

Original Research Article

To Compare the Effects of Dexmedetomidine and Midazolam for Conscious Sedation in Patients Undergoing Upper Gastrointestinal Endoscopic Procedures- an open labelled prospective study

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Abstract: Our aim was to compare the hemodynamic parameters, sedation profile, duration of procedure and recovery profile of intravenous Dexmedetomidine and Midazolam in patients undergoing upper gastrointestinal endoscopic (UGIE) procedures. Hundred subjects posted for elective UGIE procedures were randomised into 2 groups. Both groups received fentanyl 1 mcg/kg IV at beginning of procedure. Group M received IV midazolam (0.04mg/kg) until Ramsay Sedation Scale (RSS) reached 3-4. Group D received Dexmedetomidine at loading dose of 1 mcg/kg over 10 minutes till RSS reached 3-4. The intraoperative hemodynamics was recorded. The time to achieve RSS 3-4 and Modified Aldrete Score (MAS) of 9-10 was assessed. The total duration of procedure and facial pain score (FPS) were compared during the procedure. We found that RSS of 3-4 was achieved earlier in group M (3.64 min) as compared to group D (9.92 min); (P<0.001). The total time taken for the procedure was higher in D group than group M (P<0.001). In our study, no patient had respiratory depression or hypoxemia during the procedure. No patient had coughing in group D while 16% of patients in group M had cough during the procedure which was significant (p=0.003). Overall better recovery profile (MAS) was seen in group D (P<0.001). Dexmedetomidine seems to be promising agent for conscious sedation than Midazolam in UGIE procedures.

Keywords: Dexmedetomidine, Midazolam, upper gastrointestinal endoscopic (UGIE) procedures, conscious sedation, Ramsay sedation score, recovery profile

INTRODUCTION:

UGIE has evolved from simple diagnostic to therapeutic procedure of increasing duration and complexity requiring a high degree of patient's cooperation. Sedation and analgesia allows the conduct of procedure by allaying anxiety, discomfort or pain. It also alleviates the sympathetic response that follows thereby improving patient tolerance and technical success of procedure [1].

Most endoscopists favour Midazolam because of its high amnesic properties, faster onset and short

duration of action. The adverse effects of Midazolam include anterograde amnesia, prolonged recovery, hypoxemia, hypotension and respiratory depression when paired with an opioid [2,3]. In recent years, Dexmedetomidine a potent and highly selective α -2 adrenoceptor agonist with sympatholytic, sedative, amnesic and analgesic properties is being used as an adjuvant for sedation in various procedures [4, 5]. It provides a unique "conscious sedation" (patients appear to be asleep but are readily aroused) and analgesia without respiratory depression. It decreases central nervous system (CNS) sympathetic outflow in a dose

dependent manner and has analgesic effects best described as opioid-sparing. There is increasing evidence of its vital organ protective effects against ischemic and hypoxic injury [6].

In October 2008, the FDA approved its use in non-intubated patients prior to and/or during surgical and other procedures. However, there is scarcity of literature over use of these drugs in Asian race. Therefore, our study was aimed at comparing the efficacy of Dexmedetomidine with Midazolam in providing conscious sedation for UGIE procedures.

MATERIALS AND METHODS:

After approval by the Ethics and Scientific Committee of Fortis Escorts Hospital, Jaipur, a written informed consent was obtained from all study participants prior to the initiation of study cases. One hundred patients scheduled for elective upper gastrointestinal endoscopic procedures (UGIE) were randomized into two groups. Dexmedetomidine- group (D) and Midazolam- group (M). Randomization was done using period randomization where alternate months either of the two drugs was given and various parameters recorded. Duration of study was 6 months (December 2014 to May 2015).

Inclusion criteria:

Patients between 18-65 years of age; ASA grade I and II; undergoing diagnostic and therapeutic UGIE able to give consent for the procedure.

