COMPARISON BETWEEN DEXMEDETOMIDINE AND A COMBINATION OF MIDAZOLAM AND FENTANYL FOR SEDATION DURING AWAKE FIBEROPTIC INTUBATION - A PROSPECTIVE RANDOMIZED PARALLEL GROUP DOUBLE-BLINDED STUDY

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ABSTRACT

BACKGROUND

Peter Murphy, in England, in 1965 used a fiberoptic choledocosope to intubate nasally a patient with Still's disease**.** Fiberoptic nasotracheal intubation is one of the techniques available for the management of patients with difficult airways.

This study compares the effectiveness and safety of dexmedetomidine with a combination of fentanyl and midazolam for procedural sedation during awake fiberoptic intubation.

MATERIALS AND METHODS

This was a single centre, prospective, randomised, parallel group, double-blinded study. To compare the effectiveness and safety of dexmedetomidine with a combination of fentanyl and midazolam for procedural sedation during awake fiberoptic intubation. Data was analysed using Sigma Stat 3.5 version.

RESULTS

This study shows that dexmedetomidine is a safe and highly efficacious drug in providing sedation, amnesia, anxiolysis, analgesia, better haemodynamics without producing respiratory depression for awake fiberoptic intubation.

CONCLUSION

We conclude that ease of intubation, cough suppression, comfort score and sedation scale were better with Dexmedetomidine.

KEY WORDS

Fiberoptic Bronchoscope, Dexmedetomidine, Fentanyl, Midazolam.

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BACKGROUND

Peter Murphy, in England, in 1965 used a fiberoptic choledocosope to intubate nasally a patient with Still's disease**.** Fiberoptic nasotracheal[1] intubation is one of the techniques available for the management of patients with difficult airways. Fiberoptic and video technologies are widely used for airway management at recent times. Awake Fiberoptic Intubation (AFOI)[2] is indicated for patients with anticipated difficult airways because of their anatomy, airway trauma, morbid obesity and unstable cervical spine injuries. This[3] procedure is providing adequate sedation and anxiolysis while maintaining a patent airway and adequate ventilation, especially with difficult or critical airways. Hence, there is need for an ideal sedation regimen which would provide patient comfort, blunting of airway reflexes, patient cooperation, haemodynamic stability, amnesia and maintenance of a patent airway with spontaneous ventilation. This study compares the effectiveness and safety of dexmedetomidine with a combination of fentanyl and midazolam for procedural sedation during awake fiberoptic intubation.

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MATERIALS AND METHODS

Based on the previous study, 40 adult patients of both sexes within the age group of 25 to 50 years belonging to ASA 1 and 2 physical health status undergoing thyroid surgery were taken for convenience. This study was conducted in Govt. Dharmapuri Medical College, Dharmapuri from 2014 - 15. This was a single centre, prospective, randomised, parallel group, double-blinded study. To compare the effectiveness and safety of dexmedetomidine with a combination of fentanyl and midazolam for procedural sedation during awake fiberoptic intubation. Ethical Committee clearance was duly obtained from the hospital.

They were randomised using computer generated random numbers and allocated into two groups, Group D and Group FM as follows-

Group D: Received 1 mcg/kg of Dexmedetomidine administered over 10 mins followed by infusion dose of 0.7 mcg/kg/hr.

Group FM: 2 mcg/kg of Fentanyl with 40 mcg/kg of midazolam over 10 mins followed by an infusion of normal saline.

The study was carried out in a double-blinded fashion. The patients on whom study was conducted were blinded and they did not know what drug they were administered.

The drugs, both for bolus administration and infusion was prepared by an anaesthesiologist who was not involved in the study and hence the investigator who conducted the study was also blinded.

Inclusion Criteria

1. Age: > 25 years < 50 years.
2. ASA (American Society of Anaesthesiologists) 1 and 2 patients.
3. BMI: 20 - 30.
4. Patients undergoing thyroid surgery with euthyroid status.

