Indian J.Sci.Res. 5(1) : 39-46, 2014

ISSN : 0976-2876 (Print)
ISSN : 2250-0138 (Online)

A COMPARATIVE STUDY OF BUPIVACAINE 0.25% ALONE AND WITH FENTANYL OR DEXMEDETOMIDINE FOR PERCUTANEOUS NEPHROLITHOTOMY (PCNL) UNDER EPIDURAL ANAESTHESIA

RAVI PRAKASH[a1], B. B. KUSHWAHA[b], SHASHIBHUSHAN[c], V. K. BHATIA[d], GIRISH CHANDRA[e] AND B. P. SINGH[f]

[abcdef]Department of Anaesthesiology, K.G. Medical University, Lucknow, U.P., India

ABSTRACT

Low concentration of bupivacaine has been used to provide perioperative analgesia. This study was undertaken to compare low concentration bupivacaine (0.25%) when given alone and with fentanyl (1µg/kg) or dexmedetomidine (1µg/kg) in epidural anaesthesia in patients undergoing PCNL. Sensory and motor blocks were more pronounced in the dexmedetomidine group along with superior sedation. None of the patients in the study had any major complication and surgery underwent smoothly without requirement of general anaesthesia. From our study, it can be concluded that PCNL can be performed using 0.25% bupivacaine as epidural anaesthetic agent. Further, dexmedetomidine is a better adjuvant than fentanyl in epidural anaesthesia. Dexmedetomidine combined with 0.25% of bupivacaine in epidural anaesthesia provides adequate operating conditions for PCNL with minimal motor blockade.

KEYWORDS : Dexmedetomidine, bupivacaine, fentanyl, percutaneous nephrolithotomy, epidural

Percutaneous nephrolithotomy (PCNL) is a common urological procedure done nowadays and both regional and general anaesthesia are used for PCNL.

This surgery requires intense analgesia upto T- 6 level but profound muscle relaxation is not required. There is no study which has used analgesic concentration of bupivacaine in epidural anaesthesia for PCNL. We performed this study to assess whether PCNL can be performed under analgesic concentration (0.25%) of bupivacaine and the effect of fentanyl and dexmedtomidine as adjuvants to epidural bupivacaine.

It is emphasized that the combination of epidural opioids and local anesthetics provide synergistic and superior analgesia, and can be accomplished with less toxicity than either class of drugs alone (Topcu et al., 2005).

Dexmedetomidine provides pain relief by an opioid independent mechanism. It produces anti nociception by stimulating post synaptic α2 adrenergic receptors in the dorsal horn of spinal cord (Grosu and Lavand'homme, 2010).

This study was undertaken to compare low concentration bupivacaine (0.25%) when given alone and with fentanyl (1µg/kg) or dexmedetomidine (1µg/kg) in epidural anaesthesia in patients undergoing PCNL.

MATERIALS AND METHODS

It is a randomized, prospective, double blind, case control study. After getting approval from the institutional ethical committee, an informed consent was taken from the patient and attendants. The study was conducted on 75 patients of either sex, aged between 20 to 50 years belonging to ASA physical status I or II scheduled to undergo PCNL. Patient having absolute or relative contraindication for epidural catheter insertion, pregnant or lactating females, patient not willing to participate in the study, morbid obesity and patient of obstructive sleep apnea or difficult airway, patient known to have allergy to any drug under the study or patients with neurological or hepatic diseases were excluded from study. Power calculation for the study was based on the primary end point of systolic and diastolic pressure. The sample size calculation was adjusted for the 2 primary comparisons using Bonferroni correction and a corresponding Z value for a two-sided of 0.025. Preliminary data indicated that enrollment of 25 patients in each groups was necessary to detect difference in blood pressure with a power of 95.0% using a two-sided P value of 0.025. Patients were randomly allocated in three groups using a computer generated random number table:

Group A (n=25): patient receiving only 20 ml epidural 0.25% bupivacaine.

Group B (n=25): patient receiving 20 ml epidural

[1]**Corresponding author**

0.25% bupivacaine along with fentanyl (1mcg/kg).