Exclusion criteria:

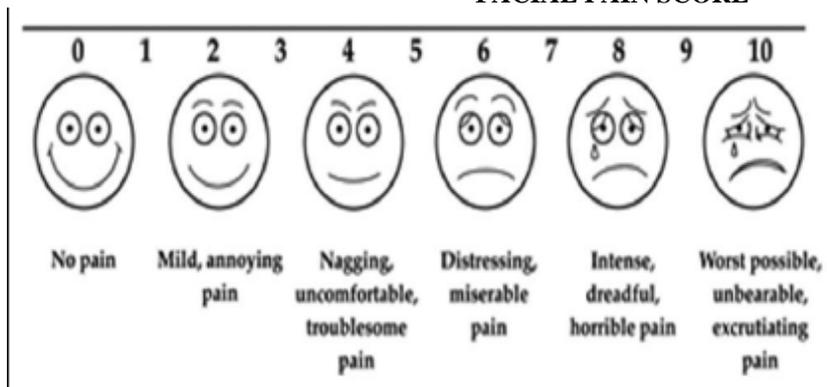
Patients receiving drugs like Dexmedetomidine or other alpha 2 agonists within 28 days of procedure or hypersensitivity ; second or third degree heart block ;renal insufficiency ; a baseline systolic blood pressure(SBP) less than 90 mm of Hg; current history of psychotropic medication ; chronic use or addiction to opiates/ sedative agents/alcohol abuse; history of Obstructive sleep apnea(OSA) ; Basal metabolic index(BMI)>30 kg/cm²

Venous access was established on dorsum of hand with 20/22 G and 0.9% NS. Patients in both groups were given fentanyl 1mcg/kg at beginning of procedure. Subjects in D group received a loading dose of Dexmedetomidine 1 mcg/kg iv over 8-10 minutes followed by 0.5mcg/kg/hour infusion until Ramsay sedation scale (RSS) Score reached 3-4 [7].

Group M received single dose of 0.04mg/kg iv Midazolam and additional doses of 0.5 mg till RSS reached 3-4.

Vital parameters such as heart rate (HR), SBP, diastolic blood pressure (DBP), mean arterial pressure (MAP), respiratory rate (RR) and SpO2 were continuously recorded. . Time to achieve RSS score of 3-4 was recorded. Duration of UGIE was taken into account from the time when patient reached RSS 3-4 till completion of procedure. The total duration of procedure was considered from the beginning of sedation till the completion of procedure.

FACIAL PAIN SCORE



RAMSAY SEDATION SCALE SCORE

Ramsay Sedation Assessment Scale		
Awake	Patient anxious or agitated or both	1
Levels :	Patient cooperative, oriented and tranquil	2
	Patient responds to commands only	3
Asleep	A brisk response to a light glabellar tap	4
Levels:	A sluggish response to a light glabellar tap	5
	No response	6

During the procedure any of the problems if observed were recorded and treated accordingly.
 Hypoxemia- (SpO₂< 92% for >10 sec).
 Hypotension – (MAP<60 mm of Hg or 20% decrease from baseline);
 Hypertension – (SBP>150mm of Hg or 20% increase from baseline)

Others such as Gagging, Retching, Restlessness, Nausea, Vomiting, Hiccups and Coughing.

In recovery room MAS of patients was recorded every 2 minutes by anesthesiologists and adverse effects if any were observed and recorded [8].

MODIFIED ALDRETE SCORE

Parameter	Description of patient	Score
Activity level	Moves all extremities voluntarily/ on command	2
	Moves 2 extremities	1
	Cannot move extremities	0
Respirations	Breathers deeply and coughs freely	2
	Is dyspneic, with shallow, limited breathing	1
	Is apneic	0
Circulation (blood pressure)	Is 20 mm Hg > preanesthetic level	2
	Is 20 to 50 mm Hg > preanesthetic level	1
	Is 50 mm Hg > preanesthetic level	0
Consciousness	Is fully awake	2
	Is arousable on calling	1
	Is not responding	0
Oxygen saturation as determined by pulse oximetry	Has level > 90% when breathing room air	2
	Requires supplemental oxygen to maintain level > 90%	1
	Has level < 90% with oxygen supplementation	0

STATISTICAL ANALYSIS:

The Sample size was calculated at power 80% and alpha error 0.05 assuming Standard Deviation (SD) of 3 minutes in time to achieve mean sedation score and 10% difference in the intra procedural mean blood

pressure and heart rate. It was further enhanced and rounded off to 50 cases equally divided into each group.

