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COMPARING DEXMEDETOMIDINE VERSUS COMBINATION OF MIDAZOLAM-FENTANYL FOR MIDDLE EAR SURGERIES UNDER MONITORED ANAESTHESIA CARE- A PROSPECTIVE RANDOMISED DOUBLE-BLINDED STUDY

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Abstract

Introduction: Analgesia and sedation are usually required for the comfort of the patient and surgeon during all middle ear surgeries done under local anaesthesia. Common middle ear surgeries includes tympanoplasty, mastoidectomy, myringotomy, grommet insertion and cochlear implantation can be performed under local anaesthesia and sedation as outpatient surgery[1]; thus rapid recovery, early ambulation and decreased length of hospital stay.

Materials and Methods: A study entitled, "Comparing Dexmedetomidine versus combination of Midazolam-Fentanyl for middle ear surgeries under monitored anaesthesia care- a prospective randomized double-blinded study", was undertaken in S Nijalingappa Medical College and HSK Hospital and Research Centre, Bagalkot from December 2015 to July 2017. The study was undertaken after obtaining ethical committee clearance as well as written informed consent from all patients.

Results: The minimum age was 18yrs and maximum age was 60yrs. Most of the patient's age in both the groups ranged between 21-30yrs.Mean age in group Dexmedetomidine was 33.30 and SD of 10.66. In group Midazolam-Fentanyl mean age was 31.40 with SD of 9.78. P-value of 0.506 and was statistically insignificant and the group receiving dexmedetomidine and other group receiving midazolam-fentanyl combination were comparable. Among the dexmedetomidine group 92.5% were ASA 1 and 7.5% were ASA II. And in the group that received midazolam-fentanyl combination 87.5% were ASA I and 12.5% were ASA II. The two groups were comparable and was statistically insignificant p=0.71.

Conclusion: On the basis of the findings of the present study, dexmedetomidine seems to be better for MAC when compared to midazolam-fentanyl combination. Dexmedetomidine provides a calm patient with better intra and post operative analgesia, reducing need of rescue

sedation and analgesic requirement in patients undergoing tympanoplasty under local anaesthesia leading to increased satisfaction of both patient and surgeon. However haemodynamic parameters and adverse effects like dry mouth, bradycardia are need to be closely monitored.
Key Words: Analgesia, tympanoplasty, mastoidectomy, myringotomy, grommet insertion.

INTRODUCTION

Analgesia and sedation are usually required for the comfort of the patient and surgeon during all middle ear surgeries done under local anaesthesia. Common middle ear surgeries includes tympanoplasty, mastoidectomy, myringotomy, grommet insertion and cochlear implantation can be performed under local anaesthesia and sedation as outpatient surgery[1]; thus rapid recovery, early ambulation and decreased length of hospital stay.

Middle-ear surgeries pose a different set of challenges for the patient, surgeons and anaesthesiologists. Patients may feel discomfort due to pain, noise due to suction, special considerations taken during middle ear surgeries include: Provision of a bloodless surgical field, attention to patient's head positioning, airway management, facial nerve monitoring, the effect of nitrous oxide on the middle ear, a smooth and calm recovery, and prevention of postoperative nauseaand vomiting (PONV).[2,3,4]

Dislocation of the ossicular chain with and without opening of the labyrinth, injuries to the facial nerve, PONV and haemorrhage from large arteries and veins may occur.[3,4] Most-middle ear procedures can be performed as outpatient surgery; thus rapid recovery, good analgesia, and avoidance of nausea andvomiting are essential.[7]

Sympathetic stimulation and movements of an anxious patient cause increased bleeding and disturb the fine microscopic nature of the surgery which may even lead to graft failure. The advantages of local anaesthesia include testing hearing intraoperatively, immediately detecting complications and a truncated postsurgical emergence. Proper patient selection, preoperative counseling and use of appropriate sedation are important factors for success of this surgery under local anesthesia.[2]

Several pharmacological agents have been tried for sedation in middle ear surgeries like dexmedetomidine, midazolam, fentanyl, propofol, clonidine, and a different combination of these drugs with varying risk benefit ratio.

Midazolam with its quick onset, but a relatively long half-life can cause prolonged sedation after repeated administration. Combining midazolam with opioids increases the risk for hypoxemia and apnea. Over sedation leading to respiratory depression has been reported tocause patient injuries during MAC.

Dexmedetomidine is a selective α2 receptor agonist with properties of analgesia, sympatholysis and titrating sedation without major respiratory depression. It reduces opioid requirements and

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stress response to surgery ensuring a stable hemodynamic state. Dexmedetomidine is increasingly being used as a sedative for MAC for various surgical procedures.

In our study we compared dexmedetomidine versus combination of midazolam- fentanyl regarding their efficacy, safety and the overall patient and surgeon satisfaction.

MATERIALS AND METHODS

A study entitled, "Comparing Dexmedetomidine versus combination ofMidazolam-Fentanyl for middle ear surgeries under monitored anaesthesia care- a prospective randomized double-blinded study", was undertaken in S Nijalingappa Medical College and HSK Hospital and Research Centre, Bagalkot from December 2015 to July 2017. The study was undertaken after obtaining ethical committee clearance as well as written informed consent from all patients.

Inclusion criteria: Eighty patients scheduled for various middle ear surgeries under local anesthesia of ASA grade I/II aged between 18 to 60 years were included in the study.
Exclusion criteria for the study group: Patients with known sensitivity to anesthetic drugs**,** Pregnant and lactating women**,** Recent history of use of any opioid or sedative medications or anyanalgesic medications**,** Body mass index >30 kg/m^2**,** Intellectual impairment or psychiatric condition precluding adequate communication**,** History of cardiac disease, hepatic or renal impairment.

Study design: Prospective, randomized double blinded clinical study

Study period: December 2015 to July 2017.

Sample size: Forty in each group. It was calculated using OPEN-EPI version 2.3.1 software.

According to a study done by Devangi A Parikh et al Proportion of patients getting rescue anesthesia in Group D is 11% Proportion of patients getting rescue anesthesia in Group MF is 40%At 95% confidence interval and 80% power of the study

Sample size calculation done using the formula:

$$N = \frac{2(Z\alpha+Z\beta)^2 P(1-P)}{\Delta^2}$$

Sample size required is 36 in each group, total of 80 patients were
Considered- Group D (Dexmedetomidine) = 40
Group MF (Midazolam-Fentanyl combination) = 40

Sampling: In this study 80 patients were divided randomly into two groups. Allocation into two groups was be done by computer generated randomization table.

- Pre-anesthetic evaluation was done before surgery. A routine pre-anesthetic

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examination was conducted assessing: General condition of the patient, airway by modified Mallampatti grading, and body weight of the patient and a detailed examination of the cardiovascular system and Respiratory system.

- The following investigations were done in all patients:
- Complete blood count estimation, Urine examination for albumin, sugar and microscopy, Standard 12-lead electrocardiogram, X-ray chest, Blood sugar, Blood urea and Serum creatinine.

