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Comparative Evaluation of two different bolus doses of Ephedrine to prevent Post Spinal Hypotension in patients undergoing PCNL: A Prospective Randomized study.

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ABSTRACT: Spinal anaesthesia is a recently accepted technique for PCNL.Hypotensionfollowingspinalblockisprimarilyduetopreganglionicsympatheticblockaderesultinginvasodilation andpoolingofbloodinthelowerlimbs. Vasopressors for prophylaxis and treatment of spinal hypotension have grown inpopularity inrecentyears.Theaimofourstudywastoevaluatetheeffectivenessof two different bolus doses of ephedrine for prevention of hypotension duringspinal anaesthesia in patients undergoing PCNL and also to evaluate any associatedadverse effects.Atotal60patientsundergoingPCNLunderspinalanaesthesiawere enrolled in the study to receive either prophylactic ephedrine bolus 10 mg(group A) or 15 mg (group B) immediately after spinal anaesthesia. Eight patientsin group A developed hypotension requiring a rescue dose of vasopressor, whiletwo patients in group B developed hypotension requiring a rescue dose ofvasopressor. We noticed that maximum hypotension was encountered after thepatient was put in prone position from supine position. Fall in blood pressure(systolicanddiastolic)werecomparablebetweentwogroups.From theabovestudy we concluded that 15mg IV bolus significantly decreases the incidence ofmaternalhypotensionwithoutserioussideeffectslikereactivehypertension.

Keywords:
Ephedrine,spinalanaesthesia,percutaneousnephrolithotomy(PCNL).

I. INTRODUCTION:

Percutaneous Nephrolithotomy (PCNL) is a popular method for removal of kidneyand ureteral calculi. PCNL has largely replaced open surgery in the management ofrenal stones (1). Definitive indications include renal stones of≥ 20 mm, multiplecalculi,staghornstonesorstonesnotamenable toextracorporealshockwavelithotripsy(ESWL)(2).PCNLcanbedoneunderlocal,generalorregionalanaesthesia. General anaesthesia has been postulated to confer many advantagesover regional anaesthesia (RA) in term of better hemodynamic and airway control,better patient and surgeon satisfaction (3). The other advantages of GA for PCNLprocedure include better control of tidal volume, airway control especially in proneposition, and extensibility of anaesthesia time(4). However it is associated withcomplicationslikeendotrachealtubedisplacements,hemodynamicchanges,neurologicandshoulderdislocationeventsespeciallyatthetimeofshiftingposition from lithotomy to prone positions and vice versa (5)**.** Moreover, studieshave suggested that patients who underwent PCNL under regional anaesthesia hadshorter mean operative time (ORT), discharge of patients was earlier, andless painon first postoperative day (6), less consumption of medication and overall low costinviewofearlydischarges(7).

The simplicity of the technique, reliable effect and lack of all those complicationsthat are associated with general anaesthesia has made it a safe alternative to generalanaesthesia. Various strategies have been used to manage spinal blockade inducedhypotensionwhichincludes:patientlegelevation,headdowntiltanduseofpressure stockings augment venous return and increase cardiac output and may besufficient to restore bloodpressure to anacceptable level**.**Volumeexpansion canbedonewitheithercrystalloidorcolloidinfusion.Mostofthestrategiesfordecreasing the incidence of hypotension during spinal anaesthesia have proved farfrombeingsatisfactoryorreliable.

This has shifted the focus to various vasopressor agents for prevention as well astreatment of spinal block induced hypotension. Vasopressors directly counter thesympatheticblock derangements.

This is because the neuraxial blockade is associated with cardiovascular effectssimilartoalpha1andbetablocker,thedecreasein systemicvascularresistanceand cardiac output can lead to complications especially in geriatric

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patients whoform the bulk of urological surgeries (8). Usage of high dose of heavy bupivacaineand level of blockade higher than T5are two modifiable risk factors associatedwith hypotension during spinal anaesthesia. As such avoidance of high block and alowerdoseofheavybupivacainecanreducetheincidenceandseverityofhypotension(9).