Descriptive studies were used to describe the baseline characteristics. Dichotomous outcomes were

compared by Chi square test with continuity correction or Fisher's exact test as applicable. Numerical variables were compared by Student's t test or Mann Whitney U test depending on distribution. Analysis was done using STATA 12. Microsoft word and MS excel was used to generate graphs and tables.

RESULTS:

Table -1 shows time to achieve RSS of 3-4 was different in both groups. The mean time to achieve RSS in group M was 3.64 minutes while it was 9.92 minutes in group D (p< 0.001). Table -2 shows the number of patients who achieved MAS of 9-10 at various time points. Only 2 (4%) patients in group M in contrast to 14 (28%) patients in group D achieved MAS of 9-10 at 6 minutes(p value = 0.001) .Similarly at 8 minutes

3(6%) patients in group M as compared to 18 (36%) patients in group D achieved recovery score of 9-10 (p=0.001). Table -3 Mean duration of endoscopy procedure was 5.36±1.57 minutes (p>0.001); the time taken to perform the endoscopy by the endoscopist after patient is under sedation. But the total time taken for procedure which is inclusive of time taken to sedate the patient to achieve RSS score 3-4 was 15.08 minutes in group D as compared to 9.2 minutes in group M(p <0.001). Table -4 There was no incidence of cough in D group while 8 patients coughed during procedure in M group which was statistically significant (p=0.003). Other complications such as gagging/retching, restlessness, nausea/vomiting and hiccups were comparable in both the groups.

Table 1: Comparison of Time to achieve RSS of 3-4 among Two Groups

S. No	Indications	Group M N= 50 Mean ± SD	Group D N=50 Mean ± SD	T Statistic	P value
1	Time to achieve RSS (3-4)	3.64±0.87	9.92±1.52	- 25.27	<0.001

Table 2: Comparison of Time to achieve Modified Aldrete Score (9-10) at various Time Points among the Two Groups

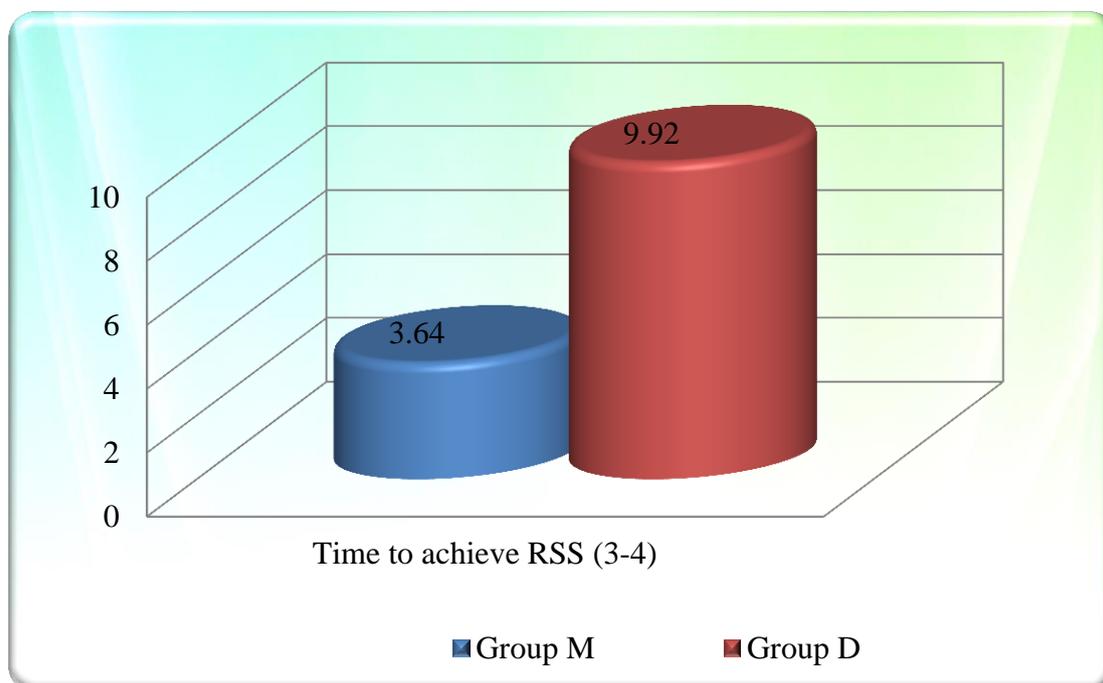
		Time to achieve MAS (9-10) in number (percentages)				
Duration (mins)		2	4	6	8	10
Group M	N	50	50	50	41	23
	Number	0	0	2	3	4
	Percentage	0	0	4	6	8
Group D	N	50	50	50	50	50
	Number	0	0	14	18	10
	Percentage	0	0	28	36	20
P value		NA	NA	0.001	0.001	.79