BLINDING: The anaesthesiologist conducting the case, the patients were blinded to the group assignment. Data was recorded by the anaesthesiologist conducting the case and the drugs were prepared by an anaesthesiologist who was not in part of patient management or data collection.

DRUG PREPARATION

Two 50 ml syringes, labelled as loading and maintenance were given for each patient. Group D patients had dexmedetomidine 1μg/kg and Group MF midazolam 0.06 mg/kg plus fentanyl 1 μg/kg in their respective loading syringes diluted up to 30 ml of normal saline.

Group D had dexmedetomidine and Group MF midazolam in their respective maintenance syringes diluted to equal volume.

All patients included in the study were kept nil per orally 10 pm onwards on the previous night. On arrival of the patient in the operating room, a 20-gauge intravenous cannula was secured and connected to IV fluid ringer lactate. Psychological assurance was given to the patients. The patients were connected to Drager multi parameter monitor which records Heart rate,

- Non-invasive measurements of SBP, DBP,
- Continuous ECG monitoring andoxygen saturation.
- The baseline systolic, diastolic blood pressure, mean arterial pressure and heart rate were recorded in the operative room. Oxygen administration via nasalcannula at 4 L/min.

The cardiac rate and rhythm were also monitored from a continuous visual display of electrocardiogram from lead II.
After recording the baseline reading, all patients were given inj.Emset 4mg iv and Inj.rantac 50mg iv. No sedative premedication was used.

Group D (n=40) received IV dexmedetomidine 1 μg/kg over 10 min followedby 0.6 μg/kg/hr infusion and Group MF (n=40) received IV midazolam 0.06 mg/kg plus IV fentanyl 1μg/kg over 10 min followed by midazolam infusion at 1μg/kg/min.

During this period, the patients were assessed every two minutes using Ramsay sedation score. The target end point is a patient having Ramsay sedation score (RSS)= 3. After the loading drug infusion if any patient in either of the groups had lesser sedation (RSS score <3) then bolus IV midazolam 0.01mg/kg was administered and was repeated if necessary till RSS 3. The maintenance infusion in both the groups were started immediately, once the loading infusionswere stopped. After completing the loading infusion of the drugs and when RSS of 3 was achieved, the blinded ENT surgeon administered local anaesthesia using 2% lignocaine with adrenaline (6-7 ml 1:2,00,000) in the postauricular area. Surgery was started after confirming adequate analgesia.

Intraoperatively heart rate (HR), Sysolic blood pressure(SBP),Diastolic blood pressure(DBP), Respiratory rate and SPO2 was recorded every 2 min during loading infusion of the study drugs and thereafter at 15 minutes intervals till the end of surgery.

Sedation level (RSS) was assessed every 15 min and if RSS <3 IV midazolam 0.01 mg/kg is administered was a common rescue sedative in both the groups. The number of rescue doses of midazolam were recorded.

Intraoperative pain intensity was evaluated using Visual analogue scale (VAS). Inadequate analgesia was treated with infiltration of 2% lignocaine with adrenaline (2-3 ml) at the surgical site and noted. If the pain, still persistent and VAS >3, then rescue IV fentanyl in the dose of 1μg/kg[1] was given. Total number of rescue doses of fentanyl during surgery were noted. The protocol specified up to a maximum of three rescue doses each of midazolam andfentanyl. At any time, if clinically indicated or if protocol-specified amounts of rescue drugs were reached, the sedation technique was converted to any alternative sedative or anaesthetic technique and the study drug were discontinued.
The maintenance infusions were discontinued at the time of closure which was approximately 15 min before end of surgery. Adverse events like bradycardia, hypotension, hypertension, bradypnea (RR <8 breaths/min), desaturation (SpO2 <90%), nausea, vomiting, dry mouth or any other event during or within two hours of the procedure were noted.

After the completion of surgery patients were shifted to the PACU and monitored for hemodynamic parameters, degree of analgesia and adverse events, if any for 2 hours. RSS Was assessed immediately on arrival in the PACU and every 30 min thereafter till 2 hours. Requirement of postoperative analgesia was noted. The first rescue dose of analgesic was given at VAS >3 and is documented. Surgeons were asked to grade the surgical conditions as well as their satisfaction with sedation technique on seven point likert satisfaction scale. Patients were asked to grade their overall satisfaction with the procedure on a similar seven point likert satisfaction scale on postoperative Day one in the surgical ward.

The primary end point of our study was the patient satisfaction score using seven point likert satisfaction scale. Efficacy of the sedation technique was defined as the ability to complete the surgery without any rescue sedatives and analgesics and safety of the technique was determined based on the frequency of analgesia/sedation related intra or postoperative adverse events.

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Statistical analysis: Statistical analysis was done using SPSS software version 19.0. Data obtained was tabulated in the excel sheet. In the present study, results are given as Mean ± Standard deviation and range values for continuous data. Students 't' test was used to compare the two groups, categorical data are expressed as number and percentages. Difference between the groups was compared by chi-square test. A "p" value of 0.05 or less was set for statistical significance.

RESULTS

The present study, comparing dexmedetomidine versus combination of midazolam-fentanyl for middle ear surgeries under monitored anaesthesia care was conducted at S.Nijalingappa Medical College and H.S.K Hospital and Research centre, Bagalkot. Eighty consenting patients belonging to ASA physical status I and II were randomly divided into 2 groups, 40 each based on computer generated randomization table. Baseline patient characteristics and demographic profile were comparable between the groups.

Table 1: Patient Characteristics

	Dexmedetomidine	Midazolam - Fenatnyl	p-Value
Age (Mean±SD) Yrs	33.30 ± 10.66	31.40 ± 9.78	0.506
Gender (M/F)	21/19	19/21	0.82
ASA (I/II)	37/3	35/5	0.71
Weight in Kgs	67.95 ± 5.42	67.65 ± 5.20	0.80

There were no significant differences in baseline patient characteristics between the two groups.

Table 2: Age Distribution of Study Groups

Age	Group			
	Dexmedetomidine		**Midazolam-Fentanyl**	
	Count	%	Count	%
≤20	4	10.0%	6	15.0%
21-30	17	42.5%	14	35.0%
31-40	9	22.5%	12	30.0%
41-50	7	17.5%	7	17.5%
51-60	3	7.5%	1	2.5%
Total	40	100.0%	40	100.0%
Mean±SD	33.3 ± 10.66		31.4 ± 9.78	
Range (Min-Max)	18-58		18-55	
t-value	0.83			
P-value	0.41			

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Above table shows the Age distribution between the two groups. The minimum age was 18yrs and maximum age was 60yrs. Most of the patient's age in both the groups ranged between 21-30yrs.Mean age in group Dexmedetomidine was 33.30 and SD of 10.66. In group Midazolam-Fentanyl mean age was 31.40 with SD of 9.78. P-value of 0.506 and was statistically insignificant and the group receiving dexmedetomidine and other group receiving midazolam-fentanyl combination were comparable.