Group C (n=25): patient receiving 20 ml epidural 0.25% bupivacaine along with dexmedetomidine (1mcg/kg).

After proper preanaesthetic assessment, patients were premedicated with tab. Pentoprazole 40 mg and tab. Alprazolam 0.5 mg night before surgery and with inj. 0.02 mg/kg Midazolam and inj. 4 mg Ondansetron intravenously before starting procedure. In the operating room, standard monitors including noninvasive blood pressure monitoring (NIBP), pulse oximetry (SpO_2) and electrocardiogram (ECG) were applied to all patients. An 18 gauge intravenous line was secured and 500 ml of lactated ringer solution was infused as preloading. An 18 gauge multiple hole epidural catheter was placed through 16 gauge Touhy needle in L1-L2 or L2-L3 intervertebral space in sitting position using loss of resistance technique via midline approach and 3 to 5 cm of catheter was placed in cephalic direction in epidural space and catheter was secured using sterile transparent tapes. 3 ml of 2% xylocaine with 1:200000 adrenaline was administered as test dose to exclude intravascular or intrathecal catheter placement.

Thereafter, patients were laid in supine position and 20 ml of study drug was given over 15 minute. After achieving sensory loss upto T-6 level, patient were laid in lithotomy position and uretric catheter was placed and then patient was turned in prone position for PCNL.

The onset and duration of analgesia, peak sensory level, time to reach maximum sensory level and associated motor block was noted in each patient. Heart rate, NIBP, ECG and SPO_2 were recorded at 3 minutes interval for initial 30 minutes, thereafter every 5 minutes for rest of the surgery and then every 15 minutes postoperatively till 3 hours. Maximum sedation using Ramsay Sedation Score was recorded in each patient at every 15 minutes. Pin prick sensation was used to determine maximum sensory level at every 5 minutes. Bromage Scale was used for assessing motor block at every 15 minutes. Surgeons were blinded for the study group and their opinion about the quality of anaesthesia was recorded on a four point scale: 0- poor; 1- satisfactory; 2- good; 3- excellent.

2^{nd} dose of midazolam (0.02 mg/kg) iv alone or followed by fentanyl (1mcg/kg) iv was used as rescue analgesia to patients complaining of pain or discomfort within 1 hour of medication. A top up bolus of 10 ml was given after the regression of sensory level two segments below the peak level or if the patient complained of pain and/or discomfort after 1 hour of loading dose.

Hypotension (fall in systolic blood pressure below 20% of baseline value or less than 90 mm Hg) was treated with bolus iv doses of (0.1mg/kg) of inj. mephenteramine. Bradycardia (heart rate less than 50 beats/min) was treated with inj. atropine (0.01 mg/kg) iv.

Patients in whom a sensory level of T-6 was not achieved even after 30 minutes of loading dose or who complained of pain within 1 hour of surgery and failed to respond to rescue medication were excluded from the study and epidural anaesthesia was converted into general anaesthesia. In our study, no patient required conversion to GA.

Any complication that occurred during anaesthesia was noted and treated promptly. Inj. dexamethasone (4 mg) iv was given to patients complaining of nausea and inj. tramadol (0.5 mg/kg) iv was given to patients who developed shivering. If securing of airway was required in emergency situation then patient could be turned to supine position by rolling over a stretcher kept ready in the OT.

ANALYSIS

The results are presented in mean±SD and percentages. The chi-sqaure test was used to compare the categorical/dichotomous variables among the groups. The one way analysis of variance (ANOVA) with Tukey's multiple comparison test was used to compares the means of the variables among the three groups. The repeated measures of analysis of variance was used to test the differences at different time intervals and among the groups. The interaction between time and groups was also tested. The Tukey's test was used for pairwise comparisons. The p-value<0.05 was considered as significant. All the analysis was carried out by using SPSS 16.0 version.

