Original Article

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A Comparison of Effects of Dexmedetomidine-Ketamine versus Dexmedetomidine-Midazolam Combination in Ambulatory Transurethral Procedures

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Abstract

Introduction: Minimally invasive transurethral procedures can be successfully performed on outpatient basis. The anaesthetic technique of choice for suchprocedures is Monitored Anaesthesia Care with a combination of local anaesthesia and sedation-analgesia. It ensures a rapid onset and early recovery with minimal cardiorespiratory adverse effects, facilitating same day discharge. Various drugs are being used in combination to achieve this goal. In this study, we have compared the effects of a combination of dexmedetomidine-ketamine and dexmedetomidine-midazolam in ambulatory transurethral procedures.

Materials and Methods: This prospective, randomised, comparative study was carried out on sixty patients aged 20-60 years, of either sex, ASA I/II physical status, scheduled for elective, outpatient transurethral procedures. These patients were randomly allocated into two groups - Group DK received a bolus of IV ketamine 1mg/kg and IV dexmedetomidine 1µg/kg and Group DM received a bolus of IV midazolam 0.05mg/kg and IV dexmedetomidine 1µg/kg, bothwere followed by amaintenance infusion of dexmedetomidine 0.2µg/kg/hr IV throughout the procedure. The heart rate, mean arterial blood pressure, analgesia using Numerical Rating Scale and sedation using the Ramsay Sedation Scale were measured intraoperatively. The recovery characteristics were assessed using the Modified Aldrete Score, time to spontaneous eye opening and length of stay in the recovery room.

Statistical analysis: The data was compared and analysed using the Unpaired t test and Fisher's exact test.

Results: Group DMshowed statistically significant lower mean arterial pressure (MAP) up to 35 mins duringthe procedure when compared with group DK ($P < 0.05$). Although the sedation scores were similar, Numerical Rating Scale scores were significantly higher in group DM than in group DK till 10 minutes of the procedure ($P < 0.001$). The Modified Aldrete score was higher and time to spontaneous eye opening, length of recovery room stay was shorter ($P < 0.001$ and$P < 0.001$, respectively) in group DK compared to group DM. The incidence of hypotension, bradycardia and postoperative nausea/vomiting was lower in group DK.

Conclusion: Although, good sedation was seen with both the combinations, the dexmedetomidine-ketamine group provided better intra operative analgesia and cardiorespiratory stability with a shorter recovery time and lower incidence of post-operative nausea/vomiting. Thus, dexmedetomidine-ketamine combination is a better, safer alternative for monitored anaesthesia care in ambulatory transurethral procedures.

Keywords: Dexmedetomidine; Ketamine; Midazolam; Ambulatory; Transurethral; Recovery.

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Introduction

Transurethral procedures which are minimally invasive are being performed on outpatient basis for some time now. Advantages of ambulatory surgery are many-it is cost effective, easy to schedule, allows discharge on the same day of surgery with a possible reduction in the risk of thromboembolism and hospital acquired infections.[15]

The choice of the anaesthetic technique can have a significant impact on post-operative recovery and discharge. Although general anaesthesia and regional anaesthesia have been used traditionally for these procedures, greater emphasis is being laid nowadays on Monitored Anaesthesia Care (MAC) wherein a combination of local anaesthesia with sedative-analgesic drugs is usually used. The advantages of MAC are avoidance of polypharmacy, airway instrumentation, lack of significant hemodynamic effects and a rapid recovery, facilitating discharge on the same day.[15] Adequate analgesia, patient comfort/satisfaction and convenience of the surgeon are also of paramount importance. Commonly used drugs for sedation-analgesia in ambulatory surgeries include propofol, midazolam, ketamine, fentanyl and more recently dexmedetomidine.