Graph 1: Age Distribution of Study Groups

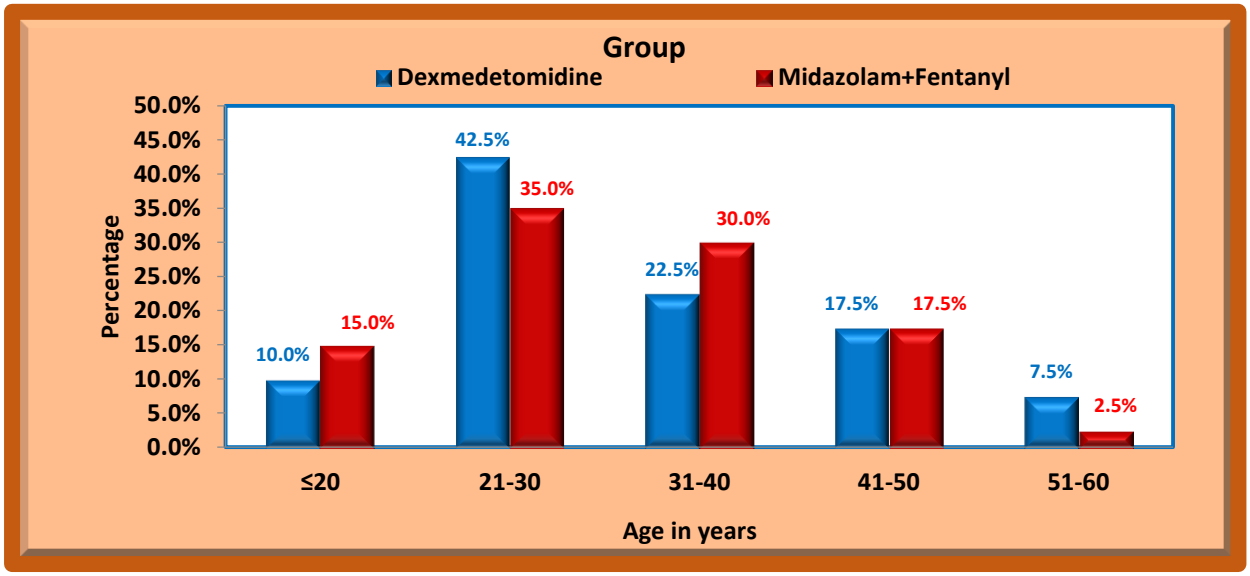

Table 3: Gender Distribution

GENDER	Dexmedetomidine		Midazolam-Fentanyl		P-value
	Count	%	Count	%	
Male	21	52.5%	19	47.5%	0.82
Female	19	47.5%	21	52.5%	
Total	40	100.0%	40	100.0%	

This table shows the Gender distribution among the study population. In the group receiving dexmedetomidine, there were 52.5% males and 47.5% were females. And in the group that received midazolam with fentanyl, the males contributed to 47.5% of study population and females contributed to 52.5%. And the two groups were comparable and there was no statistical significance p=0.82.

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Table 4: ASA Status

ASA STATUS	Group			
	Dexmedetomidine		**Midazolam-Fentanyl**	
	Count	%	Count	%
I	37	92.5%	35	87.5%
II	3	7.5%	5	12.5%
P-value	0.71			

The table shows the ASA status between the two groups. Among the dexmedetomidine group 92.5% were ASA 1 and 7.5% were ASA II. And in the group that received midazolam-fentanyl combination 87.5% were ASA I and 12.5% were ASA II. The two groups were comparable and was statistically insignificant p=0.71.

Table 5: Weight Distribution among Groups

Weight	Group			
	Dexmedetomidine		**Midazolam-Fentanyl**	
	Count	%	Count	%
60-65	16	40.0%	14	35.0%
66-70	12	30.0%	18	45.0%
71-75	9	22.5%	4	10.0%
76-80	3	7.5%	4	10.0%
Total	40	100.0%	40	100.0%
Mean±SD	67.95 ± 5.42		67.65 ± 5.20	
Range (Min-Max)	60-80		60-80	
t-value	0.25			
P-value	0.80			

Both the groups had similar body weight distribution and the mean weight in dexmedetomidine group was 67.95 with SD of 5.42 and 67.65 with SD of 5.20 in group receiving midazolam-fentanyl combination with p value 0.80 .

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Graph 2: Weight Distribution among Groups

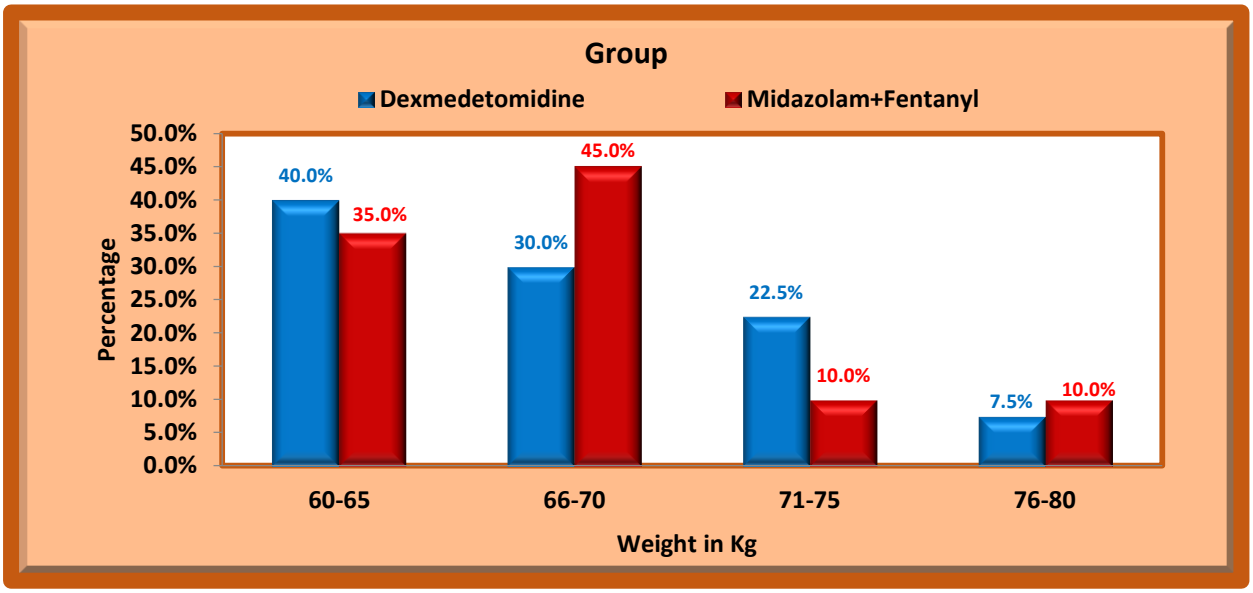

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Table 6: SURGEON SATISFACTION SCORE

Variable	Dexmedetomidine					Midazolam-Fentanyl					Z-value	P-value
	N	Minimum	Maximum	Mean	SD	N	Minimum	Maximum	Mean	SD		
Surgeon satisfaction score	40	5	7	6.13	0.56	40	5	7	5.88	0.40	-2.22	.026

The mean Surgeon satisfaction score was 6.13 with SD 0.56 in the dexmedetomidine group which was found to be superior in comparison to the group that received Midazolam-Fentanyl combination with mean score of 5.88 with SD 0.40, thus being statistically significant (p-value 0.026).

