"ONE YEAR RANDOMIZED CLINICAL TRIAL TO COMPARE THE EFFICACY OF INTRAVENOUS BOLUS PHENYLEPHRINE AND EPHEDRINE IN MAINTAINING ARTERIAL BLOOD PRESSURE DURING SPINAL ANAESTHESIA IN CAESAREAN SECTION."

DISSERTATION

BY

DR. KUSHA NAG.

SUBMITTED TO

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UNDER THE GUIDANCE OF

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"ONE YEAR RANDOMIZED CLINICAL TRIAL TO COMPARE THE EFFICACY OF INTRAVENOUS BOLUS PHENYLEPHRINE AND EPHEDRINE IN MAINTAINING ARTERIAL BLOOD PRESSURE DURING SPINAL ANAESTHESIA IN CAESAREAN SECTION."** is a bonafide and genuine research work carried out by me under the guidance of **Dr. S. N. Suresh,** **M.D.** D.A, , Professor, Department of Anaesthesiology, Jawaharlal Nehru Medical College, Nehru Nagar, Belgaum-590010.

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DR. KUSHA NAG

ABBREVIATIONS

α	- Alpha
β	- Beta
ASA	- American Society of Anaesthesiologist
BP	- Blood pressure
CNS	- Central nervous system
CSF	- Cerebrospinal fluid
CVS	- Cardio vascular system
DBP	- Diastolic blood pressure
Dl	- Decilitre
ECG	- Electrocardiogram
G	- Gauge
HR	- Heart rate
Hr	- Hour
Inj	- Injection
IV	- Intravenous
Kg	- Kilograms
mcg	- Microgram
mEq/L	- Milliequivalents / Litre.
mg	- Milligrams
min	- Minute
ml	- Millilitres
PR	- Pulse rate
RR	- Respiratory rate
SAB	- Subarachnoid block
VP	- Vasopressor drug

ABSTRACT

Background: Maternal hypotension during spinal anaesthesia for Caesarean section is a persistent problem which can result in adverse maternal and fetal outcome. Various methods are used in prevention and treatment of post spinal hypotension. The most logical approach appears to be adequate preloading and use of vasopressors. We have studied intravenous bolus Phenylephrine and Ephedrine for maintainence of arterial blood pressure during spinal anaesthesia for Caesarean section.

Objective: To compare the efficacy of intravenous bolus dose of Phenylephrine (40 mcg) and Ephedrine (6mg) for maintenance of arterial pressure following spinal anaesthesia for elective Caesarean section and to compare the number of boluses required in each group.

Study design*:* Randomized clinical trial.

Methods: After obtaining written informed consent, hundred patients with singleton full term pregnancy undergoing Caesarean section under subarachnoid block were randomly divided using computer generated randomization table, into two groups of fifty each, Group P received Phenylephrine 40 mcg and Group E received Ephedrine 6 mg IV bolus.

Baseline blood pressure and pulse rate measured. Following intravenous preload with 10ml/kg of Ringer lactate solution, all patients received intrathecal 2 ml of 0.5% hyperbaric Bupivacaine through 23 G Quincke needle at L3-L4 space in lateral position. Pulse rate, systolic, diastolic and mean arterial pressures were recorded at every 2 min for 20 min and thereafter every 5 min till 60 minutes. Whenever hypotension (fall in BP>20% of baseline or less than 90 mm of Hg) occurred, patients received the study vasopressor drug. The number of

boluses given were noted. Pediatrician assessed APGAR score of every neonate at 1 min and 5 minutes after delivery.

Results: In Phenylephrine group, the SBP is restored to more than 80% of its basal value almost immediately within 2 minutes after administration of the bolus dose and is maintained all throughout till the end of 60 minutes. In Ephedrine group, SBP is restored to its 80% of the basal value at 10 minutes, but is maintained consistently till the end of 60 min. Number of boluses required and APGAR score of the baby were comparable in both the groups.

Conclusion*:* Both the vasopressors namely Phenylephrine 40 mcg and Ephedrine 6 mg IV bolus effectively maintained arterial blood pressure during spinal anaesthesia for Caesarean section, although Phenylephrine is more efficacious and had quicker peak effects and does not cause increase in heart rate as compared to Ephedrine.

Key words: Caesarean section; Spinal anaesthesia; Hypotension; Phenylephrine; Ephedrine.

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INTRODUCTION

Pregnancy is generally expected to end with a healthy mother delivering a normal infant. However, a variety of either maternal or fetal conditions may interfere, resulting in less than the anticipated outcome. A high degree of care for the mother and the fetus is essential if desired result is to be achieved.

The obstetric patient for Caesarean section usually presents more challenges to the anaesthesiologist than other patients. Spinal anaesthesia is perhaps the most elegant approach to these challenges. It offers a fast, profound and high quality of sensory and motor block for Caesarean delivery.

However, spinal anaesthesia is also associated with some hazards. The commonest of these being hypotension of a reported incidence of greater than 80% despite fluid preload and lateral uterine displacement.[1] Maternal hypotension is associated with distressing symptoms like dizziness, nausea, vomiting and can also cause fetal bradycardia[2] and acidosis.[3]

As is rightly said that "A stitch in time saves nine", the most important question that seeks attention is the timely recognition and appropriate management of maternal hypotension.

For last 25 years left uterine displacement and volume preloading before subarachnoid block has been the cornerstone in prevention of hypotension. This notion has been questioned over time. Rapid administration of crystalloids may restore uterine blood flow, but has a short half life. Moreover, infusion of large volume of crystalloids

can cause dilutional anaemia and could also increase the risk of pulmonary oedema in the term parturient.

Several other methods have been tried for prevention of hypotension during Caesarean section, which includes left uterine displacement,[4] leg compression and elevation,[5] prophylactic administration of vasopressors including Phenylephrine and Ephedrine,[6] prophylactic Angiotensin II infusion[7] and infusion of Atrial natriuretic peptide.[8]

One of the mainstays in management of hypotension is the use of vasopressor agents, but those currently available are not perfect and there has been a controversy for years regarding the ideal vassopressor.

Ephedrine is the most widely used agent for this purpose, but causes maternal tachycardia due to its non selective action on both alpha and beta adrenergic receptors. It is difficult to titrate and also exhibits the phenomena of tachyphylaxis due to its indirectly acting nature. Hence there is a need to find an alternative drug for the treatment of hypotension, which lacks the forementioned maternal side effects and also does not cause any detrimental effect on the fetal pH. Phenylephrine is one such drug under trial.

Phenylephrine is a directly acting sympathomimetic agent with selective alpha 1 adrenergic activity. It is easy to titrate and maintains maternal blood pressure without producing undue tachycardia. Moreover, the administration of Phenylephrine is reported to be associated with lower incidence of fetal acidosis than is Ephedrine.

Numerous studies have been performed to evaluate the various doses of Phenylephrine, from 20 to 100 micrograms. On one hand a dose of 20 mcg has been found to be ineffective, on the other, a dose as high as 100 mcg has been encountered by maternal bradycardia.

Hence, an attempt has been made to compare the efficacy of intravenous Phenylephrine 40 micrograms and Ephedrine 6 milligram as a vassopressor therapy in case of hypotension associated with spinal anaesthesia in patients undergoing Caesarean section.

A safe secure and certain control of maternal blood pressure is one of the many requirements for ensuring "The perfect experience" for the mother having her baby delivered by Caesarean section under regional blockade.[9]

OBJECTIVES

The objectives of the present study are :

1. To compare the efficacy of intravenous bolus dose of Phenylephrine (40 mcg) and Ephedrine (6mg) in maintaining arterial blood pressure during spinal anaesthesia for Caesarean section.
2. To compare the dose of drug effective in maintaining arterial blood pressure within the normal range in both the groups.

REVIEW OF LITERATURE

Spinal anaesthesia, also referred to as subarachnoid block, intrathecal analgesia or central neuraxial blockade, has a fascinating historical background. Spinal anaesthesia is produced when a local anaesthetic agent is injected into the subarachnoid space and was the first major regional technique attempted.

The first planned spinal anaesthesia for surgery in man was performed in 1898 by August Karl Gustav Bier (1861-1949) on 16th August, in Keil, in Germany.[10] Bier and his assistant Hildebrandt tried spinal anaesthesia by injecting cocaine into each others theca but both experienced severe headache which lasted for days and they postulated that their headache was due to loss of large volume of cerebrospinal fluid.[11]

The technique of spinal anaesthesia was eventually well accepted all over Europe and many reports were published on its usage.

In the following years, the popularity of spinal anaesthesia had steadily increased with the introduction of newer drugs and techniques. The technique was found to be safe in expert hands and preferred over general anaesthesia for operations over lower limbs and abdomen.

The widespread use of this technique has waxed and waned over several years. The major causes for its decline being hypotension and post dural puncture headache. Hypotension has been reported in 80 percent of patients undergoing Caesarean section under spinal anaesthesia.[12] With the development of newer bevel design and better methods to control hypotension, spinal anaesthesia is again being widely practiced particularly for Caesarean sections.

Various studies have been conducted on different approaches for prevention and treatment of hypotension during spinal anaesthesia, and the effects of different vasopressor drugs on maternal and placental circulation.

One of the earliest studies was performed in 1976 to challenge the effectiveness of preloading the patient before administering spinal anaesthesia. The use of fluid loading was evaluated in 247 patients undergoing Caesarean section under spinal anaesthesia, both with and without uterine displacement compared with controls. It was found that despite the use of fluid preloading and left uterine displacement, the incidence of hypotension remains high during spinal anaesthesia for Caesarean section. A vasopressor is often required. The drugs usually recommended for this purpose are Ephedrine and Phenylephrine.[13]

Following this, the role of prophylactic Ephedrine 50 mg i.m, 5 - 23 minutes prior to subarachnoid block with both left uterine displacement and maternal hydration was studied for prevention of spinal anaesthesia induced hypotension during Caesarean section and prophylactic Ephedrine was found to be efficacious.[14]

The effect of prophylactic intravenous Ephedrine infusion during Caesarean section under spinal anaesthesia was evaluated on forty four healthy parturients and it was recommended that prophylactic Ephedrine infusion (0.01% solution, beginning with approximately 5 mg/min) immediately after subarachnoid block is safe and desirable.[15]

Subsequently, maternal and fetal effects of Ephedrine 5 mg and Phenylephrine 100 mcg intravenous bolus were compared for the treatment of hypotension due to spinal anaesthesia. After preloading the patients with 1200 ml of Ringer lactate, hypotension

was treated with Ephedrine 5 mg or Phenylephrine 100 mcg. No significant difference between the two groups was found with regard to maternal blood pressure, fetal status and number of boluses. Maternal heart rate was significantly reduced in Phenylephrine group.[16]

The inadequacy of Ephedrine for restoration of maternal blood pressure has led to interest in evaluating the efficacy of Phenylephrine. Intravenous bolus doses of Phenylephrine are found to be consistently and promptly effective in relief of maternal hypotension on a group of 100 mothers undergoing Caesarean section under spinal anaesthesia. A dose range of 20 - 100 mcg of Phenylephrine was recommended, which could be repeated as and when required.[9]

A few investigators have compared the effects of Ephedrine 5 mg or Phenylephrine 100 mcg for Caesarean section. When sensory block reached T_5 level, Ephedrine or Phenylephrine infusion was started at 50 mcg per hour and 1000 mcg per hour respectively. Although uteroplacental pulsatility index values increased following Phenylephrine at a mean dose of 448 mcg (range 344-767 mcg), no change in fetal heart rate or fetal doppler indices were noticed. Umbilical artery pH was similar in both the groups.[17]

Another study was conducted to assess maternal cardiovascular changes and neonatal acid - base status in 29 healthy women undergoing elective lower segment Caesarean section under spinal anaesthesia. In this study, an infusion of Phenylephrine 10 mcg per minute with bolus doses of 20 mcg was shown to be significantly less effective in maintaining systolic arterial pressure within 20 percent limits of baseline as compared

to an infusion of Ephedrine 1 or 2 mg per minute with bolus doses of 6 mg. Neonatal APGAR scores and acid - base profiles were similar in all the groups.[12]

Since then, various studies have been performed to evaluate the effect of different vasopressors on the mother and the fetus.

A randomized control trial was done to compare Phenylephrine or Ephedrine as intravenous bolus for maintenance of arterial pressure during spinal anaesthesia for thirty eight patients undergoing elective Caesarean section. Umbilical artery pulsatility index (PI) was measured using doppler before and after spinal anaesthesia. The median number of boluses of Phenylephrine and Ephedrine were similar respectively. Maternal systolic blood pressure and cardiac output changes were similar in both groups, but the mean maximum percentage change in maternal heart rate was larger in the Phenylephrine group than in the Ephedrine group. Mean umbilical artery pH was higher in the Phenylephrine group than in the Ephedrine group. The results supported the use of Phenylephrine for maintenance of maternal arterial pressure during spinal anaesthesia for elective Caesarean section. [18]

The usual approach to the use of vasopressors in clinical setting is reactive than proactive i.e., spinal anaesthesia induced hypotension is allowed to develop and is then treated accordingly. Given the frequency with which it occurs, a more logical approach to its prevention may be the administration of pre-emptive vasopressors according to a group of investigators. In a randomized double blind placebo controlled study on 108 patients, pre-emptive Phenylephrine 4 mg i.m. and Ephedrine 45 mg i.m. were compared. Pre- emptive i. m. vasopressors were found to reduce the severity of hypotension and the total dose of rescue i.v. Ephedrine during spinal anaesthesia for Caesarean section.[6]

In another study it was found that Phenylephrine by infusion is associated with a lower incidence of fetal acidosis and maternal nausea and vomiting than Ephedrine. There is no advantage of combining Phenylephrine and Ephedrine because it increases nausea and vomiting and it does not further improve fetal blood gas values, as compared to using Phenylephrine alone. [19]

In a quantitative, systematic review of randomized controlled trials of Ephedrine versus Phenylephrine for the management of hypotension during spinal anaesthesia for Caesarean delivery, the outcomes based on maternal hypotension, hypertension and bradycardia, neonatal umbilical cord blood pH values and APGAR scores were assessed. They concluded that, there was no difference between Phenylephrine and Ephedrine for the management of maternal hypotension. Maternal bradycardia was more likely to occur with Phenylephrine than with Ephedrine. Thus, both the vasopressors can be used safely in patients undergoing Caesarean section. [20]

A multivariate analysis of factors associated with umbilical arterial pH and standard base excess after Caesarean section under spinal anaesthesia found that the significant factors predicting uterine artery pH were : use of Ephedrine, uterine incision-to-delivery time, maximum decrease in systolic arterial pressure and the duration of hypotension. They concluded that, in order to minimize the risk of fetal acidosis, Ephedrine should not be used before delivery, uterine incision-to-delivery time should be as short as possible, and alpha-agonists such as Metaraminol or Phenylephrine should be used to minimize both the magnitude and duration of hypotension. [21]

Another similar study was done to compare the effects of bolus Phenylephrine, Ephedrine and Mephentermine for the maintenance of arterial pressure during spinal anaesthesia in Caesarean section. IV bolus of Phenylephrine 100 mcg, Ephedrine 5mg and Mephentermine 6 mg were used to prevent hypotension. They concluded that elevation of systolic blood pressure in Phenylephrine group was significantly high for first 6 minutes of bolus dose as compared to Ephedrine and Mephentermine group. There was significant reduction of heart rate in Phenylephrine group. Neonatal APGAR score was > 7 in all three groups. [22]

The effect of prophylactic Phenylephrine infusion for preventing hypotension during spinal anaesthesia for Caesarean delivery was studied and it was found that Phenylephrine infusion decreased the incidence, frequency, and magnitude of hypotension compared with control. A prophylactic infusion of Phenylephrine 100 mcg / min decreased the incidence, frequency, and magnitude of hypotension with equivalent neonatal outcome compared with a control group receiving IV bolus Phenylephrine. [23]

A comparison of Phenylephrine infusion regimens for maintaining maternal blood pressure during spinal anaesthesia for Caesarean section was done to assess the optimal Phenylephrine regimen and the optimal blood pressure to which it should be titrated. They compared umbilical blood gases, APGAR scores and maternal haemodynamics and reported that patients receiving 100 mcg of Phenylephrine had fewer episodes of hypotension compared those who received 80 mcg and concluded that for optimal management, Phenylephrine should be titrated to maintain maternal BP at near-baseline values. [24]

Further study was done to investigate if Ephedrine infusion was more effective in preventing hypotension than traditional prehydration during spinal anaesthesia for Caesarean section in African parturients. Neonatal outcome was similar in the two groups and median APGAR scores at one and five minutes were 8. Thus, they concluded prophylactic Ephedrine given by standard infusion set was more effective than crystalloid prehydration in the prevention of hypotension during spinal anaesthesia for elective Caesarean section. [25]

In a study conducted by Loughrey et al, it was found that a combination of intravenous bolus of Phenylephrine 40 mcg ± Ephedrine 10 mg was superior to Ephedrine alone for maintaining arterial pressure during spinal anaesthesia for Caesarean section in a group of 43 patients. [26]

A systematic review of vasopressors in obstetrics was performed, according to which Ephedrine was recommended as the best vasopressor in obstetrics because animal studies showed that it caused less reduction in uterine blood flow as compared to alpha-agonists. Recent clinical evidence, however, suggests that this is not as important as initially thought. Ephedrine and Phenylephrine have been most investigated. Advantages of Ephedrine include familiarity, long history and low propensity for uteroplacental vasoconstriction. Ephedrine, however, has limited efficacy, is difficult to titrate, causes maternal tachycardia and depresses fetal pH and base excess. Advantages of Phenylephrine include high efficacy, ease of titration and the ability to use liberal doses to maintain maternal blood pressure near normal and then prevent nausea and vomiting without causing fetal acidosis. Phenylephrine, however, may decrease maternal heart rate and a few data are available on its use in high-risk cases. Combination of a Phenylephrine

infusion and rapid crystalloid co hydration is the first method described that reliably prevents hypotension. In the authors' opinion, Phenylephrine is the vasopressor that most closely meets the criteria for the best vassopressor in obstetrics. [27]

The equivalent dose of Ephedrine and Phenylephrine in prevention of post spinal hypotension during Caesarean section was studied and the study demonstrates a potency ratio of 81.2 for equivalence between Phenylephrine and Ephedrine for prevention of hypotension during spinal anaesthesia for Caesarean section.[28]

