine** following hypotension.

Values obtained during hypotension following SAB are significantly different from pre-anaesthetic baseline values and post treatment values (following Ephedrine therapy).

P value is <.001 (Highly significant)

SAB - Subarachnoid block

Table-V *Haemodynamic parameter in Group A (n=26)*

Changes in systolic blood pressure (SBP) during hypotension after SAB and following Ephedrine therapy:

Haemodynamic parameter %	Systolic blood pressure (SBP) (mm Hg)	Student's *'t'* test
Pre-anaesthetic	118.23	
base line value	(±8.20)	P < .001
During	83.56	
hypotension following SAB	(±4.84)	
Following	106.67	
Ephedrine	(±8.82)	
therapy		

Data are presented as mean values (x) with standard deviation (± SD)

Group A (n=26) : Patients received **Ephedrine** following hypotension.

Values obtained during hypotension following SAB are significantly different from pre-anaesthetic baseline values and post treatment values (following Ephedrine therapy).

P value is < .001 (Highly significant),

SAB - Subarachnoid block

Table-VI *Haemodynamic parameter in Group A (n=26)*

Changes in diastolic blood pressure (DBP) during hypotension after SAB and following Ephedrine therapy:

Haemodynamic parameter °%	Diastolic blood pressure (DBP) (mm Hg)	Student's '*t*' test
Pre-anaesthetic base line value	76.24 (±7.35)	
During hypotension following SAB	61.26 (±4.94)	P < .001
Following Ephedrine therapy	70.32 (±5.67)	

Data are presented as mean values (x) with standard deviation (± SD)

Group A (n=26) : Patients received **Ephedrine** following hypotension.

Values obtained during hypotension following SAB are significantly different from the pre-anaesthetic baseline values and post treatment values (following ephedrine therapy).

P value is < .001 (Highly significant)

SAB - Subarachnoid block

Table-VII *Haemodynamic parameter in Group A (n=26)*

Changes in mean arterial pressure (MAP) during hypotension after SAB and following Ephedrine therapy

Haemodynamic parameter %	Mean arterial pressure (MAP) (mm Hg)	Student's '*t*' test
Pre-anaesthetic base line value	89.02 (±4.47)	
During hypotension following SAB	68.79 (±3.94)	P < .01
Following Ephedrine therapy	82.77 (±4.53)	

Data are presented as mean values (x) with standard deviation (± SD)

Group A (n=26) : Patients received **Ephedrine** following hypotension.

Values obtained during hypotension following SAB are significantly different from the pre-anaesthetic baseline values and post treatment values (following Ephedrine therapy).

P value is < .01 (Significant)

SAB - Subarachnoid block

Table-VIII *Haemodynamic parameter in Group B (n=27)*

Changes in heart rate (HR) during hypotension after SAB and following Epinephrine therapy:

Haemodynamic parameter °%	Heart rate (HR) (Beats/min)	Student's '*t*' test
Pre-anaesthetic base line value	87.19 (±11.24)	P < .01
During hypotension following SAB	109.34 (±11.04)	
Following Epinephrine therapy	82.85 (±5.68)	

Data are presented as mean values (x) with standard deviation (± SD)

Group B (n=27) : Patients received **Epinephrine** following hypotension.

Values obtained during Hypotension following SAB are significantly different from the pre-anaesthetic base line values and post treatment values (following Epinephrine therapy).

P value is < .01 (Significant)

SAB - Subarachnoid block

Table-IX *Haemodynamic parameter in Group B (n=27)*

Changes in systolic blood pressure (SBP) during hypotension after SAB and following Epinephrine therapy:

Haemodynamic parameter °%	Systolic blood pressure (SBP) (mm Hg)	Student's '*t*' test
Pre-anaesthetic base line value	116.78 (±8.06)	P < .001
During hypotension following SAB	84.12 (±4.36)	
Following Epinephrine therapy	115.26 (±7.82)	

Data are presented as mean values (x) with standard deviation (± SD)

Group B (n=27) : Patients received **Epinephrine** following Hypotension.

