Original Article ISSN (O):2395-2822; ISSN (P):2395-2814

Comparative Effect of Ephedrine, Mephentermine and Phenylephrine during Spinal Anesthesia

Dr. Kamalakannan M[1] and Dr. Anandha Lakshmi D[2]

[1,2]Assistant Professor, Department of Anesthesia,
Karpagam Faculty of Medical Sciences & Research, Coimbatore, Tamil Nadu-641021, India
[2]Corresponding author

Received: March 2017
Accepted: April 2017

Abstract

To compare the effects of Ephedrine, Mephentermine and Phenylephrine in the management of hypotension during spinal anesthesia for cesarean section based on the following parameters 1.Efficacy of vasopressor in treating hypotension,2.Incidence of undesirable side effects,3.Effect on neonatal outcome. Spinal (subarachnoid/intrathecal) anaesthesia is a form of centralneuraxial Block in which a temporary interruption of nerve transmission is achieved following injection of local anaesthetic and/or adjuvant solutions into the subarachnoid space. Spinal anaesthesia is one of the most frequently employed methods of regional anaesthesia. This study was done in a prospective double blind randomized manner. The patients were divided into three groups of 30 each. Patients meeting the criteria were incorporated into the study. Randomization achieved by sealed envelope technique.

INTRODUCTION

Anaesthesia to a parturient is not only unique but also requires highest degree of care because the anesthesiologist has to look after two individuals, the mother and foetus. In elective caesarean section under spinal anaesthesia hypotension has been reported in as many as 85% of patients [(1)].

Hypotension during spinal anesthesia for caesarean delivery can have detrimental effects on both mother and neonate. These effects include decreased utero placental blood flow, impaired foetal oxygenation with asphyxial stress and foetal acidosis and maternal symptoms of low cardiac output such as nausea, vomiting, dizziness and decreased consciousness. Therefore there has been much attention in the literature to methods of preventing and treating hypotension in obstetric anaesthesia. Careful positioning with left uterine displacement and volume preloading with crystalloids or colloids has been used to prevent it, but these are not complete measures [(2, 3)] and vasopressor is required to correct hypotension quickly.

Vasopressor like Ephedrine, Mephentermine, Phenylephrine, Metaraminol and Methoxamine are used for treating the hypotension. In this study we compare the efficacy of Ephedrine, Mephentermine and Phenylephrine in treating the hypotension for caesarean section and their undesirable side effects.

The vertebral canal extends from the foramen magnum to the sacral hiatus. It is formed by the dorsal spine, pedicles and lamina of successive vertebrae (7 cervical, 12 thoracic, 5 lumbar and 5 sacral). The vertebrae are held together by a series of overlapping ligaments namely the anterior and posterior longitudinal ligaments, ligamentumflavum, interspinous ligament, supraspinous ligament and the intervertebral discs.

The spinal cord, a direct continuation of the medulla oblongata begins at the upper border of the atlas and terminates distally in the conusmedullaris. The distal termination, because of the differential growth rates between the bony vertebral canal and central nervous system varies from L3 in the infant, to the lower border of L1 in the adult.

Surrounding the spinal cord in the bony vertebral column are three membranes (from within to the periphery), the piamater, arachnoid mater and dura mater. The pia mater is a highly vascular membrane that closely invests the spinal cord. The arachnoid mater is a delicate vascular membrane closely attached to the outermost dura mater. Between the two innermost membranes is the subarachnoid space. In this space are the cerebrospinal fluid, spinal nerves, blood vessels

