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COMPARISON OF DEXMEDETOMIDINE- KETAMINE AND MIDAZOLAM- KETAMINE COMBINATIONS FOR SEDATION IN PEDIATRIC PATIENTS UNDERGOING EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY (ESWL)

Anesthesiology

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ABSTRACT

OBJECTIVE : To compare the recovery parameters by achieving time to reach Aldrete score of 8 , sedative effect of dexmedetomidine versus midazolam by Modified Ramsay`s Score,the hemodynamic stability of both groups,the maintenance dose of ketamine in both groups and the side-effects in both groups.

METHODOLOGY : This prospective randomized double blind comparative study was conducted at our institution. After ethical committee approval and informed consents from parents, 80 pediatric patients of ASA I, II and aged 2-12 years, who were scheduled for Extracorporeal shock wave lithotripsy (ESWL) and were enrolled in the study and randomly divided into two equal groups The patients were premedicated with inj. Glycopyrrolate 0.004mg/kg and the patients in group D received inj.dexmedetomidine 1µg/kg over the period of 10 minutes and in group M received inj.midazolam 0.05mg/kg over the period of 10 minutes.Induction with inj. Ketamine 1mg/kg bolus slowly in both groups. Maintained with inj.ketamine (0.5mg/kg) as and when required till end of procedure. HR,BP ,SpO2 were recorded. Need of ketamine in both group was noted. Ramsay sedation score and modified aldrete score were observed postoperatively.

RESULTS: statistically significant difference in intra-operative heart rate seen at 1min,5min and 10min where p value was <0.05 after the dose of dexmedetomidine as compared to midazolam. The time to reach an Aldrete recovery score of 8 was significantly longer in group D than group M. Demand for ketamine after the loading dose in dexmedetomidine group was less(49.30±18.77mg) than midazolam group(61.81±17.26mg)which was statistically significant($p<0.01$). Time to reach modified sedation score of 3 was significantly more in group M than group D.

CONCLUSION: Combination of dexmedetomidine and ketamine may be a newer and better alternative agent for sedation than combination of midazolam and ketamine, in the paediatric population undergoing ESWL.

KEYWORDS

ESWL , dexmedetomidine, midazolam, ketamine, aldrete recovery score.

INTRODUCTION :

Treatment of urolithiasis has been revolutionized with the introduction of Extracorporeal Shockwave Lithotripsy (ESWL) due to its simplicity, non-invasive nature, efficacy, and minimal morbidity[1,2]. It has been shown to be efficacious and safe for the treatment of upper urinary tract stones in paediatric patients, with no signs of damage to the growing kidney in long term follow up.[3] Though it is a non-invasive technique, the shock waves cause transient deep sharp pain and visceral discomfort[3,4]. Although it requires minimal to no sedation/analgesia in adults, it is difficult for the paediatric patients to cope with the procedural pain or cooperate with the procedure. The anaesthetic management of paediatric patients for ESWL includes different techniques of anaesthesia/analgesia such as general anaesthesia with tracheal intubation, dissociative anaesthesia with intravenous agents like midazolam, propofol, ketamine and fentanyl. Ketamine- a NMDA antagonist is one of the most commonly used agents for sedation and analgesia in ESWL. Ketamine causes increase in heart rate, cardiac output and blood pressure without suppressing laryngeal reflexes and respiration [5,6] . It can be used alone or in combination to achieve ideal sedation.

Midazolam has both sedative and anxiolytic effects and it is used for sedation in invasive and non-invasive procedures. It has a minimal effect on recovery time [7]. Dexmedetomidine, a relatively new agent, is a highly selective alpha-2 receptor agonist and it has both sedative and analgesic effects [8,9] and may be a suitable agent for conscious sedation for ESWL, which is a mildly painful procedure because of the lack of respiratory depression.

METHODOLOGY

After ethical committee approval and informed consents from parents, 80 pediatric patients of ASA I, II and aged 2-12 years, who were scheduled for Extracorporeal shock wave lithotripsy (ESWL) were enrolled in this prospective randomized double blind comparative study conducted at our institution. All patients underwent pre-anaesthetic check-up the day before surgery and all routine investigations were noted. Patients were kept NBM for at least 6 hours for solid food. An intravenous cannula was secured in the presence of parents and crystalloid like Ringer's lactate solution was started in pre-anaesthetic room. The basal values for heart rate (ECG), blood pressure (NIBP) and O2 saturation (SpO2) recorded just before the administration of the study drug. The patients were randomized into two groups by a closed envelope method.