Values obtained during Hypotension following SAB are significantly different from the Pre-anaesthetic base line values and post treatment values (Following Epinephrine therapy).

P value is < .001 (Highly significant)

SAB - Subarachnoid block

Table-X *Haemodynamic parameter in Group B (n=27)*

Changes in diastolic blood pressure (DBP) during hypotension after SAB and following Epinephrine therapy :

Haemodynamic parameter °%	Diastolic blood pressure (DBP) (mm Hg)	Student's *'t'* test
Pre-anaesthetic base line value	74.94 (±7.05)	P < .001
During hypotension following SAB	62.19 (±4.78)	
Following Epinephrine therapy	63.06 (±3.59)	

Data are presented as mean values (x) with standard deviation (± SD)

Group B (n=27) : Patients received **Epinephrine** following hypotension.

Values obtained during hypotension following SAB are significantly different from the pre-anaesthetic base line values, but post treatment values (following Epinephrine therapy) are not significantly different.

SAB - Subarachnoid block

Table – XI *Haemodynamic parameter in Group B (n=27)*

Changes in mean arterial pressure (MAP) during hypotension after SAB and following Epinephrine therapy :

Haemodynamic parameter	Mean arterial pressure (MAP) (mm Hg)	Student's *'t'* test
Pre-anaesthetic base line value	88.24 (±4.12)	P < .01
During hypotension following SAB	69.03 (±4.01)	
Following Epinephrine therapy	80.04 (±4.38)	

Data are presented as mean values (x) with standard deviation (± SD)

Group B (n=27) : Patients received **Epinephrine** following hypotension.

Values obtained during hypotension following SAB are significantly different from the pre-anaesthetic base line values and post treatment values (following Epinephrine therapy).

P value is < .01 (Significant)

SAB - Subarachnoid Block

Table-XII *Heart Rate (HR) changes during Hypotension after SAB and following vasopressor therapy in different groups : Group A (n=26) & Group B (n=27)*

HR (beats/ min)	Group A n=26	Group B n=27	Student's *'t'* test
Pre-anaesthetic baseline value	86.55 (±10.82)	87.19 (±11.24)	
During hypotension following SAB	108.24 (±8.45)	109.34 (±11.04)	P < .001
Following vasopressor therapy	78.43 (±7.35)	82.85 (±5.68)	

Data are presented as mean values (x) with standard deviation (± SD)

Group A (n=26) : Patients received Ephedrine following hypotension.

Group B (n=27) : Patients received Epinephrine following hypotension.

P value is < .001 (Highly significant)

SAB - Subarachnoid block

Table-XIII *Systolic blood pressure (SBP) changes during hypotension after SAB and following vasopressor therapy in different groups : Group A (n=26) & Group B (n=27)*

SBP (mmHg)	Group A n=26	Group B n=27	Student's *'t'* test
Pre-anaesthetic baseline value	118.23 (±8.20)	116.78 (±8.06)	
During hypotension following SAB	83.56 (±4.84)	84.12 (±4.36)	P < .001
Following vasopressor therapy	106.67 (±8.82)	115.26 (±7.82)	

Data are presented as mean values (x) with standard deviation (± SD)

Group A (n=26) : Patients received **Ephedrine** following hypotension.

Group B (n=27) : Patients received **Epinephrine** following hypotension.

P value is < .001 (highly significant)

SAB - Subarachnoid block

Table-XIV *Diastolic blood pressure (DBP) changes during hypotension after SAB and following vasopressor therapy in different groups : Group A (n=26) & Group B (n=27)*

DBP (mmHg)	Group A n=26	Group B n=27	Student's *'t'* test
Pre-anaesthetic baseline value	76.24 (±7.35)	74.94 (±7.05)	P < .01
During hypotension following SAB	61.26 (±4.94)	62.19 (±4.78)	
Following vasopressor therapy	70.32 (±5.67)	63.06 (±3.59)	

Data are presented as mean values (x) with standard deviation (± SD)

Group A (n=26) : Patients received Ephedrine following hypotension.

Group B (n=27) : Patients received Epinephrine following hypotension.