RESULTS

The basic characteristics of three groups of patients (Group A: 0.25% bupivacaine, Group B: 0.25% bupivacaine and fentanyl, and Group C: 0.25% bupivacaine and dexmedetomidine) at admission (baseline) are summarized in table 1. Subjects of three groups were matched for age, sex, height, weight, diagnosis, operation done and duration of surgery. Thus these factors did not influence the outcome measures. The mean duration of surgery in all patients was 100.26 minutes and it did not differ stastically among three groups.

The systolic, diastolic and mean blood pressure in three groups was similar throughout the study and their comparison revealed no significant differences (table 3, 4 and 5).

Comparison of the mean heart rate between three groups, revealed significantly (P<0.001) lower heart rate of Group C as compared to both Group A and Group B while it did not differed (p value 0.235) between Group A and Group B throughout periods i.e. remain statistically the same (table 6) (figure 1). Only three patients in group C required a single dose of atropine for bradycardia. The levels of SpO_2 in all three groups remain similar over the periods.

The mean time to reach maximum sensory level was longest in Group A (17.60± 3.27 minutes) followed by Group B (17.00 ± 2.50 minutes) and Group C (16.20 ± 2.99 minutes). Although it was shortest in Group C but it does not differ statistically (P value 0.246) (as shown in table 2). The maximum sensory level achieved with equal volume of drug was higher in group C and B but T-6 level was achieved in all 75 patients which is the required sensory level for PCNL.

In our study, the mean time to two segment regression was 86.52 ± 9.07 minutes in group A, 120.00 ± 5.95 minutes in group B and 135.40 ± 9.57 in group C (table 2). Addition of fentanyl and dexmedetomedine prolonged the duration of analgesia (p<0.001). Dexmedetomidine was more effective in this respect.

The motor block (bromage scale) was observed to be more in group B and C than group A but none of the patients in the study had complete lower limb paralysis and all the patients in the study were able to ambulate after 3 hours of last dose of epidural anaesthetic agent.

Nausea was less in group C (0%) as compared to other two groups (4%) while shivering was more common in group A and B (12%) than group C (4%).

7 patients in group A and 2 patients in group B required an additional dose of midazloam 1 mg while 1 patient each in group A and B required 50 mcg of fentanyl in addition to midazolam as rescue medication. No rescue

Table 1 : Basic characteristics of three groups

Characteristics	Group A (n=25)	Group B (n=25)	Group C (n=25)	p value
Age (yrs):				
Mean ± SD	33.00 ± 11.17	35.12 ± 9.74	33.56 ± 7.76	0.725
Range (min-max)	(16-50)	(20-50)	(24-50)	
Gender:				
Males	17 (68.0%)	19 (76.0%)	17 (68.0%)	0.773
Females	8 (32.0%)	6 (24.0%)	8 (32.0%)	
ASA physical status:				
1	15 (60.0%)	13 (52.0%)	16 (64.0%)	0.681
2	10 (40.0%)	12 (48.0%)	9 (36.0%)	
Diagnosis:				
L. Renal calculus	9 (36.0%)	7 (28.0%)	12 (48.0%)	0.24
R. Renal calulus	9 (36.0%)	14 (56.0%)	11 (44.0%)	
B/L Renal stone	7 (28.0%)	4 (16.0%)	2 (8.0%)	
Operation done:				
L. PCNL	14 (56.0%)	9 (36.0%)	13 (52.0%)	0.326
R. PCNL	11 (44.0%)	16 (64.0%)	12 (48.0%)	

