A Comparative Study Of Effect Of Rapid Crystalloid Preload And Intravenous Ephedrine In Management Of Hypotension Due To Subarachanoid Block In Elective Caesarean Section

by

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LIST OF ABBREVATIONS

ASA	American Society of Anesthesiologists
BP	Blood Pressure
CBF	Cerebral Blood Flow
cm	centimetre
CO	Cardiac Output
CSF	Cerebrospinal Fluid
CVS	Cardiovascular system
dl	decilitre
ECG	Electrocardiogram
FRC	Functional Residual Capacity
GA	General Anaesthesia
GFR	Glomerular Filtration Rate
HR	Heart Rate
I-D	Induction of spinal anaesthesia to Delivery of baby interval
IM	Intramuscular
INJ.	Injection
IV	Intravenous
Kg	Kilogram
MAP	Mean Arterial Pressure
mg	milligram
min	minute
ml	millilitre
PR	Pulse Rate
RL	Ringer's Lactate

RR	Respiratory Rate
RS	Respiratory System
SA	Spinal Anaesthesia
SBP	Systolic Blood Pressure
SD	Standard Deviation
SpO2	Oxygen saturation
U-D	Uterine incision to Delivery of baby interval

ABSTRACT

Background and objectives:

Spinal anaesthesia is a preferred technique for caesarean delivery for its distinct advantages over general anaesthesia such as avoidance of airway related complications, aspiration, neonatal depression with anaesthetic agents. However hypotension is commonly associated with spinal anaesthesia, which has detrimental effect on both mother and fetus. Thus in this study the role of pre-treatment with crystalloid preloading and prophylactic I.V. Ephedrine in preventing spinal hypotension in caesarean patients is being evaluated.

Methods:

The study was conducted on 60 healthy pregnant mothers without foetal compromise undergoing elective caesarean section under spinal anaesthesia. Patients were randomly divided into two groups. Group P (n=30) patients were preloaded with Ringer Lactate solution at 10ml/kg over 15-20 min prior to spinal anaesthesia. Group E (n=30) patients were given Inj. Ephedrine 10mg I.V. bolus immediately after spinal anaesthesia.

Results:

The incidence of hypotension was higher in Group P as compared to Group E (p value<0.05). Neonatal outcome were similar in both the groups.

Conclusion:

Prophylactic intravenous bolus dose of Injection Ephedrine 10mg is safe, quick and more effective than crystalloid preloading for maintenance of maternal blood pressure close to the baseline level in a healthy parturient undergoing caesarean section under spinal anaesthesia.

Key words:

Ephedrine, Ringer Lactate, hypotension, caesarean section.

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INTRODUCTION

Spinal anaesthesia (SA) is a preferred technique for caesarean delivery for its distinct advantages over general anaesthesia (GA) such as avoidance of airway-related complications, aspiration, neonatal depression with anaesthetic agents and ability of mother to enjoy the birth experience of her baby.[1] Spinal anaesthesia, however, is also associated with certain hazards. The most common of these is hypotension with a reported incidence exceeding 80% unless prevented.[2, 3] Maternal hypotension may have detrimental effects on uterine blood flow, fetal well-being and ultimately neonatal outcome as measured by umbilical artery pH and APGAR score.[2, 3, 4]

A number of methods have been studied to prevent hypotension, such as the use of lateral uterine displacement, the use of intravenous fluid preload, trendelenberg position, compression stockings on the legs, and prophylactic vasopressors.[2] However no single method has proved satisfactory.

Prehydration is 0.5–1 L intravenous fluid administration 15–20 minutes before spinal anaesthesia. It is aimed at filling capacitance vessels and limiting hypotension when venodilatation occurs. However, prehydration with large doses of crystalloid fluid can lead to increased central venous pressure, pulmonary edema and fetal hypooxygenation.[5]

Ephedrine is a sympathomimetic agent that has both direct (alpha and beta receptor agonist) and indirect (release of norepinephrine from presynaptic nerve terminals) mechanism of action. Ephedrine with its beneficial effect on uterine blood flow remains the preferred vasoconstrictor for treating hypotension resulting from sympathetic blockade in caesarean section.[6, 7] Selectivity for Ephedrine to constrict femoral arteries more than uterine arteries in vitro is enhanced during pregnancy.[8] However, it has been found that Ephedrine administration is associated with

significant increase in fetal heart rate and beat to beat variability. These changes are dose related and are not associated with fetal asphyxia as judged by the measurement of fetal scalp blood pH or APGAR scores.[9] The appropriate route and dose of Ephedrine that should be used to prevent spinal associated hypotension during caesarean section still remains controversial[10] and the best prophylaxis of maternal hypotension during caesarean section is still controversial. Thus in the present study the role of pre-treatment with crystalloid preloading and prophylactic I.V. Ephedrine in preventing spinal hypotension in caesarean patients is being evaluated.

AIMS AND OBJECTIVES OF THE STUDY

To compare the conventional technique of crystalloid preloading and intravenous bolus dose of Ephedrine in preventing maternal hypotension during caesarean section under spinal anaesthesia.

1. To observe incidence of hypotension in both the groups.
2. Number of rescue doses of vasopressor Ephedrine required for correction of hypotension in both the group.
3. To compare the intra-operative adverse effects observed with crystalloid preloading and I.V. Ephedrine.
4. To determine materno-fetal outcomes in both the groups.

REVIEW OF LITERATURE

Dutta, Ostheiner and Alper (1982) on evaluating methods of Ephedrine administration, nausea and hypotension during spinal anaesthesia for caesarean section noted that untreated hypotension can also pose serious risks for both mother (unconsciousness, pulmonary aspiration, apnoea or even cardiac arrest) and newborns (impaired placental perfusion leading to hypoxia, fetal acidosis and neurological injury). Even mild hypotension can decrease uteroplacental blood flow and can lead to fetal acidosis. Hence he concluded that protocols aimed at preventing hypotension during spinal anaesthesia for caesarean delivery may produce better results than those intended to treat hypotension once it has happened.[1]

Chan WS *et al.,* (1997) studied effectiveness of ephedrine infusion versus fluid preload for prevention of hypotension during spinal anaesthesia in caesarean section and they found that the incidence of severe hypotension was lower in ephedrine group than in the fluid preload group, although incidence of moderate hypotension was same. They also noticed that the incidence of shivering was lower in ephedrine group than in preload group.[11]

Vercauteren MP *et al.,* (2000) studied prevention of hypotension by single 5mg dose of ephedrine during spinal anaesthesia in prehydrated caesarean section patients and found out that single intravenous dose of 5mg ephedrine decreases the hypotension with low dose spinal anaesthesia in already prehydrated patients.[10]

Malhotra HB (2004) evaluated preloading and vasoconstrictors as combined prophylaxis for hypotension during subarachnoid block in lower limb and lower abdominal procedures including caesarean section concluded that combination of both crystalloid preloading and vasoconstrictor had maximal effect in preventing spinal induced hypotension, compared to that of vasoconstrictor alone. However they

concluded that further tightly controlled studies are required to optimise the combination of preloading and vasoconstrictors.[12]

Desalu and Kushimo (2005) studied the effectiveness of Ephedrine infusion and crystalloid prehydration in preventing spinal induced hypotension in caesarean section in African parturients and they found that prophylactic Ephedrine given by standard infusion set was more effective than crystalloid pre-hydration in the prevention of hypotension during spinal anaesthesia for elective caesarean section. They also concluded that neonatal outcome was similar in both the groups.[4]

Reidy and Douglas (2008) in their study done on the vasopressors in obstetrics have concluded that Ephedrine has been the gold standard for the treatment of hypotension in obstetric anaesthesia because of its good safety record, ready availability and familiarity to most obstetric anaesthesiologists. Ephedrine has a slow onset of action making it difficult to titrate an appropriate bolus dose.[3]

Iclal Ozdemir Kol *et al.,* (2009) in a double-blinded study to determine the efficacy and safety of 0.5 mg/kg intravenous Ephedrine for the prevention of hypotension during spinal anaesthesia for caesarean delivery, concluded that the prophylactic bolus dose of 0.5 mg/kg intravenous Ephedrine given at the time of intrathecal block after a crystalloid fluid preload, plus rescue boluses reduce the incidence of hypotension.[13]

Nevan M. El-Mekawy (2012) in their study to compare the effectiveness of Co/post loading of fluids versus immediate post spinal infusion of Ephedrine in prevention of hypotension stated that "intravenous infusion of Ephedrine 1mg/min immediately after spinal anaesthesia for emergency caesarean sections, even if there is no time for proper pre-hydration, can control effectively the hypotension without episodes of hypertension or significant tachycardia, and it had no effect on fetal well-

being. It could be as effective as Co/ post loading of 0.5ml/kg/min Ringer Lactate in controlling systolic blood pressure with fewer incidences of postoperative complications."[14]

Shah SA, Naqvi SS, Abbas MA (2015) evaluated the comparison of crystalloid preloading and prophylactic administration of Ephedrine for prevention of spinal anaesthesia induced hypotension. Group A was preloaded with Ringer Lactate at dose of 20 ml/kg body weight. Group B- Ephedrine was given prophylactically at dose of 0.25mg/kg body weight immediately after subarachnoid block. Concluded that Intravenous Ephedrine given prophylactically to prevent hypotension is more effective than crystalloid preloading.[15]

Arun Kumar Natarajan *et al.,* (2015) conducted a study on Comparison of intravenous bolus Phenylephrine and intravenous Ephedrine during crystalloid co-loading in ameliorating hypotension under spinal anaesthesia for caesarean section. Concluded that Phenylephrine and Ephedrine are equally efficient in managing hypotension during spinal anaesthesia for elective caesarean delivery. There was no difference between the two vasopressors in the incidence of true fetal acidosis and neonatal outcome.[16]

Takhelmayum Hemjit Singh *et al.,* (2016) studied the effect of bolus intravenous Ephedrine in ameliorating spinal induced hypotension, considered two groups of 25 patients each: Group 1 (study) and Group 2 (control) to receive either 1 ml of 5 mg bolus intravenous Ephedrine or equal volume of Normal Saline, respectively, just after 10mg of 0.5% intrathecal Bupivacaine. Significant fall in systolic blood pressure from its baseline value occurs at all time intervals in both the groups, except up to the 4th min in the Ephedrine group. The incidences of hypotension between the two groups were 60% and 72% in the Ephedrine and control

group, respectively (P > 0.05). Hence concluded that Prophylactic use of intravenous Ephedrine did not significantly decrease the incidence of maternal hypotension.[17]

Kulkarni KR, Naik AG, Deshpande SG (2016) in their study to evaluate the efficacy of 15 mL/kg of crystalloid preloading versus prophylactic intravenous bolus of 10 mg Ephedrine as an antihypotensive measure for caesarean section, concluded that Prophylactic intravenous bolus of 10mg Ephedrine with spinal injection is more effective in maintaining maternal hemodynamic stability and better neonatal outcome as compared to crystalloid preloading during caesarean delivery.[18]

Heba Omar Ahmed *et al.,* (2016) in their study on volume preloading of 15ml/kg Ringer lactate and ephedrine infusion of 5mg in 1st min and 5mg in 2nd min and 1mg every min for 15min found that the incidence of hypotension in volume preload group was 48% and ephedrine group was 24%. They concluded that ephedrine infusion after spinal anaesthesia was more effective than volume preloading in prevention of hypotension and without causing significant tachycardia.[19]

Hegde BK, Bhat MT. (2017) Prophylactic crystalloids or prophylactic crystalloids with Ephedrine: Comparison of hemodynamic effects during caesarean section under spinal anaesthesia using 0.5% Bupivacaine. Demonstrated that prophylactic Ephedrine given by infusion along with crystalloids is not only a simple and effective method for preventing hypotension during spinal anaesthesia in elective caesarean section in ASA Grade I patients but also contributes to less incidence of intraoperative nausea and vomiting.[20]

ANATOMY OF VERTEBRAL COLUMN[21,22]

Before administration of any type of regional anaesthesia, a clear knowledge of that region is mandatory. Any variation from normal should be kept in mind. So, it is relevant to discuss anatomy of spinal cord.

Spinal cord is elongated part of CNS which is situated in the upper 2/3rd of the vertebral canal. It extends from the foramen magnum up to the lower border of 1st lumbar vertebra in adults or between the discs of 1st and 2nd lumbar vertebrae due to differential growth of the cord and vertebrae. In neonates, the cord continues upto the lower border of 3rd lumbar vertebra. This differential growth also gives rise to elongated lumbar and sacral roots to reach their corresponding intervertebral foramina resulting in the formation of the caudaequina. [23]

The average length of the spinal cord in males is 45cm and females it is 42cm. The spinal cord is a continuation of the medulla oblongata below the level of foramen magnum and it tapers off into a conical extremity known as conus medullaris. A delicate fibrous filament descends to the back of 1st segment of coccyx from apex of conus medullaris. This is known as the filum terminale.

At birth, the tip of spinal cord lies at the level of lower border of L3 vertebra. In the adult, the vertebral level of termination of spinal cord may be as follows-

Lower border of L1- 50%

Upper border of L2- 40%

Upper border of L3- 03%

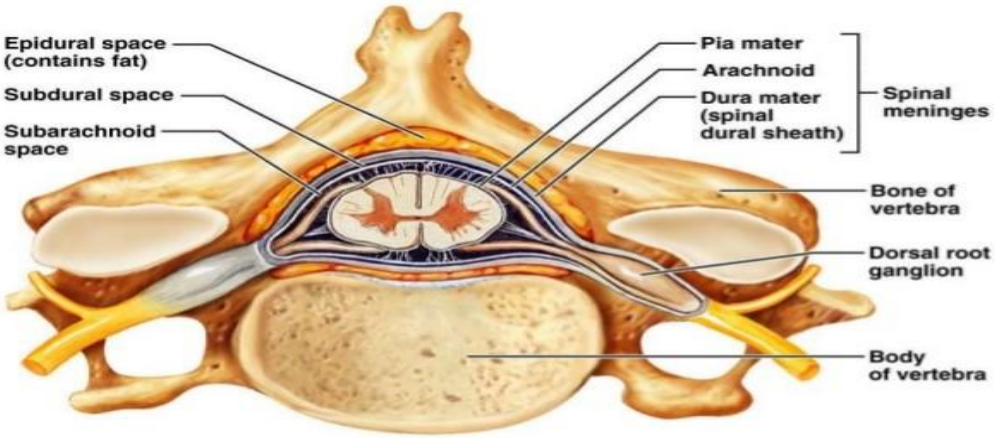


Figure 1: Cross section of spinal cord

There are three membranes (from the innermost to the outermost) covering the spinal cord in the bony vertebral column: the pia mater, the arachnoid and the dura mater. The cerebrospinal fluid (CSF) lies in the space between the pia mater and the arachnoid mater called intrathecal (subarachnoid) space.

This space is traversed by cobweb trabeculae plus the cranial and spinal nerves; it is bathed in spinal fluid. The space of the cranial and thoracic vertebrae is annular and approximately 3 mm deep. And it is circular below the first lumbar vertebrae.

The pia mater is a extremely vascular membrane that invests the spinal cord and brain. The choroid plexuses of the cerebral ventricles form about 500 mL of CSF daily, with 30 to 80 mL occupying the subarachnoid space below T11-T12 level.

The arachnoid mater is a delicate, nonvascular membrane that functions as the principal barrier to drugs crossing into (and out of) the CSF and is estimated to account for 90% of the resistance to drug migration.

The dura is the outer most layer. Surrounding the dura mater is the epidural space, which extends from the foramen magnum to the sacral hiatus and surrounds the dura mater anteriorly, laterally, and posteriorly. Epidural space contains the nerve

roots, fat, areolar tissue, lymphatics and blood vessels including the well-organized Batson venous plexus.

VERTEBRAL COLUMN:

Composed of 33 vertebrae

Cervical – 7

Thoracic - 12

Lumbar - 5

Sacrum - 5 (fused)

Coccyx - 4 (fused)

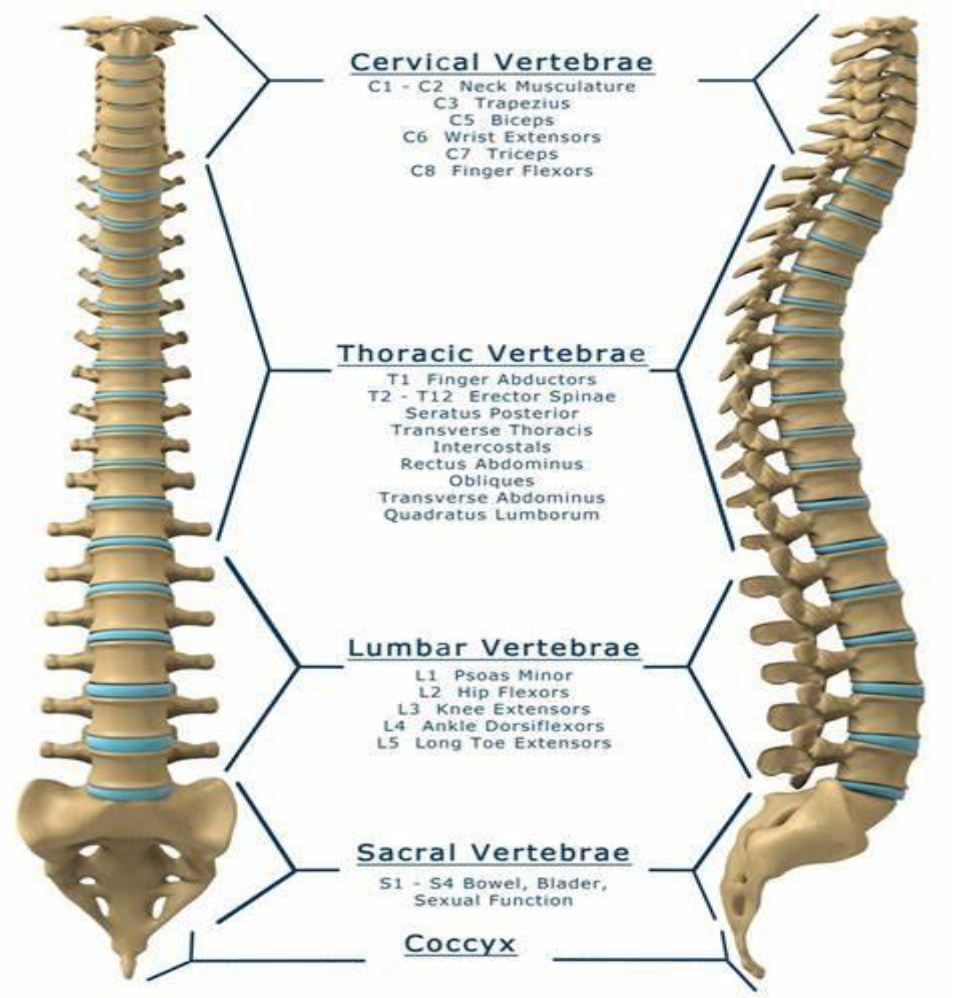


Figure 2: Vertebral column

The posterior element of vertebrae is formed by -the vertebral arch, spinous process, pedicles, and laminae. The anterior element is formed by the vertebral body. The vertebrae are joined together anteriorly by the fibrocartilaginous joints and posteriorly by the zygapophyseal (facet) joints. The spinous process of thoracic vertebrae is angulated steeply downward, whereas in lumbar vertebrae it is almost horizontal. This is a clinically important for direction of needle insertion and advancement in the thoracic and lumbar levels.[24]

The cervical and lumbar curves are convex anteriorly while the thoracic and sacral curves are convex posteriorly. These curves have a significant effect on the spread of local anaesthetics in subarachnoid and epidural space.