Dexmedetomidine is a selective α2 adrenergic receptor agonist, which providesanxiolysis,sedation and modest analgesia by inhibiting the release of endogenous catecholamines at adrenoreceptors locatedon locus ceruleus and substantia gelatinosa of the spinal cord respectively. It provides arousable sedation mimicking natural sleep, allowing spontaneous respiration. It has a distribution half-life of 8 minutes, terminal half-life of 3.5 hrs making it suitable for ambulatory anaesthesia. It also has antiemetic and anti-sialagogue properties.[4] However, sympatholysis may result in adverse effects like hypotension and bradycardia. Also, amnesia with dexmedetomidine is not predictable, particularly at lower doses.[14]

Ketamine, a phencyclidine derivative, is a N-methyl-D-aspartate antagonist which provides excellent analgesia and amnesia. It does not suppress laryngeal reflexes and respiration, is a potent bronchodilator, with distribution half-life of 45 minutes and terminal half-life of 2-3 hours, making it one of the favoured agents for sedo-analgesia.[4] Ketamine has a potential role in lowering the risk of chronification of pain, modified by analgesic and anti-inflammatory effects.[2] However, due to its sympathomimetic effects, it increases heart rate, cardiac output and blood pressure and may also result in psychogenic adverse effects.

Midazolam is a short acting benzodiazepine with sedative-hypnotic properties and a rapid onset. It provides excellent antegrade amnesia, moderate sedation, anxiolysis and has a relatively stable hemodynamic profile. However, its metabolites have longer half-lives which may lead to prolonged sedation and psychomotor impairment/ disinhibition on repeated dosage.[9] It also depresses ventilatory response to carbondioxide causing respiratory depression, which may interfere with readiness for discharge.

A combination of these drugs may complement each other, lower their individual dosages, thus offsetting some of their adverse effects. This study was carried out to compare the analgesic/ sedative effect and the recovery characteristics of a combination of dexmedetomidine-midazolam with dexmedetomidine-ketamine in patients undergoingout patient transurethral procedures under monitored anaesthesia care.

Materials and Methods

This prospective, randomised study was carried out on sixty patients, after obtaining a written informed consent, in a tertiary referral hospital. The study population consisted of patients aged 20-60 years, of either sex, belonging to ASA I/ II physical status, scheduled for elective, outpatient transurethral procedures.

Patients with ASA III/ IV physical status, age <20yrs and >60 years, with a history of drug dependence, psychological disorder, 2 or 3-degree heart block, chronic use of alpha agonist / sedatives, history of sleep apnoea / respiratory disorders, chronic renal insufficiency, liver dysfunction and procedures taking longer than one hour were excluded from the study.

A detailed history, thorough clinical examination and a written informed consent was taken a day prior to the surgery. Routine investigations including complete blood count, random blood sugar, urine analysis, electrocardiogram (ECG) was done. Special investigations were done only when indicated.

None of the patients received any premedication. On arrival at the operating room, a 20-G intravenous catheter was placed, standard monitors applied (ECG; Non-Invasive Blood Pressure; SpO2; Capnography) and baseline parameters were noted. These parameters were recorded every five mins throughout the procedure. Randomization into two groups was done using sealed envelope method.

The first group, Group DM, patients received midazolam 0.05mg/kg IV and dexmedetomidine 1µg/kg IV in 20ml normal saline over 10 min followed by a continuous infusion of dexmedetomidine 0.2 µg/kg/hr throughout the procedure. The second group, Group DK, received ketamine 1mg/kg IV and dexmedetomidine 1µg/kg IV in 20 ml normal saline over 10 min followed by a continuous infusion of dexmedetomidine 0.2µg/kg/hr throughout the procedure.

All the patients received 2-4 litres/min of O_2 by nasal cannula to maintain a saturation of >95%.After positioning of the patient, ten ml of 2% lignocaine jelly was topically instilled in the urethra by the surgeon prior to the procedure. Pain was assessed using the Numerical Rating Scale (NRS) with a 5 minute interval during procedure (0 = no pain,10 = worst pain imaginable). If pain score was greater than 3 or if patient asked for additional analgesia, arescue bolus of IV fentanyl 1mg/kg was administered. Sedation scores were assessed using Ramsey Sedation Scale (0=patient paralysed, unable to assess sedation; 1=patient anxious, agitated or restless; 2=patient cooperative, oriented and tranquil; 3=patient sedated but responds to command; 4=patient asleep but responds to glabellar tap; 5=patient asleep but responds to nail bed pressure; 6=patient asleep, no response to nail bed pressure). The goal was to maintain a score of 3. If the initial regime failed to achieve so, maintenance infusion was increased to 0.4µg/kg/hr. If the sedation score was greater than 4, the dexmedetomidine infusion was stopped immediately.