Exclusion Criteria

1. Patient refusal.
2. Emergency surgeries.
3. Difficult airway.
4. Coagulopathies or any bleeding disorder.
5. Fracture base of skull.
6. Ischaemic heart disease/ Valvular heart disease/ arrhythmia or any conduction abnormalities.[4]
7. Known hypersensitivity to any of the study drugs.
8. Raised intracranial pressure.
9. Uncontrolled seizure disorder.
10. Known psychiatric illness receiving treatment in the past two weeks, where either dexmedetomidine or benzodiazepine administration is contraindicated.
11. Heart rate < 50 bpm and Systolic blood pressure < 90 mmHg.
12. Patients with respiratory system disorders, renal disorders and liver disorders.

Procedure

After pre-anaesthetic evaluation,[5] the more patent nostril (right or left sided) was identified. Inj. Glycopyrrolate 0.2 mg intramuscularly was given as premedicant 45 mins before the procedure. Nasal and oral part of airway was anaesthetised by means of nasal packing and oral gargling with 4% Lignocaine, 15 mins before the start of procedure.[6] Nasal packing was done with 4 cotton pledgets soaked in 4 mL of 4% Lignocaine mixed with adrenaline (1: 200000 dilution), two each for both the nostrils. Oral gargling was performed with 2 mL of 4% lignocaine. IV infusion of ringer lactate was started in the non-dominant arm after securing intravenous access. ECG, NIBP, SpO_2 monitors were connected to the patient and $ETCO_2$ after intubation. Anaesthetist who is experienced and well trained with fiberoptic scope and a skilled technician was called for and made ready in case if any help is needed. Fiberoptic scope, light source and appropriately sized endotracheal tubes were kept ready. All the components of Boyle's checklist were verified and ensured that nothing is missed before administering the drug.

Baseline heart rate, BP, SpO2 were recorded and noted down after which the bolus drug,[7] Dexmedetomidine or Fentanyl and midazolam based on the group was administered over 10 minutes followed by infusion. Sedation level was graded as 1, 2, 3 and 4. Intubation commenced when sedation level reached grade 2. Local anaesthetic was sprayed as the fiberoptic scope went past the oropharynx, after the glottis was visualised. Time taken for[8] intubation, ease of intubation and comfort scores of the patient were noted down. Haemodynamic variables like heart rate, SpO2, systolic BP, diastolic BP, mean arterial pressure and respiratory rate were noted at the end of intubation, 6th, 8th and 10th minute after the procedure. After which patients were observed for the following secondary outcomes.

Statistical Analysis

Data was analysed using Statistical Package for Social Science Sigma Stat 3.5 version (2012). Using this software frequencies, percentage, mean and standard deviation was calculated by Student's 't' test and Chi-square test. The comparison of proportion was calculated using independent 't' test. The P value of < 0.05 was taken as significant.

RESULTS

Group	Mean	SD	P value	T value
Fent and Midaz	36.6	13.03	0.513	0.66
Dexmed	39.2	11.85		

Table 1. Showing the Mean, Standard Deviation, P and T value regarding to Age

The age incidence of our study belonged to patients of all ages in the range of 25 to 50 years as shown in Table 1 with mean falling in the mid-range.

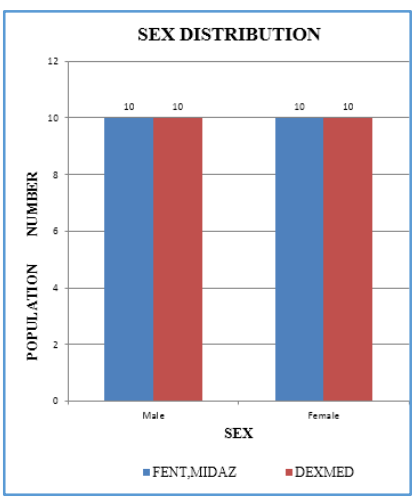

Figure 1. Comparison of Sex distribution between the Two Groups

The male and female populations of our study was distributed equally with ten in each group and in each category.

Group	Mean	SD	P value	T value
Fent and Midaz	62.45	13.14	0.783	0.278
Dexmed	63.75	16.28		

Table 2. Comparison of Weight distribution between Two Groups

Group	Mean	SD	P value	T value
Fent and Midaz	22.46	4.38	0.587	0.548
Dexmed	23.28	5.05		

Table 3. Comparison of BMI distribution between Two Groups

Group	Mean	SD	P value	T value
Fent and Midaz	165.5	5.79	0.672	0.426
Dexmed	164.65	6.77		
Total				

Table 4. Comparison of Height distribution between Two Groups

The difference in height, weight and BMI of the study population between the two study groups were comparable, but not statistically significant.

