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ABSTRACT Background: Percutaneous nephrolithotomy(PCNL) has become the mainstay of treatment for renal-calculi over the			

ABSTRACT Background: Percutaneous nephrolithotomy(PCNL) has become the mainstay of treatment for renal-calculi over the past 40years, the practice of which has been defined and redefined over-time.GA had been the anaesthesia of choice for decades, but now, SA has proven its efficacy for the same. In this study of ours, we compare the feasibility of SA over GA for PCNL.

Methods: A retrospective study was done with 60 patients who underwent PCNL. They were divided into 2 groups: Group A(n=30 patients), who underwent the surgery under SA, and Group B(n=30 patients), who underwent the surgery under GA. Hemodynamic stability in terms of HR, MAP, total blood loss, post-operative analgesic requirements, patient's and surgeon's comfort, use of poly-pharmacy and OT utilization time were recorded intra-operatively and post-operatively.

Results: MAP and HR did not show significant difference between the 2 groups(p value>0.05). Blood loss was minimal in both groups, however post-op analgesic requirements, use of poly-pharmacy and OT utilization time were significantly reduced in Group A.

Conclusion: It was observed that the patients were hemodynamically more stable and comfortable when operated under GA, however post-operative analgesia,OT utilization time was better when done under SA, also minimizing the inadvertent use of poly-pharmacy. Hence,SA is reaching equal efficacy with that of GA for PCNL cases.

KEYWORDS: Percutaneous Nephrolithotomy, Spinal Anesthesia, General Anesthesia.

INTRODUCTION

PCNL is a minimally invasive therapy for treatment of upper ureteral and renal stones [1-3]. It is the treatment of choice for kidney stones larger than 20 to 30 mms, staghorn stones and stones that are multiple or resistant to ESWL [4].

Despite good results of PNCL with GA, it may cause atelectasis, drug reactions, nausea, and vomiting (4, 5). In abdominal and lower extremities surgeries, SA is mainly employed by a single drug and comprises some advantages such as less bleeding, and reduces venous pressure in the surgery field (6, 7). However, there are recent reports regarding the use of SA in PNCL demonstrating lower post-operation pain, less drug intake, and reduced adverse effects. Some studies have also shown that surgeries with SA had better outcomes in spinal surgeries (4, 5, 8)

In recent years, RA is preferred over GA due to its advantages including less postoperative pain, low dose analgesic requirement and less drug intake, low cost shortened surgery as well as anaesthesia time, prevention from multiple drug allergies or side effects resulting from GA, complications and costs of GA are higher than SA[7].

Due to high cost and rate of complications in patients undergoing PCNL under GA it is planned to compare them with those undergoing the same procedure under SA.

OBJECTIVES OF THE STUDY

Considering the type of anesthesia as well as patients' hemodynamics that can influence on surgery outcomes and relevant morbidity and mortality of the intervention, and that these factors directly reflect on regional health-care, we aimed this study to compare the feasibility of SA over GA in terms of efficacy and safety in patients undergoing PCNL.

MATERIALS AND METHODS

Study Design: Observational study.
Study Period: 10 months (Oct. 2018 to July.2019).
Study Area: PESIMSR, Kuppam.
Source Of Data: Collected from patients undergoing PCNL under SA and GA in Operation Theatres of PESIMSR, Kuppam.

• Inclusion Criteria : Age : 20-60 yrs Gender : male and female

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ASA grading : I and II Stone size: 8 mm – 20 mm Mode of anaesthesia : SA and GA Elective cases

 Exclusion Criteria : Age < 20 yrs and > 60 yrs ASA grading : III and above Cases taken up under emergency Stone size : > 20 mm Contraindicated for SA due to gross spinal deformity Derranged Coagulopathy.

All patients referred to PESIMSR in 2018 and 2019 as PNCL candidates were included sequentially if they met these inclusion criteria: age between 18-65 years with physical status I or II of American Society of Anesthesiologists (ASA). All patients with spinal deformity, local infection at injection site, pregnancy, history of any neuromuscular or psychiatric disorder or chronic pain, who were suffering from hypertension, diabetes and coagulation disorders, patients with hypersensitivity to any anesthesia drugs, substance abusers, and patients who needed anesthesia higher than T4 and lower than T10 levels were excluded.