ISSN (O):2395-2822; ISSN (P):2395-2814

that supply the spinal cord and the denticulate ligaments. Although the spinal cord ends at the lower border of L1 in adults, the subarachnoid space continues to S2. The outermost membrane in the spinal canal is the longitudinally organized fibro elastic membrane, the duramater. This layer is the direct extension of the cranial dura mater and extends as the spinal dura mater from the foramen magnum to S2, where the filumterminale (an extension of the pia mater beginning at the conusmedullaris) blends with the periosteum of the subdural space which contains only small amounts of serous fluids to allow the dura and arachnoid move over each other. Surrounding the dura mater is the epidural space which extends from the foramen magnum to the sacral hiatus. Posterior to the epidural space is the ligamentumflavum which extends from the foramen magnum to the sacral hiatus. Immediately posterior to the ligamentumflavum is the interspinous ligament. Extending from the external occipital protuberance to the coccyx, posterior to these structures is the supraspinous ligament. Lumbar puncture is routinely done below the L2 vertebrae down to the L5-S1 interspace to avoid damaging the spinal cord which ends at the lower border of L1 in adults.

This double blind prospective randomized control study was designed to evaluate the efficacy of Ephedrine, Mephentermine and Phenylephrine in treating hypotension during spinal anaesthesia for cesarean section. The incidence of undesirable side effects and neonatal outcome in terms of Apgar score were also studied.

PREVIOUS WORK

Dinesh Sahu et al (2003) studied the effects of bolus Ephedrine, Mephentermine, Phenylephrine for the maintenance of arterial pressure during spinal anesthesia for LSCS. Sixty patients in the age group of 20-35 yrs of age with ASA-1, 11 are divided into three groups of 20 each as per the study drugs. Group P: Phenylephrine 100µg,Group E: Ephedrine 6 mg,Group M: Mephentermine 6 mg. They concluded that all the three vasopressor are effective in IV bolus form in maintenance of arterial pressure within 20% limit of baseline though Phenylephrine has quicker peak effect and it causes reduction in heart rate which may be advantageous in cardiac patients and patients in whom tachycardia is Undesirable. Moran DH et al (1991) compared Ephedrine and Phenylephrine in the prevention of maternal hypotension following spinal anesthesia for caesarean section. Patients were randomly assigned to receive either Ephedrine in 10 mg IV bolus injections or Phenylephrine in 80 µg IV bolus injections to maintain systolic BP above 100 mmHg. Finally they concluded that Phenylephrine is as effective as Ephedrine in the treatment of maternal hypotension, and when used in small increments, it appears to have no adverse neonatal effects in healthy non-laboring parturients. Laporta et al (1995) compared maternal and neonatal catecholamine concentrations, following the use of either Phenylephrine or Ephedrine to treat a drop in maternal blood pressure after spinal anesthesia for caesarean section. They found that Phenylephrine appears to be safe and effective as Ephedrine in treatment of drop in blood pressure in healthy non-laboring parturient undergoing LSCS. The use of Phenylephrine was associated with neither significantly lower concentrations of nor adrenaline in both mother and neonate. Anna Lee et al (2002) In their quantitative systematic review, they compared the efficacy and safety of Ephedrine with Phenylephrine for the prevention and treatment of hypotension during spinal anesthesia for cesarean delivery. Seven randomized controlled trials were identified after a systematic search of electronic databases, published articles, and contact with authors. This systematic review does not support the traditional idea that Ephedrine is the preferred choice for the management of maternal hypotension during spinal anaesthesia for cesarean delivery in healthy non laboring parturients. Anna Lee et al (2002) In their quantitative systematic review, they compared the efficacy and safety of Ephedrine with Phenylephrine for the prevention and treatment of hypotension during spinal anesthesia for cesarean delivery. This systematic review does not support the traditional idea that Ephedrine is the preferred choice for the management of maternal hypotension during spinal anaesthesia for cesarean delivery in healthy non laboring parturients. Thomas DG et al (1996) In their study they compared the efficacy of bolus Ephedrine and Phenylephrine for maintenance of arterial pressure during spinal an aesthesia for caesarean section. They concluded that in both groups median (range) number of boluses of Ephedrine and Phenylephrine was similar. Maternal systolic BP and cardiac output changes are similar in both groups, but the mean maximum percentage change in maternal HR was larger in Phenylephrine group than in the ephedrine group. NganKee et al (2006) Ephedrine and Phenylephrine have been most investigated. Advantages of ephedrine include familiarity, long history and low propensity for uteroplacentalvasoconstriction.They finally concluded based on their observations, that, Phenylephrine is the vasopressor that closely meets the criteria for the best vasopressor in Obstetrics.Cyna AM et al (2006) They studied the randomized controlled trials comparing the interventions to prevent hypotension with placebo or alternative treatment in women having spinal anaesthesia for cesarean section.They finally