Values obtained during hypotension following SAB are significantly different from the pre-anaesthetic base line values in both groups. Post treatment values are significantly different in Group A, but are not significantly different in Group B.

SAB - Subarachnoid block

Table-XV *Mean arterial pressure (MAP) changes during hypotension after SAB and following vasopressor therapy in different groups : Group A (n=26) & Group B (n=27)*

MAP (mmHg)	Group A n=26	Group B n=27	Student's *'t'* test
Pre-anaesthetic baseline value	89.02 (±4.47)	88.24 (±4.12)	
During hypotension following SAB	68.79 (±3.94)	69.03 (±4.01)	P < .01
Following vasopressor therapy	82.77 (±4.53)	80.04 (±4.38)	

Data are presented as mean values (x) with standard deviation (± SD)

Group A (n=26) : Patients received **Ephedrine** following hypotension.

Group B (n=27) : Patients received **Epinephrine** following hypotension.

Values obtained during hypotension following SAB are significantly different from the pre-anaesthetic base line values and post treatment values in both groups.

P value is < .01 (Significant)

SAB - Subarachnoid block

Table-XVI *Changes in systolic blood pressure (SBP), 1 min after vasopressor therapy in both groups (Group A & Group B) during 1st episode of hypotension.*

SBP (mmHg)	Group A n=26	Group B n=27	Student's *'t'* test
During hypotension following SAB (mm Hg)	83.56 (±4.84)	84.12 (±4.36)	
1 min after vasopressor therapy (mm Hg)	92.92 (±7.44)	115.26 (±7.82)	P < .01
Changes of SBP (mmHg)	10.06 (±6.12)	30.90 (±5.42)	

Data are presented as mean values (x) with standard deviation (± SD).

Group A (n=26) : Patients received **Ephedrine** following hypotension.

Group B (n=27) : Patients received **Epinephrine** following hypotension.

P value is < .01 (Significant)

SAB - Subarachnoid block

TableXVII *Frequency of both vasopressor therapy for the management of hypotension after SAB.*

	Group A n=26	Group B n=27	Student's *'t'* test
Number of injections (initial & incremental doses)	2.03 (±0.54)	2.52 (±1.06)	P < 0.05

Data are presented as mean values (x) with standard deviation (± SD).

Group A (n=26) : Patients received Ephedrine following hypotension.

Group B (n=27) : Patients received epinephrine following hypotension.

P value is < 0.05 (significant)

SAB - Subarachnoid block

Table-XVIII *Comparison of the neonatal Apgar score in Group A (n=26) & Group B (n=27).*

Parameters ¼%	Group A n=26	Group B n=27
Apgar score at 1 min	8 (7-9)	8 (7-9)
Apgar score at 5 min	9 (9-10)	9 (9-10)

Data are presented as mean values.

Group A (n=26) : Patients received **Ephedrine** following hypotension.

Group B (n=27) : Patients received **Epinephrine** following hypotension.

Adverse effects:

The incidence of hypotension during this study was sixty (60) out of one hundred and sixty seven (167) patients (35.93%). Nausea was common in those in whom hypotension developed and invariably responded to vasopressor therapy.

Four patients in **Group A** did not respond to repeated ephedrine therapy & developed severe hypotension (SBP < 70 mm of Hg) and were treated with intravenous bolus epinephrine. These four patients were omitted from the study.

Two patients in **Group B** complained of shortness of breathing & became restless and one patient developed arrhythmia following repeat dose of epinephrine. These three patients were omitted from the study.

Delivery was difficult in one patient in **Group A**, with a uterine incision to delivery time of greater than 4 minutes. There were no other operative complications.

Discussion:

Hypotension is a potentially serious complication during caesarean section under regional anaesthesia because it provokes disturbing symptoms for the mother and may lead to an episode of ischaemia for the foetus. Hypotension may occur by three main mechanisms : i) reduced venous return secondary to posture, venacaval compression, and haemorrhage, ii) peripheral vasodilatation, iii) a fall in cardiac output.[46]

Careful attention to preload, sufficient left uterine displacement, an intravenous vasopressor agent is more rationale and effective.

Our data showed that, when maternal hypotension was recognized, it was rapidly corrected with ephedrine and epinephrine.