On completion of the procedure, patient was shifted to the post anaesthesia care unit and recovery was assessed using the Modified Aldrete Score (Table 1). The time taken to achieve a score of 10 was recorded. The time to spontaneous eye opening and the length of stay in the recovery room was also noted.

Table 1: Modified Aldrete Score.

Criteria	Description	Score
Consciousness	Fully awake and oriented	2
	Arousable on calling	1
	No response	0
Activity	Moves all 4 extremities voluntarily or on command	2
	Moves all 2 extremities voluntarily or on command	1
	Unable to move extremities on command	0
Circulation	Blood Pressure ±20% of pre anaesthetic level	2
	Blood Pressure ±20-50% of pre anaesthetic level	1
	Blood Pressure ±50% of pre anaesthetic level	0
Respiration	Able to breathe and cough freely	2
	Dyspnoea, Limited breathing, Tachypnoea	1
	Apnoeic or on mechanical ventilation	0
Oxygen saturation	SpO2> 92% on room air	2
	Needs supplemental O2 to maintain SpO2> 90%	1
	SpO2< 90% even with O2 supplementation	0
Maximal Score		10

Adverse effects like bradycardia (HR of <50/min), tachycardia (HR of >100/min), hypotension (MAP of <60mm of Hg), hypertension (MAP of >20% of baseline), desaturation (SpO2 of <90%), apnoea of more than 30 seconds, bronchospasm, laryngospasm, nausea/vomiting, if any, were noted. Atropine 0.02 mg/kg IV was used to treat bradycardia and a bolus of 5ml/kg of 0.9% normal saline used in case of hypotension.

Statistical Analysis

The data of the parameters observed was presented as Mean ± SD. Since normality assumption was followed, parametric tests were applied. The demographic profile and inter-group parameters were compared using the unpaired t-test. The data was analysed using SPSS software, version 21. Categorical intergroup data was compared using the Chi-square test/Fischer's exact test. Statistical significance was accepted when P value was less than 0.05.

Results

This study was carried out in sixty patients undergoing elective transurethral outpatient procedures. The demographic data is as shown in Table 2. Both the groups were comparable with respect to age, sex distribution, weight, ASA status and duration of surgery($p > 0.05$).

The heart rate (bpm) was recorded at five-minute intervals, as shown in Table 3, Figure 1. The baseline values were comparable. There was no statistically significant difference in the heart rate between the two groups in all the intervals, except at 30 minutes. Bradycardia was noted in 5 patients

(16%) in group DM and 2 patients (6.7%) in group DK and was treatable with IV atropine.

Table 2: Demographic Details.

	Group DM (n=30)	Group DK (n=30)	P value
Age (years) Mean ± SD	45.37±7.17	44.50±8.96	0.681
Weight (kgs) Mean ± SD	70.80±5.45	71.03±4.92	0.863
Number of Patients Male/ Female	17 / 13	20 / 10	>0.05
Asa Status I/ II	17 / 13	17 / 13	>0.05
Duration of Procedure Mean ± SD	49.17±5.43	47.17±5.52	0.162

#p<0.05 significant

Table 3: Comparison of Heart Rate.

HEART RATE (bpm)	Group DM		Group DK		P value
	Mean	± SD	Mean	± SD	
Baseline	80.93	7.50	81.10	6.62	0.928
After 5 mins	83.93	9.26	85.00	7.09	0.618
After 10 mins	81.50	12.10	84.47	11.32	0.330
After 15 mins	78.90	11.18	83.40	13.37	0.146
After 20 mins	77.03	8.88	81.13	10.09	0.060
After 25 mins	74.17	6.33	77.50	7.07	0.064
After 30 mins	72.27	4.68	75.43	6.31	0.031#
After 35 mins	71.03	4.15	73.90	6.47	0.05
After 40 mins	71.37	4.82	72.93	6.14	0.276
After 45 mins	68.50	3.79	69.03	4.14	0.605