ISSN (O):2395-2822; ISSN (P):2395-2814

concluded that interventions like colloids, Ephedrine, Phenylephrine or lower leg compression can reduce the incidence of hypotension; none have been shown to eliminate the need to treat maternal hypotension during spinal anesthesia for cesarean delivery.Ram Nathan et al (1988) impedance cardiograph was used to measure stroke volume, ejection fraction and end diastolic volume.

SPINAL ANAESTHESIA

The spinal cord, a direct continuation of the medulla oblongata begins at the upper border of the atlas and terminates distally in the conusmedullaris. The distal termination, because of the differential growth rates between the bony vertebral canal and central nervous system varies from L3 in the infant, to the lower border of L1 in the adult. The first step in the successful application is proper patient selection. This is accomplished by evaluation of the patient through history, physical examination, laboratory data and communication with the patient and surgical staff about details of the procedure. The spinal anaesthetic technique can be broken down into a series of steps, the four P`s; Preparation, Position, Projection and Puncture.[7, 8].Spinal needles of various diameters with various types of points are available. Spinal needles fall into two main categories; those that cut the dura and those that designed to separate the dural fibers. The choice of position of the patient for performing the subarachnoid block depends on a number of factors, the proposed surgery being the most important. The three primary methods of positioning include lateral decubitus, sitting and prone positions, each with its own advantages in specific situation. In the lateral decubitus position, the patient is placed with his/her back parallel to the edge of the operating table nearest the anaesthesiologist, with thigh flexed upon the abdomen and neck flexed to allow the forehead to be as close to the knees as possible. The spinal puncture can be performed either by a midline or a Para median approach, usually at the L2-L3, L3-L4, or L4-L5 interspaces. The procedure is carried out under strict aseptic conditions.

PHYSIOLOGICAL CHANGES DURING PREGNANCY [9, 10]

The mean weight increase during pregnancy is 17% of prepregnant weight (12 kg approximately).This increase results from:Increase in size of the uterus and its contents: Uterus 1 kg, Amniotic fluid 1 kg, Fetus and placenta 4 kg. increase in Blood volume and interstitial fluid 2 kg each .Deposition of new fat and protein: 4 kg. Oxygen consumption is Increases by 30% to 40% during pregnancy. Progressive rise is caused by metabolic needs of fetus, uterus and placenta and secondarily by increased cardiac and respiratory work. Tidal volume increases by 45% during pregnancy with half occurring during 1st trimester. Minute ventilation increases by 45% during pregnancy with an increase evident early in the first trimester. This change results from the increase in tidal volume. Although respiratory rate declines slightly during midgestation, it is essentially unaltered during pregnancy.

PHARMACOLOGY [11, 12] EPHEDRINE

Ephedrine is a synthetic, sympathomimetic, no catecholamine drug primarily used as a vasopressor in various clinical situations. Ephedrine has direct effects on α, $ß_1$ and $ß_2$ receptors and indirect effects by releasing endogenous nor epinephrine from synaptic storage sites. Ephedrine causes increase in systolic and diastolic blood pressure, heart rate and cardiac output. Renal and splanchnic blood flows are decreased, whereas coronary and skeletal muscle blood flows are increased. Systemic vascular resistance may be altered minimally because vasoconstriction in some vascular beds is offset by vasodilatation ($ß_2$ stimulation) in other areas. These cardiovascular effects are due, in part, to α receptor mediated peripheral arterial and venous vasoconstriction. The principal mechanism, however for cardiovascular effects produced by ephedrine is increased myocardial contractility due to activation of $ß_1$receptors. In the presence of preexisting ßadrenergic blockade, the cardiovascular effects of ephedrine may resemble responses more typical of α adrenergic stimulation.