A group of scientists recently reviewed prevention and treatment of hypotension during Caesarean delivery. Regional anaesthesia for Caesarean delivery is often accompanied by a reduction in maternal blood pressure, which may lead to a reduction in uteroplacental blood flow with consecutive fetal acidosis. In order to avoid reduction in uteroplacental blood flow, the avoidance of aortocaval compression, compression of the lower extremities, and prehydration with colloids are effective measures. Further means include the recent introduction of low dose spinal anaesthesia with a combination of small amounts of local anaesthetics and opioids. Nevertheless, maternal hypotension is not always preventable and the use vasopressors is still frequently required. Although Ephedrine has been considered the vasopressor of choice over the last decades, current studies show that fetal acidosis is less frequently encountered with the use of Phenylephrine which should thus be considered as a first-line agent. [29]

The effect of intravenous vasopressor on spread of spinal anaesthesia and fetal acid-base equilibrium was investigated and found that the block height was similar for both groups at all of the assessment times. Umbilical artery pH was higher with

Phenylephrine than with Ephedrine. There was a strong negative correlation between umbilical artery pH and SAB - delivery interval, but only with Ephedrine group. Five - minute APGAR scores were higher with Phenylephrine than Ephedrine. They observed an unexpectedly high incidence of fetal acidosis with Ephedrine and found evidence that longer SAB - delivery intervals increase the risk of fetal acidosis developing with Ephedrine, but not Phenylephrine.[30]

The effect of "Spinal anaesthesia for Caesarean section: fluid loading, vasopressors and hypotension" was studied by a group of scientists. They analyzed different preventive and curative strategies for the management of hypotension during spinal anaesthesia for Caesarean section with data from Medline database. Hypotension can induce complications for the mother and/or the fetus. Crystalloid preload alone is ineffective. They concluded that hypotension during spinal anaesthesia for Caesarean section must be systematically prevented, detected and treated without delay. Phenylephrine with or without Ephedrine with a rapid crystalloid loading at the time of spinal injection represent the most interesting strategy to prevent hypotension associated with spinal anaesthesia. [31]

Most of the clinical studies performed previously were performed on healthy, low risk, elective Caesarean sections and very few data are available for non elective cases in whom there is already fetal compromise, which may get exaggerated by change in uteroplacental perfusion with the use of vasopressors. Hence, a study was conducted to compare bolus doses of Phenylephrine 100 mcg with Ephedrine 10 mg for treating hypotension in 204 patients undergoing non-elective Caesarean sections. They concluded that Phenylephrine and Ephedrine are both suitable for use in non elective Caesarean

sections, however umbilical vein lactate concentration was found to be higher in Ephedrine group as compared to Phenylephrine group.[32]

An on-going clinical trial is being performed to determine the ED 90 i.e. the effective dose at which 90 % of parturients will have a "positive response to Phenylephrine". The secondary outcomes include need for additional vasopressors, need to use Glycopyrrolate to treat bradycardia, and presence of hypertension following administration of Phenylephrine.[33]

Various other clinical trials are still being conducted to determine the minimum effective dose and the various fetal and maternal effects of Phenylephrine.

Hence, this study has been conducted to evaluate the efficacy of Phenylephrine 40 mcg in comparison with Ephedrine 6 mg to maintain arterial blood pressure during spinal anaesthesia for Caesarean section.

ANATOMY

Sound knowledge of anatomy of vertebral column and its contents is essential to all the anaesthesiologists for safe and successful administration of spinal anaesthesia, not only in terms of performance but also in terms of spread of drug in CSF and level of block achieved.

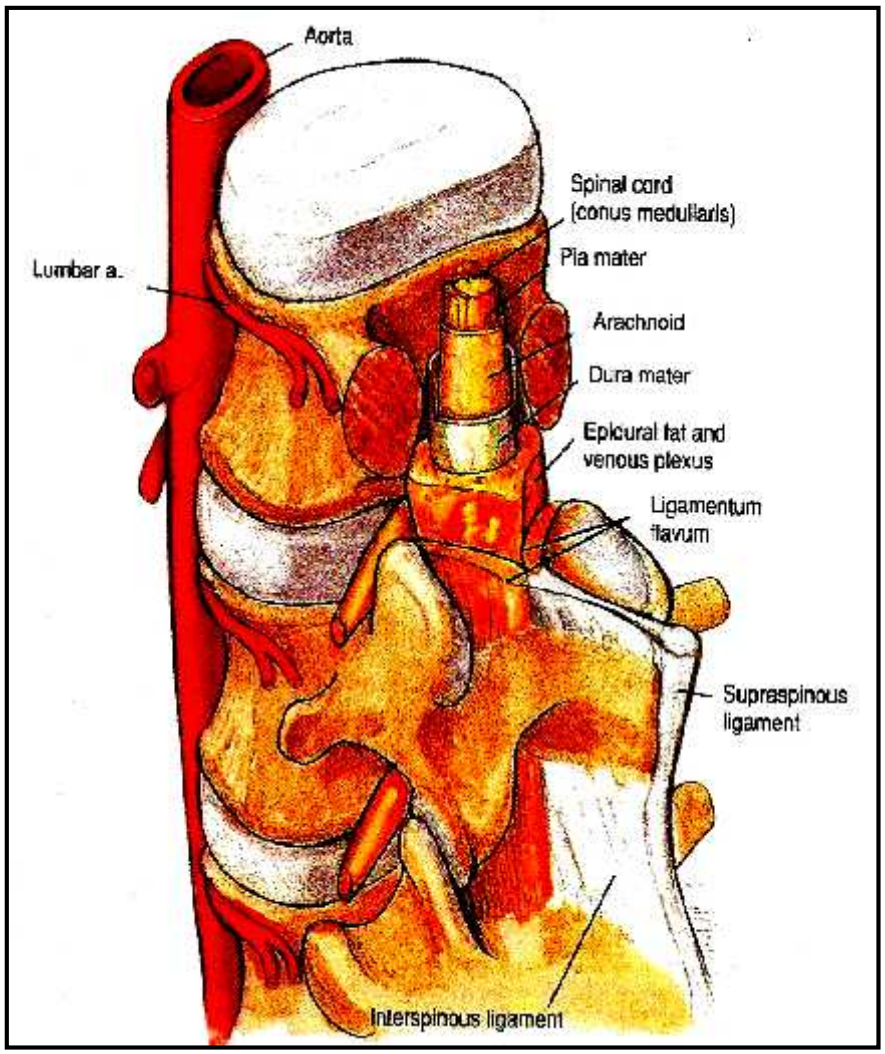


Figure 1: Anatomy of vertebral column

Vertebral column

The vertebral column comprises total of 33 vertebrae and includes 7 cervical, 12 thoracic, 5 lumbar, 5 fused sacral and 4 coccygeal vertebrae. The vertebral column has 4 curves which have significant effect on spread of drugs in sub arachnoid space. Cervical and lumbar curves are convex anteriorly whereas thoracic and sacral curves are convex posteriorly. The highest point of cervical and lumbar curves in supine position are at C5 and L5; lowest points of thoracic and sacral are at T5 and S2 respectively. Main function of vertebral column is to protect the spinal cord.

Vertebral ligaments

Vertebral column is bound together by following ligaments which give stability and elasticity.

Supraspinous ligament**:** This is a strong fibrous cord which connects apices of spinous processes from sacrum to C5 where it is continued as the ligamentum nuchae.

Interspinous ligament**:** This is a thin membranous ligament which connects spinous processes blending anteriorly with ligamentum flavum and posteriorly with supraspinous ligament.

Ligamentum flavum**:** This ligament comprises yellow elastic fibres and connects adjacent lamina. Laterally this ligament begins at the root of articular processes and extends posteriorly and medially to the point where laminae join to form spinous process.

Longitudinal ligaments**:** There are 2 longitudinal ligaments (anterior and posterior) that bind vertebral bodies together.

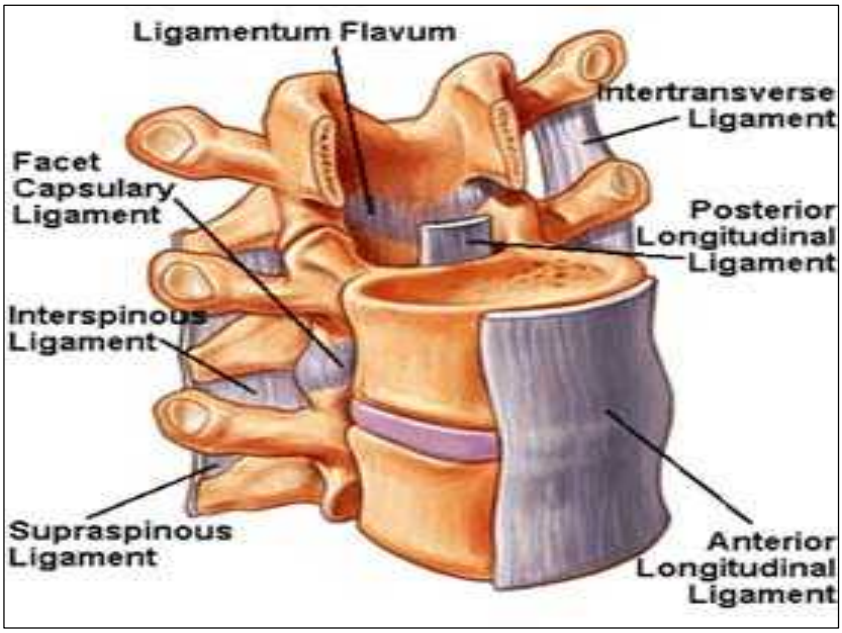


Figure 2: Spinal Ligaments

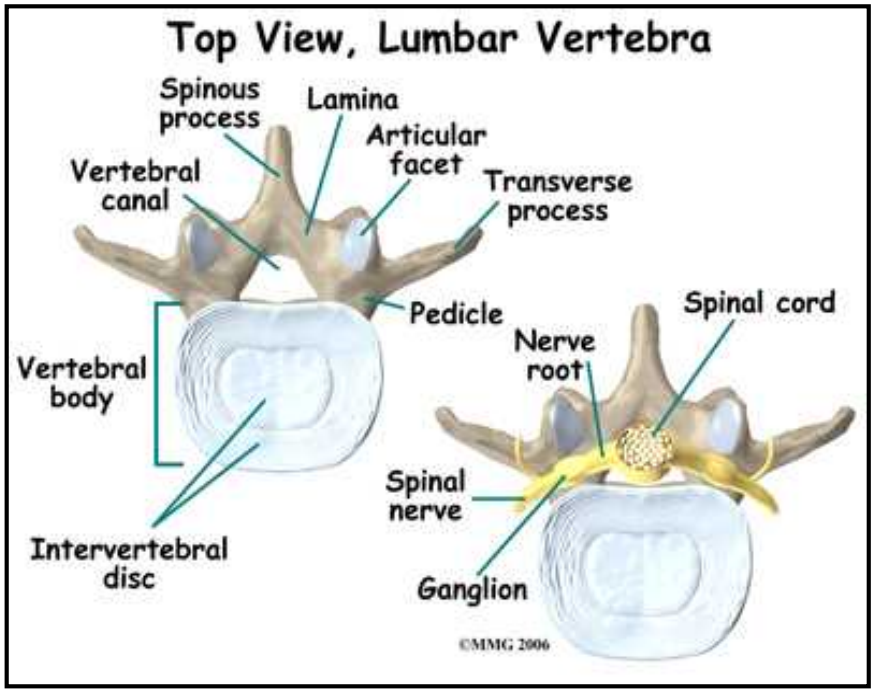


Figure 3: Typical Lumbar Vertebra

Lumbar vertebrae

A typical lumbar vertebrae consists of

1. A kidney shaped body.
2. Two pedicles directed backwards from the upper part of the body.
3. Two transverse processes which are slender
4. Two laminae meeting posteriorly and enclosing the triangular vertebral foramen.
5. Spinous processes which are thick, broad and quadrilateral in shape.
6. Two upper and lower articular processes which prevent rotation but allow limited flexion and extension between contiguous vertebrae.

Vertebral canal

Vertebral canal is bounded posteriorly by spinous processes and interspinous ligaments, laterally by the pedicles and posterolaterally by the laminae and ligamentum flavum. This ends superiorly in the foramina magnum and inferiorly in the sacral hiatus. The vertebral canal consists of spinal cord, spinal membranes, adipose tissue, blood vessels, CSF and the roots of the spinal nerves.

Spinal cord

The spinal cord which is the extension of central nervous system into the vertebral canal begins at the level of foramen magnum and ends below as the conus medullaris. At birth spinal cord ends at the level of L3 but rises as age progresses and reaches the lower border of L1 in adults. It measures about 42-45 cm.

The spinal cord receives blood supply from three arteries, one anterior and two posterior spinal arteries.

Anterior spinal artery is a single vessel lying in the substance of pia matter overlying the anterior median fissure. It receives communications from intercostals, lumbar and other small arteries and supplies the lateral and anterior columns, comprising three quarters of substance of the cord. Thrombosis of this artery causes anterior spinal artery syndrome.

There are two pairs of posterior spinal arteries, one pair on each side arising from posterior inferior cerebellar arteries at the level of foramen magnum. They supply posterior column of the cord.

Spinal meninges

Along with the bony vertebral column spinal cord is also protected with three connective tissue coverings called meninges.

Dura mater : This is a tough outermost fibro elastic covering consisting of outer endosteal layer and inner meningeal layer. Fibres of dura run longitudinally, thus it is important to insert the spinal needle so as to split these fibres and not to cut them. Dural sac ends at lower border of S2, where it is pierced by filum terminale.

Arachnoid mater : It is a delicate, non vascular, middle covering and is closely attached to the dura. There is a capillary interval or potential space between dura and arachnoid mater called subdural space and contains serous fluid.

Pia mater : It is a delicate highly vascular covering closely investing the spinal cord and brain.

Subarachnoid space

The space between the arachnoid and pia is called the subarachnoid space and is filled with cerebrospinal fluid and contains numerous arachnoid trabeculae which form delicate sponge like mass. This space has three divisions which are free communication to each other: cranial (surrounding the brain), spinal (surrounding the spinal cord) and root (surrounding the dorsal and ventral nerve roots). In the spinal cord these nerve roots are covered only by pia and bathed in CSF. As these spinal nerve roots pass beyond the spinal dura and traverse the epidural space, they carry with them all the three meningeal layers and have a distinct epidural, subdural, subarachnoid and sub pial spaces. The subarachnoid space extends separately along both the dorsal and ventral roots to the level of dorsal root ganglion, where arachnoid and pia continue as perineural epithelium of peripheral nerve.

Cerebrospinal fluid

It is a clear colourless fluid found in the cranial and spinal subarachnoid spaces and in the ventricles. CSF is mainly formed by either secretion or ultrafiltration from the choroidal plexus of lateral ventricles. CSF flows from the lateral ventricles into the third ventricle through the foramina of Monro into the fourth ventricle through the Aqueduct of Sylvius into the cerebromedullary cisterna (cisterna magna) through foramen of Magendie and foramina of Luschka. From the cisterna magna, CSF enters subarachnoid space circulating around brain and spinal cord before being absorbed into the arachnoid granulations over the cerebral hemispheres.

Composition of cerebrospinal fluid:

Specific gravity: 1.003-1.009 at 37 c.

Volume: 120 ml-150 ml (25 ml-35ml in spinal space).

CSF pressure: 60-80 mm of Hg in lumbar space.

pH: 7.27- 7.37

PCO_2: 48 mm of Hg

HCO_3:23 mEq/L

Sodium-135-145 mEq/L

Calcium:2-3 mEq/L

Phosphorous:1.6 mg/dl

Magnesium: 2-2.5 mEq/L

Chloride: 15-20 mEq/L

Proteins: 23-38 mg/dl

It is important to know that certain drugs alter the rate of formation of CSF. Carbonic anhydrase inhibitors like acetazolamide reduce the rate of CSF formation by as much as 50%. Furosemide in large doses may reduce the CSF formation where as steroids have an inconsistent effect. Inhalational anaesthetics like isoflourane and vasoconstrictors decrease the CSF formation. CSF formation is decreased when the serum osmolality is increases and increased when the serum is made hypotonic. During equilibrium, rate of formation equals the rat of absorption (500 ml/day).

PHYSIOLOGY OF SUBARACHNOID BLOCK

Physiological responses to intra and extra dural blockade results from autonomic blockade with its effects on both vascular beds and cardiac action from addition of somatic pain and the reflex responses associated with it and from the effects of blockade of motor fibres.

1) Autonomic blockade

Order of blocking nerve fibres,

a) Autonomic pre ganglionic B fibres.

b) Temperature fibres.

c) Pin prick fibres.

d) Fibres conveying pain greater than pin prick.

e) Touch fibres.

f) Deep pressure fibres.

g) Somatic motor fibres.

h) Fibres conveying vibratory sense and proprioceptive impulses.

During recovery, return of sensations in the reverse order assumed, but it has been suggested that sympathetic activity returns before sensation.

In SAB sympathetic fibres are blocked two to three segments higher than sensory fibres and sensory block is two segments higher than motor block.

2) Effects of SAB on cardiovascular system

Spinal block can influence CVS in various ways.

a. Vasodilatation of resistance and capacitance vessels.
b. Block of cardiac efferent sympathetic fibres from T1-T4 resulting in loss of chronotropic and inotropic drive and fall in cardiac output.
c. Bainbridge reflex causing bradycardia.
d. Depression of vascular smooth muscle and beta adrenergic blockade of myocardium with fall in CO following systemic absorption of local anaesthetic drug.

Block extending above T4 is associated with fall in BP. Slowing of HR is caused if any of anterior roots carrying sympathetic cardiac accelerator fibres are blocked as may happen in high spinals above T4-T5. Bradycardia may also be due to lowering of BP in the right atrium consequent to diminished venous return.

Theories of causation of fall in BP.

a. Diminished cardiac output due to reduction of venous return to cardia and lack of muscular propulsive force in veins.
b. Dilatation of post arteriolar capillaries and small venules due to paralysis of vasoconstrictors.
c. Paralysis of sympathetic nerve supply to heart.
d. Paralysis of sympathetic nerve supply to adrenal glands with consequent catacholamines depletion.
e. Ischemia and hypoxia of vital centres.
f. Compression of great vessels in abdomen by pregnant uterus or abdominal tumours.

3) Effects of SAB on respiratory system

Due to motor blockade and deafferentation, with reduction of sensory input to respiratory centre, breathing becomes quiet during spinal anaesthesia. Intercostal paralysis is compensated by descent of diaphragm which is made easier by lax abdominal wall. This is not accompanied by hypoxia or hypercapnia although the ability to cough forcibly to expel secretions is impaired. Spinal anaesthesia as such does not interfere significantly with gas exchange.