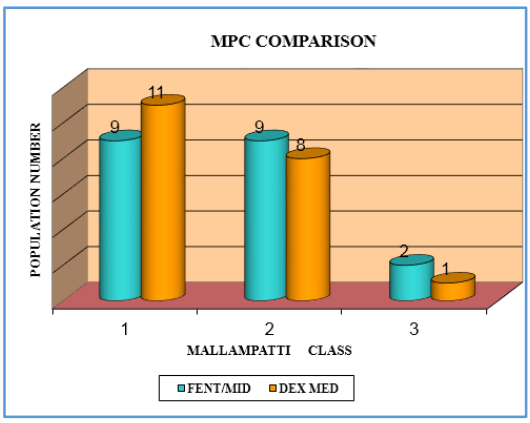

Figure 2. Comparing the distribution of Population based on their Mallampati Airway Class

Fifty percent of the population in our study group belong to Mallampati class 1, above 40 percent to class 2 and remaining to class 3. None of our study population belonged to Mallampati class four airway.

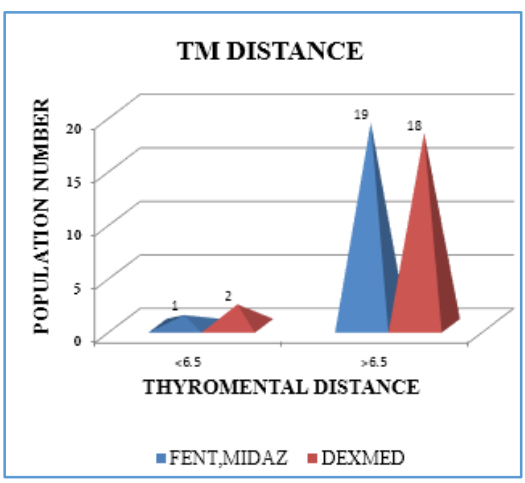

Figure 3. Comparing the distribution of Population based on Thyromental Distance

Over 90 percentage of our population had TMD > 6.5.

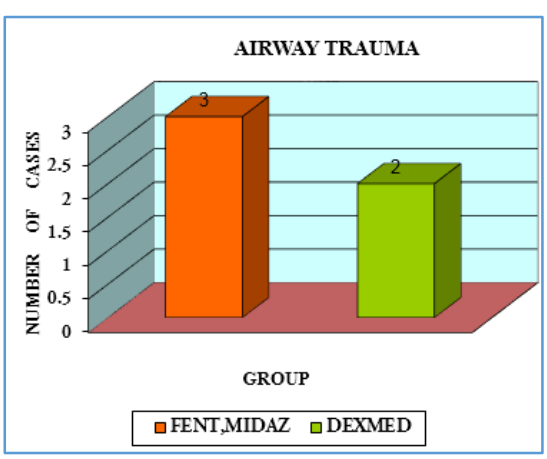

Figure 4. Comparing the Incidence of Airway Injury between the Two Groups

Ninety five percent and ninety percent of the population did not have Airway trauma in Group D and Group FM respectively.

Statistical Significance existed between Two Groups in terms of-

- Intubation time in seconds.
- Sedation scale.
- Comfort score.
- Haemodynamic variables.

Group	Mean	SD	P value	T value
Fent and Midaz	1.55	0.76	0.005	2.97
Dexmed	2.15	0.49		

Table 5. Comparison of Sedation Scale between Two Groups

Dexmedetomidine group had a better sedation score when compared with fentanyl midazolam group. The sedation score was adequate providing the patient with anxiolysis and a good conscious sedation with amnesia as well.

Group	Mean	SD	P value	T value
Fent & Midaz	20.87	4.27	<0.001	4.45
Dexmed	15.92	2.56		

Table 6. Comparison of Intubation Time between Two Groups

Except for 3 patients, the intubation time was less in dexmedetomidine group when compared with fentanyl-midaz group with statistical significance (P value being <0.001).