# p<0.05 significant

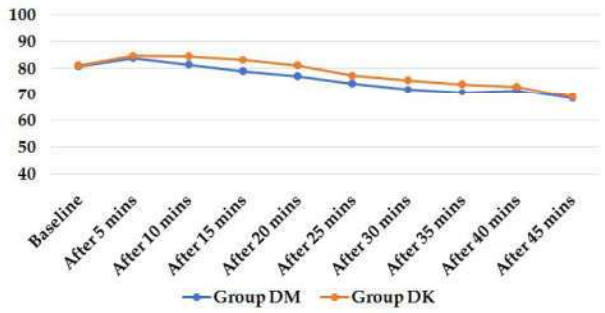

Fig. 1: Comparison of Heart Rate.

The mean arterial blood pressure (MAP) was recorded at five-minute intervals, as shown in Table 4, Figure 2. The baseline values were comparable. There was a statistically significant difference between the two groups at 5, 10, 15, 20, 30 and 35 minutes (p<0.05).The MAP in the DM group was below baseline values throughout the procedure, whereas in DK group there was an increase of about 8% after 5 minutes, with MAP returning to baseline values after 15 minutes. Hypotension was noted in 10 patients (33%) in group DM and 3 patients(10%) in group DK(p-0.057).

Table 4: Comparison of Mean Arterial Pressure.

Mean Arterial Pressure (Mm Hg)	Group DM		Group DK		P value
	Mean	± SD	Mean	± SD	
Baseline	85.97	7.86	84.73	4.40	0.456
After 5 mins	77.73	6.43	91.63	6.52	<0.001##
After 10 mins	74.83	8.33	86.80	5.00	<0.001##
After 15 mins	75.10	6.96	83.80	5.91	<0.001##
After 20 mins	72.07	8.56	78.43	7.46	0.003#
After 25 mins	72.77	8.16	76.73	8.78	0.075
After 30 mins	74.13	8.28	79.40	8.24	0.012#
After 35 mins	72.37	7.66	76.20	6.76	0.044#
After 40 mins	70.70	6.20	71.97	4.81	0.380
After 45 mins	70.07	5.68	70.83	6.14	0.617

##p<0.001 highly significant # p<0.05 significant

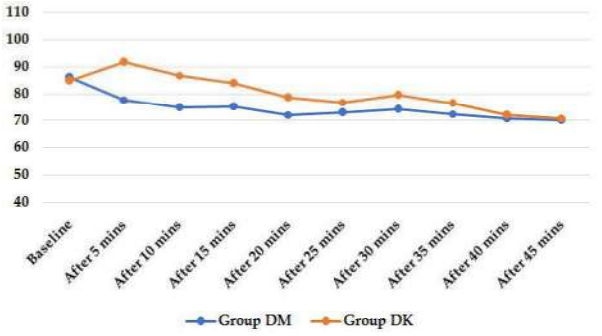

Fig. 2: Comparison of Mean Arterial Pressure.

Pain was assessed using Numerical Rating Scale at five-minute intervals during the procedure, as shown in Table 5, Figure 3. Pain score was significantly lower at 5 and 10 minutes in group DK(p<0.001). The score was comparable thereafter. The number of patients requiring rescue analgesia was nine (30%) in group DM, statistically higher in comparison to group DK where it was only one (3.3%)(p-0.012). The target sedation score of 3 (RSS) was maintained throughout the procedure in both the groups, with only one patient in group DK requiring escalation of maintenance dose of dexmedetomidine to 0.4 µg/kg/min.

Table 5: Comparison of Numerical Rating Scale Scores.

Numerical Rating Scale	Group DM		Group DK		P value
	Mean	± SD	Mean	± SD	
After 5 mins	2.93	0.64	2.27	0.45	<0.001##
After 10 mins	2.43	0.57	2	0.26	<0.001##
After 15 mins	2.1	0.31	1.9	0.48	0.059
After 20 mins	1.9	0.40	1.74	0.45	0.136
After 25 mins	1.37	0.49	1.33	0.48	0.791
After 30 mins	1.4	0.50	1.37	0.49	0.795
After 35 mins	1.3	0.47	1.33	0.48	0.786
After 40 mins	1.63	0.49	1.67	0.48	0.791
After 45 mins	1.63	0.49	1.67	0.48	0.791