The vertebral column is bounded together by several ligaments which give it stability and elasticity.[24]

a. Supraspinous ligament

b. Interspinous ligament

c. Ligamentum flavum

d. Anterior and posterior longitudinal ligament.

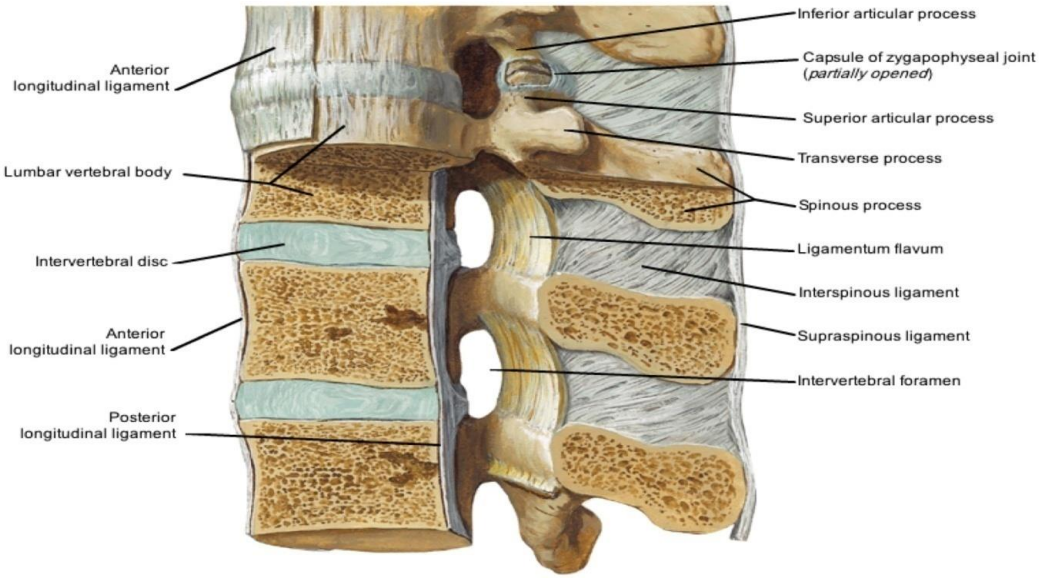


Figure 3: Ligaments of spine

SURFACE LANDMARKS [25]

To understand the neuraxial anatomy it is necessary to develop a concept of the relationship between surface and bony anatomy pertinent to the neuraxial structures.

Beginning cephalad, the spinous process of the seventh cervical vertebra, the vertebral prominence, is the most prominent midline structure at the base of the neck. A line drawn between the lower borders of the scapula crosses the vertebral axis at approximately the spinous process of T7. The lower extent of the spinal cord, the conus medullaris, ends in the adult at approximately L1 (In the infant the conus medullaris may extend upto L3). The line between the iliac crests (Tuffier's or the intercrestal line) most often crosses through the spinous process of L4. A line drawn between the posterior superior iliac spines identifies the level of the second sacral vertebra and the caudal extent of the dural sac containing cerebrospinal fluid (CSF).

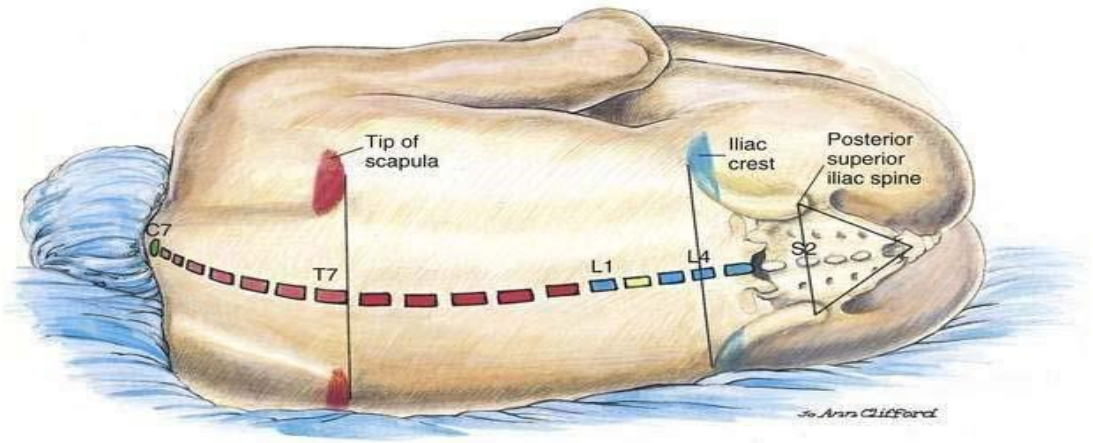


Figure 4: Neuraxial anatomy-Surface landmark

SPINAL NERVES:

Near the spinal cord each spinal nerve branches into two roots. One, composed of sensory fibers, enters the spinal cord via the dorsal root; its cell bodies lie in a spinal ganglion that is outside the spinal cord. The other, composed of motor fibers, leaves the spinal cord via the ventral root; its cell bodies lie in specific areas of the spinal cord itself.

Spinal nerves are formed by fusion of anterior and posterior roots. Sympathetic preganglionic axons arise from cells in the intermediolateral horn of the spinal cord from T1 to L2. The posterior root is larger than anterior and afferent impulses from the whole body including the viscera pass through these roots.

Each posterior root has a ganglion and conveys fibers of pain, touch, temperature and deep sensation from bone joints, muscles tendons, efferent from the viscera (accompanying sympathetic) and vasodilator fibers.

TABLE 1: SEGMENTAL LEVELS

Till inguinal ligament and crest of ilium	T12- L1
Umbilicus	T10
Xiphoid cartilage	T6
Nipple	T4
Clavicle	T1

The skin above the nipple has double innervations from C3 and C4 and from T2, T3, T4, so even with a successful block to C8 there will be some sensation above the nipple line.

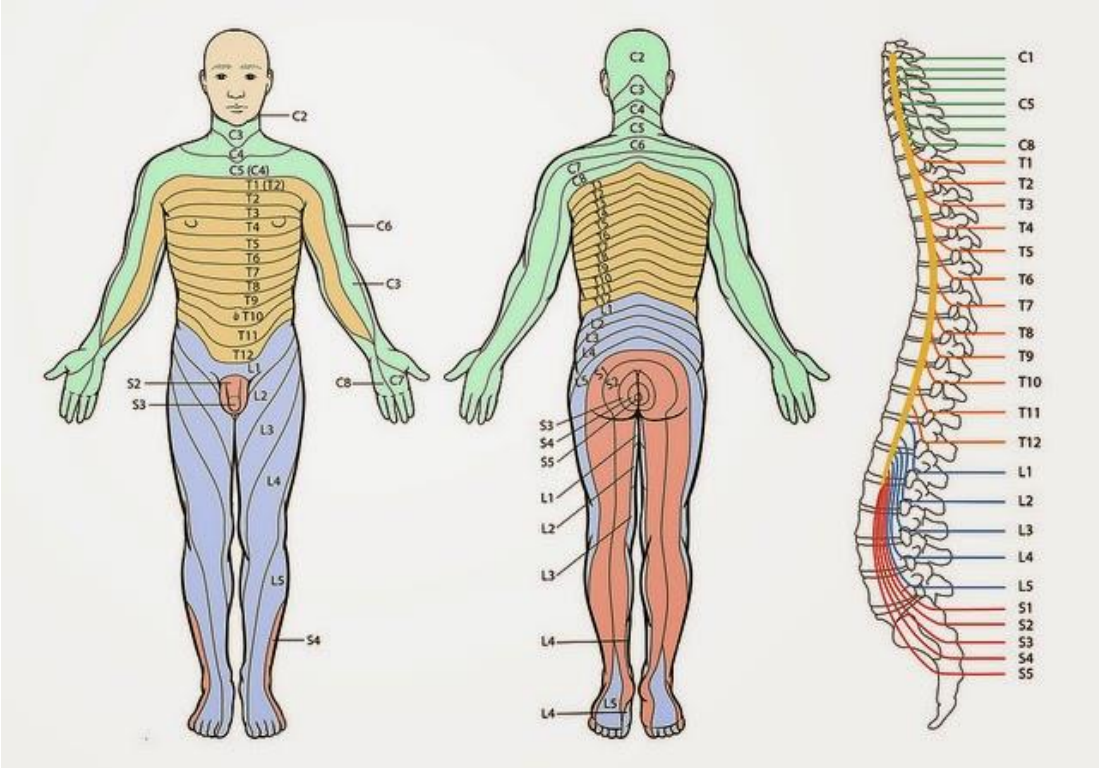


Figure 5: Spinal nerves and dermatomal distribution.

BLOOD SUPPLY OF THE SPINAL CORD [24,26]

The principal arterial supply to the spinal cord is derived from one anterior and two posterior arteries that descend from level of foramen magnum.

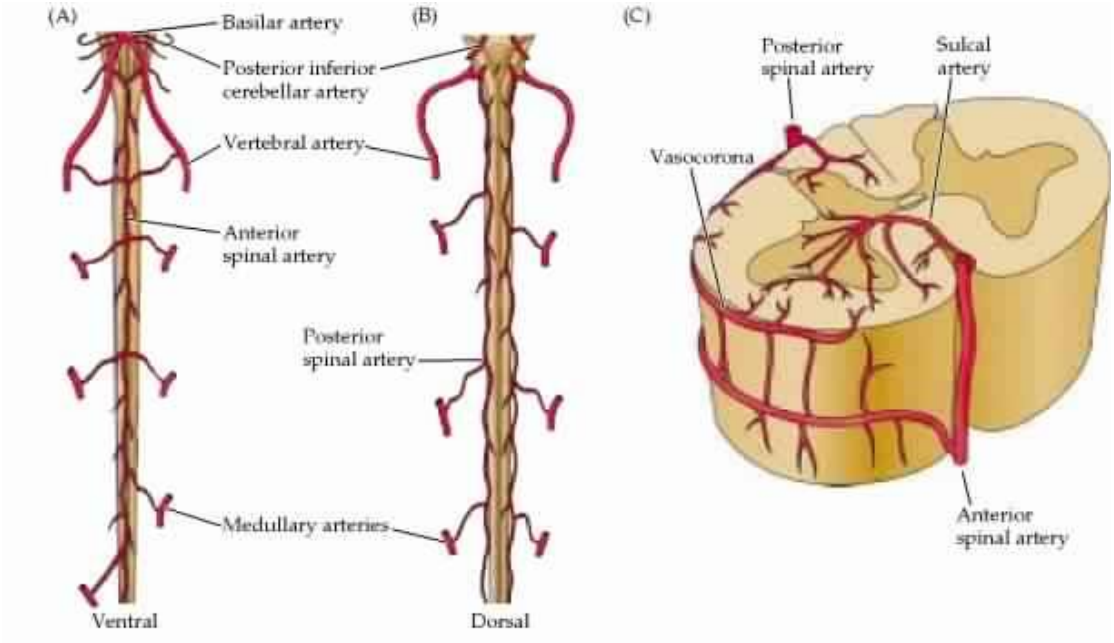


Figure 6: Blood supply of the spinal cord

Anterior spinal artery is single in number, formed by union of branch from each vertebral artery at foramen magnum and passes down the whole length of spinal cord. It receives communications from lumbar, and other small arteries. There are commonly 2-3 communications in cervical and thoracic region, and there is only one artery, the radicular magna (Artery of Adam Kiewicz) which is unilateral supplying lumbar enlargement. It supplies lateral and the anterior columns about 3/4 of the substance of the cord.

Posterior spinal artery -two posterior spinal arteries -one on each side. They are derived at the base of the brain directly from the vertebral artery or more often from posterior inferior cerebellar arteries. They supply the posterior one-third of the spinal cord. This supply is reinforced by spinal braches of vertebral, ascending cervical, posterior intercostal, lumbar and lateral sacral arteries, which pass through the intervertebral foramina.

Venous drainage:

Anterior and posterior spinal veins drain into segmental veins in the neck, the azygous veins in the thorax, lumbar veins in the abdomen, and lateral sacral veins in the pelvis.

Nerve supply of the meninges:

The posterior aspect of the dura and arachnoid mater contain no nerve fibres, hence there is no pain on dural puncture. The anterior aspect is supplied by sinovertebral nerves, each of these enters an intervertebral foramina and passes up for a segment and down for two segments.

CEREBROSPINAL FLUID (CSF):

The CSF is an ultra-filtrate of plasma and is a clear and colourless fluid bathing the brain and spinal cord. Its main function is to cushion the neural structures. CSF is produced by the choroid lateral plexus of the 3rd and 4th ventricles. It is reabsorbed via the arachnoid villi. Replacement of a volume of total spinal fluid under ordinary normal physiological circumstances is every 6 hrs.

Total volume of CSF is about 150 ml.

With the patient lying in the lateral position normal CSF pressure is 8 to 10cm of H2O.

Table 2: Characteristics of CSF

Specific gravity	1.004-1.009
Total volume	130-150 ml
Volume in subarachnoid space	20ml
Opening pressure	10-20 cm of H20

Table 3: Composition of CSF

Protein	15-45 mg/dl
Glucose	50-80 mg/dl
Non-protein nitrogen	20-30 mg/dl
Chloride	120-130 mEq/L
Sodium	140-150 mEq/L
Bicarbonate	25-30 mg/ml
pH	7.40-7.60

CSF in Lumbosacral region has a constant pressure of approximately 15 cm H2O, but its volume varies depending upon patient's body habitus and weight.[22] It is estimated that CSF volume accounts for 80% of the variability in peak block height and regression of sensory and motor blockade. Nevertheless, except for body weight (less CSF in subjects with high body mass index [BMI]), the volume of CSF does not correlate with other anthropomorphic measurements available clinically.

PHYSIOLOGICAL EFFECTS OF NEURAXIAL BLOCKADE[24,27]

The credit for introducing neuraxial block into clinical practice for the first time goes to August Bier in 1898.

Normal physiologic manifestations of neuraxial blockade such as hypotension are not necessarily complications but normal physiological effects of neuraxial blockade. A thorough understanding of these effects will allow the anaesthesia provider to anticipate alterations and treat the patient in a timely manner, preventing complications. A brief review of the mechanism of action, somatic and autonomic blockade as well as cardiovascular, respiratory, gastrointestinal, renal, and metabolic/endocrine effects are as follows.

NEURAXIAL BLOCKADE: MECHANISM OF ACTION, SPREAD, UPTAKE & ELIMINATION[24]

Local anaesthetic binds to the nerve tissue and disrupts nerve transmission, resulting in neural blockade. For spinal and epidural anaesthesia, the target binding sites are located within the spinal cord and on the spinal nerve roots in the subarachnoid and epidural spaces. The spinal nerve roots and dorsal root ganglia are considered the most important sites of action. Nerves in the subarachnoid space are highly accessible and easily anaesthetized, even with a small dose of local anaesthetic, compared with the extradural nerves, which are often ensheathed by dura mater (the "dural sleeve").

The speed of neural blockade depends on the size, surface area, and degree of myelination of the nerve fibers exposed to the local anaesthetic. Anatomic studies show that the S1 and L5 posterior roots are the largest and thus most resistant to blockade during epidural anaesthesia. Smaller nerves are more sensitive to the effects of local anaesthetics because of their relatively high membrane surface area to axon

unit volume ratio. For example, the small preganglionic sympathetic fibers (B fibers, 1 to 3 μm, minimally myelinated) are most sensitive to local anaesthetic blockade. Among the sensory nerves, the C fibers (0.3 to 1 μm, unmyelinated), which conduct cold temperature sensation, are blocked more readily or earlier than the A-delta fibers (1 to 4 μm, myelinated), which conduct pinprick sensation. The A-beta fibers (5 to 12 μm, myelinated), which conduct touch sensation, are the last to be affected among the sensory fibers. The larger A-alpha motor fibers (12 to 20 μm, myelinated) are more resistant than any of the sensory fibers.

Regression of blockade("recovery") follows in the reverse order: motor function followed by touch, then pinprick and finally cold sensation.[28] Another manifestation of relative sensitivity or susceptibility to the effects of local anaesthetics is the observed differences in the peak block height (highest or most cephalad level of anaesthesia) according to each sensory modality, which is termed differential sensory block.