Group	Mean	SD	P value	T value
Fent and Midaz	15.95	1.73	< 0.001	9.82
Dexmed	11.3	1.22		

Table 7. Showing the Comparison of Comfort Score between Two Groups

Dexmedetomidine group patients were better comfortable with the procedure than fentanyl midazolam group. Comfort score was calculated out of 35 based on 7 entities. Dexmed group had a mean value of 11.3 when compared with fentanyl midazolam group which had a mean value of 15.95 (lower the comfort score, better the patient was).

In case of haemodynamic variables again, dexmedetomidine group patients had better haemodynamic scores than fentanyl midazolam group patients.

Time	Fent and Midaz		Dexmed			
	Mean	SD	Mean	SD	P value	T value
Baseline	84.6	8.78	82.95	11.66	0.616	0.505
Before intubation	83.5	6.76	81	7.64	0.28	1.09
After intubation	115.4	9.03	101.9	9.39	<0.001	4.63
6th min	103.9	11.36	94.25	9.65	0.006	2.89
8th min	95.55	8.13	89.55	7.84	0.023	2.37
10th min	85.2	10.47	82.4	7.79	0.343	0.96

Table 8. Comparison of Pulse Rate Scores between Two Groups

Pulse Rate Distribution

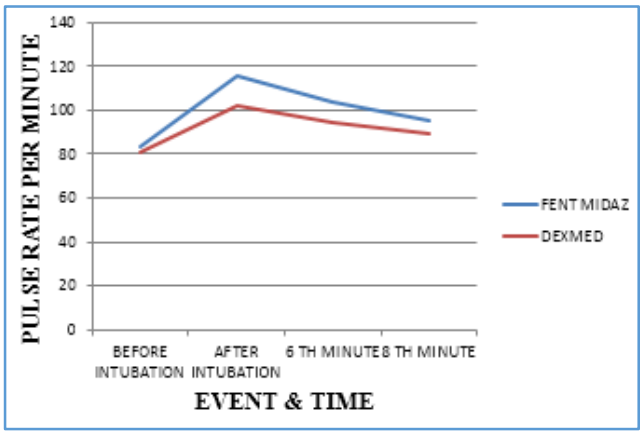

Figure 5. Line Graph showing Pulse Rate Variations among Two Groups

After intubation, 6th and 8th minute pulse rate scores were statistically significant with P value being < 0.001, 0.006, 0.023 respectively.

Time	Fent, Midaz		Dexmed			
	Mean	SD	Mean	SD	P value	T value
Baseline	125.8	16.72	126.05	13.97	0.959	0.051
Before intubation	119.75	15.01	124.35	14.05	0.323	1.001
After intubation	149.25	12.47	140.95	15.01	0.065	1.902
6th min	142.6	14.73	133.75	12.37	0.047	2.06
8th min	131.4	17.03	129.9	9.86	0.744	0.329
10th min	122.75	20.79	126	13.33	0.562	0.586

Table 9. Comparison of Systolic BP Scores between Two Groups

Systolic BP Distribution

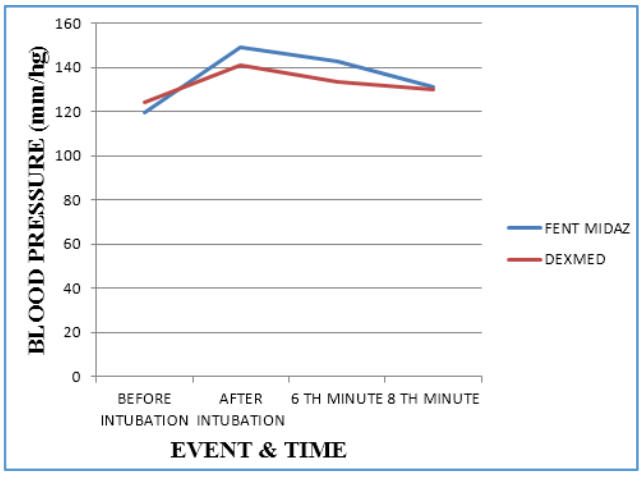

Figure 6. Comparing Systolic BP variations between Two Groups

After intubation and 6th minute scores were statistically significant.