Indication:

As a vasopressor to treat hypotension caused by sympathetic nervous system blockade or hypotension due to inhaled or injected anesthetics, As a vasopressor in shock,As a chronic oral medication to treat bronchial asthma, Nasally as nasal decongestant to treat vasomotor rhinitis, acute sinusitis, hay fever and acute coryza, As an antiemetic.

Contraindication are Angle closure glaucoma, Thyrotoxicosis, Obstetrics when maternal BP is >130/80.Precaution taken are Geriatric patients may be at a higher risk to develop prostatic hypertrophy,In patients with coronary insufficiency or IHD, hypertension may cause intracranial hemorrhage or angina pain.Side effects includesCNS: Nervousness, confusion, delirium and hallucinations can occur. Anxiety and nervousness may occur after prolonged use. Precordial pain and excessive doses may cause hypertension sufficient to result in intracranial hemorrhage.Genitourinary: Difficult and painful urination with urinary retention can occur in males with Prostatism. Also urine formation is decreased.

ISSN (O):2395-2822; ISSN (P):2395-2814

Dosage and administration:

Oral: For Bronchial asthma, Systemic Nasal decongestion:-12.5-25mg, 4th hourly, not to exceed 150mg in 24hrs.Parentral: For Bronchial Asthma:Adults: 25-50mg SC 5-25 mg slow IV, if needed repeated every 5-10mts ,Children: 0.5mg/kg SC or IM, 6thhourly.Vasopressor:Adults: 25-50mg IM, SC,5-25mg IV, repeated at 5-10mts intervals ,Children: 0.5mg/kg IM, IV.Nasal decongestion: 0.25% Spray, Topically.Antiemetic:0.5mg/kg IM.

Tolerance:

A second dose of Ephedrine produces a less intense systemic blood pressure response than the first dose. This phenomenon known as Tachyphylaxis occurs with many sympathomimetics and is related to the duration of action of these drugs. Tachyphylaxis may also be due to depletion of nor epinephrine stores

MEPHENTERMINE

Mephentermine is a synthetic, sympathomimetic, noncatecholamine drug which is structurally closely related to methyl amphetamine. Mephentermine indirectly stimulates beta adrenergic receptors and possibly to a lesser extent alpha adrenergic receptors of sympathetic nervous system by releasing noradrenalin from its storage sites. The main effect of therapeutic doses of Mephentermine is cardiac stimulation. Mephentermine also dilates the coronary, cerebral, splanchnic and renal blood vessels and also stimulates central nervous system.

IndicationareHypotension due to anesthesia, ganglionic blockade or hemorrhage.Shock accompanying myocardial infarction.ContraindicationareTo treat hypotension caused by Chlorpromazine.In combination with MAO inhibitors.Precautions taken are Hypoxia, Hypercapnia, Acidosis may reduce the effectiveness of and/or increase the adverse effects of the drug.Drug interactions: The vasoconstrictor effects of Mephentermine may be enhanced by concurrent administration of drugs with similar effects like Ergot alkaloids or Oxytocin.Administration of Mephentermine to patients who are receiving cyclopropane or halogenated hydrocarbon general anesthetics may increase cardiac irritability which may result in arrhythmias.Side effects are Anxiety,Cardiacarrhythmias,Hypertension (especially in those with heart disease).

Dosage and administration:

Hypotension secondary to spinal anesthesia(Prophylaxis),IM: 30-45mg, administered 10-20 mts prior to anesthesia, operation or termination of operative procedure, Hypotension secondary to spinal anesthesia(Treatment) ,IV: 10-25 mg given as a single dose. May be repeated as needed to maintain the desired level of blood pressure ,IV infusion: as 0.1 %(1mg/ml) solution in 5%Dextrose in water, the rate of administration and duration of therapy being adjusted according to patient response. Shock accompanying Myocardial Infarction: An initial dose 60mg IV bolus followed by IV infusion of 0.1%Mephentermine in 5% Dextrose in water or IV administration of serial doses of Mephentermine 30-45mg, as necessary.