The patient was given Premedication : Inj. Glycopyrrolate 0.004mg/kg in all children. Patients in group D received dexmedetomidine 1µg/kg over the period of 10 minutes and In group M midazolam 0.05mg/kg over the period of 10 minutes. All the patients Induced with inj. Ketamine 1mg/ kg bolus slowly in both groups and Maintaince with inj. ketamine (0.5mg/kg) as and when required till end of procedure.

Intraoperatively HR,BP ,SpO2 were recorded every 5 mins and Need of ketamine in both group was noted. Adverse effects such as bradycardia (above 20%decrease compared with baseline), hypotension (MAP <50 mmHg), desaturation (SpO2<92%), and nausea/vomiting were also recorded during the procedure and treated acoordingly.Post-operatively Ramsay sedation score and modified aldrete score were observed.

Statistical analysis

All Collected data are entered into the SPSS V20.2 Continuous data are expressed as mean±SD form. Continuous data follows parametric and nonParametric data both.Unpaired Student t – test and Fisher Exact test have been used for carrying out significant P-value.

TABLE -1 : DEMOGRAPHIC DATA

	GROUP D (Mean ± S.D)	GROUP M (Mean ± S.D)	P-value
Age (yrs)	5.56±2.71	4.74±2.68	0.12
Sex : M/F	25/15	27/13	0.64
Weight (kg)	14.33±3.72	13.56±4.08	0.24

Duration of surgery (min.)	52.5±11.09	56.50±9.49	0.09
Duration of anaesthesia(min)	59.63±11	63.38±8.65	0.12

Patients in our study were demographically comparable in both groups. There were no statistically significant difference in the two groups with regard to age, sex, weight, duration of surgery and anaesthesia (P >0.05).

TABLE – 2 INTRA OPERATIVE HEART RATE :

	GROUP D	Group M	p-value
	(N=40)	(N=40)	
	(Mean ± S.D)	(Mean ± S.D)	
Baseline	129.75±22.68	139.03±22.22	0.07
1min	118.50±24.74	131.73±21.50	0.02*
5min	116.95±21.44	126.55±19.67	0.04*
10min	115.00±19.00	123.35±14.91	0.03*
15min	113.68±15.99	119.35±13.87	0.09
20min	111.75±16.39	117.23±9.35	0.07
30min	112.18±13.81	114.00±11.15	0.52
45min	117.59±14.60	124.10±15.31	0.06
60min	116.16±13.19	119.35±13.02	0.32
1h15min	115.56±20.14	119.50±6.76	0.59

p value <0.05 *-significant

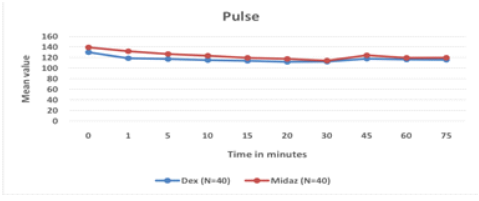
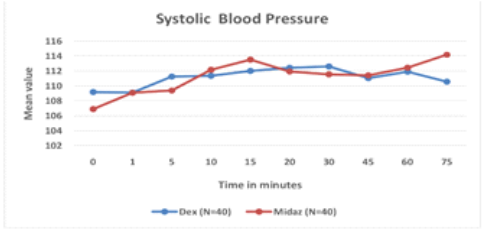
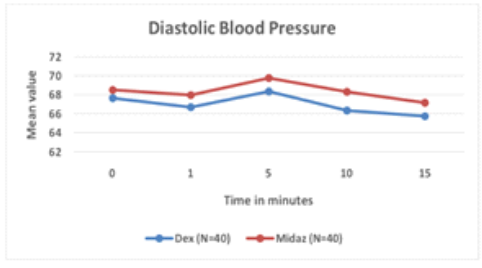


Fig.1:comparision of pulse Intra-operative heart rate was recorded in both groups at frequent intervals and there was statistically significant difference seen at 1min,5min and 10min where p value was <0.05 after the dose of dexmedetomidine as compared to midazolam.