Ephedrine was the first agent to be used successfully to treat hypotension inducedby spinal anaesthesia (10). Ephedrine is a non-catecholamine sympathomimeticdrug that stimulates alpha and beta adrenergic receptors directly and predominantlyindirectly, producing its effects by releasing norepinephrine from nerve endings inthe autonomous nervous system, which leads to an increase blood pressure, heartrate, cardiac output and systemic vascular resistance. Ephedrine is deaminated inthe liver and conjugation occurs. The slow inactivation and excretion of ephedrineare responsible for the prolonged duration of action of this sympathomimetic. OnIV injection, onset of action 3-5 mins, maintains duration of action for 10-15 mins.It crosses blood brain barrier and produces central nervous system stimulationproduces alertness, anxiety, tremor, twitching and insomnia. It has been used forprophylaxis and treatment against hypotension associated with spinal anaesthesiafor several years; but recently there are some concern about its use due to certaincomplicationssuchassupraventricular tachycardiaandtachyphylaxis**(**11).However intermittent intravenous bolus doses may be a simpler, feasible, moreacceptable method for routine practice in the low resource set up where eitherinfusionpumpsarenotavailableorthereislimited availability.Theuseofcrystalloids before spinal block is practically ineffective because of their rapidredistribution and extravasations to the 3rd space (12). Thus we decided to co-loadpatientsalongwithpre-emptivebolusofephedrine.Primaryaimwastocompare theefficacyoftwodifferentdoses10mg&15mgofephedrineonhemodynamicfor prevention of spinal hypotension inpatients undergoing PCNL and secondaryaimwas to lookforanyassociatedadverseeffects.

II. MATERIAL & METHODS:

Thisstudyentitled“ComparativeEvaluation oftwodifferentbolusdosesofEphedrine to prevent Post Spinal Hypotension in patients undergoing PCNL:AProspective Randomized study” was conducted in Department of Anaesthesiologyandintensivecareat SuperSpecialityHospitalGovt MedicalCollege,Jammu.

AfterobtainingapprovalfromtheInstitutionalEthicCommitteeaninformedwritten consent was obtained. 60 patients of American society of Anaesthesiologist(ASA) grade I and II, Patients height from 140cm to 180 cm, aged 20-60 years, ofeither sex scheduled for elective Percutaneous Nephrolithotomy(PCNL) underspinal anaesthesia were included in this prospective randomized study. Exclusioncriteria included patient refusal, contraindications to spinal anaesthesia, patientswithhistoryofallergytolocalanesthetics,patientswhoneededsupracostalpunctures for stone clearance and patients with stag horn stones. Patients weremonitored for blood pressure, electrocardiogram, and pulse oximetry prior to theprocedure and during the procedure. All patients were preloaded with ringer lactate7to10ml/kgbeforespinalanaesthesia.Ephedrinewerepreparedastwodifferent5ml syringe containing Ephedrine 10mg per cc and 15mg per cc, one ml wasrandomlyinjectedIVaspertherandomizationtable immediatelyafterspinalanaesthesia

After obtaininginformedwrittenconsent fromallthe patientsenrolledin thestudy;theyweresubjectedtodetailedgeneralphysicalexaminationaswellassystemicexamination.Basicdemographiccharacteristicslikeage,height,weight,sex werenoted.Baselinevaluesofheartrate,systolicanddiastolicbloodpressurewererecorded.Routineinvestigationsdeemednecessaryforthepatientwereundertaken. Thepatientsweredividedinto,twogroups.**GroupA**patientsinthisgroupreceivedintravenous(IV)bolusdoseof10mgephedrine.**GroupB**patientsinthisgroupreceivedintravenous(IV)bolusdoseofephedrine15mgafterspinalanaesthesia.Patientswerefastedovernightandweregivenroutineantacidprophylaxis.Onthemorningofsurgery inthepreoperativeroomintravenousaccesswith16or18Gaugecannulawassecured.Onarrivalintheoperating room,monitorslikeECG,NIBP(non-invasivebloodpressure),andpulseoximetrywereattached.Allbaselineparametersheartrate,SBP(systolicbloodpressure),DBP(diastolic bloodpressure) and SPO2(oxygen saturation) were recorded.Under allasepticprecautionspinalanaesthesiawasperformed witha25-gaugeQuinckeneedlethroughL2-L3orL3-L4interspacesand17.5mgofhyperbaric0.5%bupivacainewasinjectedinsittingposition.Simultaneouslyco-loadingwasstartedwithRLthroughadministrationset withclampfullyopen.Thepatientswerelocated in the supine position with slight head down tilt, till level of sensory blockreached T8confirmedbypinprick method.Afterstabilizationofanaesthesia,cystoscopy