Table 2 : Summary of clinical benefits and requirements of three groups

Benefits/requirements	Group A (n=25)	Group B (n=25)	Group C (n=25)	p value
Maximum sensory level:				
T4	1 (4.0%)	8 (32.0%)	5 (20.0%)	0.072
T5	0 (0.0%)	0 (0.0%)	1 (4.0%)	
T6	24 (96.0%)	17 (68.0%)	19 (76.0%)	
Time to reach maximum sensory level (min)	17.60 ± 3.27 (15-25)	17.00 ± 2.50 (15-20)	16.20 ± 2.99 (10-20)	0.246
Maximum motor level:				
B romage 1	23 (92.0%)	14 (56.0%)	11 (44.0%)	0.001
B romage 2	2 (8.0%)	11 (44.0%)	14 (56.0%)	
Maximum sedation (score)	2.0 ± 0.0 (2-3)	2.04 ± 0.20 (2-3)	2.88 ± 0.32 (2-3)	p<0.001
Time for 2 segment regression (min)	86.52 ± 9.07 (70-100)	120.00 ± 5.95 (110-130)	135.40 ± 9.57 (95-145)	p<0.001
Rescue drug/IV sedative				
1 dose of M idazolam	25 (100 .0%)	25 (100 .0%)	25 (100.0%)	NA
2 doses of M idazolam	7 (28.0%)	2 (8.0%)	0 (0.0%)	0.007
2 doses of M idazolam + 1 dose of F entanyl	1 (4.0%)	1 (4.0%)	0 (0.0%)	0.99

Table 3 : Systolic blood pressure in three groups

Time (min)	SBP (mmHg)						ANOVA F value		
	Group A (n=25)		Group B (n=25)		Group C (n=25)		Between groups (2, 72 DF)	Within groups (8, 576 DF)	Interaction (16, 576DF)
	Mean	SD	Mean	SD	Mean	SD			
0	127.76	9.08	125.92	11.08	132.28	6.57	0.92^{ns}	79.39^{***}	5.88^{***}
6	122.92	9.26	121.48	10.64	128.12	7.81			
15	119.04	10.36	114.80	14.53	121.72	7.21			
30	118.00	9.06	118.08	8.72	117.88	6.73			
60	119.64	9.19	119.72	7.67	118.80	6.30			
90	119.24	8.92	119.76	8.24	120.04	6.89			
120	119.40	8.61	118.60	9.32	120.92	6.26			
150	120.72	7.15	120.40	7.91	123.36	5.60			
180	122.80	7.68	121.44	7.69	123.92	5.28			

Table 4 : Diastolic blood pressure in three groups

Time (min)	DBP (mmHg)						ANOVA F value		
	Group A		Group B		Group C		Between groups (2, 72 DF)	Within groups (8, 576 DF)	Interaction (16, 576DF)
	Mean	SD	Mean	SD	Mean	SD			
0	80.52	8.20	80.96	8.30	80.80	6.14	0.65^{ns}	69.39^{***}	1.83^{*}
6	76.56	7.49	76.96	8.56	76.16	6.46			
15	72.08	7.69	70.28	9.52	70.80	5.61			
30	72.04	7.18	70.68	7.10	68.64	5.07			
60	70.56	7.89	72.80	6.49	68.60	3.52			
90	72.00	6.53	72.56	6.77	70.48	3.96			
120	71.80	8.52	73.04	7.19	70.56	3.84			
150	72.56	7.28	74.80	6.62	72.84	4.73			
180	76.92	7.89	77.64	6.36	74.08	7.08			

Table 5 : Mean blood pressure in three groups

Time (min)	Mean BP (mmHg)						ANOVA F value		
	Group A (n=25)		Group B (n=25)		Group C (n=25)		Between groups (2, 72 DF)	Within groups (8, 576 DF)	Interaction (16, 576DF)
	Mean	SD	Mean	SD	Mean	SD			
0	96.27	8.12	95.95	8.74	97.96	5.98	0.01 ^{ns}	105.42 ***	3.60 ***
6	92.01	7.67	91.80	8.91	93.48	6.40			
15	87.73	8.24	85.12	10.61	87.77	5.68			
30	87.36	7.13	86.48	7.22	85.05	5.19			
60	86.92	7.92	88.44	6.20	85.33	3.55			
90	87.75	6.98	88.29	6.87	87.00	3.90			
120	87.67	8.35	88.23	7.39	87.35	4.26			
150	88.61	6.86	90.00	6.41	89.68	4.16			
180	92.21	7.48	92.24	6.20	90.69	6.05			