4) Effects of SAB on gastrointestinal system

SAB up to T5 results in,

a) Narrowing of gut.

b) Active peristalsis.

c) Increase in intraluminal pressure.

d) Relaxation of sphincters.

e) Enlargement of spleen.

f) Nausea and vomiting.

5) Effects of SAB on endocrine system

The stress response to surgery results in rise in blood sugar, cortisol and catecholamine level sufficiently high and prolonged spinal blockade can minimise or even prevent these changes.

6) Effects of SAB on genito urinary system

Kidney function is not affected unless severe hypotension is present. The urinary bladder is relaxed and its spincter is contracted leading to retention of urine. Post spinal injury retention may be moderately prolonged as L2-L3 contains small autonomic fibres and their paralysis lasts longer than that of larger sensory and motor fibres.

The engorgement of flaccid penis due to paralysis of nervigentis is often the first sign of successful block. The tone of uterus is not greatly altered after spinal anaesthesia in pregnancy.

Factors affecting height of analgesia in SAB

a) Specific gravity of solution.

b) Position of patient during and after injection.

c) Volume of solution.

d) Concentration of drug.

e) Rate / force of injection.

f) The site of injection.

g) Pregnancy and intraabdominal tumours.

Spinal anaesthesia for Caesaerean section:

Changes in parturient in respect to spinal anaesthesia:

Spinal curvature

There is increase in lumbar lordosis which makes the interspinous spaces smaller making regional anaesthesia more difficult. Along with increase in lordosis of spine, distension of epidural veins increases risk of vascular damage / injection. There is about 30–50% reduction in requirement of local anaesthetics to achieve the same level of block as compared to non pregnant patients. The proposed reasons behind this includes engorged epidural veins reducing the size of intrathecal space and volume of CSFand also engorged veins block the escape of drugs though the vertebral foramina. There are greater chances of cephalad spread due to exaggerated lumbar lordosis. There is also increased secretion of the hormone relaxin which contributes to the relaxation of all the ligaments and this also contributes to increased lumbar lordosis.

Local Anesthetic and pregnancy:

Pregnancy can alter the effect of local anesthetics in different ways. Smaller amounts of local anesthetic have been shown to be needed for both spinal and epidural anaesthesia in parturient as compared with nonpregnant women in the same age group.[15,16]

The onset of blockade is also faster with the use of spinal, epiduraland peripheral nerve blocks.[17] The mechanism for this phenomenon is not known; however, progesterone, an important pregnancy hormone, may be one of the responsible factors.

Aortocaval compression:

The first report of "supine hypotension in late pregnancy" was published in 1953.[18] This described hypotension which occurred in patients upon assuming the supine positionand which resolved with lateral positioning.

It is caused by compression of the inferior vena cava by the gravid uterus with a consequent reduction in venous return. Three to seven minutes are generally required for significant hypotension to become manifest. Supine hypotension is most severe in the latent stage of labor and is more severe in patients undergoing Caesaerean section who are in labor than those who are not. The magnitude of inferior venacava compression is reduced during contractions because the uterus rides away from the inferior venacava.

During labor, aortic compression occurs almost exclusively during uterine contractions. It occurs in up to 86% of parturients. It is less dependent upon posture and less responsive to lateral tilt than inferior venacava compression. Compression of the aorta occurs at the level of maximal lumbar lordosis (L_4 - L_5).

Major problem with sub arachnoid block in this situation is difficulty in regulating upper limit of neuronal blockade. Incidence of hypotension has been described as high as 83 percent in patients in spite of fluid preloading and lateral uterine displacement. Systemic hypotension can cause reduction in uterine perfusion pressure and decrease placental flow. Degree of fetal acidosis has been associated more with duration than severity of hypotension. Therefore hypotension should be treated initially with fluid load than with vassopressors.

PHARMACOLOGY OF EPHEDRINE

Clinical Formula: $C_{10}H_{15}NO$ (Fig 5)

Molecular weight: 165.23

Melting point: - $187 – 188^0$ C

Bioavailability: - 85 % (oral)

Metabolism: - Minimal hepatic.

Elimination half life: 3 – 6 hrs.

Excretion: 22 – 99 % renal.

Routes of Administration: Oral, Intravenous, Intramuscular, Subcutaneous.

Ephedrine is a potent sympathomimetic amine which stimulates both α and β receptors and has clinical uses related to both actions.

Clinically, it is an alkaloid derived from various plants in the genus Ephedra (Family Ephedraceae).

Usually marketed as Ephedrine hydrochloride and Ephedrine sulphate.

The traditional Chinese herb Ma Huang [Ephedra sinica] contains Ephedrine as its principal active constituent. The same is true of other herbal products containing extracts from Ephedra species. The substance called soma mentioned in old Hindu books such as the Rig Veda may have been Ephedra extracts.

Chemistry: -

Ephedrine exhibits optical isomerism and has 2 chiral centres by convention; the enantiomers with opposite stereochemistry around the chiral centres are designated Ephedrine, while pseudoEphedrine has same stereochemistry around the chiral carbons.

That is (1R, 2R) – and (1S, 2S) - enantiomers are designated pseudoEphedrine, while (1R, 2S) - and (1S, 2R) - enantiomers are designated Ephedrine.

The isomer which is marketed is (1R, 2S) - Ephedrine.

As with other phenylethylamines, it is also somewhat chemically similar to methamphetamine, although the amphetamines are more potent and have additional biologic effects.

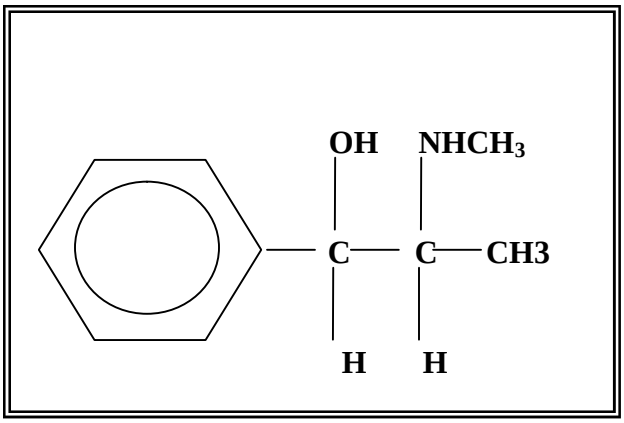
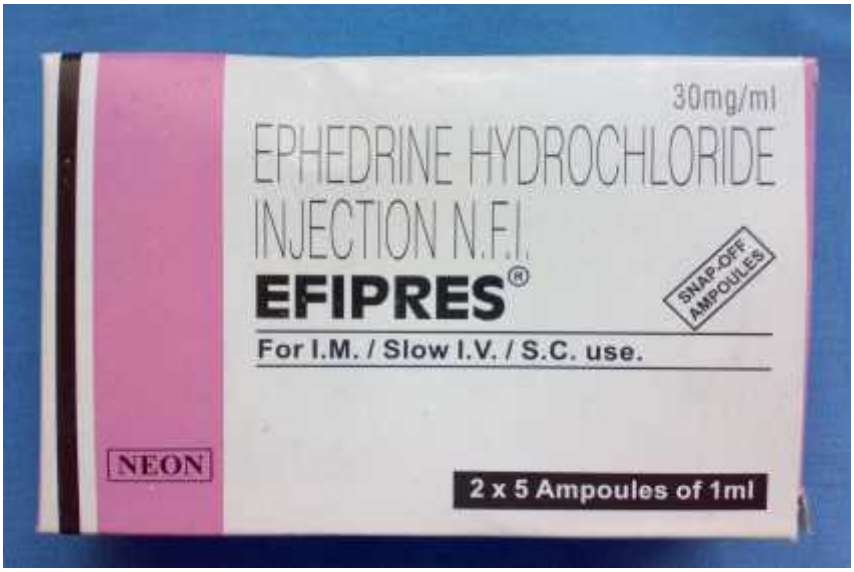


Figure 4 : Structure of Ephedrine



Photograph 1: Injection Ephedrine Hydrochloride

Mode of action: -

Ephedrine is a sympathomimetic amine. Its principal mechanism of action relies on its indirect action on the adrenergic receptor system, which is part of the sympathetic nervous system. Whilst it may have weak agonist activity at α and β adrenergic receptors, the principal mechanism is to displace noradrenaline from storage vesicles in presynaptic neurons. The displaced noradrenaline is released into the neuronal synapse where it is free to activate the postsynaptic adrenergic receptors.

Pharmacological actions: -

I.) CNS: -

- Ephedrine crosses to brain easily and is a potent stimulator of central nervous system.
- It stimulates the spinal cord and enhances spinal reflexes.
- Cerebral blood flow is reduced.

II.) CVS: -

- Cardiac output and heart rate are increased.
- Repeated frequent doses or a single very large dose may result in depression of the heart.
- Diastolic blood pressure is increased but lesser than systolic blood pressure.
- Vessels of mucus membranes are constricted following local application.
- Coronary vessels are dilated because of increased blood flow through them due to increase in cardiac output.

III.) RS: - Dilatation of the bronchial tree.

IV.) GIT and Urinary tract: -

- Increase in the tone of sphincters of the alimentary tract and the bladder.
- It may cause retention of urine.
- Renal blood flow is decreased.

Fate in the body: - It inhibits monoamine oxidase and is not destroyed by it.

It is excreted unchanged in the urine within 24 hrs.

It is also excreted in breast milk.

Preparations, Routes of Administration and Doses: -

Ephedrine sulphate available parenteral form- (25mg/ml or 50mg/ml or 30mg/ml) for SC, IM or slow IV administration (Fig 6).

- It is also available as oral preparation for patients with asthma or nasal congestion in capsules (25 or 50mg).
- Oral syrups (11 or 20mg/5ml). Oral dose is 25-50mg to be repeated every 3-4 hrs as required.
- For treatment of hypotension, drug is administered parenterally and dose is titrated according to the response.
- Adults and elderly: - up to 30 mg in increments of 3-7.5mg.
- Children: - 0.5 - 0.75 mg/ kg or 17 - 25mg/ m^2 body surface area.

Indications: -

1.) Ephedrine was once widely used as a topical decongestant (now its role in nasal congestion has largely been replaced by more potent α adrenergic receptor agonists (E.g. Oxymetazoline).

2.) Bronchodilator in the treatment of asthma: - The role of Ephedrine in asthma has been almost entirely replaced by β_2 adrenergic receptor agonists (e.g. salbutamol).

3.) Used intravenously for the treatment of hypotension following spinal or epidural anaesthesia.

Also used in other hypotensive states including overdose with:

- Ganglion blocking agents.
- Antiadrenergic drugs.
- Other drugs which lower blood pressure.

4.) Used in narcolepsy and depressive states.

5.) Used in nocturnal enuresis.

6.) Used in Myasthenia Gravis- produces a modest increase in muscle power.

7.) In Stokes-Adams syndrome with complete heart block- it has a value similar to that of epinephrine.

Contraindications/precautions:-

Ephedrine should be used with caution in patients with

- Heart disease and angina pectoris
- Inadequate fluid replacement
- Depletion of noradrenaline stores
- Hypoxia
- Hypercarbia
- Acidosis
- Hypertension
- Hyperthyroidism

- Prostatic hypertrophy
- Diabetes Mellitus
- Cardiovascular disease during delivery if maternal blood pressure > 130/80 mm of Hg.
- Lactation.

Adverse Drug Reactions: - More common with systemic administration (e.g. injection) as compared to topical administration (e.g. nasal inhalations).

I. CVS: - Tachycardia, bradycardia, arrhythmias, angina, vasoconstriction with hypertension.
II. CNS: - Anxiety, restlessness, confusion, psychoses, insomnia.
III. GIT: - Nausea, vomiting, anorexia.
IV. Dermatological: - Flushing, sweating.
V. Genitourinary: - Difficulty in micturition, retention of urine.
VI. Miscellaneous – Dizziness, headache, tremor, hypersalivation, changes in blood glucose concentration.

Drug Abuse and Dependence:-

Ephedrine has been reported to cause physical dependence after excessive long term use. This is particularly true with oral forms of Ephedrine, since parenteral administration is unlikely to occur over long periods.

Prolonged abuse of Injection Ephedrine can result in symptoms of paranoid schizophrenia.

Contraindications: -

1.) Closed angle glaucoma.

2.) Phaeochromocytoma.

3.) Asymmetric septal hypertrophy.

4.) Concomitant or recent (previous 14 days) monoamine oxidase inhibitor therapy.

5.) General anaesthesia with halogenated hydrocarbons (particularly Cyclopropane or halothane).

6.) Tachyarrhythmias or ventricular fibrillation.

7.) Hypersensitivity to Ephedrine.

8.) Psychoneurosis.

Overdosage: - The principal manifestation of Ephedrine poisoning is convulsions.

In acute poisoning, the signs and symptoms include nausea, vomiting, chills, cyanosis, irritability, fever, suicidal behaviour, tachycardia, dilated pupils, blurred vision, opisthotonus, convulsions, pulmonary edema, gasping respirations, comaand respiratory failure. Initially patient may have hypertension followed by hypotension accompanied with anuria.

Treatment:

- Artificial respiration if shallow respirations or cyanosis
- Maintain BP in case of cardiovascular collapse
- Slow IV injection of Labetalol 50- 200 mg
- Marked hypokalemia (< 2.8 mmol/ L) due to compartmental shift of potassium predisposes to cardiac arrhythmias. KCl infusion may be started.

- For hypertension, 5 mg phentolamine mesylate diluted in saline may be administered slowly IV or 100 mg orally.
- Convulsions may be controlled with diazepam or paraldehyde.
- Pyrexia- cool applications and dexamethasone 1 mg/ kg.

PHARMACOLOGY OF PHENYLEPHRINE:

Phenylephrine is a synthetic sympathomimmetic and a vasoconstrictor drug chemically related to epinephrine and Ephedrine. Structurally it is 3-hydroxyphenylethylamine. It is a synthetic non catecholamine that stimulates alpha 1 adrenergic receptors by direct action. The primary effect being on alpha 1 receptors, there is more of venoconstriction than arterial constriction. It can activate beta adrenergic receptor at higher dose.

Molecular Formula: $C_9H_{13}NO_2HCL$

Molecular weight: 203.67

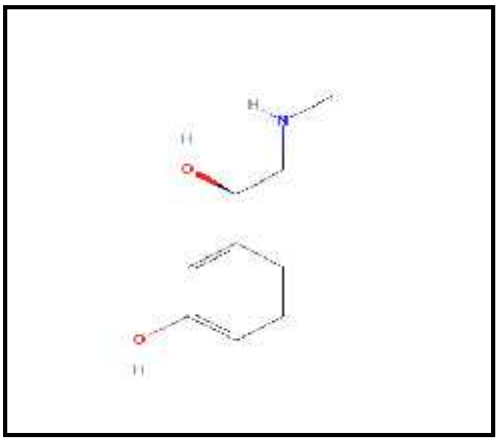


Figure 5: Structure of Phenylephrine

Photograph 2: Injection Phenylephrine hydrochloride

Clinical pharmacology:

It is a sympathomimetic agent with mainly direct effect on adrenergic receptors. It has predominantly alpha-adrenergic activity and is without significant stimulating effects on central nervous system at usual doses. After injection it produces peripheral vasoconstriction and increased arterial pressure. It also causes reflex bradycardia.

When injected subcutaneously and intramuscularly it takes 10-15 minutes to act. Subcutaneous and intramuscular injections are effective for one and 2 hours respectively. Intravenous injections are effective for 20 min. Phenylephrine is metabolized in liver by

monoamine oxidase. The metabolites, their route and rate of excretion have not been identified.

Indications:

For the treatment of hypotensive states like circulatory failure during spinal anaesthesia and drug induced hypotension.

Doses and Administration:

It can be used as Intravenous, Subcutaneous or Intramuscular injection.

Adults:

Phenylephrine injection may be administered subcutaneously or intramuscularly at doses of 2 to 5 mg with further doses of 1 to 10 mg as based on response. Intravenous 25 to 100 microgram can be given as slow intravenous injection and repeated whenever necessary.

Contraindications

1. Patients taking MAO inhibitors or within 14 days of ceasing such treatment.
2. Severe hypothyroidism and hypertension.

Adverse effects

1. Extravasation may cause tissue necrosis.
2. Rise in blood pressure with headache and vomiting which in turn may cause cerebral hemorrhage and pulmonary edema.

3. Reflex bradycardia or tachycardia
4. Other cardiac arrhythmias.

Drug Interaction

Interacts with Cyclopropane and halothane and other halogenated anaesthetic to induce arrhythmias.

Increased chances of arrhythmias in the patient taking cardiac glycosides, quinidine or tricyclic antidepressants.

Effects on different organ system:

Cardiovascular system:

Rapid intravenous infusion produces dose dependent peripheral vasoconstriction and increase in systemic blood pressure that are accompanied by decrease in cardiac output. It also produces baroreflex mediated bradycardia in response to increased diastolic blood pressure. It increases coronary perfusion pressure without any chronotropic side effects. Hence, is particularly useful in patients with coronary artery disease and in patients with aortic stenosis. It decreases renal, splanchnic and cutaneous blood flow. It also increases pulmonary artery pressure.

Placental blood flow:

With its alpha adrenergic effects it is considered to cause vasoconstriction in placental circulation, but studies have found this to be non significant and causes less alternation to acid base status then initially thought. It also increases uterine vascular resistance. Careful titrated doses of Phenylephrine restore the blood pressure in normotensive parturient and can help to maintain uterine perfusion. The advantages of Phenylephrine include high efficacy, ease of titration and the ability to use liberal doses

to maintain maternal blood pressure near normal, this results in less acid base disturbance in fetus.

Uses:

1. To treat spinal and epidural anaesthesia induced hypotension.

   Doses: 25 to 200 microgram bolus or 20-50 microgram/ min as IV infusion

2. As a prophylactic against spinal anaesthesia induced hypotension.

   Dose: 2-5 mg (up to 150 microgram per kg) Intra muscular. Onset of action after IM injection is 10-15 minutes.

3. To treat hypotension due to peripheral vasodilatation during general anaesthesia.

   Dose: 50-200 microgram bolus.

4. It can be used to prolong local anesthetic action

5. As a nasal decongestant.

Side effects

1) Bradycardia: Reflex mediated bradycardia which is caused in response to increased diastolic blood pressure
2) Hypertension: Reactionary hypertension due to alpha-1 receptor mediated peripheral vasoconstriction.