Table 3: Comparison of Total Time taken and duration of UGIE procedure(in minutes)

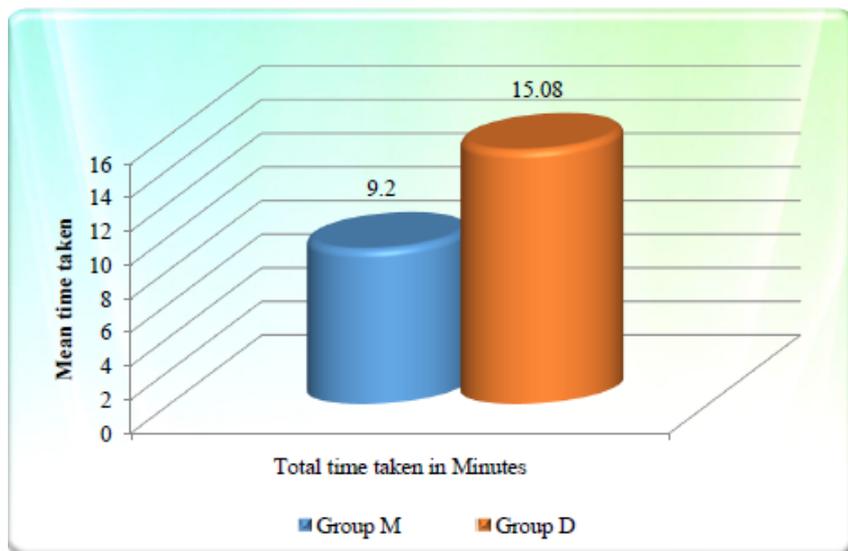
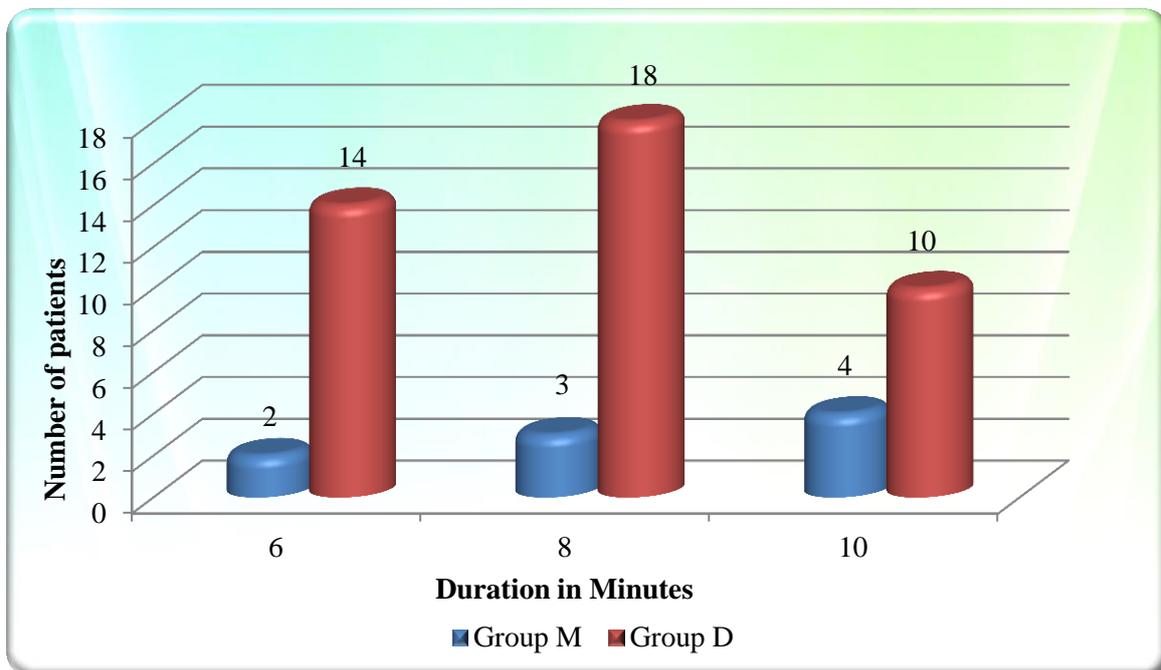
S. No	Time Taken	Group M N= 50 Mean ± SD	Group D N=50 Mean ± SD	T Statistic	P value
1	Total time taken	9.2±2.16	15.08±1.98	-14.17	<0.001
2	Duration of the procedure	5.56±1.92	5.16±1.11	1.27	0.21