##p<0.001 highly significant # p<0.05 significant

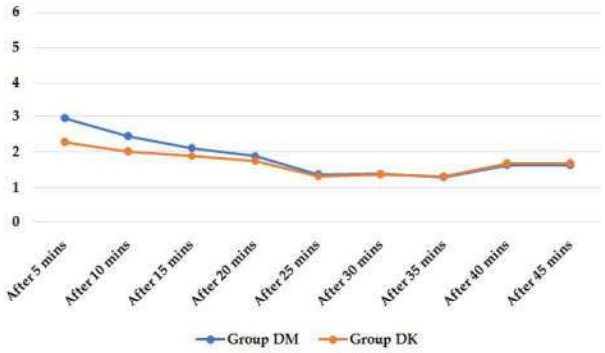

Fig. 3: Comparison of Numerical Rating Scale Scores.

The Modified Aldrete Score for recovery (Table 6, Figure 4) showed a significantly higher score in Group DK compared to group DM from 10 minutes onwards(p<0.001),with patients reaching a score of 10 faster in group DK. Time to spontaneous eye opening and the length of recovery room stay is as shown in Table 7, Figure 5. Group DK had a significantly shorter time to spontaneous eye opening of 8.23 minutes and length of stay in the recovery room of 42.33 minutes compared to group DM with time to spontaneous eye opening of 14.17 minutes and length of stay in the recovery room of 60.33 minutes (p <0.001 each).

Table 6: Comparison of Modified Aldrete Score.

Modified Aldrete Score	Group DM		Group DK		P value
	Mean	± SD	Mean	± SD	
After 5 mins	6.23	0.43	6.37	0.56	0.303
After 10 mins	6.37	0.49	6.70	0.65	0.029#
After 15 mins	6.67	0.55	7.47	0.57	<0.001##
After 20 mins	6.97	0.61	7.77	0.63	<0.001##
After 25 mins	7.30	`0.47	8.03	0.72	<0.001##
After 30 mins	7.57	0.57	8.47	0.68	<0.001##
After 35 mins	7.87	0.73	8.87	0.73	<0.001##
After 40 mins	8.20	0.66	9.30	0.70	<0.001##
After 45 mins	8.47	0.90	9.77	0.43	<0.001##
After 50 mins	8.80	0.81	9.90	0.31	<0.001##
After 55 mins	9.40	0.81	9.97	0.18	<0.001##
After 60 mins	9.63	0.61	10	0	0.002##

p<0.001 highly significant # p<0.05 significant

Table 7: Comparison of Recovery Time.

Recovery Time (in minutes)	Group DM		Group DK		P Value
	Mean	± SD	Mean	± SD	
Time to Spontaneous Eye Opening	14.17	5.59	8.23	2.05	<0.001##
Length of Recovery Room Stay	60.33	15.57	42.33	7.40	<0.001##

p<0.001 highly significant

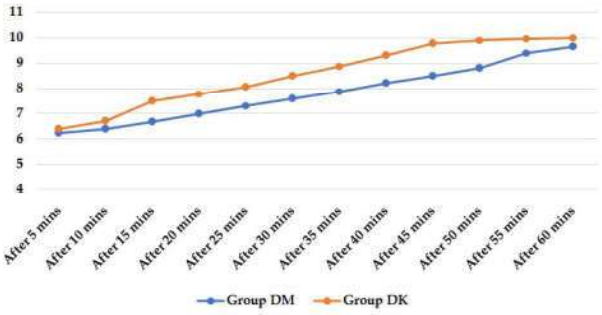

Fig. 4: Comparison of Modified Aldrete Score.

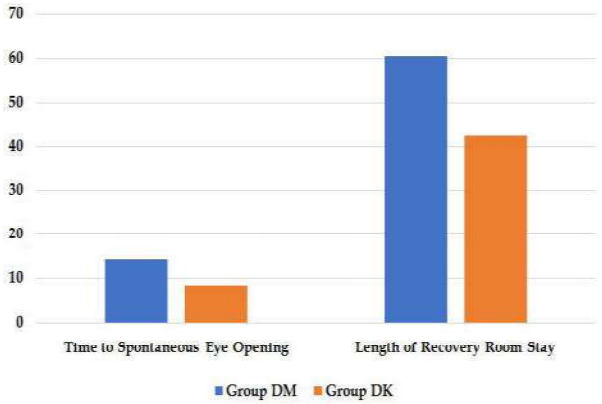

Fig. 5: Comparison of Recovery Time.