Ramanathan et al.[47] showed that transient hypotension caused by lumbar epidural anaesthesia is associated with a decreased ventricular end diastolic volume (EDV, preload). The decreased preload was probably caused by pooling of blood in the venous capacitance vessels as a result of sympathectomy. Decreased systemic pressure resulted in compensatory tachycardia. Ramanathan et al.[47] also showed that the increase in systolic blood pressure is due to increase in preload therapy suggests constriction of the capacitance vessels.

The decrease in heart rate (HR) after vasopressor therapy in both groups (Group A & B) was probably due to baroreceptor reflex initiated by improved perfusion pressure.

Our data showed that intravenous bolus injection of Epinephrine restored the systolic blood pressure (SBP) towards baseline more rapidly and effectively than injection Ephedrine but didn't raise the diastolic blood pressure (DBP), thus compromising the coronary perfusion. Our data also showed that more incremental doses of Epinephrine required to maintain the blood pressure.

Epinephrine causes more rapid correction of systolic blood pressure (SBP) by its both α and β effects. Though it causes tachycardia, the doses used in this study causes minimum tachycardia which returned toward normal after correction of hypotension.

Intravenous bolus injection of Ephedrine restored the mean arterial pressure (MAP) towards baseline by increasing both systolic & diastolic blood pressure. By increasing the diastolic blood pressure (DBP) it improves the coronary perfusion.

The pressor effect of ephedrine is believed to be due mainly to cardiac stimulation and partly to vasoconstriction. The force of myocardial contraction and cardiac output are augmented by the drug. However, at the doses used in the study, the α effects of the drug on the capacitance bed seem to over shadow its β effects.

In this study, four patients in **Group A** could not be managed by injection ephedrine 5 mg and with increments in spite of adequate fluid preload, sufficient left uterine displacement. All of the above patients were effectively managed by intravenous bolus injection of epinephrine. The hypotension refractory to intravenous ephedrine might be due to tachyphylaxis. These four patients were omitted from the study.

In **Group B** two patients complained of shortness of breathing & became restless and one patient developed arrhythmia following repeat dose of epinephrine. These three patients were omitted from the study.

Data of this study suggests that maternal hypotension corrected with ephedrine or epinephrine, neonatal Apgar score remains

unaffected. Foetal well being was assessed by Apgar score.

All patients in this study received adequate preload prior to induction of anaesthesia. Aortocaval compression was minimized by left uterine displacement. Systemic hypotension was recognized and treated promptly by administration of a vasopressor.

No patient in this study developed significant hypertension probably because the doses of vasopressor were smaller than those used in previous studies who reported.

No patient in this study developed post partum hypertension.

Conclusion:

In this study, it is concluded that the use of intravenous administration of Ephedrine and Epinephrine for the management of maternal hypotension during caesarean section under subarachnoid block does not affect the neonatal outcome; neonatal Apgar score remains satisfactory. Epinephrine raises the mean arterial pressure (MAP) by prompt increasing the systolic blood pressure but without raising the diastolic blood pressure, thus compromising the coronary perfusion and more incremental doses required to maintain the blood pressure. Ephedrine, a relatively longer acting drug, routinely used for the management of maternal hypotension during caesarean section under subarachnoid block raises the mean arterial pressure (MAP) by increasing both systolic & diastolic blood pressure but in the events of tachyphylaxis caused by ephedrine or during severe hypotension epinephrine might be the choice of drug.