METHODOLOGY

The present study was conducted in the Department of Anaesthesiology, K.L.E.Society's Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum during the period of December 2007 to December 2008.

Study Design : One year Randomized clinical trial.

Source of Data : Patients undergoing emergency and elective Casarean section at KLE Society's Dr.Prabhakar Kore Hospital and Medical Research Centre, Nehru Nagar, Belgaum - 590010, Karnataka.

Sample size : A total sample size of 100 cases.

Sample size calculation : The sample size was calculated by assuming the power of the study to be 80 percent, Alpha value of 0.05 and difference of mean of 9.

Inclusion Criteria

1. Singleton full term pregnant patients undergoing elective and emergency lower segment Casarean section.
2. Age: 25-30yrs.
3. ASA Grade I andII.

Exclusion Criteria

1. Hypertension.
2. Diabetes.

3. Patients with cardiac, pulmonary and renal diseases which could affect haemodynamic response.
4. Patients with history of drug intake like β- blockers, Magnesium sulphate or Terbutaline.
5. Contraindications to spinal anaesthesia.

Methodology

Approval from institutional ethical committee was obtained.

After explaining the anaesthetic procedure, written informed consent for participation in the study was obtained from the patient. 100 patients were randomly divided into two groups of 50 each, Group P (Phenylephrine group) and Group E (Ephedrine group) using computer generated randomization table. Study drugs were prepared and dispensed in syringes labelled “Study Vasopressor” by an anaesthesiologist not involved in the study.

In the operating room, pulse oximeter, ECGand non-invasive blood pressure monitor were attached to the patient. The baseline heart rate, systolic, diastolic and mean blood pressures were measured. Intravenous preloading was done with 10ml / kg of Ringer lactate solution, given over 15 minutes. Following this, all patients received intrathecal 2 ml of 0.5% hyperbaric Bupivacaine through 23 G Quincke needle at L3-L4 subarachnoid space in left lateral position. Immediately following the injection, patients were turned to supine position and received oxygen at the rate of 4 Litre / min by face mask. Level of sensory block was assessed by pinprick method 5 minutes after SAB.

Heart rate, systolic diastolic and mean arterial pressures were recorded every 2 minutes for 20 minutes and thereafter every 5 minutes for 1 hour or till the end of the surgery.

Whenever Hypotension (fall in BP ≥ 20% of baseline or less than 90 mm of Hg) occurred, Group P received Phenylephrine 40 mcg and Group E received 6 mg Ephedrine as intravenous bolus. Time taken to develop hypotension and the number of boluses administered were noted.

Paediatrician assessed APGAR score of every neonate at 1 min and 5 mins after delivery.

Statistical analysis

Statistical analysis was done using Student's t test and Mann-Whitney test.

'p' value of less than 0.05 was considered to be statistically significant.

Photograh 3: Spinal Tray

Photograph 4: Subarachnoid block

RESULTS

The objective of the present study was to compare the efficacy of intravenous bolus dose of Phenylephrine (40 mcg) and Ephedrine (6mg) for maintenance of arterial pressure following spinal anaesthesia for Caesarean section.

The present study was conducted on 100 patients undergoing elective and emergency Caesarean sections under spinal anaesthesia belonging to American society of Anaesthesiologists Grade I and Grade II physical status.

The study was carried out in KLES Prabhakar Kore Hospital & Medical Research Centre, Belgaum during the period of December 2007 to December 2008.

Each group consisted of 50 patients and were divided as Group P (Phenylephrine group, n = 50) and Group E (Ephedrine group, n =50) by a computer generated randomization table.

Data was collected in both the groups and observations of the analysed data are presented as mean ± standard deviation in the tabular form.

DEMOGRAPHIC PROFILE

	Group P	**Group E**
Age (yrs)	26.80 ± 1.68	26.88 ± 1.73
Weight (kg)	55.40 ± 5.55	55.20 ± 5.33
Height (cms)	151.34 ± 1.72	151.24 ± 1.78
Parity	1.60 ± 0.72	1.68 ± 0.71

Table 1 : Showing age, weight and height and parity in both the groups.

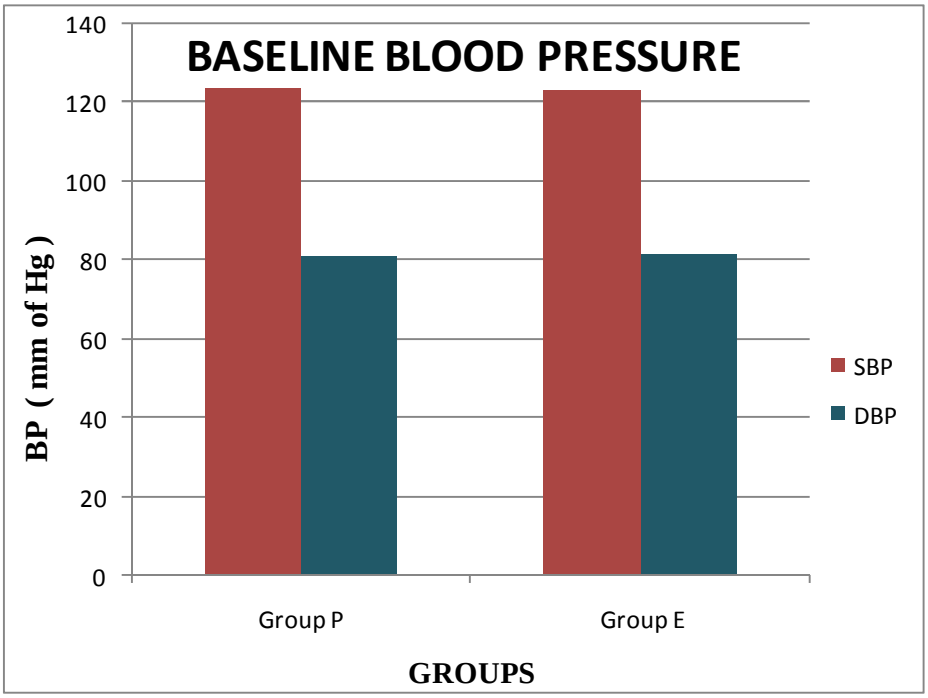
Group P = Phenylephrine group Group E = Ephedrine group

The age, weight, height and parity were comparable in both the groups.

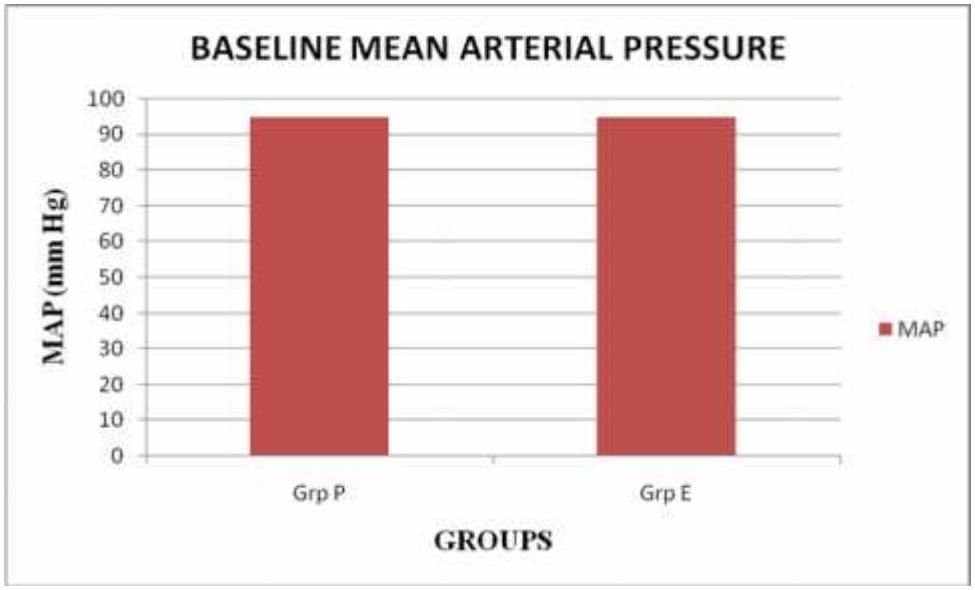
The baseline parameters recorded in the study groups were maternal heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure.

	Group P	**Group E**
Maternal heart rate (bpm)	89.52 ± 11.89	92.20 ± 11.56
Maternal SBP (mm Hg)	123.52 ± 7.84	123.14 ± 8.98
Maternal DBP (mm Hg)	80.94 ± 8.10	81.18 ± 9.12
Maternal MAP (mm Hg)	95.00 ± 7.20	95.00 ± 8.26

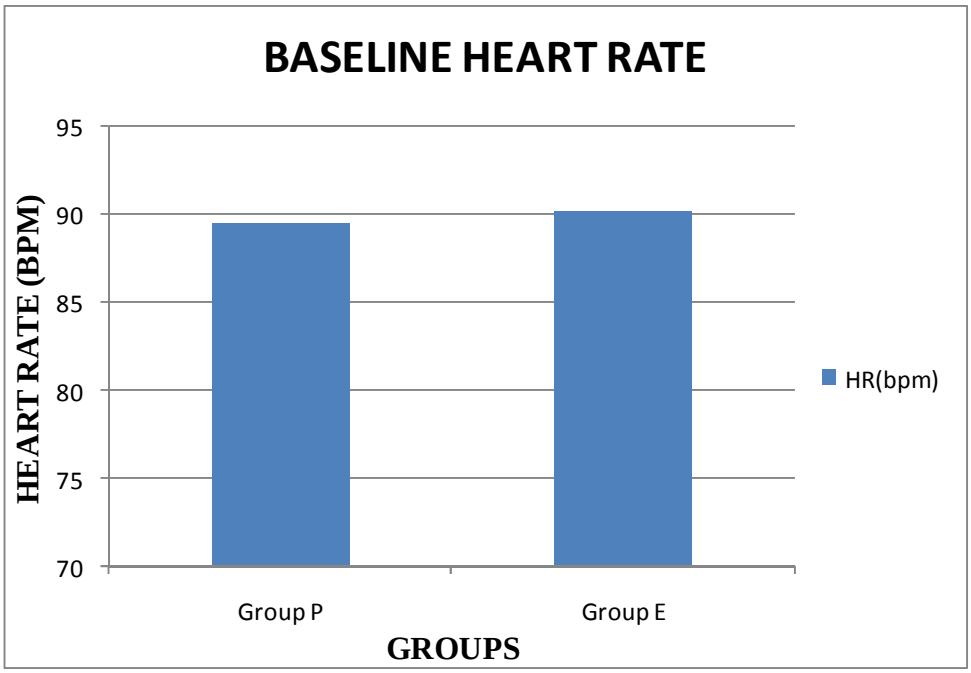
Table 2 : **Shows the baseline parameters in both the groups.**



Graph 1: Baseline systolic and diastolic blood pressure in Group P and E.



Graph 2 : Baseline mean arterial pressure in Group P and Group E



Graph 3 : Basal heart rate in Group P and E.

- The mean values of maternal baseline heart rate in group P and E are 89.52 ± 11.89 and 92.20 ± 11.56 respectively.
- The mean SBP values obtained in the two groups are 123.52 ± 7.84 and 123.14 ± 8.98 respectively.
- Similarly, diastolic blood pressure values in the two groups were 80.94±8.10 and 81.18±9.12.
- Baseline mean arterial pressure in the two groups are 95.00 ± 7.20 and 95.00 ± 8.26 mm of Hg.

  Thus, the two study groups were comparable with respect to the baseline parameters.

Time	Group P	Group E	p
SAB to hypotension	3.36±0.81	3.52±0.81	0.3265
Duration of surgery	68.28±8.46	69.40±8.18	0.5027

Table 3 : Shows SAB to hypotension time and duration of surgery

The data of subarachnoid block to hypotension time and duration of surgery were compared. There was no statistically significant difference found in the two groups ($p > 0.05$).

	Mean number of bolus	**Standard Deviation**	**Mean dose**
Group P	1.20	0.45	48 mcg
Group E	1.40	0.64	8.4mg

Table 4 : Shows number of bolus and mean drug dose required in each group

- Group P required average of 1.20 bolus, group E required 1.40 as bolus.
- Mean dose of 48 mcg and 8.4 mg was required in group P and group E respectively.

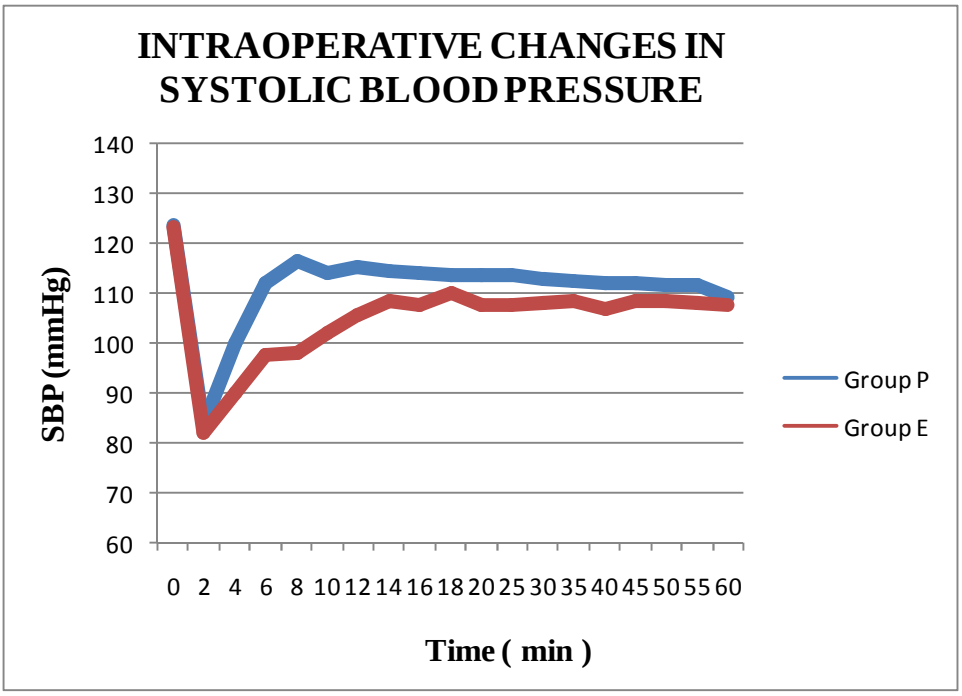
Table 5 : Shows changes in systolic blood pressure in both groups.

	Group P	Group E	P
SBP Basal	123.52±7.84	123.14±8.98	0.8222
SBP hypo (VP)	83.58±7.88	82.06±12.81	0.4766
SBP 2	100.18±12.36	89.82±17.07	**0.0008**
SBP 4	111.84±10.87	97.60±11.65	**0.0000**
SBP 6	116.28±10.92	98.20±16.55	**0.000**
SBP 8	115.92±10.28	102.14±15.38	**0.000**
SBP 10	113.82±15.12	105.80±9.71	**0.0021**
SBP 12	115.26±8.67	106.40±14.73	**0.0004**
SBP 14	114.44±7.74	108.56±7.53	**0.0002**
SBP 16	113.84±7.92	107.72±8.00	**0.0002**
SBP 18	113.54±6.98	109.83±7.256	**0.0003**
SBP 20	113.80±5.81	107.62±8.24	**0.0000**
SBP 25	113.50±5.81	107.56±7.97	**0.0000**
SBP 30	113.02±6.43	108.20±6.08	**0.002**
SBP 35	112.24±6.6.80	108.38±5.89	**0.003**
SBP 40	112.08±6.16	106.66±14.67	**0.0179**
SBP 45	122.17±5.522	108.38±5.76	**0.0037**
SBP 50	111.70±5.54	108.32±5.82	**0.0081**
SBP55	111.44±5.71	108.10±5.95	0.0891
SBP60	109.16±5.59	107.66±5.80	0.1909

SBP - Systolic blood pressure (mm of Hg).

Subscript of SBP indicates timing (in minutes) of systolic blood pressure recording.

VP – Time of administration of vasopressor.



Graph 4: Intraoperative changes in systolic blood pressure in Group P and E.

- Basal SBP in Phenylephrine group was 123.52 ± 7.84 and that in Ephedrine group was 123.14 ± 8.98.
- Similarly, SBP during hypotension were 83.58 ± 7.88 and 82.06 ± 12.81 in Phenylephrine group and Ephedrine group respectively which was found to be statistically comparable in both the groups.
- Systolic blood pressure in Group P at 2 minutes after IV bolus was 100.18 mm of Hg while in Group E was 89.82 mm of Hg. This shows a significant difference.
- Similarly, Systolic blood pressure remains significantly high in Phenylephrine group till 50 minutes as compared to Ephedrine group.
- In Phenylephrine group, the SBP is restored to ≥ 80 % of its basal value within 2 minutes after administration of the bolus dose, whereas in Ephedrine group, SBP is restored to ≥ 80% of its basal value at 10 minutes. This rise in blood pressure is maintained till the end of 60 minutes in both the groups.

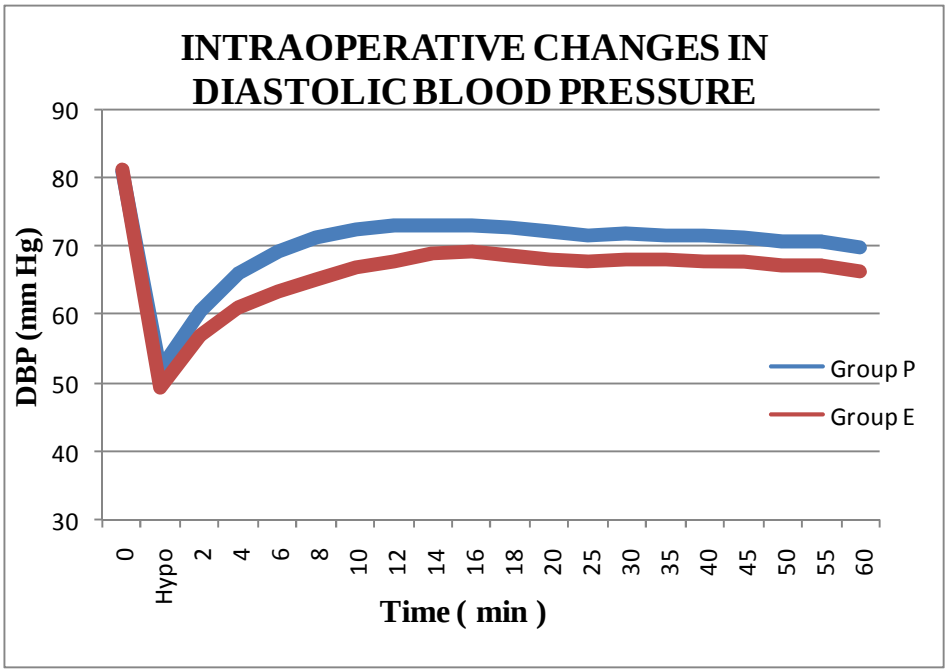
Table 6: Changes in diastolic blood pressure in both the groups.