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Volume 4, Issue 4, July-Aug 2022 pp 241-249 www.ijdmsrjournal.com ISSN: 2582-6018

and urethral catheter placement were done in lithotomy position. Thenthe patients were turned prone carefully and with the cooperation of the patients.Soft pillows of adequate thickness were placed under the patients flexed shoulderswith both arms flexed forward over them in a natural comfortable position. Thepatientswereallowedtokeeptheirheadsinneutral,leftorrightpositionsaccording to their choice and comfort. All patients received oxygen by bi-nasalprongs@4-6L/minandverbalcontactmaintainedwiththemthroughouttheprocedure.

Immediatelyafterinductionofspinalanaesthesia,blood pressure(systolic and diastolic), heart rate and oxygen saturation were measured andrecorded every 3 minutes in the first 15 minutes, then every 5 minutes until 50minutes and thereafter every 10 minutes till the end of surgery. The incidences ofhypotension (definedasfallinsystolicbloodpressure>20%of baseline)andhypertension(SBP>120%ofbaseline),bradycardia(definedasheartrate<60beats/m in) and tachycardia (>100beats/min) were recorded. Hypotension (fall insystolic blood pressure > 20% from the baseline value or a value less than 90 mmHg) were treated with 10 mg ephedrine intravenously. Any other adverse event likenausea,vomitingetcnoted.Anyepisodeofbradycardiawasmanagedwith atropine 0.6 mg. Occurance of nausea and vomiting were treated with injectionondansetron 4mg intravenously. The data was collected intra operatively and in theperioperativeperiod.

III. RESULTS:

Table1:Patientsdemographics, durationofsurgery.
Values are mean ± standard deviation andpercentage.

	GroupA	GroupB	Pvalue
Age(yrs)	36.8±13.07	38.2±12.56	0.639
M/F	50%/50%	60%/40%	
Operationtime(inmin)	74.1±7.18	72.8±7.29	0.424
BMIkg/m2	29.5±2.5	27.9±4.1	0.69

Figure1:ComparisonbasedonintraoperativeHeartrate(beats/min)betweentwogroups.

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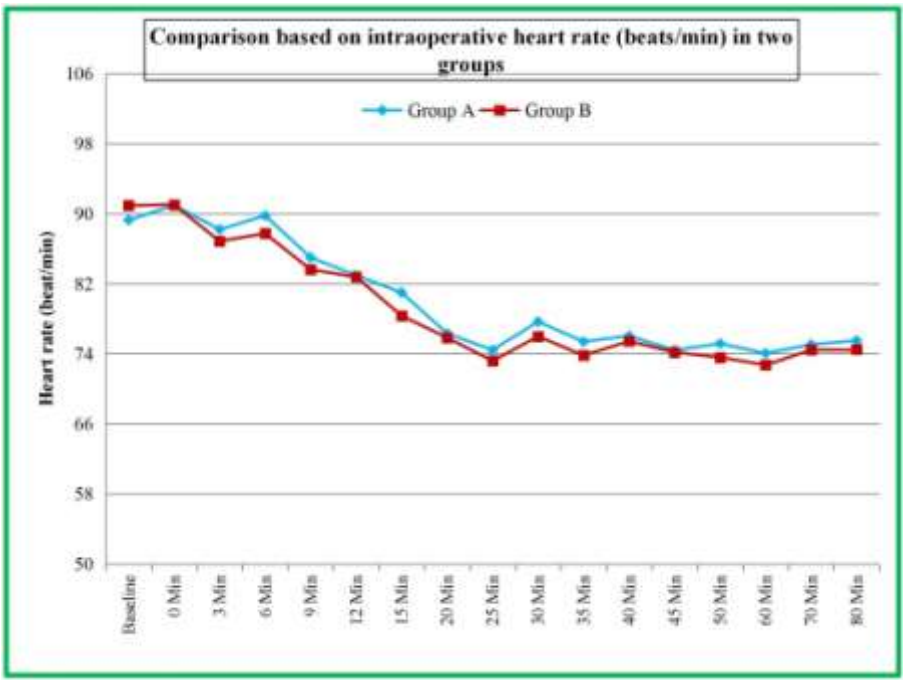

Figure2:ComparisonbasedonintraoperativeSBP(mmHg)betweentwogroups.