PHENYLEPHRINE

Phenylephrine is a synthetic sympathomimetic agent. It is a vasoconstrictor and vasopressor drug chemically related to ephedrine and adrenaline. Phenylephrine is a powerful post – synaptic α_1 receptor stimulant with little effect on ß receptors at the heart. Phenylephrine is a directly acting sympathomimetic agent. After injection it produces pronounced peripheral vasoconstriction and hence increases in both systolic and diastolic BP. Its action on the heart differs from that of adrenaline and ephedrine, in that it slows the heart rate and increases the stoke volume producing no disturbance in rhythm. At therapeutic doses it usually does not cause central nervous system stimulation. A major advantage of Phenylephrine is the fact that repeated administration produces comparable effects.

Indications are to prevent or treat hypotension during Spinal and inhalation anesthetics, Shock and shock like states,Warm septic shock,Drug induced hypotension or hypersensitivity reaction or anaphylaxis,Weaning from cardiopulmonary bypass.To overcome paroxysmal supraventricular tachycardia (high doses to produce reflex bradycardia)To prolong duration of spinal anesthesia with lignocaine.As a vasoconstrictor in regional anesthesia. Nasal: Nasal congestion due to allergies, sinusitis, common cold or hay fever. Ophthalmologic: 0.12%, 2.5%, 10%, Temporary relief of redness of the eye ,Decongestant and vasoconstrictor, Treatment of uveitis with posterior synechiae, Open angle glaucoma, Retraction without cycloplegia ,Ophthalmic examination, Fundoscopy. Contraindications includes Severe hypertension , Hyperthyroidism, Ventricular tachycardia.

Precautions taken are with extreme caution in geriatric pts, severe arteriosclerosis, bradycardia, partial heart block, myocardial disease, and hyperthyroidism. Anginal pain may be precipitated in pts with angina pectoris.To be used with caution in patients with Diabetes mellitus or closed angle glaucoma. Side effects include Phenylephrine is without significant stimulating effects on the central nervous system at usual dosesExtravasations of the drug may cause tissue

ISSN (O):2395-2822; ISSN (P):2395-2814

necrosis, CVS: Reflex bradycardia, arrhythmias, CNS: Headache, excitability and restlessness, Ophthalmologic: Rebound miosis and decreased mydriatic response in geriatric patients, blurred vision.

Dosage and administration:

Mild to moderate hypotension:SC or IM: 2 – 5 mg, initial dose should not exceed 5mg. IV: 0.2mg, range from 0.1 – 0.5mg. Initial dose should not exceed 0.5mg.Severe hypotension, shock:IV infusion: 10 mg in 500ml of 5% dextrose start at 100 180µg/min until target BP achieved, and a maintenance rate of 40 - 60µg / min.Hypotension due to central neuraxialblockade:Prophylaxis: SC or IM: 2 –3 mg administered 3-4 mts before blockade.Treatment:IV: 0.1-0.2 mg.To prolong the duration of spinal anesthesia:Addition of 2 – 5mg to local anesthetic solution, increase the duration of motor block approximately 50% without any increase in the incidence of complication such as nausea, vomiting or blood pressure disturbance. Vasoconstrictor for regional analgesia:Use of 1:2, 00,000 solution of Phenylephrine to the local anesthetic solution can act as local vasoconstrictor for regional analgesia.