For example, the level of anaesthesia to cold sensation (also an approximate level of sympathetic blockade) is most cephalad and is on average one to two spinal segments higher than the level of pinprick anaesthesia, which in turn is one to two segments higher than the level of touch anaesthesia.[29]

When local anaesthetic is injected directly into the subarachnoid space during spinal anaesthesia, it diffuses through the pia mater and penetrates through the spaces of Virchow-Robin (extensions of the subarachnoid space accompanying the blood vessels that invaginate the spinal cord from the pia mater) to reach the deeper dorsal root ganglia. Furthermore, a portion of the subarachnoid drug diffuses outward through the arachnoid and dura mater to enter the epidural space, whereas some is taken up by the blood vessels of the pia and dura maters.[30]

Drug penetration and uptake is directly proportionate to the drug mass, CSF drug concentration, contact surface area, lipid content (high in spinal cord and myelinated nerves), and local tissue vascular supply, but is inversely related to nerve root size. The concentration of local anaesthetic in the CSF is highest at the site of subarachnoid injection in the case of spinal anaesthesia (generally L2-L4 levels).

Diffusion is the primary mechanism of local anaesthetic distribution in the CSF from areas of high concentration (i.e., at the site of injection) toward other segments of the spinal cord with low drug concentration.[29] Rostral spread after the administration of a small local anaesthetic dose, often evident within 10 to 20 minutes, is related to the CSF circulation time. Longitudinal oscillations generated by the pulsations of the arteries in the skull are believed to be responsible for CSF bulk flow. This likely facilitates the cephalad distribution of local anaesthetic from the lumbar subarachnoid space to the basal cisterns within 1 hour of injection.

Regression of neural blockade results from a decline in the CSF drug concentration, which in turn is caused by non-neural tissue uptake and, most importantly, vascular absorption. Time for block regression is also inversely correlated with CSF volume. Drug is absorbed by the vessels in the pia mater or the epidural vessels through back diffusion before entering the systemic circulation.

Drug metabolism does not takes place in the CSF. The rate of elimination is also depends upon the distribution of local anaesthetic; greater spread will expose the drug to a larger area for vascular absorption and thus a shorter duration of action. Lipid-soluble local anaesthetics (e.g., bupivacaine) bind to epidural fat to form a depot that can slow vascular absorption.[31]

EFFECTS ON ORGAN SYSTEMS

Cardiovascular system:[24,27]

The effects of neuraxial blocks on blood pressure are similar in some ways to the combined use of intravenous α1- and β-adrenergic blockers on cardiac output: decreased stroke volume and heart rate caused by blockade of the peripheral (T1-L2) and cardiac (T1-T4) sympathetic fibers as well as adrenal medullary secretion.

BLOCK BELOW T4

The effect of neuraxial blockade on the cardiovascular system depends on the level and the degree of sympathetic blockade. Vasomotor tone is maintained by sympathetic fibers from T5 to L1 that innervate vascular smooth muscle. Blockade of these fibers causes venodilation with venous pooling as well as arterial vasodilatation with decreased systemic vascular resistance. The venous pooling leads to a marked decrease in venous return, right atrial pressure, and subsequently, cardiac output. The decrease in venous return can then lead to an increase in cardiac vagal tone, especially for blocks near the T5 level. Clinically, hypotension can be noted in the patients.[32]

The compensatory mechanism for the decrease in mean arterial pressure is a reflex increase in vasoconstriction above the level of the block as well as a release in catecholamines from the adrenal medulla.

If normal cardiac output is maintained either by volume loading or by physiologic mechanisms (i.e., physiologic release of catecholamine, vasoconstriction in unblocked area) the total peripheral vascular resistance will only decrease by approximately 15%, a value well tolerated by a healthy patient. In an elderly patient with cardiovascular disease, a more ominous decrease in blood pressure with significant hypotension can develop.

BLOCK ABOVE T4

The cardiovascular effects of a block above T4 are the result of a high sympathetic block. The cardiac sympathetic fibers arise from T1 to T4, and when blocked, profound hypotension (the result of a decrease in cardiac contractility) and bradycardia can occur. In addition to the cardiac effects, a high level of sympathetic blockade causes-[33, 34]

- Increased central venous pressure without an increase in stroke volume
- Vasoconstriction in the head, neck, and upper limbs
- Splanchnic nerve blockade with blockade of adrenal medullary secretion of catecholamines
- Blockade of vasoconstrictive effect on the capacitance vessels of the lower limb.

When a sympathetic block occurs at such a high level, the cardiovascular system may be left without its mechanisms for responding to low cardiac output states. This can be detrimental to a patient with limited cardiac reserve because profound hypotension with bradycardia and decreased contractility can result.[35] The anaesthesiologist must be prepared to take over the control of the circulatory system until the block subsides and the patient stabilizes.

Central nervous system

Spinal anaesthesia induced hypotension may decrease regional cerebral blood flow (CBF) in elderly patients and those with pre-existing hypertension. Both CBF and velocity decline as a result of changes in the cerebral vasculature, especially in the elderly. Whether cerebral autoregulation is impaired in the elderly is still debatable.[36]

Neuroendocrine system

Surgical stress produces a variety of changes in endocrine and metabolic function. Increased protein catabolism and oxygen consumption are common. Increased plasma concentrations of catecholamines, vasopressin, growth hormone, renin, angiotensin, cortisol, glucose, antidiuretic hormone, and thyroid-stimulating hormone have been documented and referred to as the surgical stress response.

An intraoperative manifestation of surgical stress are demonstrated as hypertension, tachycardia, hyperglycemia, suppressed immune function, and altered renal function. Afferent sensory information from the surgical site is thought to play a vital role in the response. The response can be completely abolished by an appropriate level of sensory blockade produced by regional anaesthesia.

Respiratory system

Spinal and epidural blocks to midthoracic levels have little effect on pulmonary function in patients without pre-existing lung diseases. The lung volumes, minute ventilation, dead space, arterial blood gas tensions and shunt fraction shows little or no change during spinal or epidural anaesthesia. Interestingly the ventilatory response to hypercapnia is actually increased by spinal and epidural block.[37, 38]

High blocks associated with abdominal and intercostals muscle paralysis can impair ventilatory functions requiring active exhalation. For example, expiratory reserve volume, peak expiratory flow and minute ventilation may be significantly reduced by high spinal or epidural blocks.

Gastrointestinal system

Neuraxial blockade from T6 to L1 disrupts splanchnic sympathetic innervation to the gastrointestinal tract, resulting in a contracted gut and hyperperistalsis. Nausea and vomiting may be associated with neuraxial block in as much as 20% of patients

and they are primarily related to gastrointestinal hyperperistalsis caused by unopposed parasympathetic (vagal) activity. Atropine is effective in treating nausea associated with high (T5) subarachnoid blockade.[39]

A reduction in hepatic blood flow parallels the reduction in mean systemic arterial pressure in the setting of spinal anaesthesia.[29]

Genitourinary system

Sympathetic supply to kidney is from T11-L1 via the lower splanchnic nerve. Any effects on renal function are solely due to hypotension, renal blood flow is decreased but does not cease until blood pressure has fallen to about 80mm Hg. These changes are transient and disappear when B.P. rises again. The penis is often engorged and flaccid due to paralysis of Nervi erigenti (S2-S3) and this is also a positive sign of a successful block. Post spinal retention of urine may be moderately prolonged as S2-S3 contains small autonomic fibers and their paralysis lasts longer that of larger sensory and motor fibers. During prolonged blockade of lumbar and sacral segments, the bladder must be palpated so that catheterization can be employed when necessary.[40]

PHYSIOLOGICAL CHANGES IN PREGNANCY[41]

Pregnancy causes major physiological changes in maternal organs to support fetal growth and survival and to prepare for labour. These changes are due to hormonal alterations, mechanical effects of the gravid uterus, increased metabolic and oxygen requirements, metabolic demands of the fetoplacental unit, and hemodynamic alterations associated with the placental circulation.[42,43] Such changes become more significant as pregnancy progresses, and they have major implications for anaesthetic management, especially in high-risk parturients.

Cardiovascular changes

During the first trimester cardiac output is 35% higher than in the non-pregnant state, second and third trimester it is 40-50% higher than non pregnant state.

There is a steady rise from an average of 6.7 litres/minute at 8-11 weeks to about 8.7 litres/minute flow at 36-39 weeks; due to an increase in stroke volume (35%) and heart rate (15%).

The maximum increase in CO is seen immediately after delivery (80-100% more than prelabor values) this abrupt increase is due to autotransfusion from uterine contraction, reduced vascular capacitance from loss of intervillous space and decrease lower extremity venous pressure from release of aortocaval compression.

Although CO and plasma volume increase, SBP decreases secondary to reduction in systemic vascular resistance.

SBP, DBP and MAP decrease by 5-20% by 20 wks gestational age and gradually increase towards non-pregnant values as pregnancy progresses. DBP decrease more than SBP.

Decreased resistance is mainly due to low resistance vascular bed and vasodilatation by prostacyclin and estrogen. Vascular tone is more dependent upon

sympathetic control than in the non-pregnant state, so hypotension develops more readily and more markedly consequent to sympathetic blockade following spinal or extradural anaesthesia.

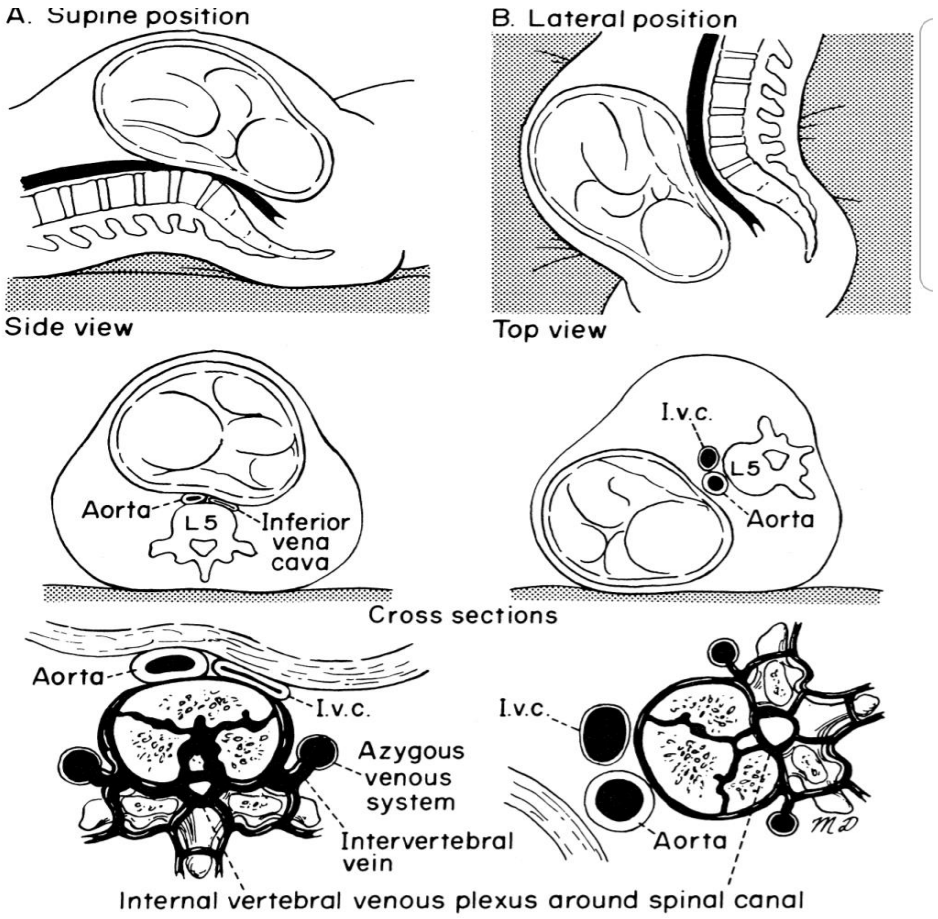


Figure 7: Aortocaval compression.[41]

Parturients at term are susceptible to hypotension, especially when in the supine position. Upto 10% of pregnant patients at term show signs of severe hypotension when assuming the supine position. This phenomenon has been termed the syndrome of supine hypotension.[44] To compensate, collateral routes of venous return develop, including the paravertebral veins to the azygos vein. Unlike compression of the vena cava, compression of the aorta is generally not associated with maternal symptoms in a healthy parturient but it may be associated with

decreased uteroplacental perfusion. Anaesthetics and drugs that cause vasodilatation or anaesthetic techniques that cause sympathectomy (e.g., neuraxial techniques) may exacerbate the impact of aortocaval compression. In the operating room, a small pillow or “wedge” should be used to provide left uterine displacement of 15 to 20 degrees. This angle can be increased as necessary by increasing the wedge or tilting the table

Respiratory system

The changes in the respiratory tract and oropharynx during pregnancy have profound anaesthetic implications. Capillary engorgement of the mucosa and edema of the oropharynx, larynx, and trachea may result in a difficult intubation. Any manipulation of the upper airway such as suctioning, insertion of airways, or laryngoscopy may cause bleeding and upper airway trauma**.** The mucosa of the nasopharynx is friable; instrumentation of the nose should be avoided if at all possible. In performing intubation of a pregnant patient, a smaller than usual endotracheal tube (size 6.0 to 7.0) should be used and repeated attempts at laryngoscopy minimized. Functional residual capacity (FRC) begins to decrease in the second trimester of pregnancy and is decreased by 20% of the nonpregnant value at full term. This decrease in FRC causes maternal hypoxemia to develop very quickly after apnea associated with the induction of general anaesthesia.

Hematologic System

Maternal blood volume begins to increase early in pregnancy as a result of changes in osmoregulation and the renin-angiotensin system, causing sodium retention and increasing total body water to 8.5 L. By term, blood volume increases by up to 45% whereas red cell volume increases by only 30%. This differential increase leads to the “physiologic anaemia” of pregnancy with an average haemoglobin and

hematocrit of 11.6 g/dL and 35.5%, respectively.[42] However, oxygen transport is not impaired by this relative anemia because the mother's body compensates for it by increased cardiac output, increased Pao2, and a rightward shift in the oxyhemoglobin dissociation curve. In pregnancy there is a state of hypercoagulation with increased levels of coagulation factors. Fibrinogen and factor VII are markedly increased, whereas the other factors increase to a lesser extent.[45] This increase in coagulation factors has been verified by thromboelastography and is probably a protective adaptation to lessen the risks associated with the acute haemorrhage that occurs at delivery.

Gastrointestinal System

Gastrointestinal tract undergoes significant anatomic and physiologic changes that increase the risk of aspiration associated with general anaesthesia. Progesterone relaxes smooth muscle; consequently, it impairs oesophageal and intestinal motility during pregnancy.[46]

Renal System

The increase in GFR 50% generally precedes the expansion of blood volume and is considered to be a marker of pregnancy-induced vasodilatation.

Central Nervous System

Pregnant women demonstrate increased sensitivity to both regional and general anaesthetics. When neuraxial anaesthesia is administered, pregnant women require less local anaesthetic than nonpregnant women do to reach a given dermatomal sensory level. Spinal anaesthetic dose requirement is reduced by 25% to 30% due to decrease in CSF volume, engorged epidural venous plexus, increased epidural fat and excessive lumbar lordosis. Also there is increase in neuronal susceptibility to local anaesthetics due to progesterone.

Pelvic widening & resultant head down tilt in lateral position cause greater degree of dermatomal spread.[47, 48]

Uterine Blood Flow

Uterine blood flow lacks autoregulation (vessels are maximally dilated during pregnancy), and uterine artery flow is therefore dependent on maternal blood pressure and cardiac output. Consequently, factors that alter blood flow through the uterus will adversely affect the fetal blood supply. Uterine blood flow decreases during periods of maternal hypotension, which can occur as a result of hypovolemia, haemorrhage, aortocaval compression and sympathetic blockade.

FETAL ASSESSMENT[49]

The fetal welfare depends upon various mechanisms at the time of birth or during caesarean section.

They are as follows:

1. Alteration in placental blood flow which occurs during maternal hypotension, aorto caval compression or due to uterine contraction.
2. Alteration in uterine contraction- uterine contraction can decrease placental perfusion which results in mild degree of fetal respiratory acidosis and hypoxemia.
3. Maternal hyperventilation and vasopressors can cause decrease in uteroplacental blood flow. The vasopressors are effective in restoring maternal blood pressure, but often cause uterine artery constriction and consequent ill effect on the fetus.

APGAR SCORE

In 1952, Dr. Virginia Apgar developed this test, for the quick assessment of newborns overall well-being. Performed at 1 and 5 minutes after birth. The 1-minute score determines how well the baby tolerated the birthing process. The 5-minute score tells the doctor how well the baby is doing outside the mother's womb.

Five cardinal signs form the basis for APGAR scoring. Numerical values are given

1. A – Appearance (color)
2. P – Pulse (heart rate)
3. G – Grimace (reflex irritability)
4. A – Activity (muscle tone)
5. R – Respiration.

Figure 8: APGAR score

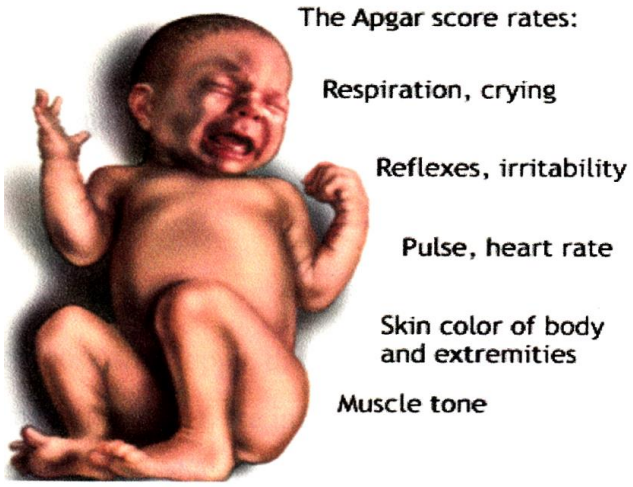


Table 4: APGAR scoring

Signs	Scores		
	0	1	2
Appearance (color)	Blue- pale	Body pink , extremities blue	Completely pink
Pulse (heart rate)	Absent	Below 100 bpm	Over 100 bpm
Grimace (reflex irritability)	No motion	Some motion	Active motion (sneeze, cough, pull away)
Activity (muscle tone)	Absent	Arms and legs flexed	Good flexion, active movements
Respiration	Absent	Weak cry, hypoventilation	Good cry

Score of 0-3 = severely depressed

Score of 4-6 = moderately depressed

Score of 7-10 = good condition and is normal.