References

1. Farragher RA, Kodali BS. Obstetric anesthesia. In: Healy TEJ,Knight PR, editor. Wylie and Churchill-Davidson's A Practice of Anesthesia. 7th ed. London: Arnold; 2003; 57: 930.
2. Rout CC, Rocke DA. Prevention of hypotension following spinal anaesthesia for caesarean section. Int Anaesthesiol Clin 1994; 32:117 – 35.
3. Morgan P. The role of vasopressors in the management of hypotension induced by spinal and epidural anaesthsia. *Can J Anaesth* 1994; 41: 404-13.
4. Clark RB, Thompson DS, Thompson CH. Prevention of spinal hypotension associated with Caesarean section. *Anaesthesiology* 1976; 45: 670 – 4
5. Burns SM, Cowan CM, Wilkes RG. Prevention and management of hypotension during spinal anaesthesia for elective caesarean section : a survey of practice. Anaesthesia 2001; 56: 777 – 98
6. Mercier JF, Riley ET, Fredericson WL, Roger-Christoph S, Benhamou D, Cohen SE. Phenylephrine added to prophylactic ephedrine infusion during spinal anesthesia for elective Cesarean section. *Anaesthesiology* 2001; 95: 668 – 74
7. Ngan Kee WD, Lau TK, Khaw KS, Lee BB. Comparison of Metaraminol and ephedrine infusions for maintaining arterial pressure during spinal anesthesia for Cesarean section.

   Anaesthesiology 2001; 95: 307 – 13
8. Corning J. L. N. Y. Med. J. 1885, 42, 483 (reprinted in 'Classical File', *Survey of Anaesthesiology* 1960, 4, 332)
9. Bier A. Versuche über Cocainisirung des Rückenmarkes. Deutsch *Zeitschrift für Chirurgie* 1899; 51: 361. (translated and reprinted in 'Classical File', *Survey of Anaesthesiology* 1962, 6, 352)
10. Swash, M, Glynn, M.(eds). 2007. Hutchison's Clinical Methods. Edinburgh. Saunders Elsevier.
11. Ellis H, Feldman S. Anatomy for Anaesthetists. 6th ed. Oxford: Blackwell Scientific Publications; 1993
12. Bernards CM. Epidural and Spinal Anesthesia. In: Barash PG, Cullen BF, Stoelting RK, editor. Clinical Anesthesia. 5th ed. Lippincott Williams & Wilkins; 2006; 25: 708-711
13. Chamberlain D, Chamberlain B: Changes in skin temperature of the trunk and their relationship to sympathetic block during spinal anesthesia. Anaesthesiology 65:139, 1986
14. Carpenter RL, Caplan RA, Brown DL, Stephenson C, Wu R : Incidence and risk