Table 4: Comparison of Complications during Upper Gastro Intestinal Endoscopy during the Procedure among the Two Groups

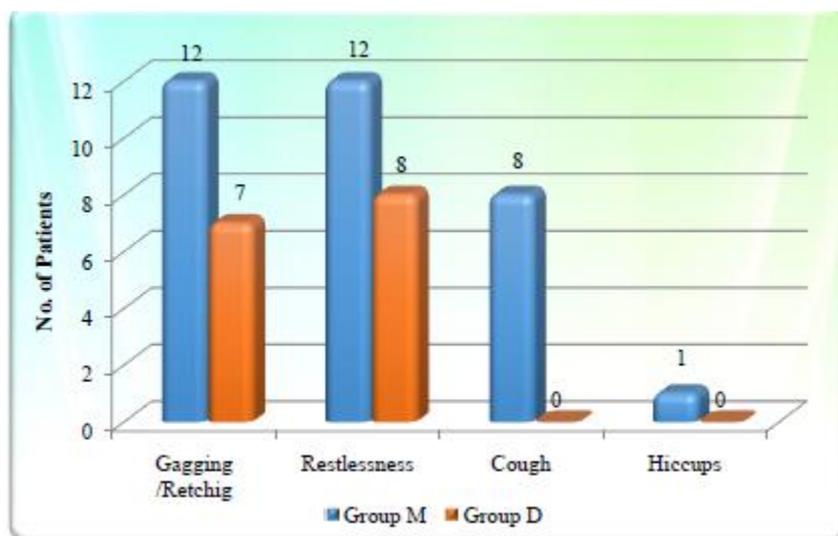
S. No	Complication	Group M N= 50 n (%)	Group D N=50 n (%)	Chi Square Statistic	p value
1	Gagging/Retching	12 (24)	7 (14)	1.62	0.20
2	Restlessness	12 (24)	8 (16)	1.00	0.31
3	Cough	8 (16)	0	8.69	0.003
4	Hiccups	1 (2)	0	1.01	0.31



Graph 1: Comparison of Time to achieve RSS of 3-4 among Two Groups



Graph 3: Comparison of Total Time taken for the Procedure among the Two Groups



Graph 4: Comparison of Complications during Upper Gastro Intestinal Endoscopy during the Procedure among the Two Groups

DISCUSSION:

Our study was an open label prospective randomized study wherein the two groups were similar with regard to demographic characteristics, baseline vital parameters and duration of UGIE. Patients in group D had statistically significantly lower HR after infusion of loading dose and at 2, 4, 6, 8 and 10 minutes during UGIE. These results are in accordance with previous study by Sethi *et al.*; who reported that after administration of Dexmedetomidine, HR was significantly decreased from baseline value [9].