EPHEDRINE[50, 51]

Ephedrine is an alkaloid solution obtained from the plants of genus ephedra or prepared synthetically. Plants of this genus are commonly encountered in northern India and china. The herb containing ephedrine, Ma-hung, has been employed in Chinese indigenous medicine for over 5000 years.

Ephedrine is a sympathomimetic with both direct and indirect effects on adrenergic receptors.[52] It has alpha and beta adrenergic activity and has pronounced stimulating effects on central nervous system. In addition, it enhances release of nor-epinephrine from sympathetic neurons and therefore is a mixed acting sympathomimetic drug.

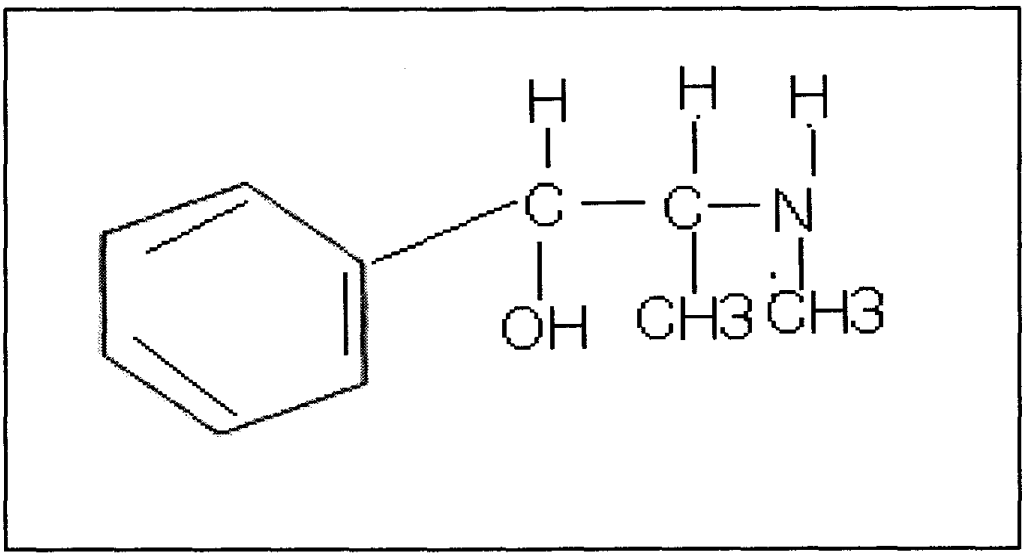
Chemical Name:

(1R, 2S) -2-(methylamino)-1-phenylpropan-1-ol

Chemical Formula:

C_{10} H_{15} NO

Figure 9: Chemical Structure:



Pharmacokinetics:

Ephedrine is readily and completely absorbed from the gastrointestinal tract. It is resistant to metabolism by monoamine oxidase and is largely excreted unchanged in the urine, together with small amounts of metabolism produced by hepatic metabolism.

Ephedrine has plasma half-life ranging from 3 to 6 hours depending on urinary pH. Elimination is enhanced in acid urine. Intramuscular injection of ephedrine is acceptable because local vasoconstriction is insufficient for greater delay in systemic absorption.

Up to 40% of single dose of ephedrine is excreted unchanged in urine, some ephedrine is deaminated by mono-amino oxidase in liver. 65-70% administered dose is excreted in 12 hrs and approximately 100% in 24hrs.

Pharmacodynamics:

The pharmacological effects of this drug are due to the endogenous release of nor-epinephrine (indirect action) also the drug has direct stimulant effects on adrenergic receptors (direct action).

Effects on Cardiovascular system:

Intravenous administration of ephedrine results in increase in blood pressure both systolic and diastolic by increasing cardiac output and by inducing peripheral vasoconstriction. Tachycardia may occur but is less frequent than with adrenaline.

Ephedrine has a more prolonged though less potent action than adrenaline. Also it causes, decrease in renal and splanchnic blood flow while, increase in coronary and skeletal muscle blood flow.

Effects on Respiratory System:

It has stimulant action on the respiratory center. It causes bronchodilatation by activation of beta 2-adrenergic receptors. Ephedrine is used as oral medication to treat bronchial asthma.[50]

Effects on genitourinary and gastrointestinal system:

Ephedrine decreases intestinal tone and motility. Ephedrine 0.5 mg/kg I.M. has an antiemetic effect.[50, 53] By alpha-receptor stimulation, enhances tone of trigone and sphincter of bladder, may increase resistance to outflow of urine.

Effects on uterus:

It maintains uterine blood flow towards normal and relaxes uterine smooth muscle.[54,55]

Effect on Eye:

It causes mydriasis on local as well as systemic administration but does not affect the light reflexes, accommodation and intraocular tension.

Effect on central nervous system:

Ephedrine stimulates the central nervous system by acting on the reticular activating system. In therapeutic doses it often produces restlessness, insomnia, anxiety, tremors and increased mental activity. Toxic doses may produce convulsion.

Metabolic effects:

It increases the metabolic rate and oxygen consumption.

Tachyphylaxis:

Repeated administration of ephedrine fails to elicit the same presser response, termed as tachyphylaxis. This is due to persistent blockade of adrenergic receptors.[52]

Adverse Effect of Ephedrine:

The common adverse effects are

- Tachycardia
- Anxiety
- Restlessness
- Insomnia

Tremors, dry mouth, vertigo and arterial hypertension.

Over dosage can give rise to paranoid psychosis, delusions and hallucinations.

Contraindications to use:

1. Ischaemic Heart Disease:

Since ephedrine has both inotropic and chronotropic effect on heart, it should be avoided in patients with ischemic heart diseases.

2. Hypertension:

It increases blood pressure so it should be avoided in hypertensive patients.

3. Thyrotoxicosis:

Patients with hyperthyroidism may be hyper susceptible to the effect of ephedrine.

Drug Interactions:

- Administration of ephedrine may cause hypertensive crisis in patients receiving monoamino oxidase inhibitors.
- Ephedrine should be avoided or used with care in patients undergoing anaesthesia with halothane; sensitizes to arrhythmias.

Preparations:

1) Ephedrine hydrochloride tablet contains 30mg of the salt. Dose- 15 to 60mg by mouth.
2) Ephedrine hydrochloride elixir -l5mg/5m1. Dose- 5 to l0 ml.
3) Ephedrine paediatric syrup NF containing 8mg of ephedrine hydrochloride/5m1. Dose 5m1 / year of age to a maximum of 20 ml per dose, 4to 6 hourly.
4) Ephedrine hydrochloride injections 30mg per ml S.C. / I.M. / I.V.
5) Ephedrine (1%) nasal drops.
6) Ephedrine (3-5%) eye drops.

LACTATED RINGER'S SOLUTION[56, 57]

It is the crystalloid intravenous fluid.

In 1880, Sydney Ringer, a British physician studied the contraction of isolated frog heart. He introduced a solution that contained calcium and potassium in sodium chloride solution to promote cardiac contraction and cell viability. This is known as Ringer's saline solution. The original solution of inorganic salts was further modified by Alexis Hartmann for the purpose of treating acidosis in children. Hartmann added lactate, which mitigates changes in pH by acting as a buffer for acid. Thus the solution became known as "lactated Ringer's solution" or "Hartmann's solution".[57]

Composition:

Sodium chloride = 6g/L

Sodium lactate = 3.1g/L

Potassium chloride = 0.3g/L

Calcium chloride = 0.2g/L

Ionic concentration of RL solution

Sodium ion = 130 mEq/L = 130 mmol/L

Potassium ion = 4 mEq/L = 4 mmol/L

Calcium ion = 2.7 mEq/L = 1.5 mmol/L

Chloride ion = 109 mEq/L = 109 mmol/L

Lactate = 28 mEq/L = 28 mmol/L

Making a total osmolarity of 273 mOsm/L and pH of 6.5 and caloric content of 9 kCal/L.

Pharmacology

Ringer's Lactate is the most physiological fluid as the electrolyte content is similar to that of plasma. Larger volumes can be infused without risk of electrolyte imbalance. Due to high sodium content (130mEq/L) RL rapidly expands intravascular volume and is effective in treatment of hypovolemia. Sodium lactate in RL is metabolised to bicarbonates in liver and is useful in correction of metabolic acidosis.[57]

Indications

- Lactated Ringer's solution is often used for fluid resuscitation after a blood loss due to trauma, surgery, or a burn injury.
- Correction of severe hypovolemia.
- In diarrhoea induced hypokalemic metabolic acidosis.
- As maintenance fluid during surgery.

Contraindications

In severe liver diseases where there is impaired lactate metabolism leading to lactic acidosis.

Simultaneous infusion of RL and blood causes inactivation of anticoagulant by binding with calcium in RL and clotting of donor blood.[58]

MATERIALS AND METHODS

SOURCE OF DATA:

This study was carried out in the Department of Anaesthesiology,

METHOD OF COLLECTION OF DATA:

Study Design: Randomised control study.

Study Period: One and half years from December 2017 to August 2019.

Sample size calculation

With Anticipated Mean Difference of hypotension cases (%) between Preloading group and Ephedrine group as 28 and Anticipated SD as 30.1, the minimum sample size per group is 30 with 90% power and 5% level of significance.

Total is 60

By using the formula:

$$n = \frac{(z_\alpha + z_\beta)^2 \, 2 \, SD^2}{MD^2}$$

Where Z= Z statistic at a level of significance

MD= Anticipated mean difference

SD= Anticipated Standard deviation

Statistical analysis

All characteristics were summarized descriptively. For continuous variables, the summary statistics of N, mean, standard deviation (SD) was used. For categorical data, the number and percentage was used in the data summaries and data was analyzed by Chi square test for association, comparison of means using t test, ANOVA and diagrammatic presentation.

Study group:

60 healthy pregnant mothers without foetal compromise of ASA I & II who will undergo elective caesarean section under spinal anaesthesia were included in the study. With the help of computer generated random number tables, these patients were assigned to one of the two groups, each consisting of 30 patients.

Inclusion criteria:

1. Women posted for elective caesarean section with term singleton pregnancy of 39-41 weeks of gestation.
2. Age between 20-40 years.
3. Weight between 45-70 kg.
4. Height between 145-160 cm.
5. Women belonging to ASA I & II category.

Exclusion criteria :

1. Parturient with obstetric complications like abruption placenta, placenta previa, PIH, obesity, pre-existing hypertension, polyhydramnios.
2. Patients with evidence of fetal anomalies and fetal compromise.
3. Patients who are contraindicated for spinal anaesthesia.
4. Patients who develop labour pains during surgery.

Preliminaries:

- Written informed consent.
- Intravenous access with a 20 gauge I.V cannula under aseptic precautions.

Study materials :

- Boyles apparatus
- Resuscitation equipments and drugs
- Hudson mask and oxygen
- Injection Ephedrine
- Ringer lactate
- Injection Bupivacaine 0.5% hyperbaric
- 20G intravenous cannula
- 25G spinal needle
- Pulse oximeter, noninvasive blood pressure and ECG monitor.

Procedure:

Patients were randomly divided into 2 groups based on computer generated random number tables.

Group P: Preloaded with ringer lactate at 10 ml/kg over 15-20 min period prior to spinal anaesthesia.

Group E:

Ephedrine group- intravenous bolus of injection Ephedrine 10mg immediately after spinal anaesthesia.

Preoperative assessment:

Patients were admitted one day before the surgery. Preoperative evaluation of all the patients were performed with detailed history, physical examination including height, weight, evidence of spinal deformity and mental status of the patient. The basal heart rate and blood pressure were recorded prior to surgery with the patient lying in left lateral position on 3 occasions, the average of these values were noted as baseline recording. All the patients were kept nil orally for approximately 8 hours.

Informed valid written consent for participation in the study was taken from all the patients.

Intraoperative assessment:

Patient was randomly allocated into either Group P (Crystalloid group) or Group E (Ephedrine group). Intravenous access is obtained in all patients with a 20G I.V. cannula. In all selected patients baseline blood pressure and pulse rate and Sp02 were recorded. All patients were premedicated with Inj. Ranitidine hydrochloride 50mg I.V. and Inj. Ondansetron 4mg I.V.

All patients received an infusion of Ringer Lactate solution during the anaesthesia at a rate of 4-5ml/kg/hour.

Maternal arterial non invasive blood pressure, heart rate and oxygen saturation was recorded throughout the procedure.

Patient was placed in the left lateral position. Under strict aseptic precautions, lumbar subarachnoid block was performed at L3-L4 interspinous space using 25G spinal needle and then 10mg of 0.5% hyperbaric Bupivacaine was injected slowly at the rate of 0.1ml/sec after free flow of CSF is confirmed. The time of institution of subarachnoid block was noted. Immediately after injection patient was replaced in supine horizontal position with 15 degree wedge under right buttock for left uterine displacement in order to prevent supine hypotension syndrome.

Surgery was started when the sensory level of block reaches T6 dermatome which is checked by loss of pinprick sensation.

Maternal heart rate and blood pressure were recorded at every 2 min interval for the first 10 min, then every 5 min for the next 20 min and thereafter every 10 min till the end of the surgical procedure.

Hypotension is defined as a decrease in systolic blood pressure >20% from the baseline or below 100 mm of Hg and was managed with rescue doses of I.V. Ephedrine (6mg). Maternal bradycardia, defined as heart rate <50 beats/min was treated with 0.6mg of intravenous Atropine. The patients were monitored for any reactive hypertension (SAP >20% of the baseline values), tachycardia >120beats/min, nausea and vomiting were recorded.

After delivery of the baby, all mothers received 20 IU of Oxytocin through drip. Neonatal APGAR scores at 1 minute and 5 minutes after delivery were recorded.

OBSERVATION AND RESULTS

Study was confined to 60 pregnant women posted for elective caesarean under subarachnoid block. With help of computer generated random number tables, these 60 patients were assigned to one of the two groups each consisting of 30 patients.

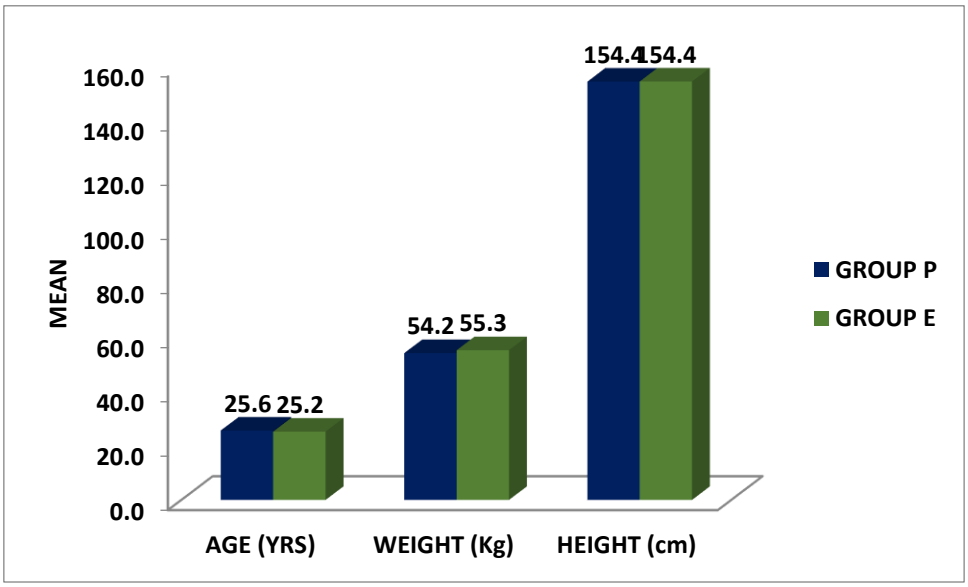
Group P (n=30) Patients received intravenous fluid preload of Ringer Lactate solution at 10ml/kg over 15-20min prior to spinal anaesthesia.

Group E (n=30) Patients received an intravenous bolus Inj. Ephedrine 10mg immediately after spinal anaesthesia.

TABLE 5: DISTRIBUTION OF BACKGROUND PARAMETERS BETWEEN STUDY GROUPS

PARAMETERS	GROUP P		GROUP E		p value
	Mean	SD	Mean	SD	
AGE (YRS)	25.6	3.5	25.2	4.3	0.694
WEIGHT (Kg)	54.2	6.3	55.3	4.6	0.441
HEIGHT (cm)	154.4	2.3	154.4	2.6	0.959

FIGURE 10: DISTRIBUTION OF BACKGROUND PARAMETERS BETWEEN STUDY GROUPS



In Preloading group the mean age of the patient was 25.6 ± 3.5 years, the mean weight 54.2±6.3 kg and the mean height was 154.4± 2.3cm, where as in Ephedrine group the mean age of the patient was 25.2±4.3 years, the mean weight 55.3±4.6 kg and the mean height was 154.4±2.6cm. Mean age, weight and height of both the groups were compared and showed no significant difference, p value >0.05.