Table 6 : Heart rate in three groups

Time (min)	Heart rate (beat/min)						ANOVA F value		
	Group A (n=25)		Group B (n=25)		Group C (n=25)		Between groups (2, 72 DF)	Within groups (8, 576 DF)	Interaction (16, 576DF)
	Mean	SD	Mean	SD	Mean	SD			
0	82.12	7.30	77.12	8.61	83.24	8.31	33.53 ***	12.95 ***	39.80 ***
6	87.16	7.53	79.48	7.92	79.08	8.94			
15	90.00	9.73	86.00	7.62	71.92	9.40			
30	88.32	10.28	88.12	7.67	67.68	8.59			
60	86.48	8.86	88.28	6.69	66.36	8.09			
90	86.88	10.96	85.92	7.50	65.24	6.31			
120	84.60	9.32	82.92	7.00	67.00	5.77			
150	84.84	7.85	83.32	7.00	67.04	6.17			
180	82.68	6.88	82.12	7.07	69.96	5.30			

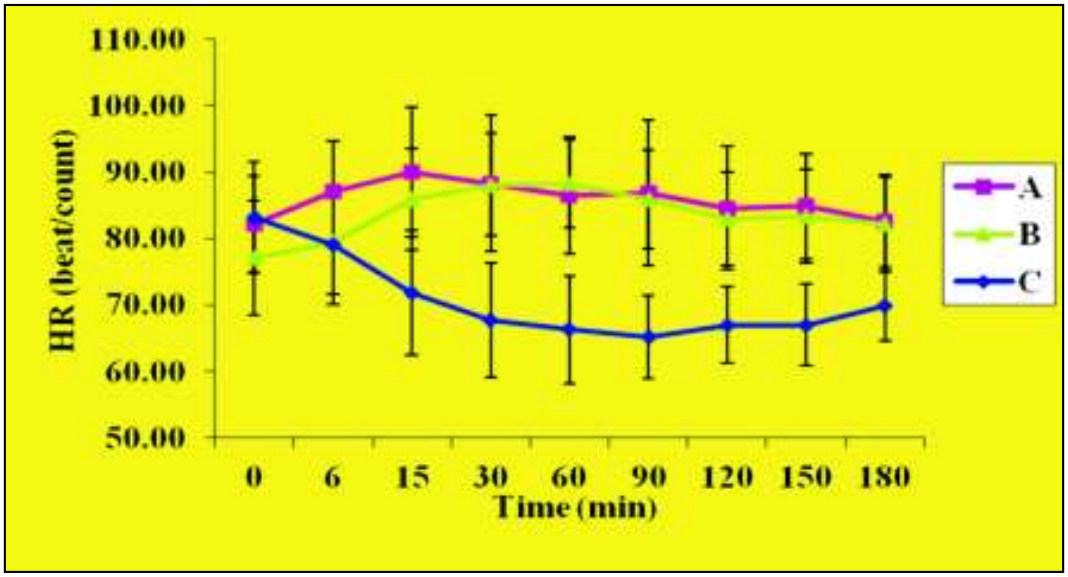

Figure 1: Heart rate in three groups

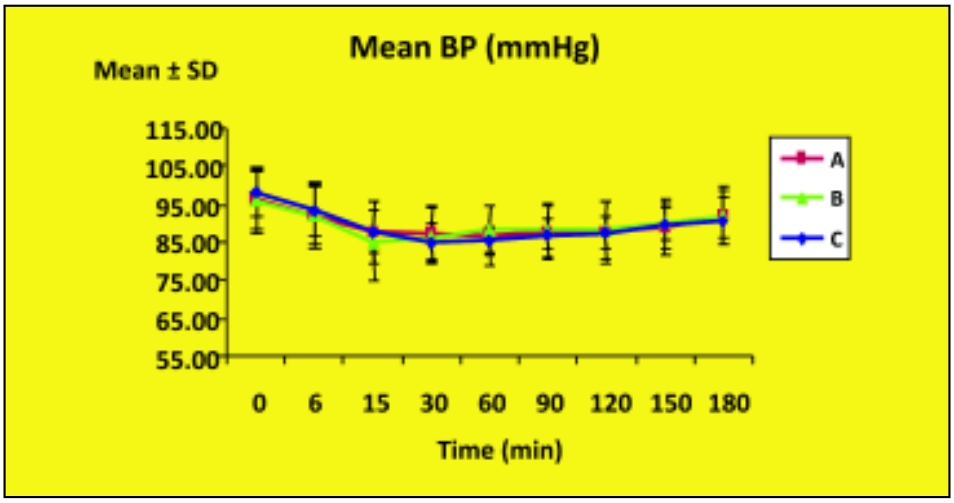

Figure 2: Mean B.P. in three groups

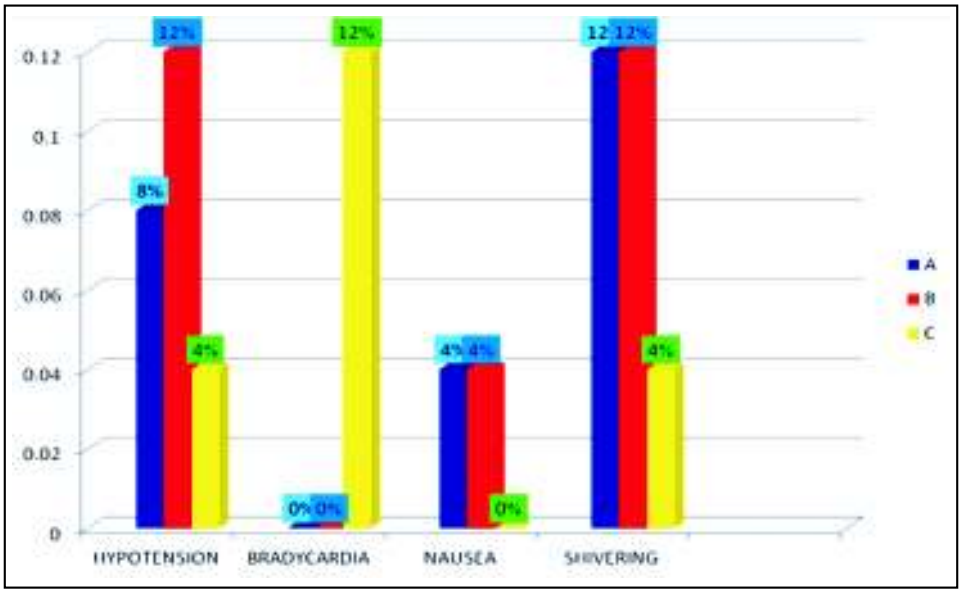

Figure 3: Incidence of adverse effects

DISCUSSION

PCNL is performed through a nephroscope inserted through a small skin incison. PCNL had been performed traditionally under general anaesthesia but multiple studies have proved that regional anaesthesia is equally safe and effective as general anaesthesia for PCNL (Singh et al., 2005; Kuzgunbay et al., 2009; Mehrabi et al., 2010). Therefore we tried to decrease the concentration of local anaesthetic in epidural anaesthesia and added fentanyl and dexmedetomidine to intensify the analgesia to minimize motor blockade of lower limb and patient can be ambulated as early as possible.

General anaesthesia (GA) is preferred in children, uncooperative patients and patients having any contraindication for regional anaesthesia (RA). It has an advantage of better control of diaphragmatic movements during insertion of nephroscope as diaphragmatic movements can cause difficulty in renal puncture by nephroscope. It also has the advantage of a secured airway especially when the surgery is done in prone position as is