Table 7: Patient Satisfaction Score

Variable	Dexmedetomidine					Midazolam-Fentanyl					Z-value	P-value
	N	Minimum	Maximum	Mean	SD	N	Minimum	Maximum	Mean	SD		
Patient satisfaction score	40	5	7	6.30	0.65	40	5	7	5.88	0.72	-2.63	.008

On comparison of the patient satisfaction score, it was found that the mean score among the patients receiving dexmedetomidine was 6.30 with SD of 0.65 which was statistically significant (p-value 0.008) than the patients receiving midazolam with fentanyl that had a mean score of 5.88 with SD of 0.72. Patient satisfaction score was found to be superior in the group receiving Dexmedetomidine compared to group receiving Midazolam-Fentanyl combination with p-value of 0.008.

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Table 8: Pulse Rate Variation during Loading Dose Infusion

Pulse Rate at	Dexmedetomidine					Midazolam-Fentanyl					Z-value	P-value
	N	Minimum	Maximum	Mean	SD	N	Min	Max	Mean	SD		
0 min	40	66	96	80.58	7.49	40	66	104	82.48	9.09	-.86	.387
2 min	40	54	96	78.25	9.67	40	54	96	77.38	9.45	-.19	.850
4 min	40	58	99	77.20	10.01	40	65	99	76.88	9.04	-.54	.588
6 min	40	50	102	75.68	15.02	40	50	102	71.38	14.52	-1.12	.262
8 min	40	57	94	73.55	10.19	40	63	88	72.63	7.01	-.08	.934
10 min	40	50	94	71.88	13.21	40	50	86	71.23	10.32	-.17	.862

This table shows Changes in pulse rate at start of loading dose infusion and were statistically insignificant in both the study groups using Dexmedetomidine and Midazolam-Fentanyl.

Graph 3: Pulse Rate Variation during Loading Dose Infusion

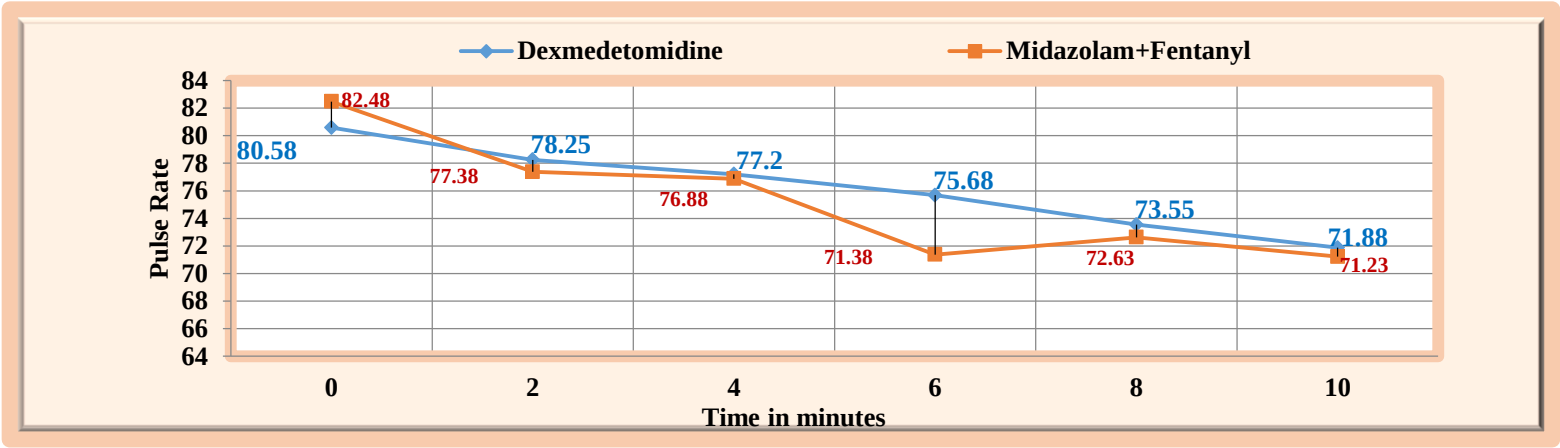

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Table 9: Respiratory Rate Variation during Loading Dose Infusion

Respiratory Rate	Dexmedetomidine					Midazolam-Fentanyl					Z-value	P-value
	N	Min	Max	Mean	SD	N	Min	Max	Mean	SD		
0 min	40	16	30	20.13	3.65	40	16	30	21.90	3.04	-2.69	.007
2 min	40	15	28	19.30	3.39	40	16	28	20.23	2.64	-2.08	.037
4 min	40	13.0	26.0	18.675	4.18	40	13.0	26.0	19.600	3.63	-1.18	.238
6 min	40	14	29	19.15	3.70	40	15	25	21.60	3.24	-2.83	.005
8 min	40	14	33	19.13	4.34	40	14	25	20.18	3.66	-1.85	.064
10 min	40	12	33	20.08	4.64	40	12	28	20.75	4.03	-1.06	.287

Above table shows Changes in respiratory rate during loading dose infusion. The variation at 0min, 2min, 6min were found to be highly statistically significant in Group Dexmedetomidine (p=0.005) compared to group Midazolam-Fentanyl.

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Graph 4: Respiratory Rate Variation During Loading Dose Infusion