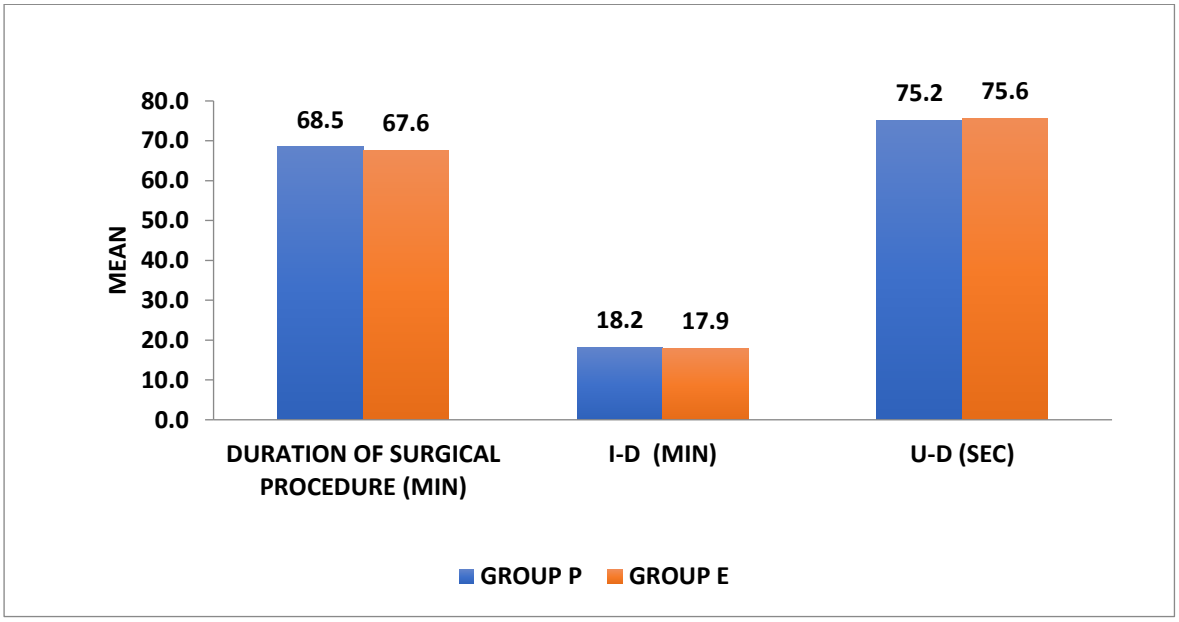
TABLE 6: COMPARISON OF DURATION OF SURGERY IN BOTH GROUPS

PARAMETERS	GROUP P		GROUP E		p value
	Mean	SD	Mean	SD	
DURATION OF SURGICAL PROCEDURE (MIN)	68.5	4.5	67.6	5.1	0.714
I-D (MIN)	18.2	2.1	17.9	1.8	0.987
U-D (SEC)	75.2	8.6	75.6	7.6	0.962

I-D – Induction of spinal to delivery of baby interval.

U-D- Uterine incision to delivery of baby interval.

FIGURE 11: COMPARISON OF DURATION OF SURGERY IN BOTH GROUPS



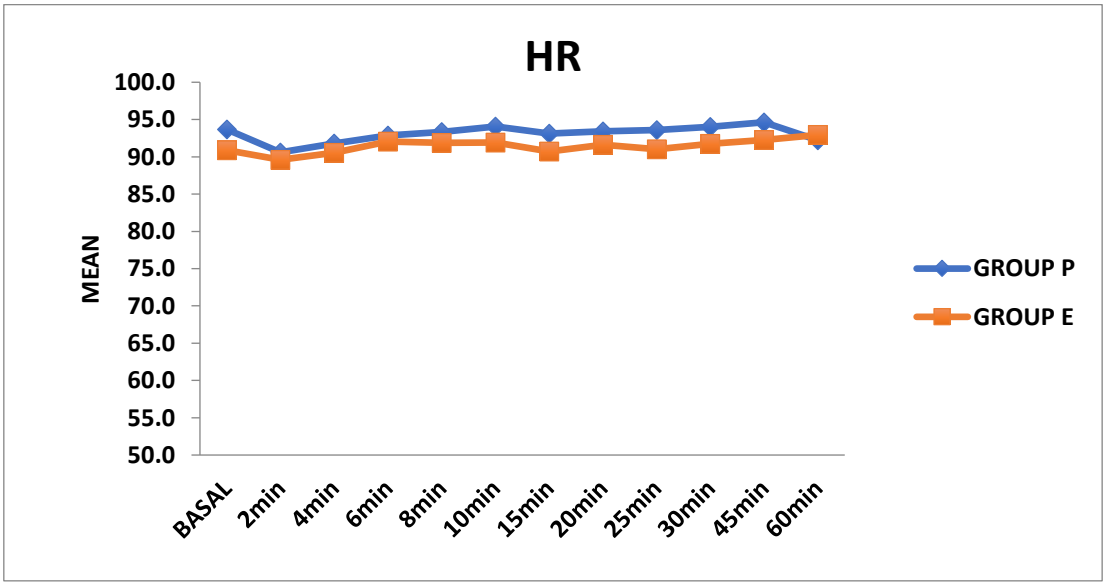
In Preload group the mean duration of surgical procedure was 68.5±4.5 min, the mean I-D was 18.2±2.1 min and the mean U-D was 75.2±8.6 sec. While in Ephedrine group, the mean duration of surgical procedure was 6.7±5.1 min, the mean I-D was 17.9±1.8 min and the mean U-D was 75.6±7.6 sec.

The mean duration of surgery, the mean I-D and the mean U-D of both the groups were comparable and showed no significant difference with p value >0.05.

TABLE 7: CHANGE IN MEAN HR OVER TIME BETWEEN STUDY GROUPS

HR	GROUP P		GROUP E		p value
	Mean	SD	Mean	SD	
BASAL	93.7	5.9	90.9	7.3	0.110
2min	90.6	8.8	89.6	6.2	0.614
4min	91.8	10.7	90.5	8.1	0.609
6min	92.9	12.6	92.1	8.9	0.778
8min	93.3	9.2	91.9	8.4	0.523
10min	94.1	8.0	91.9	7.5	0.289
15min	93.1	7.5	90.7	6.3	0.184
20min	93.4	5.8	91.6	7.3	0.295
25min	93.6	5.7	91.0	6.3	0.099
30min	94.0	5.5	91.7	7.0	0.170
45min	94.6	4.8	92.3	7.2	0.138
60min	92.2	18.0	92.9	7.3	0.837

FIGURE 12: CHANGE IN MEAN HR OVER TIME BETWEEN STUDY GROUPS



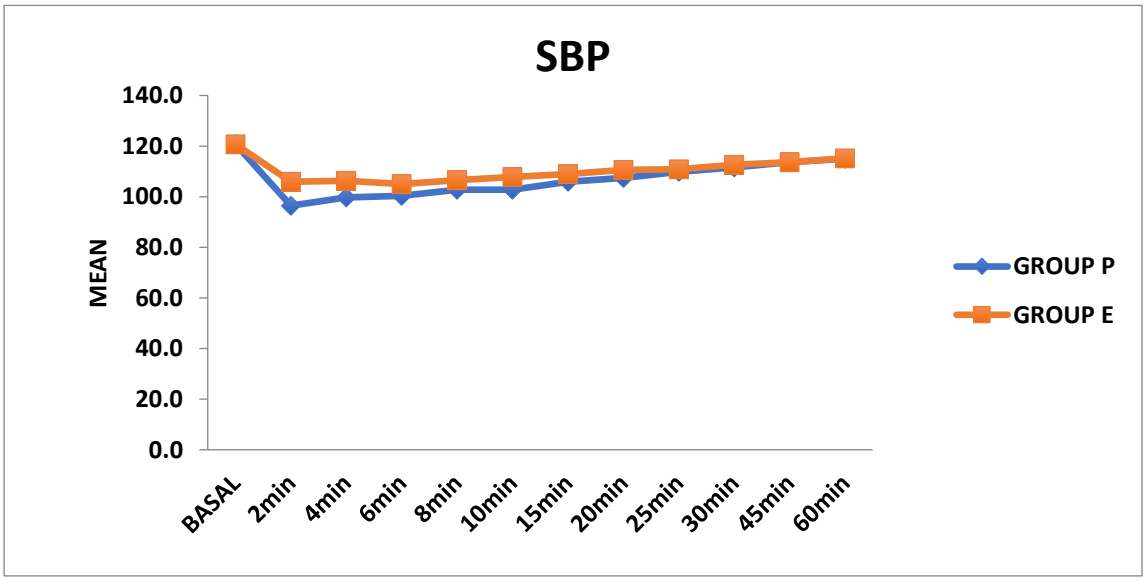
The mean heart rate of both the groups were compared and there was no statistically significant difference, p value >0.05.

TABLE 8: CHANGE IN MEAN SBP OVER TIME BETWEEN STUDY GROUPS

SBP	GROUP P		GROUP E		p value
	Mean	SD	Mean	SD	
BASAL	120.8	5.0	120.7	4.9	0.959
2min	96.5	10.6	105.9	9.3	0.001*
4min	99.7	6.4	106.3	7.4	0.001*
6min	100.4	6.4	105.0	10.0	0.038*
8min	102.8	4.5	106.6	7.7	0.023*
10min	102.7	6.0	107.8	7.8	0.006*
15min	105.9	4.1	108.9	6.8	0.038*
20min	107.4	4.6	110.6	6.5	0.032*
25min	109.9	4.0	110.8	5.3	0.444
30min	111.7	4.5	112.6	5.9	0.492
45min	113.6	4.8	113.6	5.1	1
60min	115.1	5.7	115.2	5.0	0.924

Note: * significant at 5% level of significance (p<0.05)

FIGURE 13: CHANGE IN MEAN SBP OVER TIME BETWEEN STUDY GROUPS



In our study we found that there was decline in systolic blood pressure during first 20 min in Group P compared to group E after spinal anaesthesia and values were found to be statistically significant.

The baseline SBP in Group P was 120.8±5.0 and in Group E was 120.7±4.9 with p value of 0.954 showing no significant difference.

The mean SBP in Group P was 96.5±10.6 and in Group E was 105.9±9.3 at 2^{nd} min with p value 0.001. At 4^{th} min in Group P and E were 99.7±6.4 and 106.3±7.4 with p value 0.001.

The mean SBP in Group P at 6min, 8min, 10min, 15min and 20min was 100.4±6.4, 102.8±4.5, 102.7±6, 105.9±4.1 and 107.4±4.6 respectively. Whereas in Group E was 105±10, 106.6±7.7, 107.8±7.8, 108.9±6.8 and 110.6±6.5 respectively. On comparing both the groups there was a significant difference (p value <0.05) for initial 20 minutes.

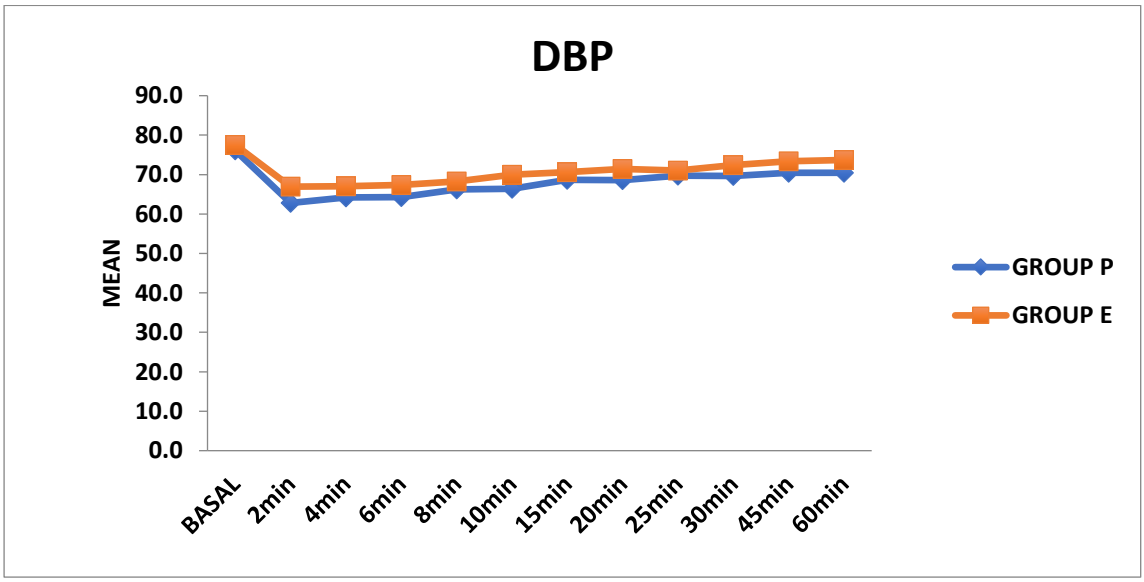
In preloading group 20 (66%) patients out of 30 patients had incidence of hypotension. Whereas in ephedrine group 8 (26%) patients out of 30 had hypotension. This shows higher incidence of hypotension in preloading group.

TABLE 9: CHANGE IN MEAN DBP OVER TIME BETWEEN STUDY GROUPS

DBP	GROUP P		GROUP E		p value
	Mean	SD	Mean	SD	
BASAL	76.1	6.7	77.5	4.3	0.341
2min	62.8	6.7	66.9	6.6	0.020*
4min	64.2	4.4	67.1	5.8	0.035*
6min	64.3	4.0	67.4	7.3	0.044*
8min	65.3	2.3	68.3	5.7	0.011*
10min	66.4	4.1	70.0	6.8	0.016*
15min	68.7	3.9	70.6	5.8	0.137
20min	68.6	5.1	71.5	6.1	0.053
25min	69.7	3.6	71.0	4.8	0.254
30min	71.2	2.2	72.4	4.5	0.197
45min	72.3	2.6	73.4	5.0	0.277
60min	72.1	2.3	73.7	4.9	0.112

Note: * significant at 5% level of significance ($p<0.05$)

FIGURE 14: CHANGE IN MEAN DBP OVER TIME BETWEEN STUDY GROUPS



The mean diastolic blood pressure of both groups were compared and there was significant drop of diastolic blood pressure in Group P for first 10min when compared to Group E with p value <0.05%.

The mean diastolic blood pressure at 2nd min was 62.8±6.7 in Group P and 66.9±6.6 in Group E with p value 0.02 (<0.05). At 4th min it was 64.2± 4.4 in Group P and 67.1±5.8 in group E, p value 0.035. At 6th min it was 64.3±4 in Group P and 67.4±7.3 in Group E with p value of 0.044. At 8th min it was 65.3±2.3 in Group P and 68.3±5.7 in Group E with p value of 0.011.

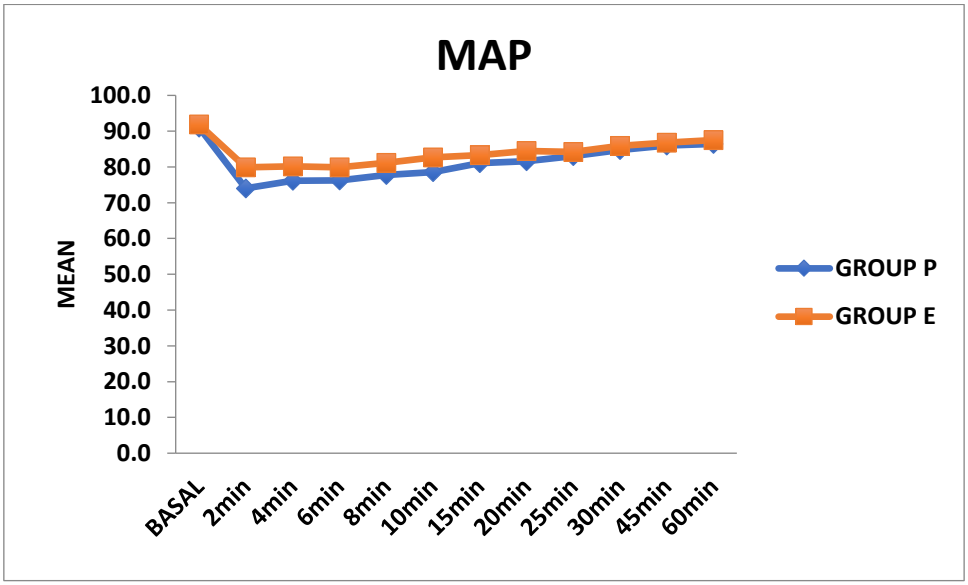
At 10th min it was 66.4±4.1 in Group P and 70±6.8 in Group E with p value of 0.016 which is statistically significant difference. Later on there was no significant changes noted.

TABLE 10: CHANGE IN MEAN MAP OVER TIME BETWEEN STUDY GROUPS

MAP	GROUP P		GROUP E		p value
	Mean	SD	Mean	SD	
BASAL	91.0	5.7	91.9	4.1	0.519
2min	74.0	7.5	79.9	7.3	0.003*
4min	76.1	4.5	80.1	6.1	0.006*
6min	76.2	4.4	79.9	8.0	0.032*
8min	77.8	2.6	81.2	6.0	0.007*
10min	78.5	4.1	82.7	7.0	0.007*
15min	80.1	3.4	83.3	5.8	0.041*
20min	81.6	4.6	84.5	6.0	0.036*
25min	83.1	3.3	84.2	4.5	0.274
30min	84.7	2.1	85.9	4.5	0.202
45min	86.0	2.5	86.8	4.5	0.382
60min	86.4	2.7	87.5	4.5	0.273

Note: * significant at 5% level of significance (p<0.05)

FIGURE 15: CHANGE IN MEAN MAP OVER TIME BETWEEN STUDY GROUPS



In our study, the changes in Mean Arterial Pressure (MAP) in both the groups were compared and it showed statistically significant fall in MAP for initial 20minutes in preloading group when compared to ephedrine group (p value <0.05).

The Mean Arterial Pressure (MAP) at different intervals in Group P and Group E respectively were 74±7.5 and 79.9±7.3 at 2 min; 76.1±4.5 and 80.1±6.1 at 4 min; 76.2±4.4 and 79.9±8.0 at 6min; 77.8±2.6 and 81.2±6 at 8min; 78.5±4.1 and 82.7±7 at 10min, 80.1±3.4 and 83.3±5.8 at 15min 81.6±4.6 and 84.5±6.0 at 20min with p value <0.05, showing statistically significant difference.