The included patients were divided into SA and GA groups using randomized number table. Standard monitoring included continuous electrocardiogram, pulse oximetry, and end-tidal carbon dioxide. Noninvasive BP measurements were performed at 5-min intervals. All patients were routed with a green (18-gauge) catheter and infused with 3-4 cc/kg isotonic crystalloids. Maintenance venous liquid during surgery was based on 4/2/1 rule. For blood loss limited to "maximum allowable blood loss", 3 mL of Ringer solution was injected for every 1 mL of blood losses. Both types of anesthesia were performed by a final year resident of anesthesiology.

GAGroup:

Premedication of 1-2 μ g/kg from fentanyl and 0.01-0.02 mg/kg from midazolam was administered. Oxygen with an inspired fraction of 1.0 was administered for 3 min before intubation. Then, GA was induced by 3-5 mg/kg thiopental-Na, and to obtain desired anesthesia, 0.5 mg/ kg of atracurium was injected intravenously for easier intubation; then, all patients were intubated by a suitable endotracheal tube. For maintaining GA, an intravenous 100 μ g/kg/min of propofol with 50% O2 and 50% N2O were induced. The ventilation protocol consisted of an inspired oxygen fraction of 1.0, inspiratory to expiratory ratio of 1:2, and a respiratory rate adjusted to normocapnia (end-tidal carbon dioxide partial pressure between 30 and 40 mmHg). Mechanical ventilation has been set with a tidal volume of 10 ml/kg ideal body weight (IBW) and ZEEP (zero-positive end expiratory pressure). Atracurium and fentanyl re-administration was based on train-offour (TOF) and every 45 minutes, respectively.

SA Group:

Premedication of 0.01-0.02 mg/kg from midazolam was administered. The patients were placed in a sitting position. The drug was administered by a 25-gauge Quincke needle in midline of L3-L4 or L4-L5 level by a physician. For inducing SA, isobar intra-thecal 15-20 mg of bupivacaine 0.5% without any additives was administered. Then, the patients' positions were changed to prone and intranasal 100% oxygen was administered. Sensory blockade was evaluated by a cotton peak (for heat perception) or a needle (for touching sense) every 15-20 seconds; then, motor blockade was tested by Bromage scale with following score: 0 = no paralysis; 1 = inability to raise extended leg; 2 = inability to flex knee; 3 = inability to move leg joints. Blood pressure below 100 mmHg of 30% from the baseline was corrected by 6 mg ephedrine and crystalloids, and all PR descents (less than 60/min) were treated by intravenous Atropine. All mentioned anesthetic drugs were provided by a regional pharmaceutical company.

The observed parameters in this study :

1.Intra-operative HR and MAP

- 2.Intra-operative blood loss
- 3.OT utilization time
- 4. Additional requirement of analgesia intra-operatively
- 5.Additional requirement of analgesia post-operatively
- 6.Post-operative nausea and vomiting

SBP, DBP, MAP, and PR were recorded in the PACU, every 10 min from entering PACU. Fifty mg from Meperidine was administered in patients suffered from additional pain. All patients were positioned in supine. MAP and PR were evaluated every 10 minutes for 1 hour. Other information were extracted from medical files and inserted into a pre-prepared checklist.

STATISTICS ANALYSIS

Using the Statistical Package for Social Science (SPSS 15.0 Evaluation version), Statistical analysis was done. To calculate sample size, a power analysis of x=0.05 and b=0.90 showed that 30 patients were the minimum required for the study group.

Mean, and Standard deviation was calculated for all the numeric data (age, weight, height, heart rate, etc.). Percentages & frequency were calculated for non-numeric data. A two-tailed paired t-test is used to compare the mean values of both groups (M & P), and for comparing two attributes (comparative of proportion) like parental separation response, venepuncture response, parental satisfaction, etc. in both the groups' chi-square test & Fischer exact was used.

The data were evaluated and analyzed by SPSS version 19 (SPSS Inc., Illinois, USA). All quantitative data were expressed as mean ± SD, and qualitative data as No. (%). For comparing the groups, t-test and Mann-Whitney-U test were used for parametric and non-parametric data, evaluated by Kolmogorov-Smirnov test, respectively. P less than 0.05 were considered as significant

RESULTS

Demographic Data:

Fifty nine patients were enrolled in the study consisting of 38 males and 21 females. The patients were randomly divided into SA (n = 29)and GA (n = 30) groups. Table 1 demonstrates all demographic data. Surgery duration (P = 0.016) and anesthesia duration (P = 0.044) were significantly lower in SA (Table 2). According to Bromage scale, motor block level was zero in all patients in SA group.