	Group P	Group E	P value
DBP Basal	80.94 ± 8.10	81.18±9.12	0.8896
DBP Hypo (VP)	51.82 ± 5.49	49.38±7.34	0.0629
DBP2	60.24 ± 6.91	56.82 ± 7.33	**0.0182**
DBP4	66.06 ± 10.82	61.00±7.97	**0.0091**
DBP6	69.32 ± 10.82	63.34±7.64	**0.0019**
DBP8	71.22 ± 10.07	65.06±7.90	**0.0010**
DBP10	72.54 ± 9.23	66.84±7.65	**0.0011**
DBP12	72.86 ± 9.25	67.72±7.30	**0.0027**
DBP14	72.90 ± 8.75	69.00±8.37	**0.0249**
DBP16	72.86 ± 8.26	69.10±9.90	**0.041**
DBP18	72.74 ± 8.09	68.70±9.81	**0.0268**
DBP20	72.04 ± 7.73	68.18±10.28	**0.0364**
DBP25	71.40 ± 7.66	67.66±9.81	**0.0361**
DBP30	71.78 ± 7.83	68.04±8.44	**0.0248**
DBP35	71.46±7.58	67.92±7.84	**0.0239**
DBP40	71.60±7.61	67.78±8.88	**0.0230**
DBP45	71.36±7.54	67.86±8.77	**0.0349**
DBP50	70.70±7.53	67.22±8.42	**0.0318**
DBP55	70.52±7.58	67.28±9.03	0.0549
DBP60	69.90±7.95	66.28±8.94	0.0554

DBP- Diastolic blood pressure (mm of Hg)

Subscript of DBP indicates timing(in minutes) of diastolic blood pressure.

VP- Time of administration of vasopressor.



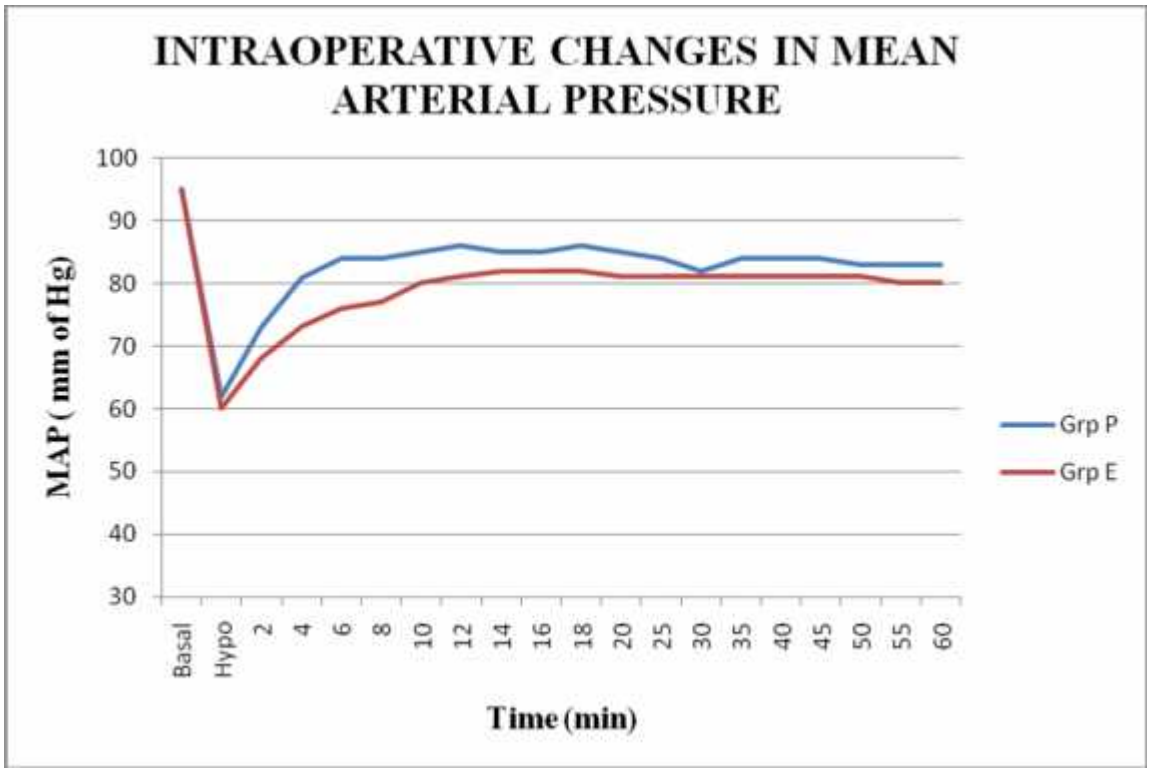
Graph 5: Intraoperative changes in diastolic blood pressure in Group P and E.

- Basal DBP and DBP during hypotension were statistically comparable in both the groups.

- Diastolic blood pressure in group P at 2 minutes after bolus dose was 60.24 ± 6.91 mm of Hg, whereas, in group E was 56.82 ±7.33 mm of Hg. This difference is statistically significant.

- Similarly, diastolic blood pressure in group P remains significantly high from 2 to 50 minutes as compared to Ephedrine group.

- In Phenylephrine group, DBP was restored to ≥ 80% of the baseline value at 2 minutes while in Ephedrine group, DBP was restored significantly only after 10 minutes, which is maintained till the end of 60 min in both the groups.



Graph 6 : Intraoperative changes in Mean arterial pressure in Group P and E.

- Basal MAP and MAP during hypotension were statistically comparable in both the groups.

- In Phenylephrine group, MAP was restored to ≥ 80% of the baseline value at 2 minutes while in Ephedrine group, DBP was restored significantly only after 10 minutes, which is maintained till the end of 60 min in both the groups.

- MAP is significantly high in group P as compared to group E.

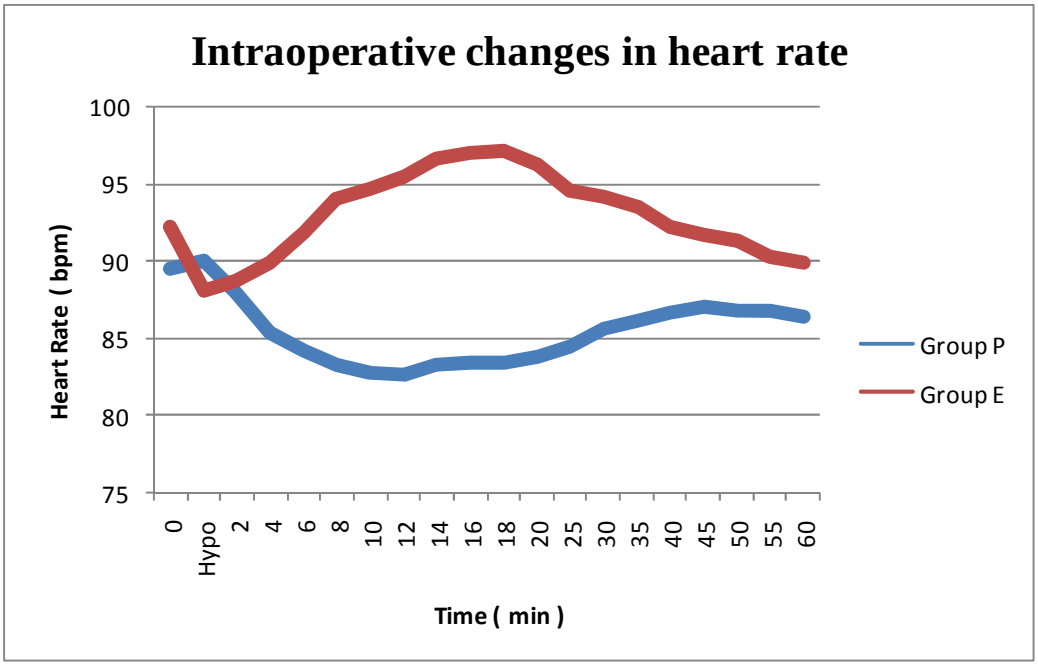
Table 7: Shows Changes in heart rate in both the groups

	Group P	Group E	P value
HR0	89.52±11.89	92.20±11.56	0.2558
HR Hypo (VP)	90.04±11.71	88.02±15.45	0.4630
HR2	87.96±10.08	88.66±14.22	0.7822
HR4	85.36±9.13	89.88±14.51	**0.0652**
HR6	84.20±8.64	91.88±14.61	**0.0019**
HR8	83.20±8.68	94.02±14.31	**<0.001**
HR10	82.68±8.62	94.64±14.75	**<0.001**
HR12	82.56±9.27	95.48±13.51	**<0.001**
HR14	83.20±9.81	96.68±13.73	**<0.001**
HR16	83.30±9.87	97.02±13.32	**<0.001**
HR18	83.36±9.28	97.18±13.13	**<0.001**
HR20	83.80±8.72	96.24±13.21	**<0.001**
HR25	84.44±8.55	94.58±14.09	**<0.001**
HR30	85.56±8.33	94.20±13.16	**<0.001**
HR35	86.08±8.17	93.46±12.61	**<0.001**
HR40	86.68±7.99	92.18±12.78	**0.0114**
HR45	86.98±7.73	91.66±12.52	**0.0267**
HR50	86.82±7.40	91.26±12.24	**0.0305**
HR55	86.82±7.32	90.30±11.43	0.0728
HR60	86.38±7.00	89.84±11.20	0.0670

HR- Heart rate (beats per minute)

Subscript of HR indicates timing (minute) of heart rate recording.

VP- Time of administration of vasopressor.



Graph 7 : Intraoperative changes in heart rate.

- Basal HR in Phenylephrine group was 89.52±11.89 and Ephedrine group was 92.20 ± 11.56 .
- Mean HR during hypotension in groups P was 90.04 ± 11.71 bpm while in group E was 88.02 ± 15.45bpm. Both were found to be statistically comparable.
- Phenylephrine group shows a significant fall in HR while in Ephedrine group there is a significant rise in the HR.

DISCUSSION

The most common side effect following spinal anaesthesia is hypotension.[1] Prevention and treatment of hypotension remains a frequent problem with no consensus in the optimal mode of management.

Fluid preloading with intravenous crystalloid or colloid solutions is a standard practice for prevention of hypotension but it has been found to be ineffective if used alone, without concomitant use of vasopressor drugs. Inadequately treated hypotension occurring during Caesarean section can cause undue effects on both mother and fetus. There have been several attempts to find the optimal therapy for hypotension occurring during Caesarean section.

Since sympathetic blockade resulting in vasodilatation is the primary cause of fall in arterial pressure, use of vasopressors in conjunction with fluid preloading appears to be a more logical approach to correct it. It has been shown that the percentage decrease in placental circulation is related to percent of reduction in maternal arterial pressure but not absolute reduction in pressure.

Incidence of hypotension clearly depends on its definition. Hypotension in most of the studies has been defined as values ranging form 20 to 30 percent reduction from baseline systolic arterial pressure or mean arterial pressure.[13] In our study we defined hypotension as decrease in systolic arterial pressure 20 percent from the baseline systolic pressure. We defined bradycardia as fall in heart rate of 20 percent or more from the baseline value.

The role of intravenous vassopressors has been well established in case of post spinal hypotension during Caesarean section. Ephedrine acts directly as well as indirectly on alpha and beta adrenergic receptors. Phenylephrine has selective alpha adrenergic activity due to which it was considered to cause reduction in uterine blood flow, but it has been mentioned that Phenylephrine causes less fetal acidosis than Ephedrine in a review by Ngan et al. [28]

In this study both the vasopressors maintained arterial blood pressure within 80 percent of limit of baseline value, although Phenylephrine maintained a better blood pressure starting in first 2 minutes of administration than Ephedrine. **(Table 5)**. These results correlate with a previous study conducted by Sahu et al.[22] This is because Phenylephrine has peak effect within 1 minute whereas Ephedrine has up to 5 minutes.

The blood pressure rise in Phenylephrine group was more as compared to Ephedrine group. **(Table 5 and 6, Graph 4, 5 and 6).** This finding is similar to that of the previous study where there was significant rise in blood pressure in Phenylephrine group than in Ephedrine group.[22] This can be attributed to direct action of Phenylephrine on alpha receptor where as less rise with Ephedrine can be explained by their indirect action of releasing catecholamine.

Moran and colleagues[34] gave Ephedrine 10 mg or Phenylephrine 80 mcg bolus to maintain systolic blood pressure above 100. They concluded that Phenylephrine is as effective as Ephedrine and when used in incremental bolus, it appears to have no adverse effect on the mother and the fetus. Thomas and colleagues[18] reported that bolus Phenylephrine 100 mcg is as effective as Ephedrine 5 mg in restoring maternal blood pressure above 100 mm of Hg.

In our study we also found that both the drugs maintained blood pressure ≥ 80 % of baseline values **(Table 5, 6),** although the dose of Phenylephrine used was comparatively less than in the similar studies.[34]

In our study, cardiovascular stability was better with Phenylephrine. A significant reduction in heart rate after the bolus dose of Phenylephrine was observed which may be attributed to positive inotropic and negative chronotropic effect of Phenylephrine. This has been consistent effect in other studies also.

In the study by Moran DH [34], there was significant bradycardia which was treated with Atropine. Similarly, Thomas DG et al[18] showed 58 % incidence of bradycardia (defined as heart rate below 60 beats per minute) when 100 mcg of Phenylephrine was given as intravenous bolus after induction of spinal anaesthesia. In our study although there was bradycardia, after administration of Phenylephrine, but it was not significant enough to warrant treatment. This can be attributed to less dose of drug administered. [34]

In Ephedrine group, the heart rate increased after the bolus dose, compared to the pre - drug administration values which we found statistically significant and the data was consistent with study of Shau[22]. This tachycardia may be attributed to beta adrenergic effect of Ephedrine which Phenylephrine lacks.

Other studies had compared neonatal effects based on umbilical cord blood pH for both the drugs. In our study we had compared only APGAR score, and there was no significant effect on the APGAR score of baby at 1 and 5 minutes in both the groups, which correlated well with study by Sahu. [22]

Use of Phenylephrine in pregnant patients has always been an issue of debate and controversy, because of its alpha effect causing placental vasoconstriction. In a recent metanalysis by Ngan et al[28] Phenylephrine was suggested to be the ideal agent for hypotension caused by spinal anaesthesia. Other studies using Phenylephrine in pregnant patients have found that although it causes fetal acidosis, it's less than that caused by Ephedrine and is non detrimental to neonatal outcome. [12, 16, 17, 18]

To summarize, we found that SBP was significantly high in Phenylephrine group within 2 min of administration of a bolus dose as compared to Ephedrine. A mean dose of 48 mcg and 8.4 mg was used for Phenylephrine and Ephedrine respectively.

There was a reduction in heart rate with Phenylephrine. Number of boluses required and neonatal APGAR scores were comparable in both Phenylephrine and Ephedrine groups.

CONCLUSION

From our study we conclude that, Phenylephrine in a dose of 40 microgram is more efficacious in comparison to Ephedrine 6 milligrams in maintaining arterial blood pressure following spinal anaesthesia for Caesarean section.

Phenylephrine has a quicker peak effect (within 2 minutes of IV bolus) as compared to Ephedrine (within 10 minutes of IV bolus) and causes a reduction in heart rate as compared to Ephedrine.

A dose of 48 mcg of Phenylephrine and 8.4 mg Ephedrine was found to be effective in maintaining arterial blood pressure within the normal range.

SUMMARY

The present study "One year randomized clinical trial to compare the efficacy of intravenous bolus Phenylephrine and Ephedrine in maintaining arterial blood pressure during spinal anaesthesia in Caesarean section" was carried out in the Department of Anaesthesiology , KLE Society's Dr. Prabhakar Kore Hospital and Medical Research Centre, Belgaum .

The study included 100 patients undergoing elective as well as emergency Caesarean section under spinal anaesthesia who developed hypotension after subarachnoid block. They were randomly allocated to one of the groups to receive an IV bolus of following

Group P– Phenylephrine 40 mcg each IV bolus.

Group E– Ephedrine 6 mg each IV bolus.

The study vasopressor drug was given whenever hypotension occurred following subarachnoid block. Hypotension was defined as fall in SBP ≥ 20 percent from baseline value or SBP < 90 mm of Hg.

Our study revealed that SBP was significantly high in Phenylephrine group within 2 min of administration of a bolus dose as compared to Ephedrine. A mean dose of 48 mcg and 8.4 mg of Phenylephrine and Ephedrine respectively was required. There was a reduction in heart rate with Phenylephrine. Number of boluses required and neonatal APGAR scores were comparable in both Phenylephrine and Ephedrine groups.

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ANNEXURE - I

CONSENT FOR PARTICIPATION IN RESEARCH STUDY

Mrs. _____ we request you to enroll yourself in this study titled, **" ONE YEAR RANDOMIZED CLINICAL TRIAL TO COMPARE THE EFFICACY OF INTRAVENOUS BOLUS PHENYLEPHRINE AND EPHEDRINE IN MAINTAINING ARTERIAL BLOOD PRESSURE DURING SPINAL ANAESTHESIA IN CAESAREAN SECTION"** conducted by Dr. Kusha Nag, Post Graduate in M.D. Anaesthesiology under the guidance of Dr. S. N Suresh M.D DA., Professor, Department of Anaesthesiology, KLE Society's Prabhakar Kore Hospital and Medical Research Centre, Belgaum.

Respected Sir/Madam we request you to enroll yourself to participate in our study as you are eligible for participating in the study. During the study you will be asked some questions regarding your present complaint and you are supposed to answer to the best of your knowledge.

Your participation in research is voluntary. Your decision whether or not to participate in the study will not affect your relationship with J. N. Medical College. If you decide to participate you are free to withdraw at any time.

The purpose of research is to compare the efficacy of Phenylephrine and Ephedrine to maintain blood pressure during spinal anaesthesia in Caesarean section.