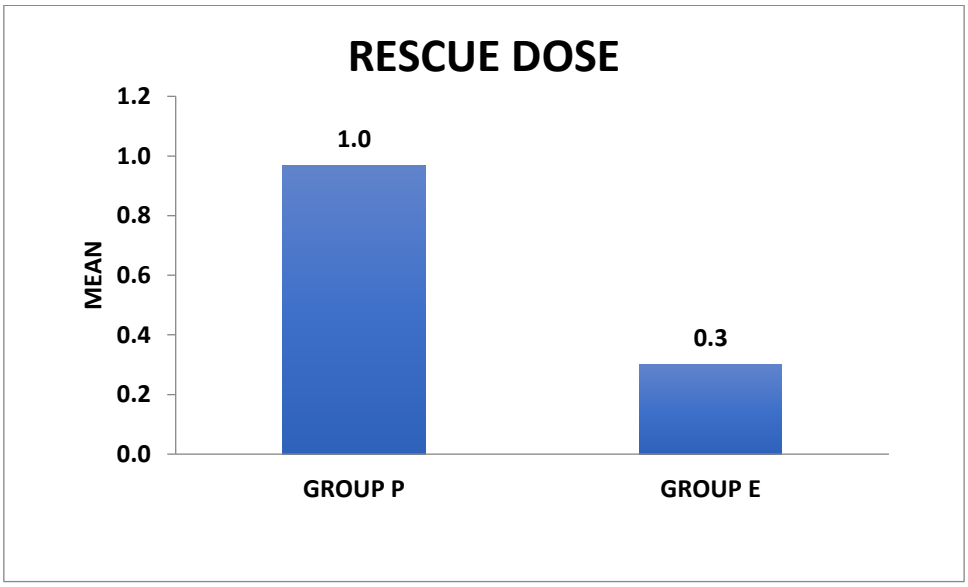
No significant difference between the groups was noted later on, from 25minutes to 60minutes.

TABLE 11: MEAN RESCUE DOSE BETWEEN STUDY GROUPS

RESCUE DOSE	GROUP P		GROUP E		p value
	Mean	SD	Mean	SD	
	1.0	0.8	0.3	0.5	<0.001*

Note: * significant at 5% level of significance (p<0.05)

FIGURE 16: MEAN RESCUE DOSE BETWEEN STUDY GROUPS



On comparing the mean rescue doses between the groups showed that Group P required more rescue doses of Inj. Ephedrine than Group E to combat hypotension and the results were statistically significant.

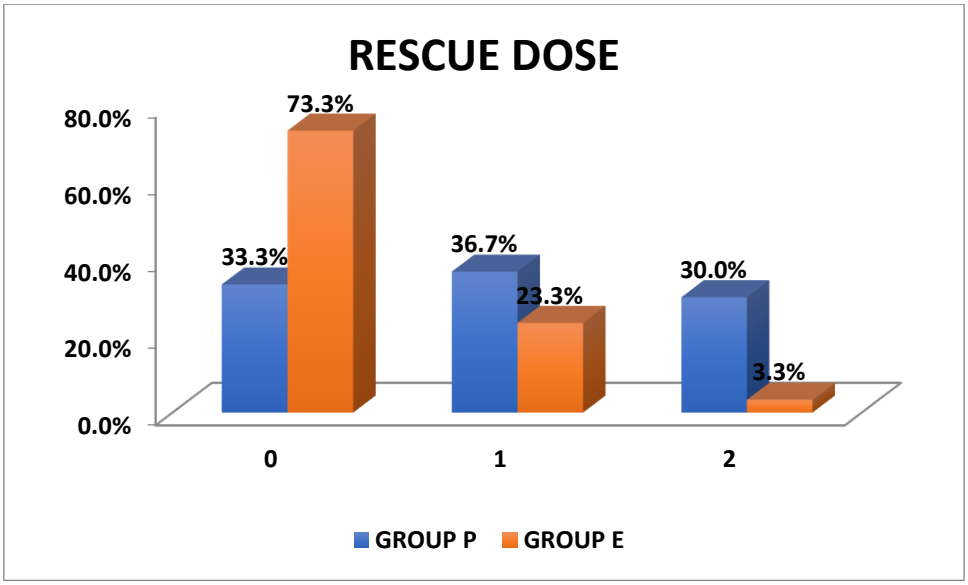
This also shows that incidence of hypotension was more in Group P when compared to Group E.

TABLE 12: NUMBER OF RESCUE DOSE BETWEEN STUDY GROUPS

RESCUE DOSE	GROUP P		GROUP E		p value
	N	%	N	%	
0	10	33.3%	22	73.3%	0.003*
1	11	36.7%	7	23.3%	
2	9	30.0%	1	3.3%	
Total	30	100.0%	30	100.0%	

Note: * significant at 5% level of significance ($p<0.05$).

FIGURE 17: NUMBER OF RESCUE DOSE BETWEEN STUDY GROUPS



The number of rescue doses of Inj. Ephedrine to combat hypotension required in both the groups were compared and showed statistically significant difference.

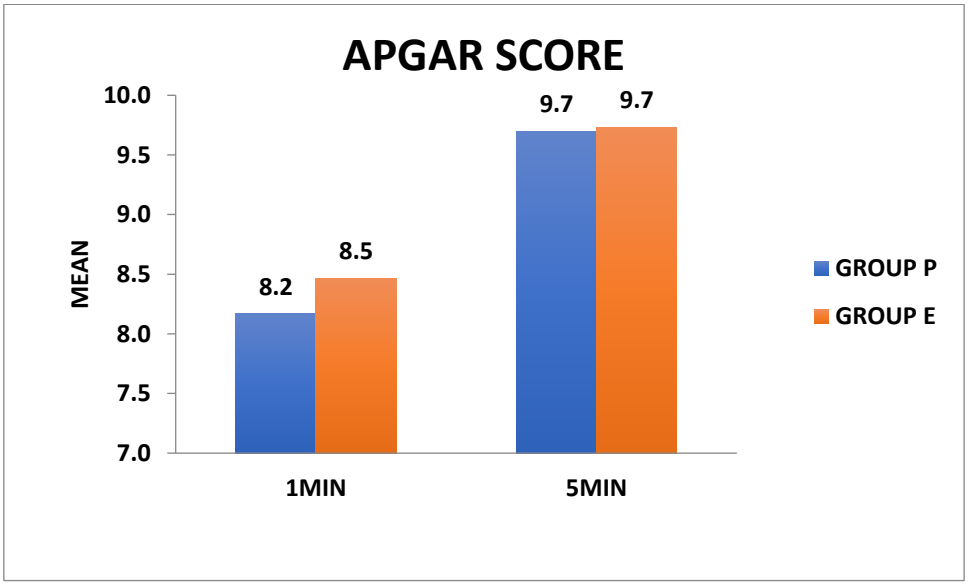
In preload group out of 30 patients, 11 (36.7%) patients required single rescue dose of Inj. Ephedrine and 9 (30%) patients required double dose of rescue ephedrine. Totally 20 (66.7%) patients required rescue doses of Inj. Ephedrine during the procedure.

In ephedrine group out of 30 patients, 7 (23.3%) patients required single rescue dose of Inj. Ephedrine and only 1 (3.3%) patient required double dose of rescue ephedrine. Totally 8 (26.7%) patients from Group E required rescue doses of Inj. Ephedrine during caesarean section.

TABLE 13: MEAN APGAR SCORE BETWEEN STUDY GROUPS

APGAR SCORE	GROUP P		GROUP E		p value
	Mean	SD	Mean	SD	
1MIN	8.2	0.7	8.5	0.6	0.074
5MIN	9.7	0.5	9.7	0.4	0.779

FIGURE 18: MEAN APGAR SCORE BETWEEN STUDY GROUPS

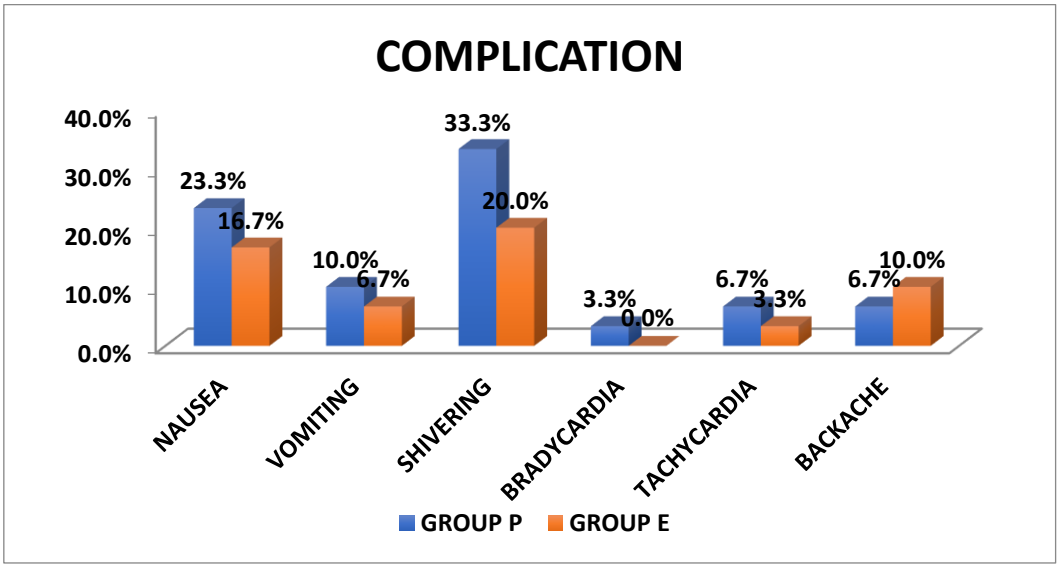


The mean APGAR scores at 1min in Group P and E were 8.2±0.7 and 8.5±0.6 respectively. At 5min the mean APGAR scores in Group P and E were 9.7±0.5 and 9.7±0.4 respectively. There was no significant difference in APGAR scores between the two groups.

TABLE 14: COMPLICATIONS BETWEEN STUDY GROUPS

COMPLICATION	GROUP P		GROUP E		p value
	N	%	N	%	
NAUSEA	7	23.3%	5	16.7%	0.519
VOMITING	3	10.0%	2	6.7%	0.64
SHIVERING	10	33.3%	6	20.0%	0.243
BRADYCARDIA	1	3.3%	0	0.0%	0.313
TACHYCARDIA	2	6.7%	1	3.3%	0.554
BACKACHE	2	6.7%	3	10.0%	0.64
Total	30	100.0%	30	100.0%	

FIGURE 19: COMPLICATIONS BETWEEN STUDY GROUPS



In preloading group out of 30 patients the incidence of nausea was 7 (23.3%) patients, vomiting was seen in 3 (10%) patients, shivering in 10 (33.3%) patients, bradycardia in 1 (3.3%) patient, tachycardia was noted in 2 (6.7%) patients and backache in 2 (6.7%) patients.

In ephedrine group out of 30 patients the incidence of nausea was 5 (16.7%) patients, vomiting was seen in 2 (6.7%) patients, shivering in 6 (20%) patients, tachycardia was noted in 1 (3.3%) patient and backache in 3 (10%) patients.

The comparison of both the groups with respect to the above parameters showed no statistically significant difference with p value >0.05.

There was no incidence of rebound hypertension or post dural puncture head ache in both the groups.

DISCUSSION

Spinal anaesthesia is a popular anaesthetic technique employed in lower segment caesarean section because of its technical simplicity, usage of small dose of drugs, minimal disturbance in physiology and good postoperative analgesia. Although spinal anaesthesia has all these benefits, its administration is invariably associated with hypotension. It has detrimental effect on both mother and fetus if not prevented.[2,3,4]

Preloading with intravenous crystalloids is the most common non pharmacological method of prevention of hypotension. Earlier studies have shown impressive results and it became established routine.[59] Some had shown that it is effective in reducing severity of hypotension[60] and some showed that it has limited effect on incidence of hypotension.[61]

Vasopressors remain the mainstay of drugs used in management of hypotension. Various studies have repeatedly proven the efficacy of ephedrine as vasopressor of choice in obstetric practice which increases blood pressure by increasing cardiac output and also has favourable effect on uteroplacental circulation.[6,7]

60 patients were enrolled in this study and were randomly divided into Group P and Group E of 30 patients each. Group P received fluid preloading of Ringer lactate solution at 10ml/kg over 15-20min prior to spinal anaesthesia, while Group E received IV bolus dose of Inj. Ephedrine 10mg immediately after spinal anaesthesia.

Dosage selection- various authors have studied the efficacy of ephedrine for prophylaxis and treatment of hypotension using various routes of administration such as intramuscular, intravenous bolus or intravenous infusion.

The efficacy of intramuscular administration has been inconsistent and its use may be associated with unacceptable hypertension, especially when subarachnoid block fails.[62,63] Ephedrine has a relatively slow onset and long duration of action. Hence it is difficult to titrate, especially when given by IV infusion compared with direct acting vasopressors. Intravenous infusion also adds to the complexity of the procedure. Hence intravenous bolus seems to be appropriate for management of spinal induced hypotension. Higher doses of intravenous ephedrine, though effective in the management of spinal hypotension are frequently associated with lower umbilical artery pH values. In our study we choose the dose of Inj. Ephedrine 10mg IV bolus as per studies conducted by Tsen LC *et al.*, in 2000.[64]

Patient characteristic:

In our study there was no significant difference between the two groups with respect to maternal demographics. Table 5 shows distribution of 60 patients with respect to their age, body weight and height.

In both the groups, age distribution ranged from 20- 40 years, with mean age in preloading group 25.6 years and mean age in ephedrine group was 25.2 years which were comparable with p value 0.694 (>0.05).

Mean weight in preloading group was 54.2 kg and in ephedrine group was 55.3 kg which were comparable with p value 0.441 (>0.05).

Mean height in preloading group was 154.4 cm and in ephedrine group was 154.4 cm which were comparable with p value 0.959 (>0.05).

Duration of surgery

In our study the mean duration of surgical procedure in preloading group and ephedrine group were 68.5 min and 67.6 min respectively, which were comparable. In both the groups the upper sensory level was T4. The mean duration between induction

of spinal anaesthesia to delivery of the baby in preloading and ephedrine group were 18.2 min and 17.9 min respectively, which were comparable. The mean duration between uterine incision to delivery of the baby in Group P and E were 75.2 sec and 75.6 sec respectively, which were comparable.

Blood pressure changes

Our study showed that there was statistically significant decline in systolic blood pressure during the first 20 mins in Group P compared to Group E after spinal anaesthesia.

The mean systolic blood pressure in Group P and E at 2^{nd} min were 96.5$\pm$ 10.6 mmHg and 105.9$\pm$ 9.3 mmHg respectively which was statistically significant difference with p value 0.001. At 4^{th} min Group P 99.7$\pm$ 6.4 mmHg and Group E 106.3$\pm$ 7.4 mmHg with significant difference with p value 0.001. At 6^{th} min Group P 100.4$\pm$ 6.4 mmHg and Group E 105$\pm$ 10 with p value 0.038. At 8^{th} min mean SBP in Group P was102.8$\pm$ 4.5 and in Group E was 106.6$\pm$ 7.7 with p value 0.023. At 10^{th} min in Group P was 102.7$\pm$ 6 and Group E 107.8$\pm$7.8 with p value 0.006. At 15^{th} min in Group P was 105.9$\pm$4.1 and in Group E was 108.9$\pm$6.8 with p value 0.038. At 20^{th} min the mean SBP in Group P and Group E were 107.4$\pm$4.6 and 110.6$\pm$6.5 with p value 0.032 which was a statistically significant difference. Later on there was no significant difference between the groups.

The mean diastolic blood pressures of both the group showed significant drop in Group P for first 10 min when compared to Group E with p value <0.05.

The changes in Mean Arterial Pressure (MAP) in both the groups were compared and it showed statistically significant fall in MAP in preloading group when compared to ephedrine group for initial 20minutes (p value <0.05) after spinal anaesthesia.

Out of 30 patients in preloading group 20 (66%) patients had hypotension while in ephedrine group out of 30patients 8 (26%) patients had hypotension. Hence the incidence of hypotension was higher in preloading group.

Shah SA, Naqvi SS, Abbas MA (2015) in their study of Comparison of crystalloid preloading and prophylactic administration of Ephedrine for prevention of spinal anaesthesia induced hypotension in 50 patients found that, out of 25 patients in each group, 11(44%) patients with 20ml/kg ringer lactate solution preloading had hypotension and 4(16%) patients with ephedrine prophylaxis of 0.25mg/kg body weight had incidence of hypotension. Their conclusion was that Intravenous Ephedrine given prophylactically to prevent hypotension is more effective than crystalloid preloading.[15]

Malhotra HB (2004) conducted a study on preloading and vasoconstrictors as combined prophylaxis for hypotension during subarachnoid block in lower limb and lower abdominal procedures including caesarean section. 90 patients were randomly allocated into three different groups. Group I patients received preloading with 15 ml/kg of ringer lactate. Group II patients received prophylactic ephedrine. Group III patients received preloading with half the volume as in group I and ephedrine in half the dose as in group II. The incidence of hypotension was only 3.33% in group III, 16.66% in group II and 43.33% in group I. The duration of significant fall in systolic arterial pressure, hypotensive episodes and requirement of I.V. fluids and ephedrine for management of hypotension were least in group III and maximum in group I. Concluded that combination of both crystalloid preloading and vasoconstrictor had maximal effect in preventing spinal induced hypotension, compared to that of preloading or vasoconstrictors alone. [12]

Heba Omar Ahmed *et al.*, (2016) in their study on volume preloading 15ml/kg Ringer lactate and ephedrine infusion of 5mg in 1st min and 5mg in 2nd min and 1mg every min for 15min found that the incidence of hypotension in volume preload group was 48% and ephedrine group was 24%. They concluded that ephedrine infusion after spinal anaesthesia was more effective than volume preloading in prevention of hypotension and without causing significant tachycardia.[19]

Hegde BK, Bhat MT. (2017) Prophylactic crystalloids or prophylactic crystalloids with Ephedrine: Comparison of hemodynamic effects during caesarean section under spinal anaesthesia using 0.5% Bupivacaine. Showed that incidence of hypotension was 70% in the crystalloid group and 5% in the crystalloid with ephedrine group. They concluded that prophylactic Ephedrine given by infusion along with crystalloids is not only a simple and effective method for prevention of hypotension during spinal anaesthesia during elective caesarean section patients but also contributes to less incidence of intraoperative nausea and vomiting.[20]

Incidence of hypotension in preloading group and ephedrine group from our study is comparable with the above different studies.