Endpoint Results:

In operation time-to-time analysis, SBP was significantly lower in GA group only in 120th minute; DBP in 60th, 90th, and 120th minutes, and MAP in 90th and 120th minutes (P < 0.05). The trend was not significantly different in none of 4 items (Figure 1; P > 0.05). Table 2 demonstrates blood loss, analgesic demand, and blood transfusion amount in both groups. As seen, blood loss (P = 0.001) and analgesic demand (P=0.038) were significantly higher in GA group.

Parameter Evaluated

- 1 Patient Characteristics 2.MAP (in mm Hg)
- 3.Additional analgesia required
- 4.HR (in bpm)
- 5.Intra-operative blood loss (in ml)
- 6.OT utilization time (in min)
- 7.Post-operative analgesia required

8.Post-operative nausea & vomiting

Comparison Of Intra-operative Outcome In Spinal Anaesthesia Vs General Anaesthesia (n=60)

Variable	Type of A			
	Spinal <u>Anaesthesia</u> (n=30)	General <u>Anaesthesia</u> (n=30)	p-value	
MAP (in mm Hg)				
0 min	66.3 ± 4.1	72.8 ± 3.5	< 0.001*	
5 min	70.1 ± 3.6	78.3 ± 7.2	< 0.001*	
15 min	60.4 ± 3.4	90.6 ± 4.7	< 0.001*	
45 min	72.3 ± 5.6	78.2 ± 6.4	0.0003*	
95 min	66.4 ± 3.1	72.5 ± 5.1	< 0.001*	
125 min	64.8 ± 4.5	78.7 ± 6.3	< 0.001*	
175 min	58.4 ± 2.9	70.8 ± 3.7	< 0.001*	
Additional analgesia required				
Yes	6	30	< 0.001*	
No	24	0		

Comparison Of Intra-operative Outcome In Spinal Anaesthesia Vs General Anaesthesia (n=60)

Variable	Type of A		
	Spinal Anaesthesia (n=30)	General Anaesthesia (n=30)	p-varue
HR (in bpm)			
0 min	96.3 ± 1.7	86.4 ± 5.2	< 0.001*
5 min	94.5 ± 4.3	94.7 ± 3.8	0.8493
15 min	116.7 ± 5.6	106.3 ± 6.7	< 0.001*
45 min	88.9 ± 6.1	90.5 ± 4.3	0.2451
95 min	76.2 ± 3.5	82.4 ± 7.1	< 0.001*
125 min	77.4 ± 1.9	76.3 ± 5.5	0.3048
175 min	83.6±4.7	90.2 ± 3.8	< 0.001*
Intra-operative blood loss (in ml)	200.3 ± 42.2	217.5 ± 36.4	0.0963
OT utilization time (in min)	172.7 ± 27.6	195.4 ± 15.9	0.0002*

Comparison Of Post-operative Outcome In Spinal Anaesthesia Vs General Anaesthesia (n=60)

Variable	Type of A					
	Spinal <u>Anaesthesia</u> (n=30)	General <u>Anaesthesia</u> (n=30)	p-value			
Post-operative analgesia required						
Yes	9	23	< 0.001*			
No	21	7				
Post-operative nausea & vomiting						
Yes	4	6	0.488			
No	26	24				

DISCUSSION

Using SA in PNCL surgery is acceptable and more secure. By faster discharge and reduced recovery time, the patients' quality of life can be improved using SA, which can be a good choice for urologist (18). Overall, our study demonstrated that SBP, DBP, MAP, and PR in the whole surgery and recovery times did not have any significant difference between 2 groups, and that the trend was also somewhat similar in SA and GA; however, patients' hemodynamics were more stable in GA group. Furthermore, bleeding and analgesic demand were significantly higher in GA group. None of the patients needed blood transfusion. These results were similar to other studies demonstrating that SA group had better hemodynamics and lower bleeding during and after the surgery (19-26).

- 60 patients, were enrolled in this study (45% males and 55% females).
- Mean age \pm SD at the time of presentation was 43 ± 11 years in GA group VS 44 ± 11 years in SA group.
- Mean stone burden was similar between both groups.
- No significant difference was found between both groups regarding patients' demographics characteristics.

It seems that SA can result in vasodilation and hypotension following sympathetic block. On the other hand, reduced intra-thoracic pressure and epidural vein distension, due to spontaneous ventilation, result in reduced bleeding. Therefore, the results do not seem to be irrational because SA can inhibit stress hormone secretion better than GA (27-30).