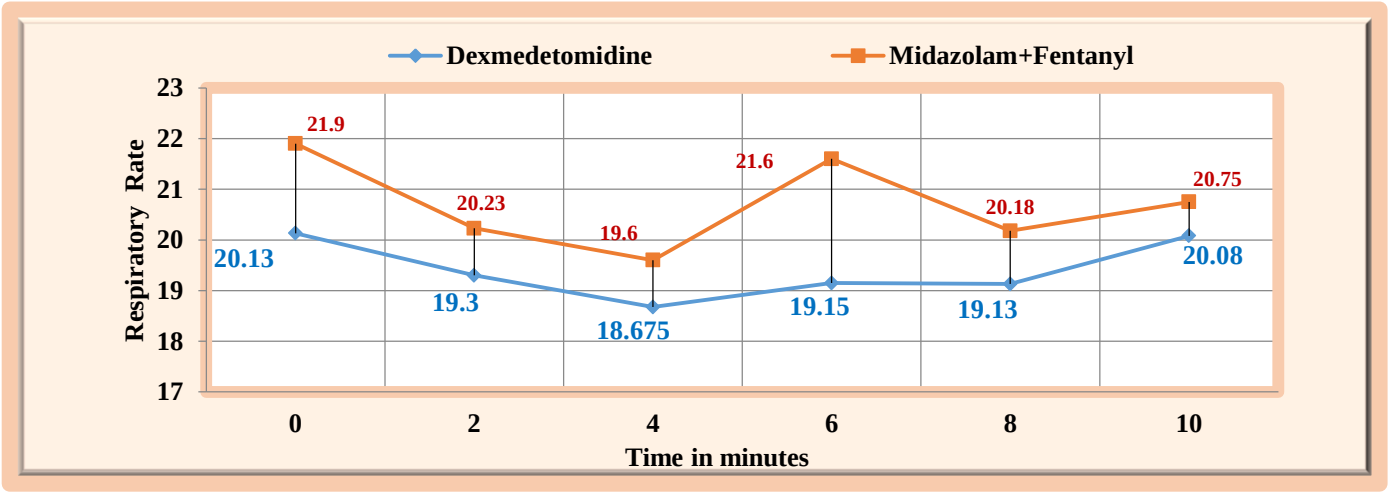

Table 10: Systolic Blood Pressure Variation during Loading Dose Infusion

Systolic blood pressure	Dexmedetomidine					Midazolam-Fentanyl					Z-value	P-value
	N	Min	Max	Mean	SD	N	Min	Max	Mean	SD		
0 min	40	108	138	120.93	10.06	40	108	138	121.55	9.10	-.73	.464
2 min	40	107	124	116.48	5.53	40	108	126	117.83	5.52	-.93	.353
4 min	40	105	125	112.93	5.81	40	105	129	118.15	5.88	-3.85	<0.0001
6 min	40	96	138	113.63	7.74	40	109	141	122.53	10.84	-4.06	<0.0001
8 min	40	98	135	114.08	8.68	40	102	135	122.58	8.60	-4.16	<0.0001
10 min	40	100	129	111.03	7.03	40	103	129	114.10	8.73	-1.33	.184

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Table shows the mean systolic pressure changes. SBP showed a decline to 112.93±5.81 in group Dexmedetomidine at 4 minutes after loading dose infusion was started and found to be highly statistically significant (p=0.0001) compared to group Midazolam-Fentanyl.

Graph 5: Systolic Blood Pressure Variation during Loading Dose Infusion

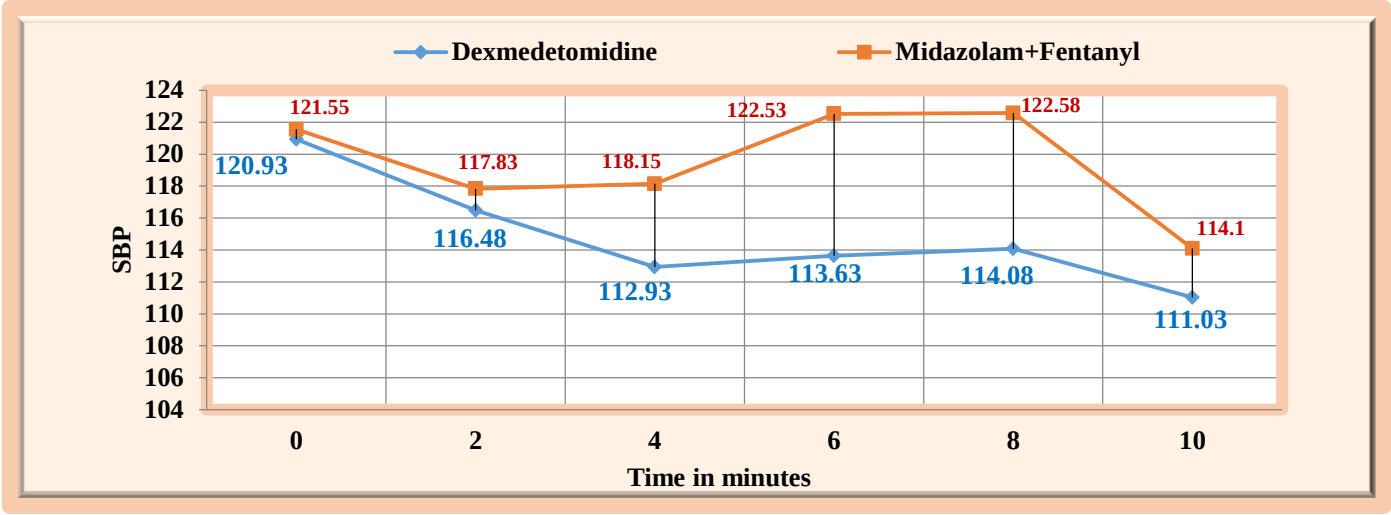

Table 11: Diastolic Blood Pressure Variation during Loading Dose Infusion

Diastolic blood pressure	Dexmedetomidine					Midazolam-Fentanyl					Z-value	P-value
	N	Min	Max	Mean	SD	N	Min	Max	Mean	SD		
0 min	40	56	98	74.98	11.87	40	56	96	81.58	9.49	-2.82	.005
2 min	40	54	90	71.53	11.38	40	57	90	76.78	7.17	-2.10	.036
4 min	40	48	98	70.85	12.41	40	48	98	76.33	13.50	-1.90	.057
6 min	40	57	89	69.13	10.50	40	58	98	77.80	10.70	-3.48	<0.0001

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8 min	40	50	87	67.93	11.82	40	57	88	77.78	9.85	-3.74	<0.0001
10 min	40	44	91	65.50	13.88	40	50	93	76.23	13.78	-3.24	.001

The mean fall in DBP in group Dexmedetomidine at 0,2,6,8,10 minutes after loading dose infusion was found to be highly statistically significant (p=0.0001) when compared to group receiving Midazolam-Fentanyl combination.