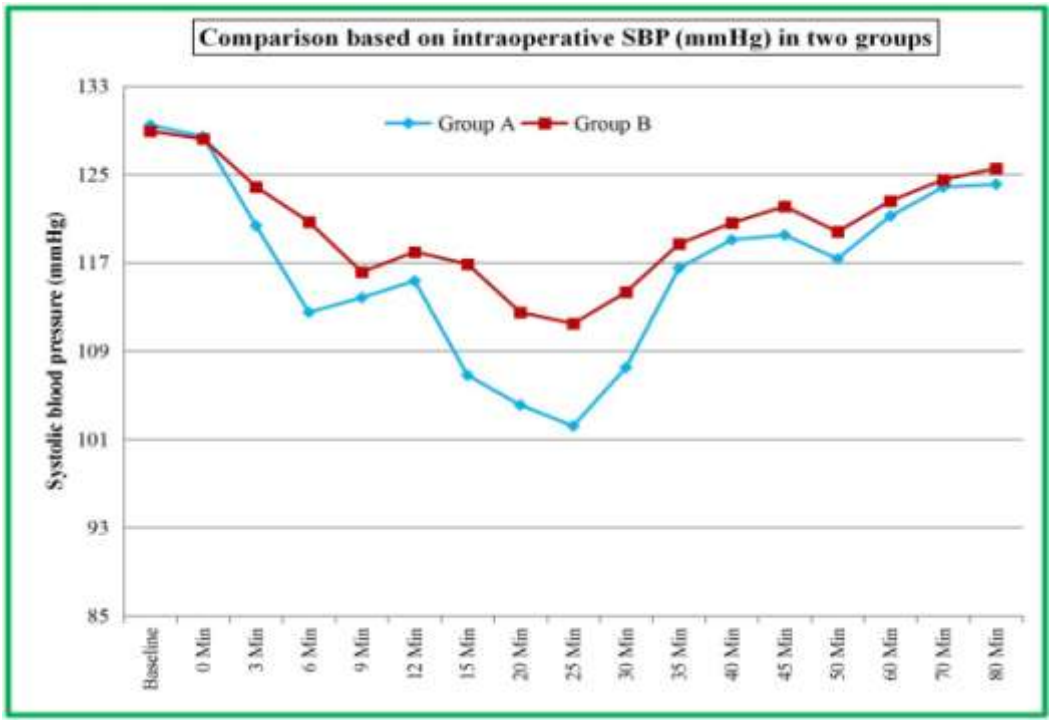

Figure 3: Comparison based on intraoperative DBP (Diastolic blood pressure)betweentwo groups.