Procedure Involved :

If you agree to enroll yourself in my study, I will ask your present past and family history. Then you will be clinically examined in detail and investigations like Hemoglobin, urine analysis for albumin, sugar and microscopy will be done.

Risks and Benefits :

Phenylephrine may be associated with sudden rise in blood pressure, headache or episodes of nausea and vomiting but it shows a rapid and sustained control of arterial hypotension due to spinal anaesthesia without any metabolic side effects on the fetus.

Alternatives :

Even if you decline the participation in the study, you will get the routine line of management.

Privacy and Confidentiality :

The only people to know that you are a research subject are members of the research team.

No information about you or information provided by you during the research will be disclosed to others without your written permission except :

1. In emergency to protect your rights and welfare.
2. If required by law.

Authorization to Publish Results :

When the results of the research are published or discussed, in a conference, no information will be displayed that would disclose your identity. Any information that is obtained in connection with this study and that can be identified with you will remain confidential.

Compensation :

In the event of injury related to the study, treatment will be made available through KLE Society's Prabhakar Kore Hospital and Medical Research Centre, Belgaum. There is no compensation or payment for such medical treatment by law.

If you are injured you may contact Dr. Kusha Nag M. D Anaesthesiology, Jawaharlal Nehru Medical college, Belgaum. Phone : 9916190661.

Questions : In case you have any questions related to the study, you can contact Dr. Kusha Nag. Phone : 9916190661.

In case you have any questions about your rights as a study participant, you can contact Dr. V. D. Patil (0831-2471350).

CONSENT STATEMENT

I, Mrs _____ voluntarily agree for the participation as a subject of study. By signing this consent form I am not giving up any of my legal rights, I may withdraw from the study anytime. I am signing the consent form after having read or been read for me in vernacular language, including the risks and the benefits and having all my questions answered.

Subject Name : _____

Signature or the Left thumb print of subject : _____

Witness Name : _____ ***Signature :*** _____

Investigators name: _____ Signature : _____

Date : _____

Place : _____

ANNEXURE – II

PROFORMA

Name & Address of the patient : _____

_____

Age of the patient : _____ years

IP.No. _____

Anaesthesiologist : _____ ***Surgeon:*** _____

PREANAESTHETIC EVALUATION :

Chief Complaints :

Past History :

Family History :

General Physical Examination :

Weight : Temperature : Pallor : Height

Cyanosis : Pedal Edema : Clubbing :

Pulse : B.P : RR :

SYSTEMIC EXAMINATION :

Respiratory System : Cardiovascular System :

Central Nervous system:

Per Abdomen :

Air way assessment :

Spine assessment :

INVESTIGATIONS :

Hb%:

Urine: Albumin -

Sugar -

Microscopy -

Others(if any) :

Diagnosis :

Proposed Surgery :

Inclusion Criteria :

1) Singleton full term pregnant patients undergoing elective and emergency
2) Caesarean section.
3) Age: 25-30yrs.
4) ASA Grade I &II.

Exclusion Criteria

1) Multiple pregnancies.
2) Hypertension.
3) Diabetes.
4) Cardiac, Pulmonary or renal diseases.
5) Fetal abnormalities.
6) Contraindications to spinal anesthesia.

Methodology:

After having met all the inclusion and exclusion criteria and obtaining written informed consent, parturients will be randomized into two groups of 50 using computer generated randomization table. Study drugs will be prepared and dispensed in syringes labeled as "Study Vasopressor." by an anaesthesiologist not involved in this study.

Each patient will receive 10ml / kg of Ringer lactate solution before spinal anaesthesia. On arrival to the operating room baseline systolic, diastolic blood pressure, mean arterial pressure, pulse rate, pulse oximetry values will be recorded using routine monitoring devices.

Patients receive an intrathecal injection of 2.0 cc of 0.5% hyperbaric Bupivacaine at L_3- L_4 level. Immediately after the injection patient will be placed on supine position. And oxygen administered at rate of 5 Litre / min. Level of sensory block assessed after 5 min by pinprick method.

Arterial blood pressure measurements performed at 2 min interval for initial 10 min and at 5 min interval thereafter.

Each time hypotension occurred (systolic blood pressure fall > 20% of basal value or less than 90 mm of Hg.), Phenylephrine group (group P, n=50) will receive 40 mcg intravenous bolus Phenylephrine and Ephedrine group (group E, n=60) will receive 6 mg Ephedrine intravenous bolus.

Time taken to develop hypotension and number of boluses will be noted. Paediatrician will assess APGAR score of every neonate at 1 min and 5 min after delivery.

Observations :

Post block arterial pressure & pulse rate:

Time	0	2	4	6	8	10	12	14	16	18	20
NIBP(mmHg)											
PR(bpm)											

Time	25	30	35	40	45	50	55	60
NIBP(mmHg)								
PR(bpm)								

Block height achieved after 5 min:

Study drug administered at (…….min after administration of spinal anaesthesia):

1st dose:

2nd dose:

3rd dose:

4th dose:

5th dose:

Number of bolus:

Total dose of study drug given:

Uterine incision (time):

Delivery of baby:

Neonatal data:

APGAR SCORE(1min):

APGAR SCORE(5min):

Total amt of fluids given intra-operatively:

Duration of surgery:

Side effect, if any:

Signature of staff in charge:

Group P	Age	IP no.	Height	Hb	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	DBP
S.N.	Yrs		(cms)		Basal	Hypo	2	4	6	8	10	12	14	16	18	20	25	30	35	40	45	50	55	60	Basal
1	25	257213	150	10.8	134	88	98	112	110	104	114	114	112	112	130	129	132	128	129	128	120	122	120	120	84
2	26	256149	154	11.2	116	80	98	130	132		28	112	109	112	108	110	124	120	116	114	109	106	102	102	80
3	25	261593	152	12.4	126	88	94	101	102	87	92	97	100	108	105	110	111	100	103	102	100	102	103	101	86
4	26	259499	151	9.8	130	86	90	130	132	130	132	128	128	132	122	120	124	120	118	116	117	118	116	119	80
5	25	256591	150	10.4	114	88	128	132	130	132	131	128	122	124	122	118	120	119	118	119	118	117	116	117	60
6	28	257594	148	11.2	120	86	110	111	116	118	117	116	117	108	104	106	105	106	108	110	112	114	112	108	80
7	26	277610	156	10.8	115	80	114	121	130	125	120	122	118	116	114	115	112	110	111	112	108	109	110	111	82
8	27	288184	152	12.4	122	86	110	116	120	122	118	116	114	116	112	110	112	108	109	112	114	118	119	117	82
9	26	277898	152	10.2	130	88	113	122	132	130	126	126	124	120	124	121	120	118	119	117	118	119	116	114	92
10	25	277838	150	11.2	138	88	117	132	142	136	134	128	124	122	119	118	113	111	112	113	110	112	108	106	89
11	26	277841	151	11.5	130	88	120	125	128	124	120	118	118	116	117	114	114	112	111	110	110	108	106	108	90
12	28	277272	154	12.4	130	88	110	112	126	124	120	118	118	116	114	115	115	114	110	111	108	107	106	104	86
13	25	278189	151	11	130	80	88	108	112	120	124	128	126	128	120	118	116	114	114	115	116	116	118	119	82
14	28	277986	153	12.1	134	100	106	114	117	118	116	114	114	112	107	108	107	104	106	105	104	105	108	110	84
15	26	278192	154	10.2	116	80	98	118	124	121	120	118	116	114	112	110	111	113	111	109	110	108	107	105	82
16	25	278055	152	11.4	126	80	100	102	100	104	105	98	86	111	118	116	119	118	116	114	114	113	112	110	82
17	26	278608	150	11.4	125	110	85	98	114	116	120	118	116	114	113	113	114	114	112	108	109	110	108	107	84
18	27	278924	151	12	122	63	68	84	84	89	95	101	98	98	97	104	103	103	102	102	103	102	101	100	73
19	28	279991	150	12.2	110	94	112	114	113	112	116	126	124	121	118	119	117	118	115	113	108	109	110	113	70
20	29	280001	154	11.2	112	78	126	131	130	126	104	110	110	112	111	111	110	100	104	106	107	104	102	103	78
21	32	288755	153	11.2	120	80	100	110	112	90	90	80	100	100	100	100	100	96	98	98	100	104	102	102	76
22	28	288941	149	12.4	125	88	118	122	126	124	120	118	116	117	115	116	114	114	115	118	114	110	108	106	80
23	28	288276	148	10.8	118	82	116	118	122	121	118	116	115	114	114	115	113		112	110	109	108	107	104	86
24	27	288327	150	12.1	122	63	89	108	118	121	116	114	113	113	108	109	106	107	104	106	104	104	103	101	73
25	29	288450	153	11.8	106	84	93	98	98	107	106	104	104	106	108	107	108	106	103	102	101	100	101	102	60
26	28	288474	151	10.8	133	86	118	118	120	118	116	115	116	114	117	118	120	119	116	114	112	114	109	110	60
27	28	288843	149	11.4	124	86	95	114	124	122	120	118	119	116	114	112	110	106	108	109	111	114	110	109	79
28	27	288868	152	12.2	112	78	96	114	116	118	118	116	114	113	111	110	108	109	107	106	110	104	118	120	78
29	26	288876	151	11.8	132	86	98	114	116	118	120	118	119	116	114	112	113	112	110	108	109	106	104	102	92
30	25	288884	152	10.8	110	85	98	117	118	116	115	114	113	112	113	118	120	120	116	114	113	112	113	114	70
31	28	288892	150	12.6	128	86	94	96	111	114	118	117	117	116	114	115	114	113	111	112	110	109	107	108	84
32	30	288760	151	11.4	130	90	98	112	118	120	121	119	119	118	117	115	115	116	116	116	117	118	119	117	92
33	29	288842	154	9.8	122	84	98	100	106	108	112	114	115	117	118	118	114	112	90	98	112	116	118	121	84
34	26	288954	151	10.6	130	84	101	108	121	124	120	121	118	118	119	119	120	120	118	118	116	115	108	109	94
35	25	288968	149	11.6	124	87	92	105	107	110	112	114	112	111	110	109	109	109	108	107	111	113	112	110	86
36	27	288975	150	11	110	72	98	110	114	112	105	102	101	84	112	114	112	116	118	117	120	121	118	114	72
37	30	294321	152	11.8	124	86	95	114	124	122	120	118	119	112	110	106	108	110	112	110	108	109	109	110	79
38	26	295457	150	12.2	130	85	90	110	114	118	120	120	119	119	118	119	118	120	120	119	116	117	118	117	90
39	28	297986	150	12.2	134	92	98	112	110	114	110	114	114	112	112	107	108	107	104	106	105	104	108	106	84
40	27	298765	152	11.6	133	86	118	118	120	118	116	116	115	116	114	117	118	118	120	120	119	118	119	116	96
41	27	295152	150	11.4	120	80	98	112	114	115	117	117	116	115	115	114	115	116	115	114	112	108	109	108	80
42	23	295682	152	10.8	128	85	98	117	118	116	115	114	114	113	112	113	115	117	118	120	118	119	118	117	70
43	28	296004	153	12.2	112	70	96	114	116	118	114	114	112	113	112	110	110	109	110	112	111	109	108	106	78
44	26	297542	150	12.2	130	83	95	114	116	118	120	120	120	118	118	119	119	120	122	120	120	119	118	119	90
45	25	296003	152	10.8	120	78	98	104	108	110	110	112	104	90	87	98	110	112	114	116	114	112	111	110	86
46	28	297854	150	11.6	120	82	92	104	108	110	112	114	116	118	120	122	120	118	119	118	119	117	117	117	80
47	25	298783	154	11.2	124	78	84	86	87	94	104	108	110	116	118	120	122	120	118	118	119	117	116	116	82
48	26	299856	152	11.4	130	84	90	110	114	112	114	116	118	117	116	117	117	116	116	114	114	113	112	112	80
49	25	300104	150	11.8	115	68	72	88	110	118	122	124	122	120	120	120	119	119	118	119	118	117	116	112	80
50	26	299474	152	12.2	130	82	98	112	114	116	118	120	118	116	114	116	112	111	112	109	108	106	104	105	80

Group P	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	MBP	MAP	MAP	MAP	MAP	MAP
S.N.	Hypo	2	4	6	8	10	12	14	16	18	20	25	30	35	40	45	50	55	60	Basal	Hypo	2	4	6	8
1	45	60	63	60	56	60	68	60	68	64	64	64	82	80	84	80	78	72	74	101	59	73	79	77	72
2	60	62	98	100	98	92	90	84	72	76	70	68	69	70	78	82	79	75	72	92	67	74	109	111	65
3	54	57	65	63	52	56	57	65	64	68	64	58	62	64	60	62	58	60	56	99	65	69	77	76	64
4	52	60	94	92	89	90	84	84	82	80	76	70	72	76	70	72	76	74	70	97	63	70	106	105	103
5	54	78	82	89	92	89	86	82	84	78	76	74	75	80	78	76	78	80	79	78	65	95	99	103	105
6	54	62	72	68	65	60	62	58	60	62	81	60	58	60	62	64	68	70	68	93	65	78	85	84	83
7	60	65	86	84	78	75	77	78	80	78	75	74	75	74	76	74	72	72	70	93	67	81	98	99	94
8	52	70	78	72	68	66	68	70	68	67	62	65	62	64	67	65	62	64	67	95	63	83	91	88	86
9	54	68	72	86	84	87	92	87	86	84	82	84	82	78	80	82	79	76	77	105	65	83	89	101	99
10	45	98	100	102	98	92	89	87	84	82	78	70	76	72	70	72	68	62	64	105	59	104	111	115	111
11	54	62	74	78	82	80	78	78	76	76	74	74	72	70	68	68	67	68	70	103	65	81	91	95	96
12	45	58	62	65	68	72	71	68	65	66	67	64	58	58	56	56	58	54	54	101	59	75	79	85	87
13	52	50	52	63	62	64	68	69	70	68	69	67	68	69	70	78	74	72	76	98	61	63	71	79	81
14	54	43	60	63	60	62	63	65	68	64	60	62	61	56	58	58	56	62	64	101	69	64	78	81	79
15	56	62	65	68	71	70	68	67	68	66	65	61	64	65	67	63	64	63	64	93	64	74	83	87	88
16	50	62	62	60	62	64	54	48	54	58	60	58	61	64	62	61	64	62	60	97	60	75	75	73	76
17	62	54	62	64	68	72	70	68	68	68	64	65	69	64	64	68	69	71	70	98	78	64	74	81	84
18	57	34	31	47	47	49	45	44	41	42	52	41	42	52	51	52	54	52	50	89	59	45	49	59	61
19	50	76	78	82	78	78	82	78	78	82	82	78	62	64	65	64	67	68	72	83	65	88	90	92	89
20	42	64	77	78	54	67	70	60	62	64	71	70	64	64	62	64	62	60	61	89	54	85	95	95	78
21	50	64	62	60	64	67	54	56	60	64	60	62	64	60	62	64	65	62	60	91	60	76	78	77	73
22	54	62	70	78	82	80	78	76	76	75	72	72	68	68	64	62	64	65	64	95	65	81	87	94	96
23	49	52	58	64	68	72	72	70	68	66	68	71	72	70	72	70	73	74	75	97	60	73	78	83	86
24	34	36	38	42	47	52	52	54	52	56	58	54	52	48	50	46	48	46	50	89	44	54	61	67	72
25	41	46	51	59	58	54	58	62	60	58	54	52	52	48	48	50	52	54	50	75	55	62	67	72	74
26	52	58	60	62	64	64	68	67	67	68	67	68	67	65	68	70	72	70	68	84	63	78	79	81	82
27	55	62	66	81	89	86	84	82	80	78	74	68	68	72	75	79	82	80	78	94	65	73	82	95	100
28	48	52	56	60	62	64	65	64	68	72	68	70	72	70	69	68	71	74	74	89	58	67	75	79	81
29	34	48	57	62	68	72	72	74	72	727	68	68	70	69	67	64	62	62	64	105	51	65	76	80	85
30	54	62	64	65	68	68	65	65	64	65	62	68		68	72	70	68	66	65	83	64	74	82	83	84
31	56	58	62	64	67	69	72	70	71	70	70	68	64	65	68	66	67	69	70	99	66	70	73	80	83
32	54	58	62	68	69	72	72	74	76	77	75	78	78	82	84	85	84	84	87	105	66	71	79	85	86
33	48	57	62	64	68	74	78	82	86	85	88	86	84	84	82	75	60	78	76	97	60	71	75	78	81
34	54	68	74	78	82	78	79	80	78	76	77	75	74	75	72	71	70	71	72	106	64	79	85	92	96
35	54	58	62	67	72	76	78	82	80	81	78	76	75	75	72	74	72	71	70	99	65	69	76	80	85
36	42	40	46	52	62	58	56	54	58	62	66	68	72	74	74	76	74	76	74	85	52	59	67	73	79
37	55	66	81	89	86	84	82	80	78	74	68	68	72	74	78	82	80	78	78	94	65	76	92	101	98
38	54	60	68	72	78	80	80	82	82	82	80	80	78	78	79	79	79	80	80	103	64	70	82	86	91
39	43	60	60	68	64	64	60	62	61	58	58	60	58	59	58	59	60	60	58	101	59	73	77	82	81
40	52	58	60	62	64	68	72	71	70	72	70	70	71	68	68	68	69	68	67	108	63	78	79	81	82
41	45	60	64	67	68	68	64	64	62	60	60	59	58	58	60	62	60	60	58	93	57	73	80	83	84
42	54	62	68	70	72	70	68	68	69	69	70	71	70	68	69	68	68	70	68	89	64	74	84	86	87
43	48	52	56	62	64	64	64	72	68	69	69	70	72	72	79	70	72	74	72	89	55	67	75	80	82
44	53	62	64	68	74	78	78	80	82	80	80	82	82	84	82	80	80	78	79	103	63	73	81	84	89
45	55	54	52	54	60	62	62	60	58	50	58	62	68	70	72	74	76	78	74	97	63	69	69	72	77
46	43	49	52	54	58	59	62	64	68	72	74	78	80	80	78	79	80	81	80	93	56	63	69	72	75
47	48	52	50	52	58	62	64	70	72	78	78	80	80	79	78	78	76	77	78	96	58	63	62	64	70
48	50	58	60	68	70	72	78	76	78	79	80	80	82	80	79	79	78	78	80	97	61	69	77	83	84
49	45	54	62	68	74	78	82	82	80	80	80	82	80	78	76	76	77	75	74	92	53	60	71	82	89
50	53	60	62	60	72	78	74	76	74	76	74	73	74	72	70	68	70	69	70	97	63	73	79	78	87