Intra-operative heart rate and mean arterial blood pressure were comparable in both groups at the basal level, and then it continued at lower level in spinal group till 1.5 h after beginning of the procedure.

- VAS was lower in SA group till 1 h postoperatively in comparison with GA group.
- Patients in SA group started to receive rescue analgesics after the 1st hour from the end of the surgical procedures while patients in GA group received analgesics early postoperative.
- Patients in GA group reported higher overall satisfaction scores than patients in SA group.
- Similarly, over all surgeons' satisfaction score was higher in favor of GA group compared with SA group.
- Postoperative shivering was higher in SA group than GA group while nausea and vomiting was higher in GA group than SA group.
- Postoperative consumption of analgesia was significantly lower in patients in SA group in the 1st postoperative day in comparison with patients in GA group.

SA blocks preganglionic sympathetic nerves with many advantages compared to GA, such as redistribution of blood flow to musculoskeletal system, skin, and subcutaneous tissues, as well as reducing SBP, DBP, MAP, and PAP, and better hemostasis. Furthermore, other studies demonstrated better PNCL surgery results, lower blood loss, and lesser side effects (such as nausea, vomiting, and post-op pain) in SA(19, 31). Among these advantages of SA, decreasing blood loss is a main issue of SA in PCNL surgery. Recent studies investigated the effects of a 200-µg of oral clonidine tablet 60 - 90 minutes before anesthesia, which reduced blood loss significantly in several kinds of surgeries under GA that could be a future choice along with SA in PCNL (32, 33)

- In a prospective randomized study comparing spinal epidural block vs. general anesthesia Singh et al., reported lower VAS score, less need for analgesics and shorter hospital stay in spinal epidural group
- Kuzgunbay et al. found no difference between general anesthesia and spinal epidural anesthesia regarding operative time, postoperative hemoglobin level, hospital stay, success rate and postoperative complications.
- In McClain et al. study, SA could reduce the amount of anesthesia drugs, length of surgery time, and other side effects in discus decompression surgery (34).
- Tetzlaff et al. have also shown that in spinal surgeries, SA was a better choice for anesthesia compared to GA resulting in lower side effects (35).
- In an observational study, Mehrabi et al. evaluated 160 patients who underwent PCNL under spinal anesthesia in prone position. Blood transfusion was performed for ten patients (6.3%), and six patients complained of mild to moderate headache, dizziness, and mild postoperative low back pain for 2 to 4 days. Complete clearance of calculus or no significant residual calculi larger than 5 mm was achieved in 70% of patients (36).

CONCLUSION

Both GA and SA are effective and safe in PCNL.SA has fewer complications and lower consumption of analgesia postoperatively. Hence, SA has proven its efficacy as the mode of anaesthesia for PCNL