INTRA OPERATIVE BLOOD PRESSURE :

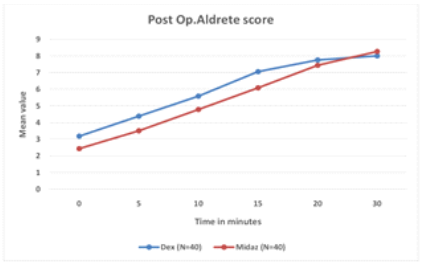


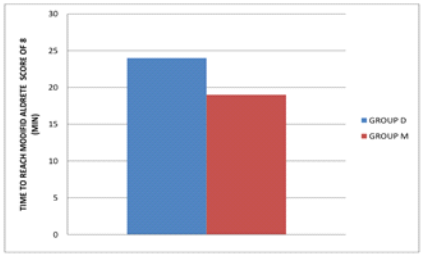


This above graph suggests that there were no statistically significant difference in both the groups with regard to systolic blood pressure and diastolic blood pressure (P > 0.05).

TABLE -3 Modified Aldrete Score:

	GROUP D	GROUP M	p-value
	(Mean ± S.D)	(Mean± S.D)	
0min	2.43±0.71	3.18±0.96	<0.01*
5min	3.50±1.04	4.38±0.93	<0.01*
10min	4.78±0.97	5.58±1.06	<0.01*
15min	6.08±1.16	7.05±0.93	<0.01*
20min	7.43±0.65	7.75±0.52	0.03*
30min	8.26±0.24	8.00	0.88
Time to reach aldrete score of 8(min)	23.82±5.51	19.63±4.58	<0.01*





For assessment of the recovery in postoperative period, Modified Aldrete score was selected. There was statistically significant difference between the groups till 30min (p-valve <0.01). The time to reach an Aldrete recovery score of 8 was significantly longer in group D than group M.

RECOVERY TIME :

TIME(minutes)	GROUP D	GROUP M	P value
	(Mean ± S.D)	(Mean± S.D)	
Eye opening time	10.65±2.27	13.33±2.54	<0.01*
Verbal response time	15.15±3.54	18±2.86	<0.01*
Cooperation time	25.9±3.13	21.8±3.761	<.0.01*

Eye-opening and verbal response were significantly shorter in the group D. The cooperation time in group D was prolong compared to group M.

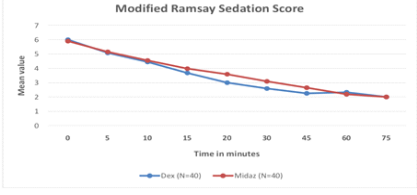
Maintenance dose requirement of ketamine

In our study, demand for ketamine after the loading dose in dexmedetomidine group was less(49.30±18.77mg) than midazolam group (61.81±17.26mg) which was statistically significant(p<0.01).

TABLE - 4 MODIFIED RAMSAY SEDATION SCORE:

Modified Ramsay sedation score at	GROUP D (Mean ± S.D)	GROUP M (Mean ± S.D)	p-value
0min	6.00	5.90±0.38	0.08
5min	5.08±0.73	5.15±0.74	0.64
10min	4.45±0.85	4.55±1.01	0.75
15min	3.68±0.69	3.98±0.89	0.10
20min	3.00±0.68	3.59±0.88	<0.01*
30min	2.59±0.70	3.09±0.85	<0.01*
45min	2.25±0.44	2.65±0.49	<0.01*
60min	2.33±0.52	2.19±0.40	0.64
75min	2.00	2.00	1.00
Time to reach score of 3	19.00±7.61	25.75±12.79	0.03*

*p valve <0.05 significant



The sedation of patients postoperatively observed with modified Ramsay sedation score and it was significant at 20min,30min and 45min (p-value <0.01). The times to reach modified sedation score of 3 was significantly more in group M than group D.