Group P	MAP	MAP	MAP	MAP	MAP	MAP	MAP	MAP	MAP	MAP	MaP	MAP	MAP	MAP	PR	PR	PR	PR	PR	PR	PR	PR	PR	PR	PR
S.N.	10	12	14	16	18	20	25	30	35	40	45	50	55	60	Basal	Hypo	2	4	6	8	10	12	14	16	18
1	78	83	77	83	86	86	87	97	96	99	93	93	88	89	98	96	94	90	92	92	94	92	94	92	90
2	71	97	92	85	87	83	87	86	85	90	91	88	84	82	84	73	74	76	74	72	69	68	63	71	72
3	68	70	77	79	80	79	76	75	77	74	75	73	74	71	86	84	86	71	73	84	88	90	93	97	92
4	104	99	99	99	94	91	88	88	90	85	87	90	88	86	82	84	82	80	78	76	76	74	75	76	78
5	103	100	95	97	93	90	89	90	93	92	90	91	92	92	92	86	88	84	84	83	84	86	86	85	85
6	79	80	78	76	76	89	75	74	76	78	80	83	84	81	100	95	92	95	94	92	90	95	96	92	90
7	90	92	91	92	90	88	87	87	86	88	85	84	85	84	80	79	80	84	85	84	87	87	86	85	83
8	83	84	85	84	82	78	81	77	79	82	81	81	82	84	92	89	89	84	86	84	82	82	84	83	83
9	100	103	99	97	97	95	96	94	92	92	94	92	89	89	92	94	91	89	87	86	82	85	86	85	86
10	106	102	99	97	94	91	84	88	85	84	85	83	77	78	97	89	82	84	82	78	76	78	82	85	84
11	93	91	91	89	90	87	87	85	84	82	82	81	81	83	76	75	70	68	64	65	66	67	69	68	68
12	88	87	85	82	82	83	81	77	75	74	73	74	71	71	67	85	58	62	64	65	67	64	68	68	70
13	84	88	88	89	85	85	83	83	84	85	91	88	87	90	104	102	98	92	86	85	86	87	85	84	86
14	80	80	81	83	78	76	77	75	73	74	73	72	77	79	110	98	100	90	92	89	87	88	87	86	87
15	87	85	83	83	81	80	78	80	80	81	79	79	78	78	84	76	74	75	76	74	72	68	70	72	76
16	78	69	61	73	78	79	78	80	81	79	79	80	79	77	98	84	86	92	98	96	94	89	92	94	95
17	88	86	84	83	83	80	81	84	80	79	82	83	83	82	92	89	89	84	82	82	78	79	76	78	77
18	64	64	62	60	60	69	62	62	69	68	69	70	68	67	84	86	82	78	76	74	75	76	74	77	78
19	91	97	93	92	94	94	91	81	81	81	79	81	82	86	108	98	94	96	95	94	86	95	96	97	95
20	79	83	77	79	80	84	83	76	77	77	78	76	74	75	112	114	102	96	94	92	93	92	94	92	88
21	75	63	71	73	76	73	75	75	73	74	76	78	75	74	112	110	108	92	80	82	76	76	86	72	74
22	93	91	89	90	88	87	86	83	84	82	79	79	79	78	80	76	75	74	72	69	70	71	72	74	73
23	87	87	85	83	82	84	85	48	84	85	83	85	85	85	80	76	74	72	70	68	69	67	68	65	66
24	73	73	74	72	73	75	71	70	67	69	65	67	65	67	84	86	85	82	78	76	75	74	72	68	67
25	71	73	76	75	75	72	71	70	66	66	67	68	70	67	98	90	86	87	90	89	90	91	90	92	89
26	81	84	83	83	84	84	85	84	82	83	84	86	83	82	87	82	78	76	75	77	76	75	75	76	74
27	97	95	94	92	90	87	82	81	84	86	90	93	90	88	78	112	102	98	92	88	86	82	85	86	87
28	82	82	81	83	85	82	83	84	82	81	82	82	89	89	100	95	94	89	88	84	87	89	92	96	92
29	88	87	89	87	523	83	83	84	83	81	79	77	76	77	62	92	89	87	84	82	78	76	78	82	84
30	84	81	81	80	81	81	85	40	84	86	84	83	82	81	98	96	92	89	86	84	83	82	83	84	87
31	85	87	86	86	85	85	83	80	80	83	81	81	82	83	72	92	94	96	97	99	102	104	110	112	111
32	88	88	89	90	90	88	90	91	93	95	96	95	96	97	86	98	96	87	86	87	85	85	85	87	88
33	87	90	93	96	96	98	95	93	86	87	87	79	91	91	75	114	110	98	92	87	84	78	79	82	86
34	92	93	93	91	90	91	90	89	89	87	86	85	83	84	70	98	96	87	85	84	82	80	78	79	82
35	88	90	92	90	91	88	87	86	86	84	86	86	85	83	98	94	89	86	84	82	80	81	80	78	80
36	74	71	70	67	79	82	83	87	89	88	91	90	90	87	72	98	97	92	90	87	86	85	82	86	85
37	96	94	93	89	86	81	81	85	87	89	91	90	88	89	90	92	92	90	89	88	89	89	88	88	89
38	93	93	94	94	94	93	93	92	92	92	91	92	93	92	90	88	89	87	88	88	87	87	88	86	87
39	79	78	79	78	76	74	76	74	74	74	74	75	76	74	110	98	100	100	90	92	90	90	92	89	89
40	84	87	86	85	86	86	86	87	85	85	85	85	85	83	87	82	78	76	77	76	75	75	76	74	74
41	84	82	81	80	78	78	78	77	77	78	79	76	76	75	80	45	60	63	68	62	67	64	62	62	60
42	85	83	83	84	83	84	86	86	85	86	85	85	86	84	98	96	96	92	92	90	91	90	90	91	89
43	81	81	85	83	83	83	83	84	85	90	84	84	85	83	100	98	99	98	98	97	98	96	95	95	96
44	92	92	93	94	93	93	94	95	97	95	93	93	91	92	96	94	92	92	90	89	89	87	87	86	87
45	78	79	75	69	62	71	78	83	85	87	87	88	89	86	96	94	92	90	92	93	94	95	96	96	95
46	77	79	81	85	88	90	92	93	93	91	92	92	93	92	87	86	84	84	82	82	84	85	84	82	80
47	76	79	83	87	91	92	94	93	92	91	92	90	90	91	86	84	86	84	82	80	78	80	79	78	79
48	86	91	90	91	91	92	92	93	92	91	91	90	89	91	86	84	82	82	82	81	82	80	80	81	82
49	93	96	95	93	93	93	94	93	91	90	90	90	89	87	80	78	76	74	75	75	74	76	76	76	78
50	91	89	90	88	89	88	86	86	85	83	81	82	81	82	100	98	96	94	94	95	95	96	96	95	95

Group P	PR	PR	PR	PR	PR	PR	PR	PR	PR	of block ac	No. of Bolus	Dose	Complications/	Intervention	Neonatal Data		Duration of	SAB to Hypotension
S.N.	20	25	30	35	40	45	50	55	60				Side effects		APGAR 1 min	APGAR 5 min	surgery	
1	94	96	95	97	98	100	95	97	98	8	1	40	-	-	9	9	80	3
2	74	72	75	76	75	76	74	73	76	7	1	40	-	-	10	10	80	3.5
3	89	78	86	92	97	98	100	96	94	6	2	80	-	-	9	9	70	4
4	79	79	82	84	84	85	83	83	84	8	1	40	-	-	9	9	75	3
5	86	87	85	84	85	84	83	83	82	8	1	40	-	-	10	10	80	3
6	89	86	87	86	90	92	94	97	95	8	1	40	-	-	10	10	75	2
7	82	84	83	83	85	87	87	87	86	7	1	40			9	9	70	4
8	84	87	89	85	83	86	87	86	89	8	1	40	-	-	9	9	60	4.5
9	87	88	87	86	85	87	86	89	87	8	1	40	-	-	10	10	60	4
10	82	84	82	85	84	82	81	80	82	8	1	40	-	-	9	10	75	3
11	69	70	70	72	73	71	72	73	72	6	1	40			9	9	50	3
12	74	75	76	78	82	85	84	92	80	8	1	40	-		10	10	50	4
13	87	84	86	87	88	90	89	86	87	6	1	40	-	-	10	10	80	3
14	91	92	93	92	91	95	94	95	92	8	1	40	-	-	9	10	60	3
15	78	80	84	86	84	85	87	83	82	6	1	40	-	-	9	10	80	4
16	92	89	90	88	87	86	87	88	87	6	2	80	-	-	10	10	90	3
17	79	82	84	85	83	84	82	83	82	6	1	40	-	-	9	9	60	5
18	80	82	81	85	83	82	78	81	82	8	2	80	-	-	10	10	60	5
19	92	92	86	88	86	89	86	87	88	6	2	80	-	-	10	10	75	4
20	86	88	90	91	90	89	91	89	90	6	3	120	-	-	10	10	75	4
21	72	76	76	74	78	78	80	82	80	7	2	80	-	-	10	10	60	3
22	73	75	76	77	78	78	79	81	82	8	1	40	-	-	10	10	65	3
23	68	70	72	73	74	75	78	75	76	7	1	40	-	-	10	10	70	3
24	69	72	74	76	78	78	79	80	83	8	1	40	-	-	10	10	60	2.5
25	87	89	91	90	92	89	90	93	91	8	1	40	-	-	9	10	65	3
26	74	75	75	74	75	76	78	77	76	8	1	40	-	-	10	10	60	2
27	92	94	96	96	94	97	92	86	84	8	1	40		-	9	10	70	3
28	94	95	97	94	99	96	95	91	89	6	1	40			10	10	75	4.5
29	86	87	92	94	90	88	89	88	87	6	1	40	-	-	9	9	55	4
30	86	87	89	92	94	92	94	96	97	6	1	40	-	-	10	10	72	3
31	109	106	104	101	99	98	98	97	94	7	1	40	-	-	10	10	75	3
32	92	92	94	94	97	97	96	99	98	8	1	40	-	-	10	10	75	3.5
33	86	89	92	92	94	94	92	90	89	7	2	80	-	-	10	10	65	3
34	84	86	88	92	94	91	90	92	94	6	1	40	-	-	10	10	70	2
35	81	82	84	82	81	80	80	82	80	7	1	40	-	-	10	10	55	5
36	83	82	86	87	89	92	94	90	87	8	1	40	-	-	10	10	60	4
37	90	90	91	92	92	90	90	89	89	6	1	40	-	-	10	10	65	3
38	88	90	90	89	91	91	92	90	90	7	1	40	-	-	9	9	65	3
39	87	87	86	87	89	91	91	92	92	6	1	40	-	-	9	10	60	4
40	75	75	74	75	76	78	78	77	78	7	1	40	-	-	10	10	60	3
41	62	60	62	60	64	68	70	72	74	6	1	40	-	-	9	9	65	4
42	89	90	92	94	94	93	94	92	92	7	1	40	-	-	10	10	72	3
43	95	97	97	96	96	95	95	96	97	7	1	40	-	-	10	10	75	3
44	88	89	90	90	91	89	89	89	88	6	1	40	-	-	10	10	70	4
45	95	96	97	98	98	99	98	98	97	7	2	80	-	-	10	10	70	5
46	80	85	86	85	83	82	82	81	80	6	1	40	-	-	10	10	70	3
47	80	80	81	82	82	83	83	82	82	7	2	80			10	10	75	2
48	80	78	80	82	81	80	78	79	79	7	1	40	-	-	10	10	70	2
49	77	78	78	79	80	80	80	79	79	6	1	40	-	-	9	9	70	2.5
50	94	95	97	97	98	98	97	98	100	6	1	40	-	-	10	10	70	3

Group E	Age	IP no.	Height	Hb	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	SBP	DBP
S.N.	Yrs		(cms)		Basal	Hypo	2	4	6	8	10	12	14	16	18	20	25	30	35	40	45	50	55	60	Basal
1	26	256488	151	12.2	120	76	110	112	112	114	114	116	114	112	111	110	112	108	108	107	105	105	107	106	68
2	26	258952	152	10	130	90	98	100	102	102	104	102	100	101	100	98	100	102	102	100	104	101	102	100	90
3	26	258604	150	10.4	110	80	100	110	110	112	112	114	112	110	111	112	109	107	108	105	106	104	102	100	60
4	28	258772	149	11.8	125	67	77	112	90	108	109	113	112	121	118	119	118	116	114	115	115	114	112	111	73
5	29	258790	148	11.2	130	80	90	92	92	92	94	94	86	92	94	100	102	104	105	106	104	107	106	108	80
6	28	269380	155	12	140	94	112	110	113	118	116	115	114	113	112	110	112	111	110	108	109	107	105	104	80
7	25	272087	151	10	110	92	108	112	110	114	116	114	112	110	109	107	106	104	102	100	101	103	102	100	98
8	25	272156	150	10.4	124	90	100	80	100	91	116	114	112	98	94	80	110	114	112	111	110	112	114	112	80
9	28	277638	151	11.2	133	80	90	100	104	105	110	108	109	108	106	108	112	110	112	111	112	114	116	115	90
10	30	277748	153	12.1	130	60	70	80	100	110	114	112	116	112	110	100	100	102	104	102	104	102	101	100	90
11	27	285730	148	10	122	92	94	105	104	103	103	108	111	109	110	108	106	104	103	101	101	100	100	100	70
12	27	287235	149	10.2	128	90	90	114	116	115	118	121	124	118	114	112	111	110	114	116	115	117	117	115	88
13	25	287245	152	11.2	104	65	72	80	86	100	98	101	100	100	102	104	106	102	104	108	110	112	114	115	68
14	31	287264	150	10.8	120	84	92	96	99	105	104	103	103	103	104	106	105	108	107	104	101	99	104	108	70
15	25	290871	151	11.2	110	70	84	89	92	98	100	102	102	101	100	99	100	101	101	100	101	100	101	100	78
16	25	278553	154	10	130	84	13	114	116	122	121	120	118	116	114	117	112	116	118	119	121	122	120	118	92
17	28	279854	152	11.4	118	82	92	98	99	104	103	108	109	110	112	114	113	113	112	113	111	108	109	110	72
18	25	278862	150	11.4	130	80	90	98	95	92	100	110	109	108	106	108	110	112	111	109	109	110	100	106	90
19	30	279029	148	10.8	130	90	100	104	102	104	110	110	112	100	102	104	106	106	108	114	116	120	124	120	70
20	25	280419	149	11.6	130	87	101	111	109	104	101	98	102	93	92	90	80	110	112	114	110	111	108	107	85
21	26	282465	150	12.4	113	88	96	98	94	92	89	102	104	106	108	110	109	106	104	103	101	102	101	100	82
22	25	282579	152	11.8	120	90	100	102	104	101	100	98	92	90	110	106	102	102	102	103	101	102	101	103	80
23	26	282765	153	11.2	120	90	100	110	100	102	104	101	98	92	96	98	100	102	104	102	100	102	102	103	80
24	27	282854	152	10.8	124	90	92	96	98	100	80	100	91	90	100	100	102	104	106	14	103	104	101	102	79
25	25	282920	151	11.2	130	60	70	75	80	100	110	108	109	107	106	104	105	107	104	102	101	102	103	101	92
26	26	283546	150	10.8	130	90	100	102	104	108	106	104	110	108	112	108	106	104	103	102	104	110	105	104	92
27	28	284424	148	11	108	83	101	104	106	104	106	108	104	103	104	104	102	100	101	104	103	104	105	108	70
28	29	288567	152	11.8	112	70	84	92	98	100	102	101	100	104	102	103	102	100	101	102	105	102	106	104	76
29	27	288646	149	11.2	130	84	113	114	116	122	120	118	116	119	120	118	114	113	112	110	108	107	109	107	92
30	28	280805	150	9.8	110	73	86	106	115	118	123	120	114	107	112	118	116	117	115	112	113	112	115	117	73
31	29	288654	152	10.2	122	78	84	87	92	100	102	100	98	100	99	94	86	98	100	114	115	112	113	111	82
32	28	288877	154	11.8	133	86	98	100	102	14	106	108	110	114	119	117	117	116	114	113	111	112	110	110	94
33	25	288931	151	1.2	140	86	98	100	10	107	108	109	110	112	112	114	115	118	121	122	121	120	118	117	94
34	27	288948	153	12.2	124	56	62	84	92	98	100	102	104	102	98	92	89	92	94	96	106	109	112	116	86
35	28	288992	151	10.4	118	76	84	92	94	96	100	16	108	107	104	105	104	102	100	101	101	100	101	100	78
36	30	289991	149	9.8	124	87	94	96	100	104	108	110	108	109	110	109	108	106	107	107	105	105	103	102	82
37	29	293852	152	12.2	128	84	92	98	108	114	118	120	120	119	118	118	116	114	115	116	114	112	113	110	84
38	26	295168	150	12.2	112	70	84	89	86	89	92	98	102	101	100	100	99	100	101	100	100	101	102	100	76
39	28	295104	152	12.2	126	82	90	87	94	98	112	116	118	120	118	117	116	115	114	114	112	111	110	110	84
40	26	295222	152	10.8	120	78	82	84	86	92	98	110	109	112	112	111	112	114	113	113	114	112	111	110	80
41	25	269380	151	12	140	92	112	110	111	108	90	98	114	116	115	114	115	116	118	118	117	117	116	117	80
42	25	296754	154	12.1	130	128	60	70	75	82	80	100	110	108	109	107	109	110	112	111	110	109	108	107	92
43	28	298632	151	10.2	120	117	111	84	92	99	108	110	112	111	110	110	109	108	109	110	112	112	111	110	70
44	26	299695	154	10.4	130	90	98	100	102	16	109	110	112	114	116	115	114	112	112	114	113	112	111	110	90
45	26	295401	152	11.2	121	66	83	111	116	115	114	115	116	118	116	114	112	110	111	110	112	111	110	109	79
46	25	298812	154	11.2	120	84	110	111	116	118	117	115	116	116	116	116	118	117	116	114	112	108	108	108	80
47	30	298595	153	11	106	72	84	93	85	98	107	108	110	109	109	108	107	105	104	106	104	103	102	100	60
48	25	297654	152	11.8	130	84	98	104	198	110	110	110	112	111	114	116	114	115	114	113	112	111	110	110	92
49	27	299614	153	11.6	130	68	70	80	100	110	114	112	112	116	117	115	114	112	111	109	108	109	110	110	90
50	25	230001	152	10.8	112	68	72	84	75	89	94	110	112	110	111	114	116	115	114	115	116	115	114	112	78