Time	Fent, Midaz		Dexmed			
	Mean	SD	Mean	SD	P value	T value
Baseline	81.9	13.56	78.3	10.33	0.351	0.945
Before intubation	76.9	11.25	77.35	12.99	0.907	0.117
After intubation	93.55	13.97	85.8	9.6	0.037	2.16
6th min	89.3	13.45	80.8	11.15	0.036	2.17
8th min	85.6	12.83	79.75	9.78	0.113	1.62
10th min	79	15.54	75.65	10.06	0.424	0.809

Table 10. Comparison of Diastolic BP Scores between the Two Groups

Diastolic BP Distribution

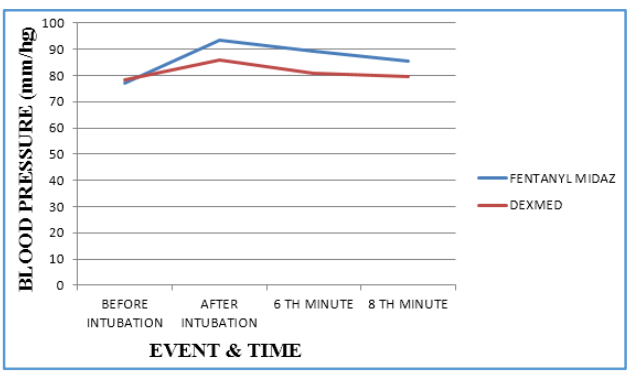

Figure 7. Comparing Diastolic BP variations between the Two Groups

After intubation and 6th minute scores were statistically significant with P value being 0.037 and 0.036 respectively.

Time	Fent, Midaz		Dexmed			
	Mean	SD	Mean	SD	P value	T value
Baseline	96.5	15.02	92.3	21.84	0.483	0.709
Before intubation	91.3	11.92	95.4	14.01	0.325	0.997
After intubation	116.55	14.45	105.5	12.5	0.014	2.58
6th min	109.6	15.86	99.2	11.5	0.023	2.37
8th min	101.4	15.56	97.9	9.09	0.39	0.869
10th min	93.65	18.37	93.6	10.04	0.992	0.011

Table 11. Comparing MAP (Mean Arterial Pressure) between the Two Groups

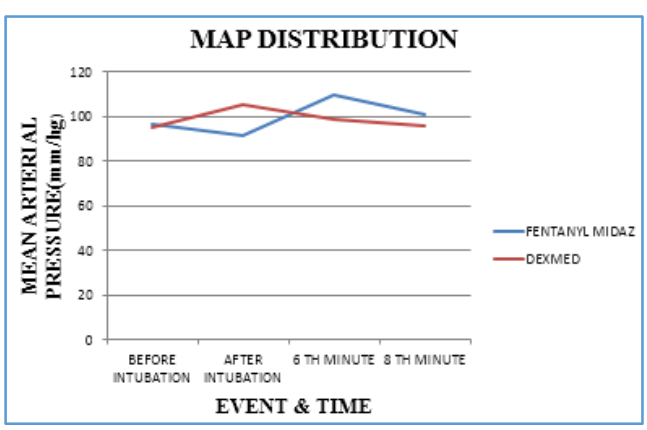

Figure 8. Comparing MAP variations between Two Groups

After intubation and 6th minute values were significant with P value being 0.014 and 0.023 respectively.

Time	Fent Midaz		Dexmed			
	Mean	SD	Mean	SD	P value	T value
Baseline	100		100		1	
Before intubation	100		100		1	
After intubation	97.5	2.67	99.2	1.74	0.022	2.38
6th min	99.4	0.41	99.85	0.49	0.003	3.15
8th min	100		100		1	
10th min	100		100		1	

Table 12. Comparison of SpO_2 Scores between the Two Groups

SPO_2 Distribution

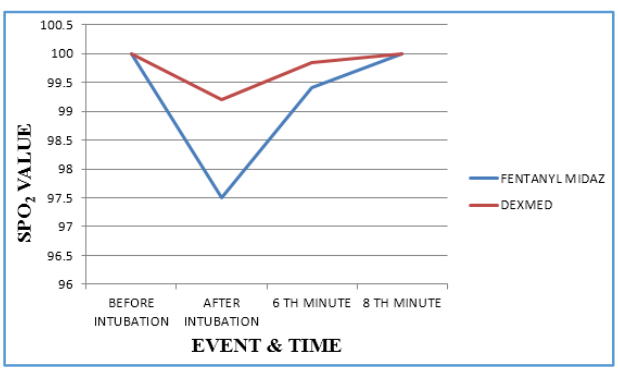

Figure 9. Showing SpO_2 variations between Two Groups

After intubation and 6th minute were statistically significant with P value being 0.022 and 0.003 respectively.