Heart rate changes

The mean heart rates of both the groups were comparable and there was no any statistically significant difference with p value >0.05. Heart rates in both the group were maintained close to baseline values.

Out of 30 patients in preloading group only 1(3.3%) patient had bradycardia and no incidence of bradycardia in ephedrine group; p value 0.313 (>0.05) no significant difference noted.

Tachycardia was noted in 2(6.7%) patients in preloading group and 1(3.3%) patient in ephedrine group with p value 0.554 , which is statistically not significant.

Heba Omar Ahmed *et al.*, (2016) in their study on volume preloading 15ml/kg Ringer lactate and ephedrine infusion showed that there was no significant difference in the heart rates of both the group and there was no significant tachycardia in ephedrine group.[19]

Hegde BK, Bhat MT. (2017) in their study of prophylactic crystalloids or prophylactic crystalloids with Ephedrine: Comparison of hemodynamic effects during caesarean section under spinal anaesthesia using 0.5% Bupivacaine. Showed that none of their patients developed hypertension and bradycardia.[20]

This could be explained by the minimum dose of ephedrine used and also effect of baroreceptor mediated reflex increase in heart rate in patients who became hypotensive.

Rescue doses of Injection Ephedrine

In our study out of 30 patients in Group P, 11 (36.7%) patients required only single rescue dose of ephedrine to correct hypotension as compared to 7 (23.3%) patients out of 30 in Group E showing significant difference in both the groups ($p < 0.05$).

Double rescue dose of ephedrine was required by 9 (30%) patients in Group P while 1 (3.3%) patient in Group E , this difference was found to be statistically significant ($p<0.05$).

In study of Hegde BK, Bhat MT. (2017) there were significant decrease in total rescue dose of ephedrine in patients receiving prophylactic ephedrine immediately after spinal anaesthesia.[20]

Kol IO *et al.*, in 2009 studied the effects of Intravenous Ephedrine during spinal anaesthesia for caesarean delivery. Intravenous preload of 15ml/kg ringer lactate was given. Shortly after spinal, Inj. Ephedrine 0.5mg/kg or Saline was injected

for 60sec. It showed that there were significant lower incidences of hypotension and nausea and vomiting in the ephedrine group compared with the preload. There was significant decrease in the total dose of rescue ephedrine in Ephedrine group.[13]

These findings suggest, the prophylactic bolus dose of intravenous ephedrine given at the time of intrathecal block reduces the incidence of hypotension.

APGAR score

In our study the neonatal APGAR scores at 1 min and 5min interval in both the groups were comparable and were statistically not significant with p value >0.05. Both the groups had good neonatal outcome.

This probably reflects the early recognition and restoration of hypotension by rescue dose of ephedrine.

Our results were similar to the study done by Desalu and Kushimo (2005) in comparing the effectiveness of Ephedrine infusion and crystalloid prehydration in preventing spinal induced hypotension in caesarean section in African parturients and they found that prophylactic Ephedrine given by standard infusion set was more effective than crystalloid pre-hydration in preventing hypotension during spinal anaesthesia for elective caesarean section. They also concluded that neonatal outcome was similar in both the groups.[4]

Nevan M. El-Mekawy (2012) in their study to compare the effectiveness of Co/post loading of fluids vs. immediate post spinal infusion of Ephedrine in prevention of hypotension, showed that intravenous infusion of Ephedrine 1mg/min immediately after spinal anaesthesia for emergency caesarean sections, even if there is no time for proper prehydration, can control effectively the hypotension without episodes of hypertension or significant tachycardia, and it had no effect on fetal well-being.[14]

Arun Kumar Natarajan *et al.,* (2015) in their study on Comparison of intravenous bolus Phenylephrine and intravenous Ephedrine during crystalloid co-loading in ameliorating hypotension under spinal anaesthesia for caesarean section, concluded that Phenylephrine and Ephedrine are equally efficient in managing hypotension during spinal anaesthesia for elective caesarean delivery. There was no difference between the two vasopressors in the incidence of true fetal acidosis and neonatal outcome.[16]

Laurent ducros *et al.,* 2002 in their study of effect of ephedrine on uterine artery velocities and resistance index, concluded that placental transfer of ephedrine is minimal and does not affect fetal hemodynamic parameters and neonatal outcome.[65]

Nausea and vomiting

In our study 7 (23.3%) patients out of 30 patients in Group P and 5 (16.7) patients out of 30 patients in Group E had incidence of nausea. Also 3(10%) patients in group P and 2(6.7%) patients in group E had vomiting. There was no significant difference between the two groups with respect to the incidence of nausea and vomiting (p value >0.05).

The results were in accordance with the study conducted by Heba Omar Ahmed *et al.,* (2016) in comparing volume Preload versus Ephedrine infusion for prevention of hypotension due to spinal anaesthesia in caesarean section. They found that incidence of nausea and vomiting was 20% in Preloading group and 12% in Ephedrine group with p value 0.23 and no significant difference between the groups with respect to incidence of nausea and vomiting.[19]

In contrast to our study, Hegde BK, Bhat MT. (2017) in their study on Prophylactic crystalloids or prophylactic crystalloids with Ephedrine: Comparison of hemodynamic effects during caesarean section under spinal anaesthesia using 0.5%

Bupivacaine, has shown that incidence of nausea and vomiting were less with prophylactic ephedrine group.[20]

Incidence of shivering

With regards to incidence of shivering our study showed no significant difference between the two groups. 10 (33.3%) patients in Group P and 6 (20%) patients in Group E had shivering, p value 0.243.

Chan WS *et al.,* in 1997 in their similar study note that 2(8.7%) patients out of 23 from ephedrine group while 9 (39.1%) patients out of 23 from preload group had shivering.[11]

Incidence of backache

In Group P 2 (6.7%) patients out of 30 patients and 3 (10%) patients out of 30 patients in Group E had mild backache. None of the patients in both the groups had post dural puncture headache. There was no significant difference between the groups, p value >0.05.

Vercauteren MP *et al.,* in 2000 evaluated the effectiveness of prophylactic ephedrine for prevention of hypotension associated with spinal anaesthesia for caesarean section. None of the patients complained of post dural puncture headache.[10]

SUMMARY

Spinal anaesthesia is a preferred technique for caesarean delivery for its distinct advantages over general anaesthesia such as airway related complications, aspiration, neonatal depression with anaesthetic agents.[1]

However spinal anaesthesia is frequently associated with hypotension in many of the cases if not prevented, which has detrimental effect on both mother and fetus.[2,3,4]

Preloading with 0.5-1 Lts of intravenous fluid fills the capacitance vessels and limit the hypotension when venodilatation occurs.[5]

Ephedrine is a sympathomimetic agent having both direct alpha and beta agonist effect and indirect effect by release of norepinephrine. It maintains uterine blood flow towards normal and restores maternal blood pressure.[6,7] it may be given prophylactically or when hypotension occurs.

The current study was to compare fluid preloading with Ringer Lactate solution and intravenous bolus dose of Ephedrine in preventing maternal hypotension during caesarean section under spinal anaesthesia.

In this study 60 patients undergoing elective caesarean section were randomly assigned to one of the two groups.

Group P: 30 patients received preload of Ringer Lactate solution I.V. at 10ml/kg over 15-20 min period prior to spinal anaesthesia.

Group E: 30 patients received I.V. bolus of Inj. Ephedrine 10mg immediately after spinal anaesthesia.

Patients from both the group received spinal anaesthesia with Inj. Bupivacaine heavy 0.5% 10mg.

Hypotension was treated with rescue dose of Inj. Ephedrine 6mg I.V.

All patients in both the groups were assessed and monitored for incidence of hypotension, number of rescue doses of injection ephedrine, APGAR score at 1 and 5 min, incidence of nausea, vomiting , shivering and post spinal adverse events and any other adverse maternal effects of ephedrine (hypertension or tachycardia).

Our study showed significant difference in systolic blood pressure between two groups as there was greater decline in blood pressure during first 20min in patients preloaded with Ringer Lactate solution compared to patients who received prophylactic intravenous bolus dose of ephedrine immediately after spinal anaesthesia.

The incidence of hypotension was 66% in patients in Group P, whereas 26% in Group E. Also 36.7% patients in Group P and 23.3% patients in Group E received single rescue dose of Inj. Ephedrine. 30% patients in Group P and only 3.3% patients in Group E required second rescue dose of Inj. Ephedrine to combat hypotension. These differences were statistically significant. Thus incidence and severity of hypotension was higher in preload group as compared to ephedrine group.

There was no significant difference between the two groups as regards to maternal heart rate and no incidence of reactive hypertension found. Maternal heart rate was maintained close to the baseline values. No significant bradycardia noted. This could be explained by both the effect of rescue ephedrine and baroreceptor mediated reflex increase in heart rate in patients who became hypotensive.

APGAR score in both the groups was comparable and there was no significant difference between the two groups. And there was no any significant difference in incidence of nausea, vomiting, shivering and backache in both the groups.

In conclusion, the prophylactic bolus dose of Inj. Ephedrine 10mg I.V. given immediately after spinal anaesthesia reduce the incidence of hypotension as compared

to fluid preloading with crystalloid solution. In other words this suggest that prophylactic intravenous bolus dose of ephedrine 10mg is more effective for maintenance of maternal blood pressure close to baseline level than crystalloid preloading in healthy parturient undergoing caesarean section under spinal anaesthesia.

CONCLUSION

From the present study we conclude that prophylactic intravenous bolus dose of Injection Ephedrine 10mg is safe, quick and more effective than crystalloid preloading for maintenance of maternal blood pressure close to the baseline level in a healthy parturient undergoing caesarean section under spinal anaesthesia.

The heart rate in patients of both the groups was maintained close to baseline heart rate. No adverse effects like reactive hypertension and no significant tachycardia was noticed.

There was no difference in the fetal outcome in both the groups as assessed by APGAR score. And there was no any significant difference in incidence of nausea, vomiting, shivering, bradycardia and backache in both the groups.

Considering the advantage of 10mg bolus dose of ephedrine over crystalloid preload, it is appropriate to administer it routinely in parturient undergoing caesarean section under spinal anaesthesia. However 10mg bolus dose of ephedrine do not completely eliminate maternal hypotension but significantly reduces the incidence of hypotension compared to fluid preloading with crystalloids.

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SAMPLE INFORMED CONSENT FORM

TITLE OF THE PROJECT: **"A COMPARATIVE STUDY OF EFFECT OF RAPID CRYSTALLOID PRELOAD AND INTRAVENOUS EPHEDRINE IN MANAGEMENT OF HYPOTENSION DUE TO SUB ARACHANOID BLOCK IN ELECTIVE CAESAREAN SECTION"**

PRINCIPAL INVESTIGATOR :

Department of Anaesthesiology,

PG GUIDE :

I have been informed that this study is **"A COMPARATIVE STUDY OF EFFECT OF RAPID CRYSTALLOID PRELOAD AND INTRAVENOUS EPHEDRINE IN MANAGEMENT OF HYPOTENSION DUE TO SUB ARACHANOID BLOCK IN ELECTIVE CAESAREAN SECTION" .** I have been explained about this study in the language which I understand. I have been explained about the reason for doing this study and selecting me/my ward as a subject for this study. I have been told that my participation in the above study is voluntary and I am aware that I can opt out of the study at any time without having to give any reasons for doing so. I am also informed that my refusal to participate in this study will not affect my treatment by any means.

I agree to participate in the above study and cooperate fully. I agree to follow the Doctor's instructions about my treatment to the best of my ability.

CONFIDENTIALITY:

I understand that medical information produced by this study will become a part of this Hospital records and will be subjected to the confidentiality and privacy regulation of this hospital. Information of a sensitive, personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by a code number. The code key connecting name to numbers will be kept in a separate secure location.

If the data are used for publication in the medical literature or for teaching purpose, no names will be used and other identifiers such as photographs and audio or video tapes will be used only with my special written permission. I understand that I may see the photograph and videotapes and hear audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at any time and available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which might influence my continued participation.

If during this study, or later, I wish to discuss my participation or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me and that a copy of this consent form will be given to me for my careful reading.

REFUSAL OR WITHDRAWL OF PARTICIPATION:

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital.

I also understand that will terminate my participation in this study at any time after she has explained the reasons for doing so and has helped arrange for my continued care by my own physician or therapist.

INJURY STATEMENT:

I understand that in the unlikely event of injury to me/my ward, resulting directly to my participation in this study, if such injury were reported promptly, then medical treatment would be available to me, but no further compensation will be provided.

I understand that by my agreement to participate in this study, I am not waiving any of my legal rights.

I have been explained about the purpose of this research, the procedures required and the possible risks and benefits, in my own language.

I have been explained all the above in detail and I understand the same. Therefore I agree to give my consent to participate as a subject in this research project.

Patient's Signature:	Witness Signature
Name :	Name :
Date :	Date :
(Guide)	(Investigator)

PROFORMA

STUDY: **"A COMPARATIVE STUDY OF EFFECT OF RAPID CRYSTALLOID PRELOAD AND INTRAVENOUS EPHEDRINE IN MANAGEMENT OF HYPOTENSION DUE TO SUBARACHANOID BLOCK IN ELECTIVE CAESAREAN SECTION."**

Name of the patient: I.P. No. :

Age: Height:

Weight: Date:

Consent taken for study: YES/NO

Group allocated: P/E

Pre anaesthetic evaluation:

Chief complaints:

Past History:

a) Presence of any comorbid condition - Diabetes/ Hypertension/ Ischemic heart disease/ Cerebrovascular accident / Asthma/ Epilepsy/ Bleeding disorder/ Drug allergy/ any other.

b) Drug Therapy

c) H/o previous anaesthetic exposure:

Family History:

General Physical Examination:

- General condition :
- Pallor / Icterus / Cyanosis / Clubbing / Lympadenopathy / Pedal edema.
- Temperature:
- Pulse rate:
- Respiratory rate:
- Blood Pressure :

AIRWAY ASSESSMENT:

- Mallampati grade

Systemic Examination:

- Cardiovascular system
- Respiratory system
- Central nervous system
- Others

Investigations:

- Complete blood picture:
  - Haemoglobin% :
  - Total Leucocyte count :
  - Platelet count :
- Random Blood sugar :

- Urine routine:
- Blood Grouping and Rh Typing:
- Any other:

ASA GRADING

Diagnosis:

Written informed consent:

Nil by mouth status:

STUDY GROUPS:

- Group P- Preloading group-patients received a preload of ringer lactate solution 15ml/kg over 10 to 20 min before spinal anaesthesia.
- Group E- Ephedrine group- patient received intravenous bolus of injection Ephedrine 10mg immediately after spinal anaesthesia.

PREMEDICATION:-

- Inj. Ranitidine hydrochloride 50mg I.V.
- Inj. Ondansetron 4mg I.V.

ANAESTHESIA TECHNIQUE- Spinal anaesthesia.

TIME (MIN)	SBP (mmHg)	DBP (mmHg)	MAP (mmHg)	HR (bpm)	RR (cpm)	SpO2	SIDE EFFECTS	TREATMENT
Basal								
2min								
4min								
6min								
8min								
10min								
15min								
20min								
25min								
30min								
40min								
50min								
60min								

Following parameters were studied:

1. Incidence of hypotension
2. Number of rescue doses of INJ. Ephedrine needed
3. Total duration of procedure, uterine incision to delivery interval and spinal injection to delivery interval
4. Neonatal APGAR score at 1min and 5min
5. Incidence of nausea , vomiting and shivering
6. Adverse effect of Ephedrine.
7. Post operative adverse effect due to spinal anaesthesia.