Group E	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	DBP	MAP	MAP	MAP	MAP	MAP	MAP
S.N.	Hypo	2	4	6	8	10	12	14	16	18	20	25	30	35	40	45	50	55	60	Basal	Hypo	2	4	6	8
1	56	70	78	80	76	78	74	72	68	65	62	60	62	61	60	68	65	67	64	85	63	83	89	91	89
2	56	60	62	60	62	64	68	70	72	68	62	60	62	68	67	72	74	68	67	103	67	73	75	74	75
3	54	58	57	62	60	60	58	62	58	54	56	58	62	60	58	62	60	62	60	77	63	72	75	78	77
4	45	50	58	60	62	72	73	77	83	71	70	70	68	64	66	64	62	64	60	90	52	59	76	70	77
5	50	58	60	61	62	64	66	64	62	64	64	62	64	64	65	67	64	62	58	97	60	69	71	71	72
6	46	59	62	58	46	72	70	68	65	64	60	62	67	64	62	60	64	63	64	100	62	77	78	76	70
7	56	62	68	72	74	72	70	74	72	68	64	62	60	56	51	54	56	52	50	102	68	77	83	85	87
8	54	60	68	65	64	60	58	60	60	62	74	74	76	72	72	68	64	67	65	95	66	73	72	77	73
9	54	58	60	60	59	62	64	64	68	70	72	70	71	72	70	72	70	72	70	104	63	69	73	75	74
10	50	52	56	58	60	62	64	61	60	64	68	62	64	62	64	60	62	58	58	103	53	58	64	72	77
11	32	48	49	52	54	56	57	58	56	54	57	54	52	51	48	47	48	50	52	87	52	63	68	69	70
12	48	45	48	64	68	64	62	62	58	60	62	64	66	65	67	64	68	65	67	101	62	60	70	81	84
13	46	52	58	62	60	62	68	71	71	70	70	74	72	71	70	68	68	64	67	80	52	59	65	70	73
14	34	49	52	56	56	57	58	57	48	51	52	54	54	62	61	58	54	48	50	87	51	63	67	70	72
15	43	46	54	62	68	64	63	62	65	64	62	63	60	58	56	61	60	59	60	89	52	59	66	72	78
16	52	58	68	71	72	74	73	72	72	74	76	76	74	68	68	65	64	64	62	105	63	43	83	86	89
17	34	49	52	55	58	57	58	62	64	66	67	68	70	70	72	68	64	62	64	87	50	63	67	70	73
18	50	54	60	58	54	50	58	52	51	54	52	56	62	64	63	58	61	60	58	103	60	66	73	70	67
19	54	60	70	60	70	72	70	72	68	68	70	71	74	72	68	70	69	70	67	90	66	73	81	74	81
20	58	65	67	68	65	58	62	62	64	59	55	62	64	62	60	60	62	60	60	100	68	77	82	82	78
21	56	64	68	67	65	62	58	64	68	70	71	72	70	70	68	69	68	67	68	92	67	75	78	76	74
22	56	60	68	70	68	72	72	72	70	70	68	64	60	68	70	70	70	70	70	93	67	73	79	81	79
23	54	60	68	70	68	64	60	58	60	64	62	64	68	70	70	70	68	68	68	93	66	73	82	80	79
24	46	52	58	60	62	64	60	54	62	60	60	64	64	68	68	69	69	70	72	94	61	65	71	73	75
25	56	68	74	80	81	84	86	92	100	101	106	105	97	94	102	104	101	102	103	105	57	69	74	80	87
26	54	58	62	64	62	60	64	68	65	64	65	62	60	62	61	62	60	61	62	105	66	72	75	77	77
27	40	42	45	45	48	54	58	62	50	48	46	50	52	54	56	58	60	62	62	83	54	62	65	65	67
28	42	46	52	54	62	64	63	60	63	60	59	61	60	59	58	60	59	59	60	88	51	59	65	69	75
29	52	71	72	74	76	75	74	74	76	82	79	72	74	71	68	69	64	62	60	105	63	85	86	88	91
30	42	49	58	69	74	70	65	78	72	68	65	64	66	67	68	72	74	5	72	85	52	61	74	84	89
31	52	58	64	67	68	62	64	66	65	64	62	54	58	62	68	72	74	76	72	95	61	67	72	75	79
32	56	64	67	68	72	74	78	82	85	87	87	79	75	72	72	73	71	70	70	107	66	75	78	79	53
33	60	64	67	69	72	74	78	82	84	82	80	78	78	74	76	72	70	72	74	109	69	75	78	49	84
34	43	56	62	64	67	68	72	72	75	72	62	58	64	67	68	73	71	70	72	99	47	58	69	73	77
35	52	58	62	64	65	67	68	66	64	63	62	60	64	62	66	64	65	65	62	91	60	67	72	74	75
36	56	64	67	68	72	71	70	74	76	78	76	75	74	72	71	71	70	68	68	96	66	74	77	79	83
37	58	60	68	72	76	78	82	80	80	78	79	78	76	77	75	75	76	76	75	99	67	71	78	84	89
38	42	64	54	52	58	64	64	63	60	58	58	56	61	60	60	59	58	60	60	88	51	71	66	63	68
39	40	58	54	50	48	52	58	64	68	72	78	82	80	80	82	78	79	78	78	98	54	69	65	65	65
40	46	58	60	62	68	74	78	82	80	78	77	79	78	76	74	75	74	72	70	93	57	66	68	70	76
41	58	64	62	58	67	68	70	72	74	72	70	70	72	74	78	76	74	72	70	100	69	80	78	76	81
42	50	48	58	62	68	72	74	78	80	80	79	78	74	76	74	72	70	72	70	105	76	52	62	66	73
43	34	46	48	54	62	68	64	62	60	62	63	64	62	60	60	60	58	59	60	87	62	68	60	67	74
44	60	72	78	82	80	82	80	80	78	79	79	78	79	80	82	82	80	80	78	103	70	81	85	89	59
45	38	46	68	72	74	78	76	78	78	76	74	76	76	75	74	72	72	74	76	93	47	58	82	87	88
46	54	62	64	64	72	75	76	75	78	76	75	72	70	68	64	62	62	60	61	93	64	78	80	81	87
47	38	48	45	58	62	68	72	74	75	74	68	62	62	64	62	62	60	58	60	75	49	60	61	67	74
48	54	58	58	62	68	72	72	72	76	78	80	80	82	80	80	78	78	79	76	105	64	71	73	107	82
49	42	52	50	58	60	62	68	72	74	75	72	70	70	78	78	80	78	76	74	103	51	58	60	72	77
50	45	58	62	64	58	64	68	72	74	74	72	74	72	70	68	68	69	70	68	89	53	63	69	68	68

Group E	MAP	MAP	MAP	MAP	MAP	MAP	MAP	MAP	MAP	MAP	MAP	MAP	MAP	MAP	PR	PR	PR	PR	PR	PR	PR	PR	PR	PR
S.N.	10	12	14	16	18	20	25	30	35	40	45	50	55	60	Basal	Hypo	2	4	6	8	10	12	14	16	18
1	90	88	86	83	80	78	77	77	77	76	80	78	80	78	76	75	78	79	82	84	84	85	85	83	83
2	77	79	80	82	79	74	73	75	79	78	83	83	79	78	90	92	94	94	95	97	104	106	108	110	112
3	77	77	79	75	73	75	75	77	76	74	77	75	75	73	100	108	110	108	114	116	112	112	112	114	108
4	84	86	89	96	87	86	86	84	81	82	81	79	80	77	78	76	77	78	81	93	84	92	91	90	92
5	74	75	71	72	74	76	75	77	78	79	79	78	77	75	98	96	96	97	98	100	102	104	102	98	96
6	87	85	83	81	80	77	79	82	79	77	76	78	77	77	120	124	118	122	126	118	119	114	113	108	109
7	87	85	87	85	82	78	77	75	71	67	70	72	69	67	98	100	101	102	104	106	110	108	104	102	101
8	79	77	77	73	73	76	86	89	85	85	82	80	83	81	100	99	98	92	94	97	95	92	93	94	96
9	78	79	79	81	82	84	84	84	85	84	85	85	87	85	82	66	67	68	69	68	65	70	74	76	78
10	79	80	79	77	79	79	75	77	76	77	75	75	72	72	92	86	84	78	80	84	86	88	90	88	90
11	72	74	76	74	73	74	71	69	68	66	65	65	67	68	86	84	85	88	92	91	93	92	94	95	94
12	82	82	83	78	78	79	80	81	81	83	81	84	82	83	87	88	84	79	76	78	77	74	82	84	86
13	74	79	81	81	81	81	85	82	82	83	82	83	81	83	112	114	116	114	112	113	111	115	118	122	121
14	73	73	72	66	69	70	71	72	77	75	72	69	67	69	78	76	77	77	79	80	82	83	84	86	85
15	76	76	75	77	76	74	75	74	72	71	74	73	73	73	102	100	97	97	98	102	101	101	100	102	98
16	90	89	87	87	87	90	88	88	85	85	84	83	83	81	92	94	96	97	102	106	110	111	115	117	118
17	72	75	78	79	81	83	83	84	84	86	82	79	78	79	87	86	85	84	88	92	95	96	97	94	92
18	67	75	71	70	71	71	74	79	80	78	75	77	73	74	110	98	100	102	106	107	110	108	109	111	112
19	85	83	85	79	79	81	83	85	84	83	85	86	88	85	78	80	81	82	76	78	74	76	70	70	70
20	72	74	75	74	70	67	68	79	79	78	77	78	76	76	79	74	77	78	83	96	101	96	101	96	92
21	71	73	77	81	83	84	84	82	81	80	80	79	78	79	78	72	74	78	83	82	84	86	92	98	101
22	81	81	79	77	83	81	77	74	79	81	80	81	80	81	80	78	82	86	90	92	94	101	98	97	96
23	77	74	71	71	75	74	76	79	81	81	80	79	79	80	80	78	81	82	86	90	92	94	101	98	97
24	69	73	66	71	73	73	77	77	81	50	80	81	80	82	69	60	64	66	68	64	68	70	74	76	80
25	93	93	98	102	103	105	105	100	97	102	103	101	102	102	80	50	52	54	56	60	62	64	60	68	66
26	75	77	82	79	80	79	77	75	76	75	76	77	76	76	78	80	82	84	85	86	85	87	85	84	83
27	71	75	76	68	67	65	67	68	70	72	73	75	76	77	92	88	89	90	91	92	92	94	95	97	96
28	77	76	73	77	74	74	75	73	73	73	75	73	75	75	100	98	98	101	102	104	110	108	109	106	107
29	90	89	88	90	95	92	86	87	85	82	82	78	78	76	92	90	89	92	94	97	97	98	97	95	93
30	88	83	90	84	83	83	81	83	83	83	86	87	42	87	86	72	71	74	74	76	75	77	78	82	84
31	75	76	77	77	76	73	65	71	75	83	86	87	88	85	97	92	94	96	97	97	98	100	109	110	112
32	85	88	91	95	98	97	92	89	86	86	86	85	83	83	100	98	102	105	105	109	109	112	112	114	112
33	85	88	91	93	92	91	90	91	90	91	88	87	87	88	110	92	98	99	104	108	110	110	112	114	118
34	79	82	83	84	81	72	68	73	76	77	84	84	84	87	100	102	104	107	111	114	115	115	117	116	115
35	78	51	80	78	77	76	75	77	75	78	76	77	77	75	112	110	98	100	101	14	105	107	107	110	112
36	83	83	85	87	89	87	86	85	84	83	82	82	80	79	100	104	105	107	107	109	109	110	109	112	114
37	91	95	93	93	91	92	91	89	90	89	88	88	88	87	92	90	92	94	95	97	98	97	97	96	98
38	73	75	76	74	72	72	70	74	74	73	73	72	74	73	100	98	101	102	104	198	110	108	109	106	107
39	72	77	82	85	87	91	93	92	91	93	89	90	89	89	86	84	83	84	85	87	86	86	87	88	89
40	82	89	91	91	89	88	90	90	88	87	88	87	85	83	86	84	83	84	87	89	88	89	92	93	91
41	75	79	86	88	86	85	85	87	89	91	90	88	87	86	120	124	118	126	128	128	130	124	128	129	127
42	75	83	89	89	90	88	88	86	88	86	85	83	84	82	90	58	62	64	68	68	72	75	76	78	80
43	81	79	79	77	78	79	79	77	76	77	77	76	76	77	92	94	89	84	86	87	84	85	87	88	92
44	91	90	91	90	91	91	90	90	91	93	92	91	90	89	90	92	94	96	97	95	94	93	95	94	95
45	90	89	91	91	89	87	88	87	87	86	85	85	86	87	105	58	62	64	68	72	74	86	89	92	92
46	89	89	89	91	89	89	87	86	84	81	79	77	76	77	86	88	89	90	94	97	96	96	95	93	94
47	81	84	86	86	86	81	77	76	77	77	76	74	73	73	90	86	87	92	94	96	94	92	94	93	92
48	85	85	85	88	90	92	91	93	91	91	89	89	89	87	92	87	88	92	92	96	96	97	97	95	95
49	79	83	85	88	89	86	85	84	89	88	89	88	87	86	92	89	91	93	94	97	98	98	100	99	98
50	74	82	85	86	86	86	88	86	85	84	84	84	85	83	90	89	90	92	93	94	92	92	91	90	90

Group E	PR	PR	PR	PR	PR	PR	PR	PR	PR	of block ac	No. of Bolu	Dose	Complications/	Intervention	Neonatal Data		Duration of Surgery	SAB to Hypotension
S.N.	20	25	30	35	40	45	50	55	60				Side effects		APGAR 1 min	APGAR 5 min		(min)
1	84	84	85	86	82	82	83	81	79	7	1	6	-	-	9	9	80	3
2	108	109	104	100	98	96	95	97	93	7	1	6	-	-	10	10	75	2
3	104	103	101	98	96	98	96	95	97	6	1	6	-	-	10	10	60	3
4	91	87	89	86	87	88	89	86	88	8	2	12	-	-	10	10	70	4.5
5	97	96	97	97	98	98	99	94	98	6	2	12	-	-	9	9	60	4
6	110	114	115	109	108	102	101	100	98	8	1	6	-	-	10	10	75	3
7	98	97	95	96	94	97	93	94	95	8	1	6	-	-	10	10	75	3
8	95	94	93	95	97	95	97	98	96	6	3	18	-	-	9	9	80	3.5
9	77	76	78	76	75	74	76	79	82	7	1	6	-		9	10	75	3
10	89	86	87	88	90	92	89	88	84	8	1	6	-	-	9	9	70	2
11	92	90	91	92	89	88	87	89	86	6	1	6	-	-	10	10	60	5
12	72	74	70	68	66	65	68	69	67	8	2	12	-	-	9	10	75	4
13	118	114	109	104	98	97	98	99	98	8	1	6		-	10	10	75	3
14	82	83	81	80	79	78	79	81	82	8	2	12	-	-	9	9	75	3
15	97	96	95	96	95	97	98	96	97	8	1	6	-	-	9	9	80	4
16	116	115	115	113	112	108	102	102	100	8	1	6	-	-	9	10	60	3
17	89	89	87	86	85	86	89	92	87	6	1	6	-	-	10	10	60	4
18	109	107	108	104	104	105	102	98	100	8	2	12	-	-	10	10	70	3
19	74	76	78	82	80	78	76	76	74	7	1	6	-	-	9	9	75	3
20	89	88	82	86	92	94	92	91	92	7	3	18	-	-	10	10	55	4
21	96	94	96	92	89	90	91	90	89	6	2	12	-	-	9	10	75	5
22	96	95	96	97	94	93	92	92	90	8	1	6	-	-	9	10	70	3
23	98	60	68	70	70	70	68	68	70	8	1	6	-	-	10	10	75	2
24	78	74	75	74	73	72	73	75	74	6	2	12	-	-	10	10	60	3
25	64	62	67	64	60	60	60	62	60	7	3	18	-	-	9	10	60	2.5
26	82	81	80	82	78	72	68	64	65	7	1	6	-	-	10	10	75	3
27	95	95	97	98	97	95	96	95	94	8	1	6	-	-	10	10	60	3
28	108	106	104	102	98	97	98	95	98	6	1	6	-	-	9	10	70	3
29	94	96	95	93	91	92	90	89	86	8	1	6	-	-	10	10	65	4
30	86	84	85	87	84	83	80	78	80	7	1	6	-	-	9	9	60	3
31	114	111	110	109	108	106	108	105	105	7	2	12	-		10	10	75	3
32	113	111	107	106	106	104	104	98	98	7	1	6	-	-	10	10	80	4
33	119	121	122	124	120	119	118	116	114	7	1	6	-	-	10	10	60	4
34	114	113	112	112	111	110	108	107	104	6	1	6	-	-	10	10	80	4.5
35	114	113	112	111	110	108	107	106	102	7	1	6	-	-	10	10	60	4
36	108	107	104	105	105	102	100	99	98	7	1	6	-	-	10	10	55	3
37	98	97	98	97	96	95	95	94	95	8	1	6	-	-	10	10	90	4
38	106	104	105	100	102	102	100	100	98	7	2	12	-	-	9	10	70	4
39	89	88	87	87	88	89	92	90	90	7	2	12	-	-	10	10	60	3
40	90	90	89	88	87	86	87	86	87	6	1	6	-	-	10	10	65	3
41	126	124	122	120	118	118	117	108	107	7	2	12		-	10	10	70	4
42	80	78	79	78	72	74	72	70	70	7	3	18	-	-	9	10	60	3
43	94	92	91	90	90	89	91	87	92	8	1	6	-	-	9	9	75	5
44	94	95	96	95	94	93	92	90	91	7	1	6	-	-	9	9	70	5
45	95	96	94	92	91	90	90	89	89	8	1	6	-	-	10	10	80	4
46	95	93	92	91	90	92	93	92	91	7	1	6	-	-	10	10	75	4
47	92	91	90	90	90	89	89	89	88	8	1	6	-	-	9	9	70	5
48	94	92	92	91	90	91	89	89	88	7	1	6	-	-	9	9	65	3
49	98	97	96	97	95	95	96	95	96	7	1	6	-	-	10	10	60	3
50	91	91	89	89	87	89	90	92	90	7	2	12	-	-	10	10	75	5