International Journal Dental and Medical Sciences Research
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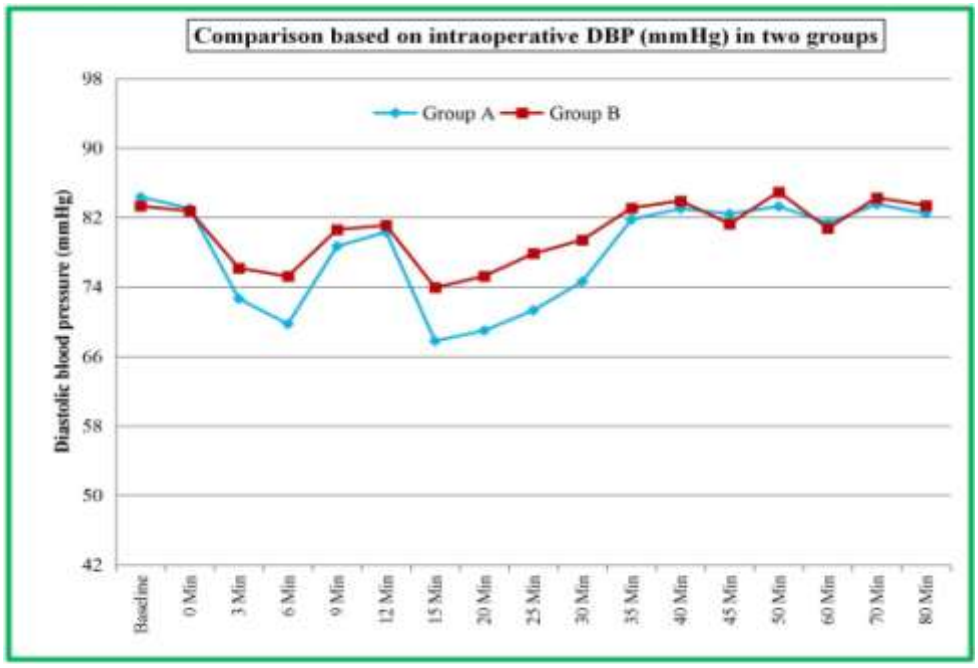

Figure4:Comparisonbasedonintraoperativeoxygensaturationbetweentwogroups.

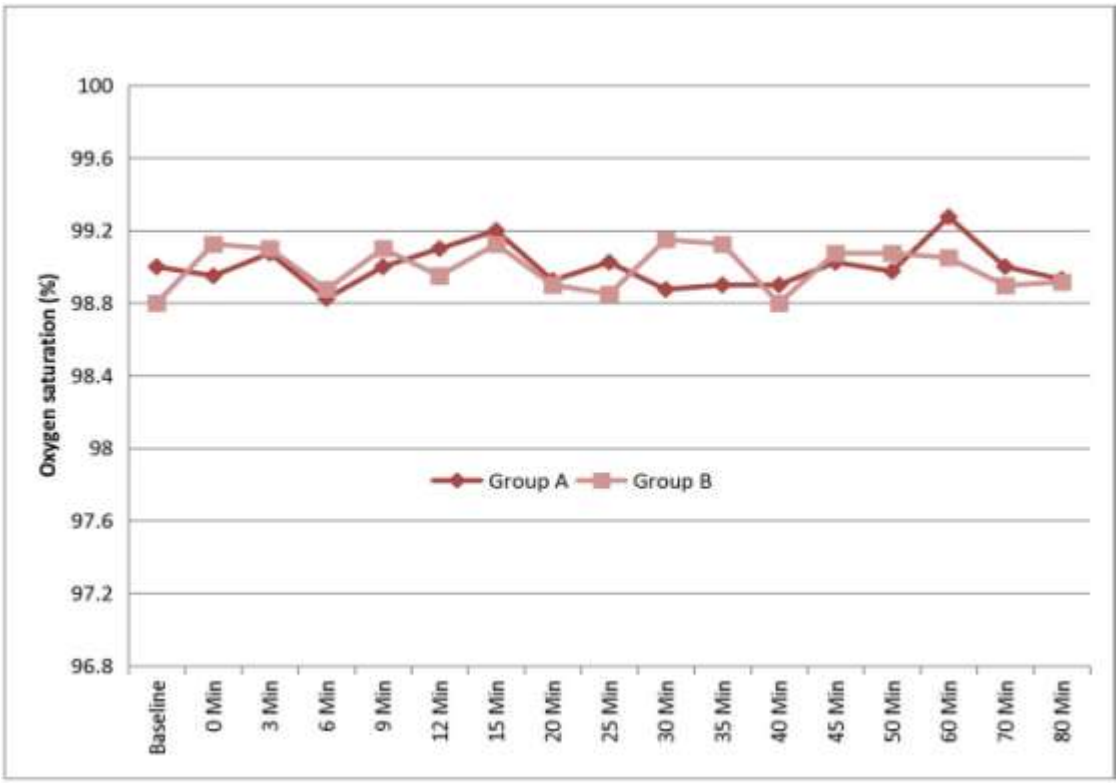

Figure4:Comparisonofpatientsreceiving repetitionofvasopressor.