REFERENCES

- Dale O, Hjortkjaer R, Kharasch ED. Nasal administration of opioids for pain management in adults. Acta Anaesthesio Scand 2002; 46(7):759-70.
- Fundamentals of Otolaryngology. A Textbook of Ear, Nose and throat diseases. 6th Ed.Philadelphia, PA: W B Saunders Co; 1989:184. 2. 3
- Reves JG, Robert MD, Fragen MD. Midazolam pharmacology and uses . Anaesthesiology 1985;62:310-324. 4.
- Skidgel RA, Erdos EG. Goodman & Gilman's the Pharmacological basis of therapeutics. 11th Ed. McGraw-Hill Professional; 2006. 5.
- Katzung BG. Katzung-Basic & Clinical Pharmacology. 9th Ed. McGraw-Hill Professional: 2003. Taylor G, Houston JB, Shaffer J, Maweri G. Pharmacokinetics of Promethazine and its 6.
- sulphoxide metabolite after intravenous and oral administration to man. Br. J. clin.Pharmac 1983;15:287-93
- E Rose, D Simon, JP Haberer. Premedicaton with intranasal midazolam in pediatric anesthesia 1990; 9(4), 326-330. 7. 8.
- R Vivarelli, F Zanotti, D Battaglia, G Caggese, G Stella, G Gilli, A Guberti. Premedication with intranasal midazolam in children of various ages 1998;64(11), 499-
- Dallman JA, Ignelzi MA Jr, Briskie DM. Comparing the safety, efficacy and recovery of 9 intranasal Midazolam vs. oral chloral hydrate and Promethazine. Pediatr Dent 2001;23(5):424-30.
- Shashikiran ND, Reddy SV, Yavagal CM. Conscious sedation-An artist's science! An 10. Indian experience with Midazolam. J Indian Pedod Prev Dent 2006; 24:7-14
- Bhaktha P, Ghosh BR, Roy M, Mukherjee G. Evaluation of intranasal Midazolam for 11. Dirakina F, Ghosh DK, Koy M, Mukheljee D. Evaluation of indunasal MidaZollar for preanaesthetic sedation in paediatric patients. Indian J Anaesth 2007; 51: 111-6.
 Wolfe TR, Braude DA. Intranasal Medication Delivery for Children: A Brief Review
- 12
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- and Update. Pediatrics 2010;126(3):532-7. Mathai A, Nazareth M, Raju RS. Preanesthetic sedation of preschool children: 13 Comparison of intranasal midazolam versus oral promethazine. Anesth Essays Res. 2011 Jan-Jun:5(1):67-71.
- Koppal R, Adarsh ES., Ambi U, Anilkumar G. Comparison of the Midazolam Transnasal 14 Atomizer and Oral Midazolam for Sedative Premedication in Paediatric Cases. Journal of Clinical and Diagnostic Research 2011;5(5):932-4.
- Baldwa NM, Padvi AV, Dave NM, Garasia MB. Atomised intranasal midazolam spray as 15. premedication in pediatric patients: comparison between two doses of 0.2 and 0.3 mg/kg. Journal of Anesthesia 2012;26(3):346-50.
- Derakhshanfar H, Modanlookordi M, Amini A, Shahrami A. A comparative study of the sedative effect of oral Midazolam and oral Promethazine medication in Lumbar 16. Puncture. Iran J Child Neurol 2013 Spring;7(2):11-6. Narendra K, Rohit S, Mamta S, Indu V, Meenaxi S. Midazolam Pre-medication in
- 17 Paediatrics: Comparison of the Intranasal and sublingual Routes by using an Atomizer Spray. Journal of Clinical and Diagnostic Research. 2012 February;6(1):65-68. Mostafa G. Mostafa, Khaled M. Morsy. Premedication with intranasal
- 18. dexmedetomidine, Midazolam and ketamine for children undergoing bone marrow biopsy and aspirate. Egyptian Journal of Anaesthesia 2013;29,131-5.
- Mitra S, Kazaland S, Lakesh KA. Intranasal Clonidine vs. Midazolam as Premedication in children: A Randomized controlled Trial. Indian Pediatrics 2014;51:113-8. 19.
- Malinovsky JM, Lejus C, Servin F, Lepage JY, Le Normand Y, Testa S et al. Plasma 20. concentration of Midazolam after intavenous, nasal or rectal administration in children. British Journal of Anaesthesia 1993; 70:617-620.
- Davis PJ, Tome JA, Mc Gowan FX Jr, Cohen IT, Latta K. Preanesthetic medication with intranasal Midazolam for brief pediatric surgical procedures. Effect on recovery and 21. hospital discharge times. Anaesthesiology 82:2-5. Al-rakhaf H, Bello LL, Turkustani A, Adenubi JO. Intra-nasal Midazolam in conscious
- 22. sedation of young pediatric dental patients. International Journal of Pediatric Dentistry 2001.11.33-40
- Kogan A, Katz J, Efrat R, Eidelman LA. Premedication with Midazolam in young children: a comparison of 4 routes of administration. Pediatr Anesth 2002; 12:685-9.
- Roelofse JA, Shipton EA, de la Harpe CJ, Blignaut RJ. Intranasal Sufentanil/Midazolam versus Ketamin / Midazolam for ralgesia / sedation in the pediatric population prior to undergoing multiple dental extractions under general anaesthesia: a prospective,