Graph 6: Diastolic Blood Pressure Variation during Loading Dose Infusion

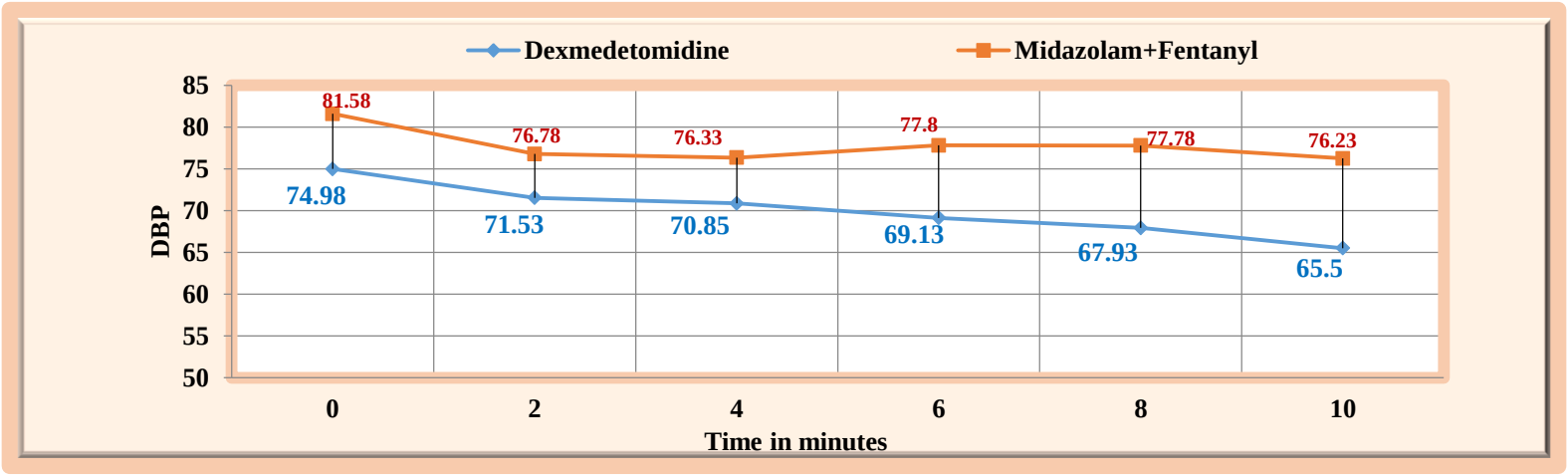

Table 12: Spo2 Variation during Loading Dose Infusion

SPO2	Dexmedetomidine					Midazolam+Fentanyl					Z-value	P-value
	N	Min	Max	Mean	SD	N	Min	Max	Mean	SD		
0 min	40	100	100	100.00	0.00	40	100	100	100.00	0.00	0.00	1.000
2 min	40	100	100	100.00	0.00	40	96	100	99.90	0.63	-1.00	.317
4 min	40	100	100	100.00	0.00	40	98	100	99.95	0.32	-1.00	.317

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6 min	40	99	100	99.93	0.27	40	99	100	99.90	0.30	-0.39	.694
8 min	40	99	100	99.98	0.16	40	96	100	99.90	0.63	-0.02	.986
10 min	40	97	100	99.88	0.56	40	95	100	99.88	0.79	-0.56	.579

The above table shows the variation in Spo2 at start of loading dose infusion. There was no significant variation among the groups in our study.

Graph 7: Spo2 Variation during Loading Dose Infusion

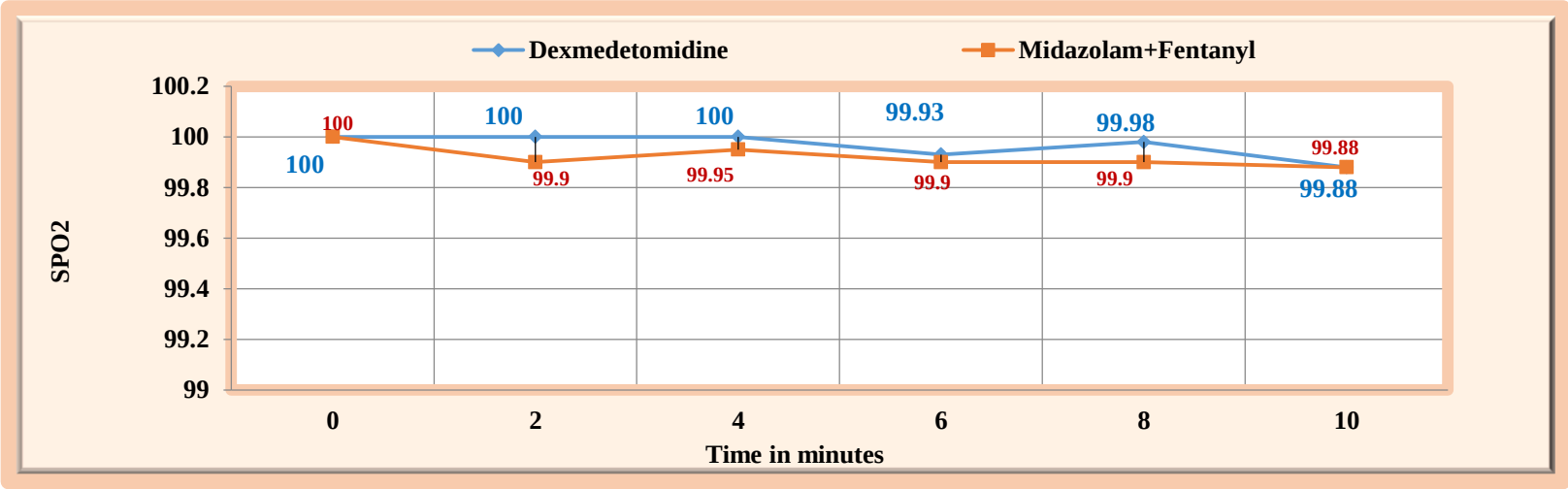

Table 13: Pulse Rate Variation during Maintenance Dose Infusion

Pulse Rate	Dexmedetomidine					Midazolam+Fentanyl					Z-value	P-value
	N	Min	Max	Mean	SD	N	Min	Max	Mean	SD		
15 min	40	49	100	70.90	15.75	40	50	110	77.13	14.33	-1.81	.070

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30 min	40	44	101	70.40	14.35	40	44	101	75.30	13.60	-1.92	.055
45 min	40	49	135	73.35	24.37	39	49	87	71.15	12.14	-0.36	.719
60 min	40	46	111	69.98	17.30	39	46	85	69.90	9.06	-1.20	.232
75 min	40	56	114	73.15	17.00	39	56	89	71.85	9.28	-1.13	.260
90 min	38	53	99	68.97	13.07	35	59	81	70.66	6.95	-1.81	.071
105 min	31	60	107	79.77	17.39	33	64	111	88.06	17.42	-2.17	.030
120 min	23	56	103	75.09	18.58	26	60	103	90.62	15.55	-2.97	.003
135 min	17	54	105	72.82	16.20	18	54	105	92.67	19.63	-2.78	.005
150 min	12	58	90	72.92	12.40	16	58	91	84.13	12.97	-2.40	.016
165 min	3	79	88	82.33	4.93	13	79	88	82.69	3.40	-0.41	.679
180 min	3	78	79	78.67	0.58	13	78	80	78.92	0.64	-0.63	.532

Table number 13 showing the variation of pulse rate during maintenance dose infusion among the study groups. We observed statistically significant fall of pulse rate at 120 min with mean of 75.09 and SD of 18.58 in the group that received dexmedetomidine (p=0.003).