The complications observed are as shown in Table 8, Figure 6. Desaturation, apnoea, bronchospasm, laryngospasm and hypertension was not observed in any of the patients. Nausea/vomiting was observed in 6 patients (20%) in group DM and 2 patients (6.7%) in group DK(p-0.25).

Table 8: Table of Complications.

Complications	Group DM	Group DK	P Value
Bradycardia	5 (16.7%)	2 (6.7%)	0.423
Hypotension	10 (33.3%)	3(10%)	0.057
Pain requiring rescue analgesia	9 (30%)	1 (3.3%)	0.012#
Nausea/Vomiting	6 (20%)	2 (6.7%)	0.254
Inadequate sedation	0	1 (3.3%)	1.00

# p<0.05 significant

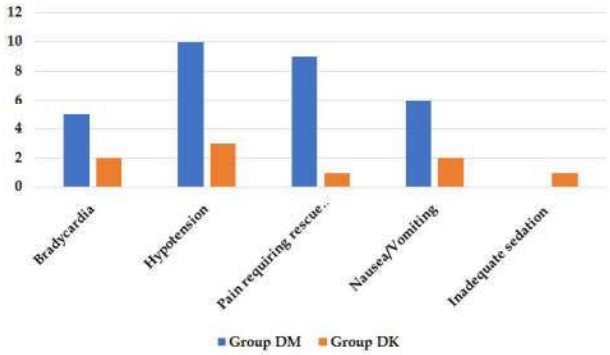

Fig. 6: Table of Complications.

Discussion

Minimally invasive transurethral procedures such as ureteroscopy for extraction of lower urethral stones, stent placement, cystoscopy, incision and dilation of urethral strictures can be performed successfully on outpatient basis.[4]

The anaesthetic technique for such ambulatory procedures dictates the need of rapid onset and recovery, devoid of any cardiorespiratory side effects, while ensuring patient comfort and surgeon satisfaction. Monitored Anaesthesia Care (MAC) with a combination of local anaesthesia and sedative-analgesic drugs(like propofol, ketamine, dexmedetomidine, midazolam, remifentanil) can be used to achieve the same.[15]

Dexmedetomidine possesses many properties that are advantageous for ambulatory procedures; it has shown to provide sedation that parallels natural sleep, anxiolysis, analgesia, sympatholysis, with an anaesthetic-sparing effect and minimal respiratory depression. In addition, there is increasing evidence supporting its organ-protective effects against ischaemic and hypoxic injury.[11] Increasing concentrations of dexmedetomidine results in progressive increases in sedation and analgesia, decrease in heart rate, cardiac output, and memory.[9] Although generally effective in non-invasive procedures as a sole agent, the use of dexmedetomidine in invasive procedures has been limited due to its distressing side effects, hemodynamic instability and prolonged recovery.[10] However, if other sedative-analgesic drugs were to beadded, the dose-sparing effect of dexmedetomidine will enhance the already superior safety profile of it. Also, dexmedetomidinehas the ability to unlock the full potential of other drugseven at lower doses.[14]

Sim JHet alin 2014 studied the effects of different loadingdoses,0.5and1.0µg/kg,ofdexmedetomidine on sedation. They concluded that a higher loading dose (1.0 µg/kg) of dexmedetomidine can lead to faster sedation without any severe complications.[5] For maintenance, although infusion rates up to 2µg/kg/h have being used, effective sedation is usually seen at infusion rates of 0.2-0.4µg/kg/h. It is uncertain if a rate greater than 0.7 µg/kg/h is more efficacious and it may only increase the incidence ofside-effects.[14] Therefore, in our study we chose a loading dose of 1µg/kg of dexmedetomidineand the lowest recommended dose for maintenance i.e.,0.2µg/kg/hr to avoid prolonged recovery.