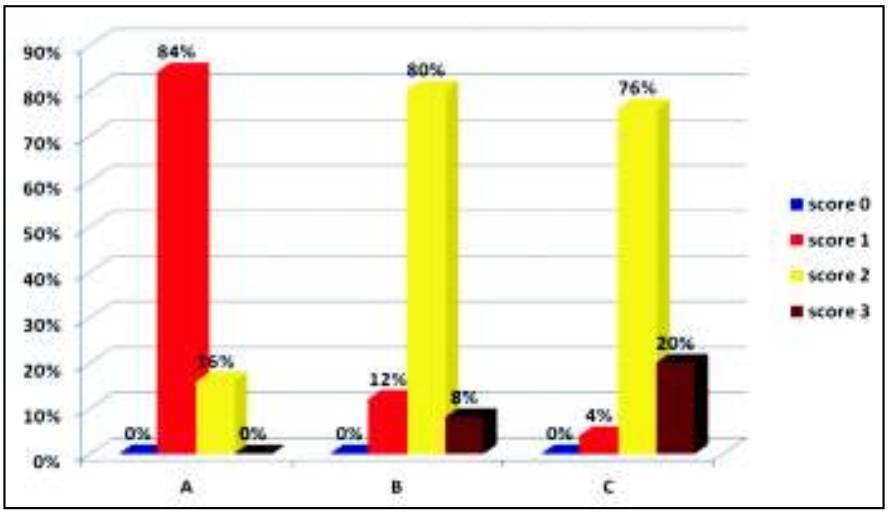

Figure 4 : Surgeon's opinion about quality of anaesthesia (P value for score 1,2 and 3 is 0.0001)

the practice in our institution. But GA has its own disadvantages such as use of multiple drugs, pulmonary and airway related complications, postoperative delayed ambulation and discharge from hospital, adverse physiological effects and stress response. Moreover, administering GA is more costly and post operative pain management requires intravenous drugs which may cause nausea and vomiting and needless sedation.

Epidural anaesthesia is safe in patient with compromised respiratory function and has been used for transcutaneous renal surgery. It also blunts the surgical stress response and provides good post operative analgesia without the need for sedation.

In our study, blood pressure (systolic, diastolic and mean) in all three groups showed similar trends and no major change occurred in blood pressure in any group. Addition of fentanyl or dexemedetomidine did not significantly increase the incidence of hypotension. 6 patients (2 in group, 3 in group B and 1 in group C) had hypotension which responded to single bolus dose of mephenteramine. So, the risk of hypotension was not significant with any of the three drug combination used. Drug concentration was more important than drug dose in determining the degree of sympathectomy following use of local anaesthetics in lumbar epidural anesthesia (Ginosar et al., 2009). We observed a lesser degree of fall in blood pressure with 0.25% epidural bupivacaine as seen in previous studies using 0.5% bupivacaine for lumber epidural anaesthesia (Kampe et al., 2004; James et al., 1980).

The mean heart rate was lower in group C than other two groups but only three patients in group C required single dose of atropine for bradycardia. No patient in group B and A required atropine for bradycardia. The heart rate was lower than observed in previous studies (Kampe et al., 2004; James et al., 1980).

The oxygen saturation in all the three groups was above 95% in all patients..

The onset time of epidurally administered local anesthetic bupivacaine 0.5% was found to be 13-19 minutes in previous studies (Johnson et al., 1989). Decreasing the concentration in our study to 0.25% did not prolong the time of onset of block (16-18 minutes). The maximum sensory level achieved with equal volume of drug was higher in group C and B but T-6 level was achieved in all 75 patients which was the required sensory level for PCNL.

The time to two segment regressions was decreased on lowering the concentration of drug to 0.25% but addition of fentanyl and dexmedtomedine prolongs the duration of analgesia. Dexmedetomidine was more effective in this respect. It was consistent with the findings of various studies (Topcu et al., 2005; Al-Mustafa et al., 2009; Bajwa et al., 2011; El-Hennawy et al., 2009) which showed that addition of dexmedetomidine and fentanyl prolongs the duration of analgesia of epidurally administered local anaesthetics.

The motor block in group B and C was more than in group A but none of the patients in the study had complete lower limb paralysis and all were able to ambulate after 3 hours of last dose of epidural anaesthetic agent.