International Journal Dental and Medical Sciences Research
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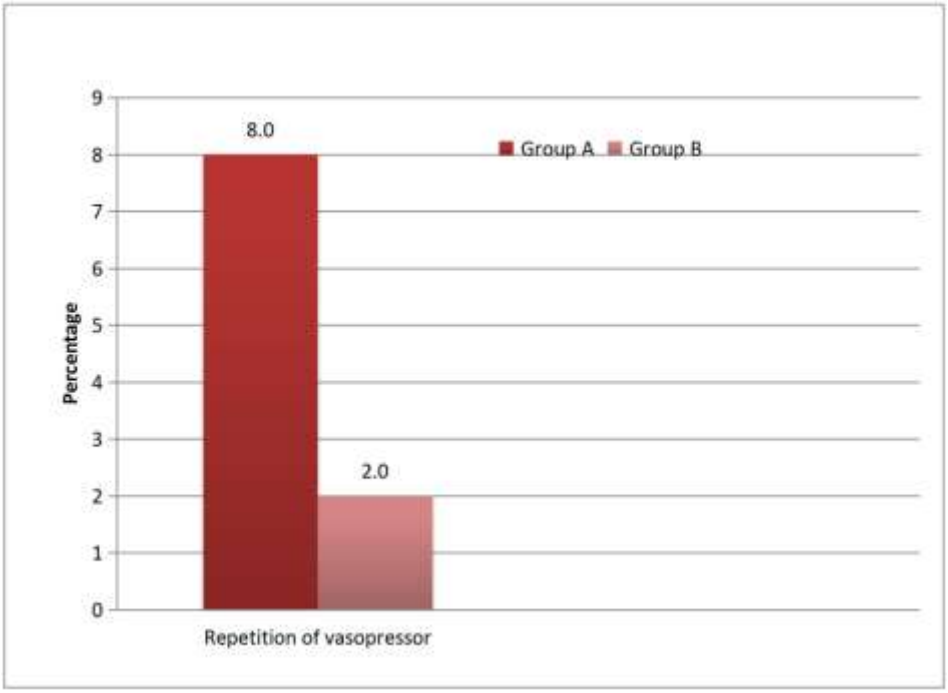

Table2:Thenumberofpeoplereceivingtherepetitionofvasopressor

Parameter	**GroupA**		**Group B**		**Significance**
	No.	**%age**	**No.**	**%age**	
Repetition ofvasopressor	8	26.6%	2	6.6%	SS

Table3:Adverseeffects

AdverseEffects	**GroupA**	**GroupB**	**Significance**
Shivering	5	7	NS
Bradycardia	1	1	NS
Nausea/Vomiting	1	1	NS
Pleuralpuncture	0	0	
Shoulderdislocation	0	0	

Localperioperativepain	0	0	

IV. DISCUSSION:

Spinal anaesthesia has proved to be an excellent alternative to general anaesthesiaforvarietyofsurgicalprocedures.Thereare manyadvantagesforspinalanaesthesiaovergeneralan aesthesia.

Various methods are employed for the management of hypotension. Nowadaysvasopressorsarebecomingoneofthemainst ayofmanagementofspinalhypotension.

Vasopressors infusions, however have been associated with a largeamount of drug being used, increasing possibilities of side effects and toxicity.Different studies have compared ephedrine different doses in prevention of spinalhypotension. We compared two different doses (10 mg and 15mg) of ephedrineintravenouslyinthis study.

The demographic profile including age, sex, BMI (body mass index) of the patientsinbothgroupswerecomparableandstatisticall ynonsignificant.Durationofsurgeryinbothgroupswer ecomparableandstatistically nonsignificant.

The difference in baseline mean heart rates and baseline blood pressure (systolic,diastolic)amongtwogroupswascomparable andstatisticallynonsignificant.Meanheartratedidnot varysignificantlyatanyintervalanddifferenceinintrao perativeheartratesamongtwogroupswas statisticallynonsignificant.