- double-blind, randomized comparison. Anesth Prog 2004; 51(4):114-21. McCornick AS, Thomas VL, Berry D, Thomas PW. Plasma concentrations and sedation scores after nebulized and intranasal Midazolam in healthy volunteers. Br J Anaesth 25 2008:100(5):631-6.
- 26 Verma RK, Paswan A, De A, Gupta S. Premedication with Midazolam Nasal Spray: An
- Alternative to Oral Midazolam in Children. Anesth Pain. 2012;1(4):248-51.
 Kain ZN, Mayes LC, O'Connor TZ, Cicchetti DV. Preoperative anxiety in children: predictors and outcomes. Arch pediatr Adolesc Med 1996;150:1238-45. 27
- Kain Z, Mayles L, Caramico L, Hofstadter M. Distress during induction of anaesthesia and postoperative behavioural outcomes. Anesth Analg 1999;88:1042-7. 28.
- 29. Sury MRJ, Cole PV. Nolbuphine combined with Midazolam for outpatient sedation. Anaesthesia 1988; 43:285-8
- Josie C, James GW, Sheelagh MK. An evidence-based review of parental presence 30. during anaesthesia induction and parent/child anxiety. Schulman JL, Foley JM, Vernon DT, Allan D. A study of the effect of the mother's 31.
- presence during anaesthesia induction. Pediatrics 1967;39:111-4. 32.
- Ryder I, Spargo P. Parents in the anaesthetic room: a questionnaire survey of parent's reactions. Anaesthesia 199; 46: 977-9. Kain ZN, Caldwell-Andrews AA, Wang SM, Krivutza DM, Weinberg ME, Mayes LC. 33
- Parental intervention choices for children undergoing repeated surgeries. Anesth Analg 2003: 96: 970-5
- Kain ZN, Caldwell-Andrews AA, Krivutza D. Trends in the practice of parental 34. presence during induction of anaesthesia and the use of preoperative sedative premedication in the United States, 1995-2002: results of a follow-up national survey. Anesth Analg 2004;98:1252-9. Shaw EG, Routh DK. Effect of mother presence on children's reaction to aversive
- 35
- 36 37
- Shaw EG, Routh DK. Effect of mother presence on children's reaction to aversive procedures. J Pediatr Psychol 1982;7:33-42.
 Bowie JR. Parents in the operating room. Anaesthesiology 1993;78:1192-3.
 American Academy of Pediatrics: Child life programs. Pediatrics 1993;91:671-2.
 Kain ZN, Caldwell-Andrews AA, Mayes LC, et al. Family-centered preparation for surgey improves perioperative outcomes in children: a randomized controlled trial.
 Anaesthesiology 2007;106:65-74.
 Melamed BG, Dearborn M, Hermezz DA. Necessary considerations for surgery 38.
- 39
- Freinica DS, Benton H, Heinez DF. Freesawa (Section 1) and Sugery preparation: age and previous experience. Psychosom Med 1983;45:517-25. Kain ZN, Mayes LC, Caramico LA. Preoperative preparation in children: a cross-sectional study. J Clin Anaesthesia 1996;8:508-14. 40.
- O'byrne K, Peterson L, Saldana L. Survey of pediatric hospitals preparation programs: evidence of the impact of health psychology research. Health psychol 1997;16:147-54. 41.
- Kain ZN, Mayes LC, Wang SM, Caramico LA, Hofstader MB. Parental presence during induction of anaesthesia versus sedative premedication: which intervention is more 42 effective? Anaesthesiology 1998;89:1147-56.
- 43.
- Cote CJ. Changing concepts in properative mediaction and "NPO" status of the pediatric patient. ASA Refresher Courses in Anaesthesiology 1994;22:101-16. Twersky RS, Hartung J, Berger BJ, McClain J, Beaton C. Midazolam enhances anterograde but not retrograde amnesia in pediatric patients. Anaesthesiology 1993; 78: 44. 51-5
- Shannon M, Albers G, Burkhart K, Liebelt E, Kelley M, et al. (1997) Safety and efficacy 45.
- Snamon M, Aloers O, Burknart K, Llebelt E, Kelley M, et al. (1997) Safety and efficacy of flumazenil in the reversal of benzodiazepine-induced conscious sedation. The FlumazenilPediatricStudyGroup.JPediatr131:582-6. Masoud Fallahinejad Ghajari, Ghaseem Ansari, Ali Asghar Soleymani,Shahnaz Shayeghi, Faezeh Fotuhi Ardakani. Comaprison of Oral and Intranasal Midazolam/Ketamine Sedation in 3-6-year-old Uncooperative Dental patients. J Dent Paer Derd Clin Dard Benzenz 2015 60/2016 for Res Dent Clin Dent Prospect 2015;9(2):61-65. Darshna D. Patel, Lisha, M.R.Upadhyay. Pre anaesthetic medication in children: A
- 47 Comparison of intranasal dexmedetomidine versus intranasal midazolam. JMR 2015; 1(2):59-63.
- Mithil Manoj, Srinivasan Swaminathan, Rithu Krishna Kamaladevi. Comparison of ease of administration of intranasal midazolam spray and oral midazolam syrup by parents as premedication to children undergoing elective surgery. Journal of Anesthesia, June 2017; 31(3):351-7.