No rescue medication was required in group C. Therefore, we can conclude that dexmedetomidine with bupivacaine provides better analgesia, optimal sedation and excellent operating comfort for patient and surgeon than bupivacaine alone or with fentanyl. No major adverse effects were noted in any of the three groups.

From our study, we conclude that PCNL can be performed using 0.25% bupivacaine in epidural anaesthesia without compromising on patient's comfort and surgeon's satisfaction. Reducing the concentration helps in decreasing motor blockade ensuring early ambulation without compromising the depth of analgesia. Addition of fentanyl and dexmedetomidine improves the quality of analgesia and prolongs the duration of anaesthesia with latter being better in this regard. The incidence of adverse effects was almost same in all groups except bradycardia which was seen with dexmedetomidine. Dexmedetomidine is a better adjuvant to 0.25% bupivacaine for PCNL than fentanyl.

Use of low concentration epidural anaesthesia helps in early ambulation of patients and thus reduces the hospital stay and overall cost of the surgery. By avoiding general anaesthesia drugs, we can reduce the incidence of post operative cognitive dysfunction in elderly patients.

We recommend that ropivacaine can also be used in place of bupivacaine due to its differential effect on motor blockade and lesser cardiotoxicity.

REFERENCES

Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, Murshidi MM, Ammari BA, Awwad ZM, et al. Effect of dexmedetomidine added to spinal bupivacaine for urological procedures. Saudi Med J 2009; **30**:365-70.

Bajwa SJ, Bajwa S, Arora A, et al. Dexmedetomidine and clonidine in epidural anaesthesia: A comparative evaluation. Indian J anaesthesia 2011; **55**:116-2.

El-Hennawy AM, Abd-Elwahab AM, Abd-Elmaksoud AM, El-Ozairy HS, Boulis SR. Addition of clonidine or dexmedetomidine to bupivacaine prolongs caudal analgesia in children. Br J Anaesth 2009; **103**:268-74.

Ginosar Y, Weiniger CF, Kurz V, Babchenko A, Nitzan M, Davidson E. Sympathectomy-mediated vasodilatation: a randomized concentration ranging study of epidural bupivacaine. Can J Anaesth. 2009; **56**:213-21.

Grosu I and Lavand'homme P. Use of dexmedetomidine for pain control. F1000 Medicine Reports 2010, **2**:90 (doi: 10.3410/M2-90).

James FM 3rd, Dewan DM, Floyd HM, Wheeler AS, Grant WM, Rhyne L et al. Chloroprocaine vs. bupivacaine for lumbar epidural analgesia for elective cesarean section. Anesthesiology 1980; **52(6)**:488-91.

Johnson C, Oriol N, Feinstein D, Ransil BJ. Onset of action between bupivacaine 0.5% and bupivacaine 0.5% plus fentanyl 75 mcg. J Clin Anesth. 1989; **1(6)**:440-3.

Kampe S, Tausch B, Paul M, Kasper SM, Bauer K, Diefenbach C, Kiencke P. Epidural block with ropivacaine and bupivacaine for elective caesarean section: maternal cardiovascular parameters, comfort and neonatal well-being. Curr Med Res Opin 2004; **20(1)**:7-12.

Kuzgunbay B, Turunc T, Akin S, Ergenoglu P, Aribogan A, Ozkardes H. Percutaneous nephrolithotomy under general versus combined spinal-epidural anesthesia. J Endourol 2009; **23(11)**:1835-8.

Mehrabi S, Karimzadeh Shirazi K. Results and complications of spinal anesthesia in percutaneous nephrolithotomy. Urol J 2010; **7**:22-5.

Singh I, Kumar A, Kumar P. Ambulatory PCNL (tubeless PCNL under regional anesthesia) - a preliminary report of 10 cases. Int Urol Nephrol. 2005; **37(1)**:35-7.

Topcu I, Luleci N, Tekin S, Kefi A, Erincler T. Effectiveness of clonidine and fentanyl addition to bupivacaine in postoperative patient controlled epidural analgesia. Anasthesiol Intensivmed Notfallmed Schmerzther 2005; **40**:521-5.