TABLE – 5 POSTOPERATIVE SIDE EFFECTS

post op side effects	GROUP D	GROUP M	P value
Hypotension	1	0	1.00(NS)
Bradycardia	2	0	0.49 (NS)

Dellusion	1	2	1.00(NS)
Vomiting	0	2	0.49 (NS)
Tachycardia	0	4	0.12(NS)
Shivering	0	4	0.12(NS)
Respiratory depression	0	5	0.05(NS)

The side effects were evaluated and the incidence of side effects were similar in Groups D and M

DISCUSSION :

Children have been under treated for painful procedures because of the wrong notion that they neither suffer or feel pain, nor responded to or remembered the painful experiences to same degree that adult did. The prime function of anaesthesiologist during ESWL in children is to relieve pain, keep the child stable and prevent any unwanted movement of the child. For that, various anaesthetic agents either sole or in combination have been tried. When ketamine is administered alone, there is an increased incidence of delirium and unpleasant dreams during the recovery period.

Aydin Erden et al[3], **Cartwright and Pingel**[10], **Toft and Romer**[11]found that midazolam–ketamine resulted in a significantly lower incidence of emergence reactions in paediatric population. **Tobias JD et al** [12] studied that when used together, dexmedetomidine may prevent the tachycardia, hypertension, salivation, and emergence phenomena from ketamine whereas ketamine may prevent the bradycardia and hypotension which has been reported with dexmedetomidine. In our study, heart rate was lower significantly lower in group D than group M at initial period of procedure i.e. at 1min, 5min and 10min. which did not require any treatment and was comparable with the study of **Waleed et al** [13]

In our study we found no significant change in blood pressure at 5min interval till end of ESWL. **Mason et al**[14] found that dexmedetomidine has no greater likelihood of blood pressure shift during bolus as opposed to infusion. Despite the deep sedation, Dexmedetomidine does not cause severe concomitant respiratory effects because of it is alpha-2 adrenergic agonist. .In our study, we did not observe any respiratory depression, hypoxia or apnoea in group D during the recovery period similar to **Walker et al** [15],**Mason et al**[14] and various authors. Midazolam is a short acting benzodiazepine which causes transient respiratory depression.The **Aldrete's scoring system** is a commonly used scale for determining when patients can be safely discharged from the post-anaesthesia care unit (PACU) to ward or discharge home.

In our study there was statistically significant difference between the groups till 30min.The time to reach modified Aldrete recovery score of 8 was more in group D (**23.82±5.51min**) than group M (19.63±4.58 min). **Kose et al**[16] had time to reach aldrete score 8 in dexmedetomidine-midazolam group around 50min and in group dexmedetomidine- ketamine around 20min which correlates with our study.

Reports for recovery times in respect to dexmedetomidine use had been reported with great variability; **P. Zeyneloglu et al** [17] found the Aldrete score more with significantly prolonged recovery despite using lowest recommended infusion rate of dexmedetomidine (2µg/kg/hr.).

In our study in group D eye opening time, was significantly shorter than group M (10.68± 2.25min vs 13.33± 2.54min, P<0.01). The verbal response time was also shorter in group D than group M (15.15±3.54min v/s18.00 ± 2.86min , p<0.01) which correlated with the study of **Kose E.A et al** [16]and **Koruk et al**.[18]

The time to reach modified Ramsay sedation score of 3 was significantly more in group D than group M at 20min,30min and 45min.(p-value <0.01).**Parul Uppal et** al[19],observed profound sedation after dexmedetomidine than midazolam like our study.In our study, demand for ketamine after the loading dose in dexmedetomidine group was less (49.30±18.77) than midazolam group(61.81±17.26) which was statistically significant(p<0.01) In the study of **Mohd. Asim Rasheed, et al** [20] found mean extra ketamine dose requirement greater but non-significant in group KM than in group KD.

CONCLUSION

We found that both dexmedetomidine-ketamine and midazolam-ketamine combinations had satisfactory sedative and analgesic effects. In the dexmedetomidine-ketamine group, the recovery time was prolonged duo to more sedation but with good hemodynamic stability and minimum side effects which is beneficial in inital recovery period. So we concluded that combination of dexmedetomidine and ketamine may be a newer and better alternative agent for sedation than combination of midazolam and ketamine, in the paediatric population undergoing ESWL.

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