Tobias Joseph D et al in 2008 evaluated a combination of ketamine (2mg/kg) and dexmedetomidine (1µg/kg) followed by a continuous infusion of dexmedetomidine 1µg/kg for sedation during cardiac catheterization in children with congenital heart disease. They suggested that it provided effective sedation without significant effects on cardiovascular or ventilatory function.[13] Tobias JD et al in 2012 have provided an account of reports from literature regarding the use of dexmedetomidine-ketamine combination for procedural sedation. They noted that when used together, dexmedetomidine may prevent the tachycardia, hypertension, salivation, and emergence phenomena from ketamine, whereas ketamine may prevent the bradycardia and hypotension, reported with dexmedetomidine. Also, ketamine eliminates the slow onset time of dexmedetomidine seen when it is used as a sole agent. Among the various regimens reported in literature, the most effective regimen appeared to be the use of a bolus dose of dexmedetomidine (1 µg/kg) and ketamine (1-2 mg/kg), followed by an infusion of dexmedetomidine (1-2 µg/kg/hr).[1]

In our study, Group DK, received bolus doses of ketamine 1mg/kg IV and dexmedetomidine 1µg/kg IV over 10 min followed by a continuous infusion of low dose dexmedetomidine 0.2µg/kg/hr throughout the procedure.

Ikeda Yet alevaluated the usefulness of

dexmedetomidine as a combination with benzodiazepines for benzodiazepines induced disinhibition during ERCP. They concluded that it yielded better sedative efficacy, lower excessive movement/disinhibition, a reduction in benzodiazepines used, and a higher procedure complete rate.[8] Park SW et al in 2018 examined whether an intravenous bolus of midazolam could replace the loading dose of dexmedetomidine for sedation during surgery in elderly patients who received spinal anaesthesia. The Patient State Index and Ramsay sedation score showed statistically significant deeper sedation in the combination group 10 minutes after drug administration, but no difference at the end of surgery. The heart rate was significantly higher in the combination group. They concluded that a combination of midazolam and dexmedetomidine is especially effective for patients whowant faster sedationor are at high risk for bradycardia.[7] Yoon DKet alin 2016 studied the effects of dexmedetomidine-midazolam (MD) versus dexmedetomidine(D) alone for sedation during spinal anaesthesia The RSS and Bispectral Index were comparable. The prevalence of bradycardia(except at 10 min), hypotension, and hypoxia did not differ statistically between the two groups. They concluded that midazolam bolus and dexmedetomidine continuous infusion may be an additional sedation method for patients who have severe bradycardia.[6]

In our study group DM, received a bolus of midazolam 0.05 mg/kg IV and dexmedetomidine 1µg/kg IV over 10 min followed by continuous infusion of dexmedetomidine 0.2µg/kg/hr throughout the procedure.

Baik,H.J.etal.in2016compareddexmedetomidine-ketamine versus dexmedetomidine-midazolam-fentanyl for monitored anaesthesia care during chemo port insertion.All patients received 1 µg/ kgdexmedetomidine over 10 min followed by 0.2–1.0 µg/kg/h in order to maintain 3 or 4 of modified Observer's Assessment of Analgesia and Sedation score checked every 3 min. The patients in addition received a bolus of 0.5 mg/kg ketamineor 0.05 mg/kg midazolam plus 0.5 µg/kg fentanylin group DK or DMF respectively. They concluded that both ketamine and midazolam-fentanyl co-administration with dexmedetomidine for MAC showedno significant differences in the onset time, time to spontaneous eye opening, recovery room stay, the incidences of inadequate analgesia, hypotension and bradycardia. However, the dexmedetomidinemidazolam-fentanyl combination showed a better sedationquality and satisfaction scores despite the lower infusionrate of dexmedetomidine, and a higher incidence of BIS <60 than the dexmedetomidine-ketamine combination.[3]