Signature of Anaesthesiologist

KEY TO MASTER CHART

Cm	centimetre
DBP	Diastolic Blood Pressure
HR	Heart Rate
Ht	Height
HTN	Hypertension
I-D	Induction of spinal anaesthesia to Delivery of baby interval
Kg	kilogram
MAP	Mean Arterial Pressure
MIN	Minute
PDPH	Post Dural Puncture Headache
SBP	Systolic Blood Pressure
Sec	Seconds
U-D	Uterine incision to Delivery of baby interval
Wt	Weight
Yrs	years

MASTER CHART

		AGE	Wt	Ht	DURATION	I-D	U-D	HR												SBP										
SL. NO.	GROUP	(yrs)	(kg)	(cm)	(MIN)	(MIN)	(SEC)	BASAL	2min	4min	6min	8min	10min	15min	20min	25min	30min	45min	60min	BASAL	2min	4min	6min	8min	10min	15min	20min	25min	30min	45min	60min
1	P	24	46	152	69	19	77	94	90	92	94	92	92	94	96	94	94	90	92	122	90	100	104	102	100	102	102	108	110	108	116
2	P	26	52	156	67	16	72	96	118	126	124	112	114	116	92	84	84	86	88	124	90	92	94	104	108	106	106	114	118	118	120
3	P	26	48	157	66	15	73	92	90	90	90	92	92	94	100	98	96	98	92	120	102	102	100	104	106	104	100	100	102	104	110
4	P	28	56	154	69	19	76	94	92	92	94	94	96	92	96	98	98	96	94	128	90	104	106	108	110	110	112	114	116	120	118
5	P	35	58	152	69	17	72	96	94	92	90	90	92	94	96	98	98	99	0	112	102	100	100	104	106	104	108	108	110	112	110
6	P	26	60	156	66	18	78	102	92	90	94	94	96	94	98	96	94	96	98	116	110	108	106	102	100	102	102	106	110	114	106
7	P	26	50	152	66	15	77	104	94	94	96	94	92	94	94	98	96	94	98	124	88	90	94	108	110	106	108	110	112	110	108
8	P	26	44	158	66	15	79	106	88	94	98	96	90	94	96	96	94	92	94	122	100	104	106	104	104	108	110	116	116	112	110
9	P	30	40	152	68	16	79	92	72	64	50	88	96	82	80	84	86	88	88	128	96	108	110	110	112	110	110	110	112	118	124
10	P	22	42	152	67	19	74	86	84	84	86	84	82	84	84	86	88	90	92	122	116	110	104	102	100	102	102	110	114	110	112
11	P	30	50	156	68	18	75	82	88	90	90	90	92	90	94	92	90	94	94	108	98	98	100	100	98	104	106	104	100	102	104
12	P	26	48	158	65	18	77	92	106	120	122	124	112	104	92	94	94	96	94	118	88	96	100	102	100	104	106	108	110	108	112
13	P	21	48	157	65	16	78	88	84	84	82	84	86	84	88	88	90	94	96	118	86	98	100	110	112	106	108	110	114	116	120
14	P	22	56	152	66	16	77	86	90	90	92	94	94	96	96	94	90	92	90	114	112	110	100	102	102	104	106	108	110	116	120
15	P	21	64	150	65	19	72	82	72	84	82	82	84	86	86	84	88	90	92	122	106	90	82	90	100	100	102	108	110	114	112
16	P	25	60	156	69	17	73	88	84	86	88	84	86	84	82	86	88	90	94	126	80	86	92	108	110	116	118	116	120	122	120
17	P	22	64	154	66	15	72	92	84	86	88	84	86	82	84	84	86	88	86	130	90	92	94	104	106	108	110	112	116	120	124
18	P	21	56	158	65	17	79	94	78	76	74	74	76	80	86	88	88	90	94	124	92	102	108	106	94	110	112	118	116	120	126
19	P	28	58	156	65	15	73	96	90	90	92	92	94	96	96	94	98	96	98	120	90	100	102	104	106	102	104	114	112	116	110
20	P	22	55	154	65	16	78	94	92	90	94	94	96	94	98	98	100	102	100	122	92	98	100	102	104	108	110	110	112	114	116
21	P	28	56	156	68	15	73	92	90	94	96	94	98	96	94	96	96	100	102	126	90	98	102	98	92	104	108	110	112	118	122
22	P	25	58	154	68	15	72	94	90	92	94	92	92	90	90	92	92	94	96	126	120	110	112	110	110	114	116	110	112	114	116
23	P	28	60	156	67	15	77	100	98	96	100	102	102	100	100	102	106	104	100	122	116	110	108	106	102	104	106	106	106	110	118
24	P	30	62	152	65	15	76	102	98	96	102	102	104	100	102	104	104	102	106	120	88	98	100	98	90	98	102	110	112	118	122
25	P	25	54	154	67	18	74	98	90	92	94	94	96	94	98	96	94	96	98	120	100	96	92	98	102	106	108	110	112	110	116
26	P	28	55	152	66	17	77	96	94	96	98	98	100	98	96	94	98	96	98	114	82	98	102	96	100	110	112	110	110	114	112
27	P	22	58	150	65	19	79	88	90	92	94	94	96	94	98	98	96	94	96	116	108	104	100	98	98	100	100	102	104	110	112
28	P	30	60	156	67	19	78	90	98	92	94	92	92	94	96	94	94	90	100	118	90	98	104	102	92	108	110	114	116	112	110
29	P	25	52	155	66	18	73	98	96	96	100	102	102	102	100	102	104	104	100	122	90	98	100	102	102	110	114	112	116	112	114
30	P	20	55	154	69	18	72	96	92	94	94	92	92	92	94	96	96	98	96	120	92	94	90	100	106	106	104	108	110	116	112

	DBP												MAP											RESCUE	APGAR	SCORE	ADVERSE	EFFECTS					
SL. NO.	BASAL	2min	4min	6min	8min	10min	15min	20min	25min	30min	45min	60min	BASAL	2min	4min	6min	8min	10min	15min	20min	25min	30min	45min	60min	DOSE	1MIN	5MIN	NAUSEA	VOMITING	SHIVERING	BRADY	TACHY	HTN	BACKACHE	PDPH
1	74	60	62	64	62	62	64	66	68	70	72	74	90	70	75	77	75	75	77	78	81	83	84	88	1	8	9			YES					
2	76	62	60	60	64	66	66	64	66	74	74	74	92	71	71	71	77	80	79	78	82	89	89	89	2	9	10	YES				YES			
3	84	70	68	66	66	66	64	60	70	70	70	70	96	81	79	77	79	79	77	73	80	81	81	83	0	8	10			YES					
4	86	60	60	62	68	66	72	70	72	74	76	76	100	70	75	77	81	81	85	84	86	88	91	90	1	8	10								
5	70	56	66	60	68	70	80	80	76	72	72	74	84	71	77	73	80	82	88	89	87	85	85	86	0	9	10								
6	70	60	64	64	66	68	68	70	72	70	72	72	85	77	79	78	78	79	79	81	83	83	86	83	0	8	9								
7	70	56	62	60	68	70	72	70	74	72	74	70	88	67	71	71	81	83	83	83	86	85	86	83	2	7	10	YES	YES	YES					
8	76	60	64	64	66	66	72	74	72	74	72	72	91	73	77	78	79	79	84	86	87	88	85	85	0	8	10			YES					
9	80	60	64	66	68	70	70	68	70	70	72	74	96	72	79	81	82	84	83	82	83	84	87	91	1	8	9				YES				
10	70	70	68	66	66	70	68	64	68	70	74	72	87	85	82	79	78	80	79	77	82	85	86	85	0	8	9								
11	64	64	62	60	64	64	66	66	64	74	74	74	79	75	74	73	76	75	79	79	77	83	83	84	0	7	10			YES					
12	66	60	60	60	62	62	64	66	68	70	72	72	83	69	72	73	75	75	77	79	81	83	84	85	1	8	9			YES		YES			
13	70	60	60	62	64	72	70	68	68	70	72	74	86	69	73	75	79	85	82	81	82	85	87	89	1	8	10								
14	66	64	66	64	66	74	72	70	70	70	72	74	82	80	81	76	78	83	83	82	83	83	87	89	0	8	10								
15	74	66	64	60	66	68	64	60	68	74	74	74	90	79	73	67	74	79	76	74	81	86	87	87	1	8	10							YES	
16	76	56	62	64	68	72	72	70	70	72	70	70	93	64	70	73	81	85	87	86	85	88	87	87	2	8	9	YES	YES	YES					
17	82	60	62	62	68	70	72	74	70	70	74	72	98	70	72	73	80	82	84	86	84	85	89	89	2	7	9	YES		YES					
18	84	62	66	70	68	64	74	80	80	76	78	76	97	72	78	83	81	74	86	91	93	89	92	93	2	8	9	YES							
19	82	64	68	72	66	66	70	72	74	70	70	72	95	73	79	82	79	79	81	83	87	84	85	85	1	9	10								
20	86	62	64	66	66	64	68	70	72	68	68	70	98	72	75	77	78	77	81	83	85	83	83	85	1	8	10								
21	84	60	66	70	68	60	66	70	68	68	72	70	98	70	77	81	78	71	79	83	82	83	87	87	2	8	10								
22	86	82	76	72	66	70	74	72	70	70	72	70	99	95	87	85	81	83	87	87	83	84	86	85	0	7	10							YES	
23	70	84	78	74	66	74	70	68	72	70	72	72	87	95	89	85	79	83	81	81	83	82	85	87	0	8	10								
24	74	56	60	64	66	64	66	64	70	72	74	74	89	67	73	76	77	73	77	77	83	85	89	90	2	9	10	YES	YES	YES					
25	76	56	58	60	64	66	68	64	66	68	74	68	91	71	71	71	75	78	81	79	81	83	86	84	1	9	10								
26	70	60	62	62	60	62	66	68	66	70	74	68	85	67	74	75	72	75	81	83	81	83	87	83	1	10	10								
27	72	70	66	64	62	62	64	60	62	74	74	74	87	83	79	76	74	74	76	73	75	84	86	87	0	9	10								
28	80	60	62	64	62	60	68	72	70	68	70	68	93	70	74	77	75	71	81	85	85	84	84	82	2	9	10								
29	84	60	64	66	64	64	68	74	70	72	70	74	97	70	75	77	77	77	82	87	84	87	84	87	1	8	10	YES							
30	82	64	62	60	62	60	62	64	66	74	64	70	95	73	73	70	75	75	77	77	80	86	81	84	2	8	9			YES					

		AGE	Wt	Ht	DURATION	I-D	U-D	HR												SBP										
SL. NO.	GROUP	(yrs)	(kg)	(cm)	(MIN)	(MIN)	(SEC)	BASAL	2min	4min	6min	8min	10min	15min	20min	25min	30min	45min	60min	BASAL	2min	4min	6min	8min	10min	15min	20min	25min	30min	45min	60min
31	E	25	53	155	68	15	73	96	88	90	94	88	86	88	84	86	82	80	86	122	102	102	100	102	100	104	106	108	110	112	116
32	E	28	48	156	68	18	73	108	100	104	102	102	104	102	106	104	100	100	102	120	100	98	100	102	102	108	110	110	116	108	110
33	E	26	50	154	66	15	73	84	84	86	86	84	88	86	82	88	88	90	96	114	110	106	104	100	98	100	100	104	106	108	110
34	E	21	52	154	68	19	74	86	88	88	86	88	88	84	84	86	88	90	86	108	102	100	98	100	100	104	106	106	104	110	108
35	E	21	53	158	66	19	72	96	96	94	98	94	92	90	90	92	94	96	96	124	100	98	90	104	106	104	102	104	106	108	110
36	E	23	62	153	67	17	73	86	84	84	86	88	90	88	86	84	88	90	92	114	90	98	102	104	100	108	110	108	108	110	112
37	E	21	48	150	67	18	72	94	98	100	102	104	98	96	98	96	98	102	98	122	100	102	90	112	110	118	120	118	116	116	118
38	E	24	52	154	67	19	76	96	92	94	94	92	90	90	88	86	86	88	84	124	100	98	98	100	102	102	100	104	108	110	112
39	E	20	58	150	66	16	74	84	86	88	88	86	84	88	84	86	86	88	80	116	100	102	104	104	106	106	108	114	118	120	122
40	E	20	56	153	67	18	76	82	80	84	88	86	84	84	86	88	90	86	88	122	110	106	94	98	100	100	102	104	106	110	112
41	E	23	59	154	68	17	79	84	96	118	122	120	106	102	98	96	96	94	98	118	100	106	102	98	100	108	110	112	112	122	124
42	E	24	54	156	68	16	78	96	90	92	92	90	90	92	94	92	94	96	96	120	90	98	102	98	100	102	104	104	106	110	112
43	E	35	55	154	66	18	74	86	84	86	88	88	90	86	88	86	86	84	86	116	100	100	102	104	104	108	110	108	106	110	112
44	E	30	54	156	68	19	75	82	90	92	92	94	96	94	94	92	96	98	96	128	96	104	106	104	108	110	110	110	112	116	118
45	E	26	55	158	66	16	73	84	80	84	90	90	92	86	88	86	86	88	88	116	100	102	104	102	106	108	110	110	112	120	108
46	E	37	55	157	68	17	75	96	92	88	90	88	86	86	88	90	90	92	94	118	88	98	100	102	104	108	110	106	100	106	110
47	E	24	58	150	66	19	79	94	98	96	98	100	102	100	104	98	100	98	104	126	114	114	118	116	120	116	118	114	116	118	120
48	E	23	48	150	68	16	74	82	88	86	90	88	92	90	94	90	88	86	88	124	120	118	116	114	112	110	108	112	116	120	120
49	E	32	52	155	68	16	72	84	78	76	76	78	80	82	84	86	86	88	90	126	118	116	118	120	122	118	120	122	124	114	118
50	E	23	56	157	66	16	73	100	102	104	110	106	108	104	106	102	104	100	102	116	104	104	102	110	112	110	114	112	116	110	114
51	E	28	54	154	68	15	79	102	94	90	92	94	96	94	98	98	96	98	98	120	110	108	112	114	116	112	114	110	118	112	122
52	E	21	50	152	67	16	72	96	94	90	92	94	96	98	100	98	102	104	102	124	112	116	114	112	116	118	114	116	118	120	118
53	E	22	50	158	66	18	76	82	86	84	84	86	88	86	88	88	82	80	84	116	110	108	88	100	102	100	100	104	108	104	106
54	E	28	60	156	66	15	73	96	90	92	94	98	100	98	96	96	98	94	100	126	118	116	120	114	118	120	122	118	120	118	116
55	E	24	62	157	68	16	73	94	96	94	98	96	94	90	92	94	96	98	96	130	126	122	124	122	120	118	118	116	120	118	122
56	E	31	64	157	67	15	73	92	90	92	88	90	92	90	94	92	96	98	100	124	114	118	120	114	116	116	118	120	120	116	118
57	E	23	60	158	66	19	78	88	88	86	86	88	94	92	96	94	96	98	98	124	116	118	118	120	120	118	120	118	116	120	120
58	E	23	62	152	68	18	75	98	90	90	92	90	94	92	96	98	100	102	100	126	112	106	90	92	96	94	116	114	118	120	120
59	E	25	60	154	67	17	75	98	84	84	86	88	82	86	84	82	86	84	82	120	108	106	110	108	112	114	110	110	112	114	118
60	E	25	58	150	66	19	77	80	82	80	78	78	76	78	78	76	74	78	78	118	106	102	104	108	106	106	108	108	110	108	110

	DBP												MAP												RESCUE	APGAR	SCORE	ADVERSE	EFFECTS						
SL. NO.	BASAL	2min	4min	6min	8min	10min	15min	20min	25min	30min	45min	60min	BASAL	2min	4min	6min	8min	10min	15min	20min	25min	30min	45min	60min	DOSE	1MIN	5MIN	NAUSEA	VOMITING	SHIVERING	BRADY	TACHY	HTN	BACKACHE	PDPH
31	82	64	66	66	66	64	64	66	68	74	76	76	95	77	78	77	78	76	77	79	81	86	88	89	0	9	10								
32	76	60	62	62	64	66	70	72	74	70	72	74	91	73	74	75	77	78	83	85	86	85	84	86	0	9	10	YES							
33	70	72	68	64	62	60	60	60	66	68	68	70	85	85	81	77	75	73	73	73	79	81	81	83	0	9	10								
34	74	64	62	60	62	62	64	64	66	66	66	68	85	77	75	73	75	75	77	78	79	79	81	81	0	8	9							YES	
35	84	66	64	62	64	64	62	62	62	64	66	64	97	77	75	71	77	78	76	75	76	78	80	79	1	9	10								
36	74	56	60	62	66	68	74	80	78	76	78	80	87	67	73	75	79	79	85	90	88	87	89	91	0	8	10								
37	70	60	60	50	60	64	66	70	70	70	72	70	87	73	74	63	77	79	83	87	86	85	87	86	1	8	9			YES					
38	80	62	62	64	62	62	66	64	66	72	74	72	95	75	74	75	75	75	78	76	79	84	86	85	0	8	10			YES					
39	70	60	62	64	66	64	74	76	74	76	78	78	85	73	75	77	79	78	85	87	87	90	92	93	0	9	10								
40	80	70	68	66	68	66	68	64	62	64	64	66	94	83	81	75	78	77	79	77	76	78	79	81	1	8	10								
41	74	60	64	62	64	64	66	70	68	70	72	70	89	73	78	75	75	76	80	83	83	84	89	88	0	8	9					YES		YES	
42	82	66	68	70	66	62	66	64	66	68	66	66	95	74	78	81	77	75	78	77	79	81	81	81	1	10	10	YES	YES						
43	76	56	60	64	66	70	72	74	72	74	80	78	89	71	73	77	79	81	84	86	84	85	90	89	0	9	10								
44	82	62	60	64	68	70	68	66	68	70	80	80	97	73	75	78	80	83	82	81	82	84	92	93	1	8	10	YES		YES					
45	80	64	66	68	66	70	72	74	74	76	72	74	92	76	78	80	78	82	84	86	86	88	88	85	0	9	9								
46	80	56	58	56	60	68	70	74	72	70	72	72	93	67	71	71	74	80	83	86	83	80	83	85	1	8	10	YES							
47	80	74	76	76	78	82	80	78	78	76	78	80	95	87	89	90	91	95	92	91	90	89	91	93	0	9	10								
48	72	74	72	72	70	74	72	70	74	76	78	76	89	89	87	87	85	87	85	83	87	89	92	91	0	8	10			YES					
49	84	80	76	74	76	80	78	80	76	78	80	80	98	93	89	89	91	94	91	93	91	93	91	93	0	9	9								
50	76	64	64	66	68	72	70	74	72	72	74	74	89	77	77	78	82	85	83	87	85	87	86	87	0	8	10			YES					
51	78	70	74	76	72	74	72	76	72	74	72	76	92	83	85	88	86	88	85	89	85	89	85	91	0	9	9								
52	80	76	72	74	76	80	78	76	76	74	78	76	95	88	87	87	88	92	91	89	89	89	92	90	0	8	9								
53	74	72	66	60	62	64	62	64	62	64	62	66	88	85	80	69	75	77	75	76	76	79	76	79	1	9	10								
54	82	78	76	78	74	76	80	82	78	80	78	80	97	91	89	92	87	90	93	95	91	93	91	92	0	8	10			YES					
55	84	70	78	82	80	78	80	78	76	80	76	80	99	89	93	96	94	92	93	91	89	93	90	94	0	8	10								
56	78	70	76	80	76	78	72	74	72	76	78	78	93	85	90	93	89	91	87	89	88	91	91	91	0	8	9							YES	
57	76	72	70	74	76	82	80	80	76	78	76	76	92	87	86	89	91	95	93	93	90	91	91	91	0	8	10								
58	78	74	66	64	66	64	66	70	68	70	72	70	94	87	79	73	75	75	75	85	83	86	88	87	2	8	10	YES	YES						
59	72	68	66	70	74	78	74	72	70	74	74	72	88	81	79	83	85	89	87	85	83	87	87	87	0	8	10								
60	78	68	70	72	70	74	72	70	74	72	70	70	91	81	81	83	83	85	83	83	85	85	83	83	0	9	10								