Table 14: Respiratory Rate Variation during Maintenance Dose Infusion

Respiratory Rate	Dexmedetomidine					Midazolam+Fentanyl					Z-value	P-value
	N	Min	Max	Mean	SD	N	Min	Max	Mean	SD		
15 min	40	16	33	20.75	4.71	40	15	33	19.45	5.55	-2.63	.009
30 min	40	12	30	18.50	4.44	40	12	28	19.08	4.16	-0.82	.413

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45 min	40	10	29	18.70	5.62	39	10	25	17.51	3.71	-0.65	.514
60 min	40	10	30	18.03	5.03	39	14	30	19.21	4.43	-1.10	.271
75 min	40	12	28	19.10	4.54	39	12	26	19.18	3.52	-0.36	.719
90 min	38	13	29	18.74	3.86	35	14	29	19.80	4.26	-0.83	.409
105 min	31	13	27	18.26	3.91	33	14	27	18.45	3.59	-0.35	.723
120 min	23	14	25	18.17	3.04	26	14	22	17.00	2.37	-1.72	.085
135 min	17	16	26	18.76	3.09	18	16	19	16.89	1.23	-1.99	.046
150 min	12	14	19	16.67	1.72	16	14	21	18.19	2.40	-2.29	.022
165 min	3	14	16	14.67	1.15	13	14	21	16.38	3.23	-0.65	.513
180 min	3	25	25	25.00	0.00	13	25	28	26.31	1.38	-1.57	.116

The mean fall in Respiratory rate at 15 minutes after start of maintenance dose infusion in midazolam-fentanyl combination group was found to be statistically significant (p=0.009) 19.45±5.55 than in group that received Dexmedetomidine .

Table 15: Systolic Blood Pressure Variation During Maintenance Dose Infusion

Systolic blood pressure	Dexmedetomidine					Midazolam+Fentanyl					Z-value	P-value
	N	Min	Max	Mean	SD	N	Min	Max	Mean	SD		
15 min	40	98	144	110.33	11.62	40	99	144	117.18	10.77	-3.60	<0.0001
30 min	40	95	129	111.90	9.38	40	101	129	115.00	7.92	-1.51	.131

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45 min	40	96	139	112.48	14.20	39	98	130	117.05	10.32	-1.85	.064
60 min	40	93	137	116.38	12.03	39	101	133	116.33	9.21	-0.33	.745
75 min	40	99	139	117.18	10.88	39	103	139	118.08	11.08	-0.17	.863
90 min	38	89	129	113.61	9.71	35	103	129	117.03	7.92	-1.48	.138
105 min	31	100	135	113.26	10.80	33	100	137	120.09	13.86	-2.04	.042
120 min	23	100	130	115.48	12.26	26	108	138	126.31	9.31	-2.80	.005
135 min	17	99	137	113.24	12.17	18	104	138	127.50	15.03	-2.25	.025
150 min	12	106	142	127.50	9.47	16	122	142	137.38	7.73	-2.66	.008
165 min	3	120	125	122.00	2.65	13	121	126	123.46	1.81	-1.18	.238
180 min	3	108	120	115.67	6.66	13	119	122	120.46	1.05	-1.87	.061

The mean fall in SBP in group receiving dexmedetomidine at 15 min was statistically highly significant with mean of 110.33 and SD of 11.62 after start of maintenance dose infusion (p=0.0001) compared to group Midazolam-Fentanyl.

Table 16: Diastolic Blood Pressure Variation During Maintenance Dose Infusion

Diastolic blood pressure	Dexmedetomidine					Midazolam+Fentanyl					Z-value	P-value
	N	Min	Max	Mean	SD	N	Min	Max	Mean	SD		
15 min	40	46	93	64.28	14.15	40	50	93	74.58	13.24	-3.10	.002
30 min	40	47	88	67.88	12.47	40	56	87	73.53	8.69	-1.85	.065
45 min	40	5	92	69.05	16.55	39	45	90	76.72	12.42	-2.18	.029

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60 min	40	43	90	69.65	15.00	39	43	93	76.33	13.00	-2.03	.042
75 min	40	39	100	68.58	14.59	39	39	100	74.74	14.78	-1.98	.048
90 min	38	39	90	66.61	13.08	35	51	90	73.14	12.67	-1.89	.058
105 min	31	43	98	67.97	16.54	33	52	98	80.67	14.07	-2.69	.007
120 min	23	44	99	68.74	19.51	26	56	103	88.73	15.98	-3.41	.001
135 min	17	47	99	63.35	17.52	18	52	99	86.00	20.20	-2.59	.010
150 min	12	59	105	75.58	16.62	16	70	107	97.63	13.87	-3.25	.001
165 min	3	96	98	96.67	1.15	13	95	98	96.85	0.90	-0.42	.671
180 min	3	91	95	92.67	2.08	13	91	95	93.38	1.33	-0.69	.491

The above table show the mean fall in DBP. In group Dexmedetomidine, the mean fall of DBP at 150 minutes after start of maintenance dose infusion was statistically highly significant (p=0.001) with mean of 75.58 and SD 16.62 when compared to group receiving Midazolam-Fentanyl.

Table 17: Spo2 Variation During Maintenance Dose Infusion

SPO2	Dexmedetomidine					Midazolam+Fentanyl					Z-value	P-value
	N	Min	Max	Mean	SD	N	Min	Max	Mean	SD		
15 min	40	100	100	100.00	0.00	40	99	100	99.98	0.16	-1.00	.317
30 min	40	98	100	99.90	0.44	40	94	100	99.75	1.03	-0.48	.630
45 min	40	99	100	99.90	0.30	39	96	100	99.82	0.68	-0.08	.940
60 min	40	98	100	99.88	0.46	39	97	100	99.87	0.57	-0.38	.701

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75 min	40	96	100	99.70	0.82	39	98	100	99.79	0.61	-0.59	.552
90 min	40	96	100	99.48	1.34	39	100	100	100.00	0.00	-2.50	.012
105 min	31	98	100	99.45	0.89	33	96	100	99.82	0.77	-2.31	.021
120 min	23	98	100	99.39	0.84	26	99	100	99.92	0.27	-2.72	.006
135 min	17	100	100	100.00	0.00	18	100	100	100.00	0.00	0.00	1
150 min	12	100	100	100.00	0.00	16	100	100	100.00	0.00	0.00	1
165 min	2	100	100	100.00	0.00	13	100	100	100.00	0.00	0.00	1
180 min	2	100	100	100.00	0.00	13	100	100	100.00	0.00	0.00	1

Changes in SPO2 after start of maintenance dose infusion were found to be statistically significant (p=0.006) in group receiving Dexmedetomidine when maintenance dose of infusion was started.

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Effect of study drugs on haemodynamic response. Intraoperatively, 3 patients (7.5%) had hypertension and hypotension in group receiving Dexmedetomidine which was found to be statistically insignificant (p=0.12).

Effect of study drugs on Heart rate. In group Dexmedetomidine, 5 patients (12.5%) had bradycardia and none in group that received midazolam-fentanyl which was found to be statistically significant (p=0.05).

Requirement of Rescue analgesia and sedation among study groups. In our study we found out that, total of 9 patients (22.5%) required rescue doses in the group Midazolam-Fentanyl which was found to be statistically significant (p=0.002).