In our study the decrease in the blood pressure(systolic and diastolic) were moreat 3, 6, 15, 20, 25 and 30 minutes post spinal anaesthesia, but this difference wasstatisticallysignificant(P<0.05).Whenpatientsw ereputinlithotomypositionafterspinalforcystoscopya ndurethralcatheterplacementbloodpressureincreased butbloodpressurefurtherdecreasedafterpronepositio n.Thereasonmay be due to return of pooled blood from the lower extremities to the heart whenpatient put in lithotomy position. Increase in the venous return was greater in thelithotomy position (13). In prone position there is significant decrease in the thecardiac index (14). We noticed maximum hypotension when patient is put in pronepositionfromsupine.

OurstudyareinaccordancewithLoughreyJPetal.(15)t heyfoundthatprophylactic bolus of ephedrine 12 mg IV given at the time of intrathecal block,plusrescuebolusesleadstoalowerincidenceofh ypotensionfollowingspinal anaesthesia for elective caesarean section compared to IV rescue boluses alone.Iqbal MS et al. (16) they found that the incidence of hypotension was significantlyhigher in patients receiving a 10 mg prophylactic dose of ephedrine than in patientsreceiving 15 mg and 20 mg ephedrine. There was however, a significantly higherincidenceofreactivehypertensioninpatientsrec eiving20mgephedrine.

Our study are not in accordance with Ngan Kee WD et al**.** (17) they found thatsystolic arterial pressure (SAP) in the first 12 min after the spinal injection wasgreater in the 30 mg group compared with other groups (P<0.05). They concludedthat smallest effective dose was 30 mg. King SW and Rosen MA 1998 (18) theydetermined whether intravenous ephedrine prophylaxis would benefit prehydratedobstetricalpatientspresentingforelective cesareansection.Theyfoundthathypotensionoccurre din6/10controlpatients,5/10boluspatientsand5/10inf usion patients.Tsen LCet al.(19) they concluded that 10mgIV ephedrinegiven at the time of spinal anesthesia, and after a 10 mL/ kg RL fluid bolus, doesnot diminish the incidence or severity of hypotension in parturients undergoingcesareandelivery.Overallincidenceofhyp otensionwas70% inbothgroups.

Various studieshave compared the effectof ephedrine and phenylephrine andfound no difference in the effectiveness to prevent spinal anaesthesia associatedhypotension. Alday Munoz Eet al.(20) they foundthat the ability of ephedrineandphenylephrinetopreventhypotensiond uringcesareansectionprovedtobesimilar.LaPortaRFe tal.(21)theyfoundthatphenylephrineisassafeandeffec tiveasephedrineintreatmentofdropinbloodpressure. MagalhaesEetal.

(22) theyfoundthatephedrinewasmoreeffectivet hanphenylephrineinthepreventionofhypotension.

In our study we found one patient in each group have bradycardia and requiredatropine for treatment. In our study eight patient in group A required ephedrine 10mg as a rescue vasopressor while two patients in group B required ephedrine, thedifference was statistically significant. In our study 5 patients in group A and 7patients in group B have shivering which was comparable and statistically nonsignificant. In our study incidence of nausea and vomiting were comparable andstatistically non significant. The mean oxygen saturation in the both groups wascomparableandstatisticallynon-significant.Noepisodesofdesaturationwereobserved withtheuseofthesevasopressors.

Therewasnoincidenceofcomplicationssuchasintract ablehypotension,significanthaemorrhage,transfusio n,localperioperativepain,pleuralpuncturesand

shoulder dislocation in our study. In our study no patients was converted togeneral anaesthesia. Our study are in accordance to Abraham AA and Das V (23)they found that PCNL can be done under spinal anesthesia to the satisfaction of thepatient, surgeon and anesthesiologist. Mehrabi S and Karimzadeh Shirazi K (24)evaluatedtheimpactofspinalanesthesiaonintra-operativeandpostoperative
outcome in patients undergoing PCNL. They found that spinal anesthesia is safeand effective for performing PCNL and is a good alternative for general anesthesia(GA)inadultpatients.
From the above study we concluded that the prophylactic use of ephedrine in 15mg IV bolus significantly decreases the incidence of maternal hypotension
withoutserioussideeffectslikereactivehypertension.

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