Kose EA et alin 2012 compared the effects of combinations of dexmedetomidine-ketamine (K) and dexmedetomidine -midazolam (M) on recovery time, hemodynamic variables, respiratory variables and side effects in transurethral procedures. Group M showed significantly lower mean arterial pressure (MAP) values at 5 and 10 minutes during the procedure when compared with group K. Visual analogue scale scores were greater in group M than in group K at 5 and 10 minutes for the transurethral procedure. Sedation scores were similar between groups during the procedure. Time to eye opening and length of recovery room stay were shorter and Aldrete scores were greater in group K than group M. They concluded that both combinations provided satisfactory sedation levels, but the dexmedetomidine-ketamine combination provided better analgesia and hemodynamic stability, with a shorter recovery time, than the dexmedetomidine-midazolam combination.[4]

In our study, we observed that the heart rate throughout the procedure was comparable in both the groups. Bradycardia was noted in 5 patients (16%) in group DM and 2 patients (6.7%) in group DK.The mean arterial pressure was significantly lower in the DM group up to 35 mins during the procedure as compared to group DK. The increase in MAP seen in group DK was 8% only, returning to baseline values after 15 minutes. The incidence of hypotension, although statistically insignificant (p-0.057) was much greater (33%) in group DM compared to group DK (10%). No tachycardia/ hypertension was seen in either of the groups. This is similar to the results of Kose EA et al and Yoon DKet al. The sympathetic stimulation and increased catecholamine levels by ketamine may be attributed to the higher mean arterial pressure in group DK. It can be said that ketamine may prevent hypotension induced by dexmedetomidine and vice versa.

The numerical rating scale score was significantly lower in group DK at 5 and 10 mins, and thereafter comparable in both the groups. However, the number of patients requiring rescue analgesia was statistically greater (30%) in group DM compared to group DK (3%). This can be attributed to the additive analgesic effects of ketamine and dexmedetomidine used in combination. Our results are comparable to that by Kose EA et al. The sedation scores of both the groups were comparable with only one patient (3%) in group DK requiring

rescue sedation. This was in contrast to the study by Baik, H. J. et al where comparable analgesia was noted between both the groups and better sedation quality and satisfaction scores was seen in the dexmedetomidine-midazolam group. In our study, we concluded that while both groups provided comparable sedation, analgesia was better with the dexmedetomidine-ketamine group.

The recovery characteristics of the groups when assessed using Modified Aldrete Score, showed a statistically higher score in group DK 15 minutes onwards. Group DK also had a statistically significant shorter time to spontaneous eye opening and length of stay in the recovery room. Thus, it can be said that the combination of dexmedetomidine-ketamine has a more favourable recovery profile, which is of paramount importance in ambulatory procedures. Our findings were similar to that of Kose EA et al.

The use of midazolam in ambulatory procedures is limited due to depression of the ventilator response to carbon dioxide leading to respiratorydepression, desaturation and apnoea. However, we did not observe any desaturation/apnoea or decrease in respiratory rate in the dexmedetomidine-midazolam group. This can be explained by the use of a single bolus dose of midazolam and the effect of dexmedetomidine which by itself allows spontaneous respiration even at moderately high doses. There was no disinhibition/disorientation observed in any of these patients as well. This was similar to the observations made by Ikeda Y et al. In our study, there were no cases of bronchospasm or laryngospasm in either groups which can be explained by the anti-sialagogic properties of dexmedetomidine. Ketamine induced psychogenic effects were also not seen.

The incidence of nausea and vomiting observed was 6 (20%) cases in group DM and 2 cases (6.7%) in Group DK. A lower incidence in group DK can be attributed to the antiemetic properties of dexmedetomidine along with a lower incidence of hypotension and need for rescue analgesic in group DK. Similar results were observed by Koruk et al[16] on comparing sedation using dexmedetomidine and ketamineto a regimen using midazolam with ketamine during shock wave lithotripsy.

Thus, the incidence of side effects both intraoperatively and post operatively were lower in the dexmedetomidine-ketamine group.

Conclusion

From our study, we conclude that although good sedation levels were seen with both the combinations of dexmedetomidine-midazolam and dexmedetomidine-ketamine, the dexmedetomidine-ketamine group provided better intra operative analgesia and hemodynamic stability with a shorter recovery time and lower incidence of post-operative nausea/vomiting. This makes the dexmedetomidine-ketamine combination a better, safer alternative for monitored anaesthesia care in ambulatory transurethral procedures.

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