In the present study, we observed HR and a BP reading were more stable with Dexmedetomidine as it decreases the release of norepinephrine and inhibits the sympathetic activity leading to decreasing heart rate (HR) and blood pressure (BP). It also produces analgesia by binding to adrenoceptors in the spinal cord. In study by Dere *et al.*; [12] and Killic *et al.*; [10] there was statistically significant lower heart rate in D group when compared to M group. Arain and Ebert [13] reported that in patients receiving Dexmedetomidine, MAP was significantly reduced during the intraoperative period and the reduction was significantly smaller than that observed with Propofol. The decreased BP was attributed to inhibition of sympathetic outflow.

These findings suggest that Dexmedetomidine has clinical advantage over Midazolam with regard to superior hemodynamic stability. Rest all vital parameters statistically showed no significant difference. The patients in group M achieved RSS of 3-

4 in 3.64 minutes while it took 9.92 minutes in patients of group D. (D) Group induction dose was given by infusion in 10 minutes followed by maintenance but in (M) group drug was given as a bolus. So onset of sedation was faster in midazolam group then D group.

The results were comparable to study conducted by Sethi *et al.*; [9] wherein there was faster onset of sedation (RSS 3-4) in Group M compared with Group D (mean time 3 min vs. 12 minutes). Duration of UGIE procedure was comparable in both the groups ($p=0.21$). But the total time taken for the procedure was significantly higher in group D (15.08 minutes) as compared to group M (9.2 minutes) as the time to achieve RSS was longer in group D.

In our study, during recovery 28% of patients in group D attained MAS of 9-10 at 6 minutes as compared to only 4% in group M. Most of the patients in group D achieved MAS 9-10 at 10 minutes. The amnestic effects of Dexmedetomidine are less pronounced than those of Midazolam resulting in profound anterograde amnesia and more confused states with Midazolam on emergence. In contrast, amnesia is achieved with Dexmedetomidine only at higher plasma levels (≥ 1.9 ng.ml⁻¹) without any retrograde amnesia [14]. Thus, patients in group D were more alert and clearheaded.

No untoward incidents such as bradycardia or profound hypotension necessitating any urgent intervention throughout the procedure. Complication

rate was significantly higher in group M than group D during the procedure.

Almost 24% of patients had gagging/retching and restlessness during the procedure in group M which was comparable to group D. There was no incidence of cough in D group while 8 patients coughed during procedure in M group which was statistically significant ($p=0.003$). Similarly, Kilic N *et al.*; [10] reported that the procedure elicited a gag response in 28% patients in group M and in 16% patients in group D which was comparable ($p>0.05$).

Abdellatif AA ER [15] suggested that Dexmedetomidine was not associated with respiratory depression despite the profound levels of sedation. Dexmedetomidine is associated with limited respiratory effects, even if plasma levels up to 15 times of normal, leading to a wide safety margin [16]. In our study, no patient had respiratory depression or hypoxemia during the procedure.

CONCLUSION:

Upper Gastrointestinal Endoscopic procedures (UGIE) may be associated with complications like airway irritation, bleeding resulting as a consequence of restlessness, anxiety and poor cooperation of patients during procedure Conscious sedation during UGIE provides patient comfort, thereby facilitating the procedure.

Our study revealed that Dexmedetomidine was more efficacious in providing hemodynamic stability, higher patient satisfaction scores, and adequacy of sedation and control of airway. It also resulted in lower complication rates and better recovery profile of patients. Neither Dexmedetomidine nor Midazolam resulted in respiratory depression. However, larger randomized controlled trials are needed to further validate our findings and prior to establishing Dexmedetomidine, a standard of care in UGIE sedation.

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