DISCUSSION

Awake fiberoptic intubation,[9] one of the modalities in difficult airway management is an unpleasant procedure which definitely needs an ideal sedative regimen satisfying patient in all aspects by providing adequate analgesia, amnesia, anxiolysis, anti-sialogogue, better respiratory and haemodynamic parameters.[10] Fentanyl midazolam combination may provide adequate analgesia, amnesia, anxiolysis but is known to produce apnoea and hypoxaemia even in healthy volunteers. But dexmedetomidine,[11] a recently introduced drug, an alpha-2 adrenoreceptor agonist seems to be satisfying all the patient's needs in all aspects.

In view of existing controversies and lack of consensus in previous literatures, this study was carried out over a one year period with the principal aim of comparing dexmedetomidine[12] alone with fentanyl-midazolam combination as an ideal agent for providing sedation for AFOI. In this study, we have shown that Dexmedetomidine[13] convincingly is a superior and better drug in terms of providing sedation for awake fiberoptic intubation in all aspects. The plane of sedation provided by this drug was excellent such that it neither produced a deep sedation making the patient well asleep depressing his respiration nor a superficial plane where the patient is anxious and agitated. It was an intermediate plane where the patient was conscious, responding to commands, calm with better haemodynamics and respiratory parameter.

Quoting other's literature, Bergese et al in his study has shown that patients belonging to dexmedetomidine group were more satisfied and comfortable than the midazolam group. Further, in our study dexmedetomidine group patient had better comfort score when compared with fentanyl midazolam group.[14] Comfort score was calculated based on 7 parameters which were calmness, alertness, crying, physical movement, respiratory response, facial tension and muscle tone. The lower the score, the better the patient was.

Also, the patients belonging to dexmedetomidine group had less airway trauma when compared with fentanyl midazolam indicating Group D patients were better prepared for the procedure. Intubation time in dexmedetomidine group patients was faster when compared with fentanyl midazolam group, which tells that Group D patients were easier to intubate as they were more cooperative and calmer.

Dexmedetomidine group patients also had better haemodynamics when compared with fentanyl and midazolam group. Further Dexmedetomidine group had better respiratory parameters in terms of SpO2.[15] Midazolam especially in combination with fentanyl is known for its respiratory depression and decrease in SpO2, whereas dexmedetomidine group has respiratory sparing effect even in high doses. Bailey et al too had quoted in his literature that fentanyl and midazolam combination produces respiratory depression and hypoxia. Kamibyashi et al has quoted that dexmedetomidine[16] has additional antisialagogue effect making intubation easier and intubation time shorter.

Study	Inference
Bailey et al	Fentanyl and midazolam use has produced significant hypoxia and apnoea even in healthy adult volunteers.
Bergese et al	Dexmedetomidine group patients were more calm, cooperative and satisfied when compared with others.
Tsai et al	Respiratory depression is lesser with dexmedetomidine group when compared with propofol group.
Avitsian et al	Dexmedetomidine had better intubating conditions in patients with cervical spine injury.
Chu et al	In oral cancers for whom intubation was difficult, dexmedetomidine was very much efficacious.
Bloor et al	Dexmedetomidine has a biphasic blood pressure response, initial hypertension due to vasoconstriction of peripheral vessels.

Table 13. Comparison of Similar Studies

CONCLUSION

We conclude that dexmedetomidine is a safe and highly efficacious drug in providing sedation, amnesia, anxiolysis, analgesia, better haemodynamics without producing respiratory depression for awake fiberoptic intubation. We also conclude that ease of intubation, cough suppression, comfort score and sedation scale was better with dexmedetomidine.

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