https://www.cibil.com/mycibil/viewHomePage

MATERIALS AND METHODS

This study was done in a prospective double blind randomized manner. The patients were divided into three groups of 30 each. Patients meeting the criteria were incorporated into the study. Randomization achieved by sealed envelope technique. Patients in age group of 18 – 35 years of age, healthy, ASA I & II patients with singleton full term pregnancy, undergoing elective and emergency LSCS were included in the study. The descriptive statistics of the variables studied were represented as two-way tables. The categorical factors were represented by the number and frequency (%) of cases. The continuous variables were represented by measures of central frequency (like mean, median & mode) and deviation (say, standard deviation and range). The differences in the proportions of are tested for statistical significance using non-parametric Chi-square test for variables measured on nominal scale. When testing for two factors, the Mann-Whitney "U" test or Wilcoxon two sample test (by Kruskal-Wallis "H" test which is equivalent to chi-square) was used. Fisher's exact probability test was used wherever indicated. For variables measured on a continuous scale, one-way analysis of variance (ANOVA) was employed to elicit the statistical significance of variation when three variables were taken together. When testing for two groups (pair wise), Student "t" test is used to test for statistical significance in the differences of the two means.

OBSERVATION AND RESULTS

All the three groups were comparable with respect to their age, height, weight, baseline systolic BP, diastolic BP, MAP, heart rate. Also the time to develop hypotension, lowest systolic BP recorded, SAB-delivery time were comparable in the three groups and was not statistically significant. The level of sensory blockade was comparable in all the three groups and was not statistically significant.

Table 1: Distribution of age of cases by groups[$]

Age	Group I	Group II	Group III	p-value
No. of cases	30	30	30	
Mean	25.0	24.6	24.1	
S.D.	2.91	3.63	2.89	0.52
Median	24.5	24	24	
Range	21 – 31	18 – 32	19 – 32	
Stat Significance	p-value			
Gr I vs Gr III	0.22			
Gr II vs Gr III	0.58			
Gr I vs Gr II	0.58			

ISSN (O):2395-2822; ISSN (P):2395-2814

Table 2: Distribution of SAB-Delivery time by groups[$]

SAB-Delivery time in mts	Group. I		Group II		Group III		p-value
	No.	%	No.	%	No.	%	
4	2	6.7	1	3.3	0	0.0	
5	1	3.3	2	6.7	1	3.3	
6	6	20.0	10	33.3	9	30.0	
7	5	16.7	4	13.3	8	26.7	0.53
8	6	20.0	5	16.7	4	13.3	
9	9	30.0	8	26.7	4	13.3	
10	1	3.3	0	0.0	3	10.0	
11	0	0.0	0	0.0	1	3.3	
Stat. Significance	p-value						
Gr. I vs. Control	0.38						
Gr. II vs. Control	0.32						
Gr. I vs. Gr. II	0.82						

The distribution of SAB-Delivery values between Group I, Group II and Group III did not reveal any statistically significant differences. The results were similar when the groups were compared in pairs.

[$] Not statistically significant

The comparison of mean lowest systolic BP values between the three groups was not statistically significant. The results were the same for pair wise comparisons of groups.

Table 8: Mean Distribution of cases by groups and baseline HR SBP, DBP, MAP[$]

At Baseline	Group I (n=30)	Group II (n=30)	Group III (n=30)	p-value
Heart rate				
Mean	86.4	83.9	90.1	0.14
SD	12.25	10.39	13.62	
Systolic BP				
Mean	119.6	119.2	119.5	0.98
SD	7.68	8.46	8.45	
Diastolic BP				
Mean	74.0	78.8	76.7	0.07
SD	6.38	7.58	7.43	
MAP value				
Mean	89.2	92.3	90.3	0.19
SD	5.57	7.11	6.93	

[$] Not statistically significant

The mean distribution of anthropometric values of the heart rate, systolic BP and MAP at baseline between the three groups was not statistically significant. . The results were the same for pair wise comparisons of groups.