factors for side effects of spinal anesthesia. Anaesthesiology 76: 906, 1992

15. Coe AJ, Revanas B: Is crystalloid preloading useful in spinal anaesthesia in the elderly? Anaesthesia 45: 241, 1990
16. Phero JC, Bridenbaugh PO, Edstrom HH et al: Hypotension in spinal anesthesia: A comparison of isobaric tetracaine with epinephrine and isobaric bupivacaine without epinephrine. Anesth Analg 66: 549, 1987
17. Shimosato S, Etsten BE: The role of the venous system in cardiocirculatory dynamics during spinal and epidural anesthesia in man. Anaesthesiology 30: 619,1969
18. Kennedy WF, Jr. , Bonica JJ, Akamatsu TJ, Ward RJ, Martin WE, Grinstein A: Cardiovascular and respiratory effects of subarachnoid block in the presence of acute blood loss. Anaesthesiology 29:29, 1968
19. Anzai Y, Nishikawa T: Heart rate responses to body tilt during spinal anesthesia. Anesth Analg 73: 385, 1991
20. Kleinman W, Mikhail M. Spinal, Epidural, & Caudal Blocks. In: Morgan GE, Jr., Mikhail MS, Murray MJ. Clinical Anaesthesiology. 4th ed. McGraw-Hill; 2006: 297
21. Vickers MD, Morgan M, Spencer PSJ, Read MS. Drugs in Anaesthetic & Intensive Care Practice. 8th ed. Butterworth-Heinemann; 1999
22. Thornburg KL, Jacobson SL, Giraud GD, et al; Hemodynamicchanges in pregnancy : Semim Perinatol. 2000 Feb;24(1):11-4.
23. Stalburg CM, Naughton NN. Reproductive physiology. In: HealyTEJ, Knight PR, editor. Wylie and Churchill-Davidson's APRACTICE OF ANESTHESIA. 7th ed. London: Arnold; 2003; 21: 353
24. Cutforth R, MacDonald CB. Heart sounds and murmurs inpregnancy. Am heart J 1966; 71: 741–7.
25. Enein M, Zina AA, Kassem M, el-Tabbakh G. Echocardiography of the pericardium in pregnancy. Obstet Gynecol 1987; 69: 851–3.
26. Conklin KA. Maternal physiologic adaptations during gestation, labor, and the puerperium. *Semin Anesth* 1991; 10: 221–34.
27. Chesnutt AN; Physiology of normal pregnancy.; Crit Care Clin. 2004 Oct;20(4):609-15.
28. Ciliberto CF, Marx GF. Physiological Changes Associated with Pregnancy; Department of Anaesthesiology, Albert Einstein College of Medicine.
29. Oxford Textbook of Nephrology by Davison, Grunfeld, Cameron and Stewart. OUP 2nd edition ISBN 019262413X
30. Oruc S, Saruc M, Koyuncu FM, et al; Changes in the plasma activities of protein C and protein S during pregnancy.; *Aust N Z J Obstet Gynaecol*. 2000 Nov;40(4):448-50.
31. Butte NF, Wong WW, Treuth MS, et al; Energy requirements during pregnancy based on total energy expenditure and energy deposition. *Am J Clin Nutr*. 2004 Jun;79(6):1078-87.
32. Foti T, Davids JR, Bagley A; A biomechanical analysis of gait during pregnancy. *J Bone Joint Surg Am*. 2000 May;82(5):625-32.
33. Lazarus JH, Premawardhana LD; Screening for thyroid disease in pregnancy.; *J Clin Pathol*. 2005 May;58(5):449-52.
34. Glinoer D; The regulation of thyroid function in pregnancy: pathways of endocrine adaptation from physiology to pathology.; Endocr Rev. 1997 Jun; 18(3):404-33.
35. Butte NF; Carbohydrate and lipid metabolism in pregnancy: normal compared with gestational diabetes mellitus.; *Am J Clin Nutr*. 2000 May;71(5 Suppl): 1256S-61S.
36. Gaw A, Cowan R, O'Reilly D, Stewart MJ, Shepherd J, Clinical Biochemistry – an illustrated colour text, 2nd edition. 1999 Churchill Livingstone ISBN 0443044813; *Section on biochemistry in pregnancy*
37. Tran H; Biochemical tests in pregnancy. Australian prescriber 2005; 28:98-101
38. Howland RH, Mycek MJ. Lippincott's Illustrated Reviews: Pharmacology. 3rd edition; Lippincott Williums & Wilkins; Reprinted 2006
39. Zaritsky AL, Chernow B: Catechlolamines, sympathomimetics. In Ziegler MG, Lake CR

(eds): Frontiers of Clinical Neuroscience, p 481. Baltimore, Williams & Wilkins, 1984

40. greene NM: Perspectives in spinal anesthesia. Reg Anesth 7:55, 1982

41. Ramanathan S, Grant GJ: Vasopressor therapy for hypotension due to epidural anesthesia for cesarean section. Acta Anaesthesiol Scan 32:559, 1988

42. Hodgkinson R, Bhatt M, Kim SS, *et al*. Neurobehavioral tests following cesarean section under general and spinal anesthesia. *Am J Obstet Gynecol* 1978; 132: 670–4.

43. Robson SC, Boys RJ, Rodecke, et al. (1992) Maternal and foetal haemodynamic effect of spinal and extradural anaesthesia for elective caesarean sections. *Br J Anaesth* ; 68 : 54–9

44. Aitkenhead AR, Smith G, Rowbotham DJ. Textbook of Anaesthesia. 5th edition. Churchill Livingstone; 2007

45. Aitkenhead AR. Maternal and neonatal physiology; Textbook of Anaesthesia. 3rd edition. 77-92

46. MCCRAE. AF and Wildsmith JAW (1993). Prevention and treatment of hypotension during central neural blockade. Br J Anaesth ; 70 : 625–80.

47. Ramanathan S. and Grant GJ. (1988). Vasopressor therapy for hypotension due to epidural anaesthesia for caesarean section : Acta, Anaesthesia Scand; 1988 ; 32 : 559-65.