In the present study, 12.5% patients complained of dry mouth (p=0.05) in dexmedetomidine group and 5% (p=0.05) of patients complained of Nausea in the group that received Midazolam-fentanyl which was statistically significant. And fall in respiratory rate was same in both groups 2.5% (p=1) which was statistically insignificant. In dexmedetomidine group, 2.5% of study population reported vomiting and 5.0% in midazolam-fentanyl combination group (p=1) and it was statistically not significant.

DISCUSSION

Monitored anesthesia care (MAC) is the practice of administrating local anaesthesia in combination with IV sedatives, anxiolytics and/or analgesic drugs during certain surgical procedures. Most of ear surgeries can be done under monitored anaesthesia care. Middle ear surgeries can be performed under local anaesthesia and sedation and can be well tolerated by the patient with minimal discomfort. Although, it has been known that majority of ear surgeries can be carried out under local anaesthesia, only a small number of surgeons feel comfortable using this technique for tympanoplasty. Drilling and manipulation of instruments with long duration of the surgery raises the concern that the patient may not tolerate the noise and discomfort. Most of the patients prefer to have no memory of the surgical procedure, and some form of sedation is necessary. The ideal sedative medication for use during surgery would provide for an easily titratable level of sleepiness, predictable amnesia, and decreased anxiety (anxiolysis), while providing for a rapid recovery with minimal side-effects[1]. Sarmento and Tomita reported that the Retroauricular tympanoplasty under local anesthesia and sedation can be well tolerated by the patient with minimum discomfort[10].

The current study was aimed at comparing, Dexmedetomidine versus combination of midazolam-Fentanyl combination in patients undergoing middle ear surgeries under MAC and to note the efficacy and safety of these in terms of requirement of rescue sedatives and analgesics, impact on hemodynamic parameters, intra or postoperative adverse events and overall patient and surgeon satisfaction.

In this prospective, randomized double blinded study conducted at S.Nijalingappa Medical College and HSK Hospital, Bagalkot, 80 ASA grade I and II patients undergoing various elective middle ear surgeries under monitored anaesthesia care were enrolled and divided

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randomly into two groups of 40 each, standard anaesthetic protocols were applied to both groups.[11]
There was no significant difference in the demographic profile between the patients in the two groups. There is no ideal drug and/or combination of drugs for patients posted for middle ear surgeries under MAC.[12]

There have been several reports on the successful use of Dexmedetomidine as the primary sedative drug for orthopedic, ophthalmic, dental, and plastic surgery, and for diagnostic procedures. Due to its analgesic properties, cooperative sedation and lack of respiratory depression, Dexmedetomidine is increasingly being used as a sedative for monitored anesthesia care. Dexmedetomidine has both sedative and analgesic properties and has been used as a single agent in many painful procedures.[13]

Fentanyl was added in the other group as midazolam has no analgesic properties and this combination is conventionally used for MAC in our setup.

We chose a loading dose of 1μ/kg of dexmedetomidine based on previous literature and studies. Reports suggest that on administration of low or moderate doses and slow rates of infusion of dexmedetomidine, α2 agonist effects are observed but not α1 effect. In view of its short distribution half-life of 5 min Dexmedetomidine necessitates that it to be given as a maintenance infusion. We selected a maintenance dose of 0.6μ/kg/hr, because the surgery was essentially done under local anesthesia. Increasing the infusion rate of dexmedetomidine to maintain desired levels of sedation would also confer additional analgesia and probably reduce the number of rescue fentanyl top-ups in Group Dexmedetomidine. To avoid this we used a fixed maintenance dose. Additional sedatives and analgesics if required were provided using midazolam and fentanyl respectively so that the rescue drugs were common in both the groups. The dose of midazolam 0.06 mg/kg was chosen based on a recent study by Eren *et al.*, that this dose is comparable to dexmedetomidine 1 μg/kg in terms of sedation.[14]

We aimed to compare equivalent doses of both the drugs to avoid any bias in our results. Also, drugs in both the study groups were targeted to a predefined end point (Ramsay score of 3).

The lower pulse rate and SBP, DBP in Group Dexmedetomidine in comparison to the midazolam-fentanyl combination could be explained by the markedly decreased sympathetic activity. Also, intraoperatively Group midazolam-fentanyl had more number of patients who complained of pain which was treated with rescue analgesia. Our findings are similar to other studies where lower HR and MAP were observed in the dexmedetomidine group.
These results suggest that dexmedetomidine has clinical advantage over midazolam in providing a better operative field for microscopic surgery. Durmus *et al.*, have evaluated this property of dexmedetomidine for providing controlled hypotension in general anaesthesia for tympanoplasty cases and concluded that it is a useful adjuvant to decrease bleeding when a bloodless surgical field is required.

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In the present study, Intraoperatively, incidence of decrease in respiratory rate in both study groups found to be statistically insignificant. Dexmedetomidine is unique in that it does not cause respiratory depression because its effects are not mediated by the gamma-aminobutyric system[66]. These findings are similar to other studies. However, Alhashemi *et al*., in there comparative study of dexmedetomidine with midazolam for cataract had observed a higher ventilatory frequency in patients receiving midazolam. They attributed the increased respiratory rate to midazolam causing decreased tidal volume and an increase in the respiratory rate as a compensation to maintain minute ventilation.

Our study demonstrated significantly higher patient and surgeon satisfaction scores with dexmedetomidine suggesting a difference in the quality of sedation of both the drugs[17]. The lower PR, SBP, DBP in these patients could have probably resulted in a better surgical field thus attributing to better surgeon satisfaction. Moreover, surgeons are satisfied if there is no patient movement during surgery. Lesser number of patients receiving dexmedetomidine demanded rescue analgesics as compared to the midazolam-fentanyl group (22.5%). Similar findings have been reported by K. Karaaslan *et al.,* where Group dexmedetomidine used significantly less rescue tramadol in comparison to Group midazolam when both the drugs were compared in FESS and nasal septoplasties. Analgesic property of α2 agonists like dexmedetomidine with its opiate-sparing properties has been documented, and has been reported in studies conducted in general anesthesia with dexmedetomidine. Other studies have also reported better satisfaction scores with dexmedetomidine.[15]

A possible limitation of this study could be that amnesia scoring and cognitive function testing for psychomotor impairment was not done as early discharge of the patients was not a concern of this study. Midazolam has a potent anterograde amnesic effect and dexmedetomidine also results in memory impairment[24]. However, tympanoplasty in our setup is not a daycare procedure, so this issue was not considered as a part of the study. Another limitation could be that the effects of the drugs were seen only in ASA I/II patients. The effects of α2 agonists on the cardiovascular system may be beneficial in high-risk patients. Further studies need to be carried out recruiting high-risk patients.

CONCLUSION

On the basis of the findings of the present study, dexmedetomidine seems to be better for MAC when compared to midazolam-fentanyl combination. Dexmedetomidine provides a calm patient with better intra and post operative analgesia, reducing need of rescue sedation and analgesic requirement in patients undergoing tympanoplasty under local anaesthesia leading to increased satisfaction of both patient and surgeon. However haemodynamic parameters and adverse effects like dry mouth, bradycardia are need to be closely monitored.

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