Haemodynamic variables:

Table 9: Mean Distribution of cases by groups and HR

HR	Group I (n=30)	Group II (n=30)	Group III (n=30)	p-value
Base line				
Mean	86.4	83.9	90.1	0.14
SD	12.25	10.39	13.62	
HP(VP given)				
Mean	90.7	90.9	87.6	0.24
SD	25.52	18.47	17.93	
2 mts after VP				
Mean	93.1	93.8	83.2	0.04*
SD	21.21	18.3	17.8	
4-mts				
Mean	93.7	93.8	91.3	0.83
SD	19.49	20.50	12.64	

6-mts Mean SD	96.2 17.58	99.0 18.16	94.6 13.10	0.58
8-mts Mean SD	96.5 17.24	98.6 15.31	94.0 12.76	0.51
10-mts Mean SD	97.2 15.36	97.2 15.51	92.7 13.07	0.40
15-mts Mean SD	96.6 16.31	96.1 15.42	92.1 12.53	0.43
20-mts Mean SD	95.6 15.96	96.7 15.88	93.8 12.17	0.74
25-mts Mean SD	N=29 96.3 15.31	N=30 95.8 14.41	N=30 93.1 11.98	0.63
30-mts Mean SD	N=28 95.5 12.38	N=30 96.1 14.67	N=29 91.9 11.94	0.42

*statistically significant

The mean value of heart rate was generally the highest in Group II followed by Group I and Group III. The mean variation of heart rate values between the three groups was statistically significant at 2mts. Pair wise comparison of groups showed that the differences in mean values were statistically significant between Group II and III and between Group I and III at 2-mts.

CONCLUSION

In conclusion, we found that all the three vasopressors namely Ephedrine, Mephentermine and Phenylephrine are effective in IV bolus form in maintenance of maternal arterial pressure within 20% limit of baseline values, though Phenylephrine has quicker peak effect, in comparison to Ephedrine and Mephentermine and it causes reduction in heart rate, which may be advantageous in patients in whom tachycardia is undesirable. All the three vasopressor had no significant adverse effects on neonatal outcome.

REFERENCE

1. Riley ET, Cohen SF, Rubenstein AJ, Flanaga B-Prevention of hypotension after spinal anesthesia for cesarean section, Anesthesia Analgesia 1995;81:838-842.
2. Robert.K.Stoelting, Sympathomimetics, In; Pharmacology and Physiology in Anaesthetic Practice, Fourth edition, Lippicott Williams and Willkins, 2006, 292-311.
3. Jonathan Moss and David Glick, The Autonomic Nervous system, In;
4. Millers Anaesthesia, Sixth edition, Elsevier-Churchill Livingstone 2005; 617-670.
5. Dinesh Sahu, Dilipkothari, AmrithaMehotra- Comparison of bolus Ephedrine, Mephentermine, Phenylephrine for maintenance of arterial pressure during spinal anesthesia for cesarean section-A clinical study. Indian Journal of Anesthesia 2003; 47(2):125-128.
6. Moran DH, Perillo M, Laporta RF, Bader AM, Datta S-Phenylephrine in the prevention of hypotension following spinal anesthesia for cesarean delivery-Journal of clinical anesthesiology; Jul-Aug;3(4):301-5 1991.
7. Laporta RF, Arthur GR, Datta S- Phenylephrine in the treating maternal hypotension due to spinal anesthesia for spinal anesthesia for cesarean delivery- Effects on neonatal catecholamine concentrations, acid-base status and APGAR scores. ActaAnesthesiologicaScandinavica 39 (7): 901-905 Oct 1995.
8. Anna Lee MPH, Warwick D et al-A Quantitative, systematic review of randomized controlled trials of Ephedrine versus Phenylephrine for the management of hypotension during spinal anesthesia for cesarean delivery. Anesthesia & Analgesia 2002; 94:920-926.
9. Thomas DJ, Robson SC, Redfern N, Hughes D et al-Randomized trial of bolus Ephedrine or Phenylephrine for maintenance of arterial pressure during spinal anesthesia for caesarean section. British Journal of Anesthesia, 1996 Jan; 76(1):61-5.
10. NganKee, Warwick D, Khaw-Vasopressors in Obstetrics: What should we be using? Current opinion in anesthesiology. 19(3):238-243, June 2006.