ORIGINAL ARTICLE

Comparative Study Between Dexmeditomidine and Midazolam for Prevention of Emergence Agitation After Nasal Surgery

Rukhsar Shaw, Arti Mahajan, Rajdeep Kour, Anjali Mehta, Renu Wakhloo

Abstract

Background Emergence agitation (EA) is a common complication that develops in the postanaesthesia care unit (PACU). It usually occurs between initial 30 and 60 minute following emergence from anaesthesia and may lasts upto 45 min to 48 hour in extreme cases. **Aims and Objective** Objective of the study was to compare incidence of emergence agitation, hemodynamic parameters, sedation score between dexmedetomidine and midazolam after nasal surgeries. **Material & Methods** This prospective, comparative study was conducted in 60 patients of age 18-60 years, ASA grade I and II scheduled for elective nasal surgeries. Patients were randomly divided into two groups: Group D received injection Dexmedetomidine- loading dose of 0.5mcgm/kg i.v over 15 minutes and then 0.1 mcg/kg/hour i.v as maintenance infusion Group M received injection Midazolam.- loading Dose 0.05mg/kg i.v over 15 minutes and then 0.05 mg/kg/ hour i.v as maintenance infusion. **Results** There was no significant difference in sex, age, height and weight of the patients between two groups ($p>0.05$). Incidence of agitation was more in group M (43.33%) as compared to group D (23.33%) but the difference was statistically insignificant ($p = 0.110$). Maximum no. of patients in Group D had Riker Sedation- Agitation Scale (RSAS) score 4 which was taken as ideal with no agitation and drowsiness as compare to group M. There was no significant difference in MAP in both groups, the incidence of hypotension and decrease in heart rate was more in group D as compare to group M **Conclusion** Midazolam and Dexmeditomidine were comparable when given as infusion for prevention of emergence agitation after nasal surgeries.

Key Words

Dexmeditomidine, Midazolam, Emergence Agitation (EA), Nasal Surgeries

Introduction

Emergence agitation (EA) is defined as state of mental confusion, agitation, and disinhibition manifesting as hyperexcitability, restlessness, hallucinations, irritability, disorientation, confusion, inconsolable crying and abnormal violent movement that may result in serious complication and morbidity during emergence from general anesthesia. [1] It may also cause complications such as hypoxia, aspiration pneumonia, re-operation although the exact pathogenesis is not clearly understood, the precipitating factors are supposed to be preoperative anxiety, postoperative pain, use of sevoflurane anesthesia and post traumatic stress disorder.[2] ENT (ear, nose, and throat) surgical procedures have a higher incidence of emergence agitation in both adults and children.[3]

Premedication with benzodiazepines, longer duration of surgery, breast surgery and abdominal surgery are also important risk factors for EA [4,5] nasal packing is also

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trigger to emergence agitation.Different medication agents such as anesthetic drugs, benzodiazepine and alpha2 agonist are proven to attenuate the EA with different efficiencies. Drugs that have potent analgesic effects (fentanyl, remifentanil, and nefopam) or an analgesic with a sedative effect (ketamine and dexmedetomidine) help to prevent EA after general anesthesia.[6] Various agents including ketamine, propofol, clonidine, opioids, etc., have also been used to prevent EA. However, these medications may increase sedation after anaesthesia, and associated side effects such as nausea and vomiting. Benzodiazepines like midazolam when given single bolus dose as premedication is not effective in preventing EA due to its short half-life.[7] Midazolam given as bolus dose at the end of surgery is helpful in preventing agitation.[8]

Dexmedetomidine is a selective alpha2 adrenoceptor agonist. It has sedative, hypnotic, anxiolytic, analgesic and sympatholytic properties without significant respiratory depression. It was proved to reduce the Emergence agitation in children. [9] Midazolam and Dexmedetomidine have been compared for various clinical parameters but not for their efficacy in prevention of EA in adults.

- Primary outcome of study was to compare the efficacy of Dexmedetomidine and Midazolam for prevention of emergence agitation after nasal surgeries.
- Secondary outcome were to compare perioperative hemodynamic parameters, sedation score and emergence in the two study groups.

Material and Methods

After obtaining approval from institutional ethical committee, the study was conducted in the Department of Anesthesiology and Intensive care GMC jammu.60 patients between 18 and 60 years of age of ASA physical Status I and II of either sex posted for elective nasal surgeries with nasal packing on each side were included in the study. Patients with ASA Physical Status III and above, psychiatric illness and anxiety disorder, history suggestive of post-traumatic stress disorder, obstructive sleep apnea, Pregnant patients and emergency surgeries were excluded. An informed written consent was taken from all the patients and Pre-anesthetic check-up was done one day before surgery which includes detailed history, thorough physical and systemic examination and relevant investigations.

Anesthetic Technique

All the patients were kept fasting for 8 hours and premedication with injection glycopyrolate 5mcg/kg i/m was given 45minutes before induction. In the operating room intravenous infusion with Ringer Lactate was started and standard monitoring was done which included ECG, HR, SPO2, NIBP. Patients were randomly divided into two groups:

Group D received injection Dexmedetomidine- loading dose of 0.5mcg/kg i.v over 15 minutes and then 0.1 mcg/kg/hour i.v as maintenance infusion

Group M received injection Midazolam.- loading Dose 0.05 mg/kg i.v over 15 minutes and then 0.05 mg/kg/hour as maintenance infusion.

Both the groups received infusion through syringe pump. For Group D, loading dose of 0.5mcg/kg and 0.1 mcg/kg/hour as maintenance so 100 mcg of Dexmedetomidine was mixed with normal saline to total volume of 50 ml. For Group M, loading Dose 0.05 mg/kg and 0.05 mg/kg/hour as maintenance, so 5 mg of Midazolam was mixed with normal saline to total volume of 50 ml. All Patients received injection Ondansetron 4 mg i.v stat as prophylaxis for nausea-vomiting. Once loading dose was started, injection Tramadol 1mg/kg i.v was given, patients were preoxygenated for 5 min and induced with injection Propofol 2 mg/kg i.v and injection Succinylcholine 1.5mg/kg i.v and intubation was done with appropriate size endotracheal tube. Anaesthesia was maintained with Oxygen, Nitrous Oxide (30%:70%) and Halothane and neuromuscular blockade was maintained with injection Vecuronium 0.1mg/kg i.v.

Infusion was started by an independent investigator who was not a part of anaesthetic management. Time of start of infusion was noted and HR, SBP, DBP, MAP were noted at 5, 15 & 30 min and every 10 minutes thereafter from start of infusion till the end of surgery. Fall in MAP of more than 20% of baseline value was taken as hypotension and treated with boluses of injection Mephenteramine and intravenous fluids. HR <50/min was taken as bradycardia and was treated with 0.6 mg of Injection Atropine. Total numbers of episodes of bradycardia were noted. Infusion and inhalational agent both were stopped at end of surgery. Injection Neostigmine 50mcg/kg i.v and injection Glycopyrolate 10mcg/kg i.v were used as reversal agent. Time of eye opening on verbal Commands was taken as time of consciousness and was noted after discontinuation of infusion. Duration of 5 min from the time of regaining of consciousness was taken as emergence.

Patients were monitored as per Riker Sedation- Agitation Scale (RSAS).

Score 1 -Unarousable to noxious stimuli

Table 1. Patient Criteria & Anaesthetic Details

Parameter	Group D	Group M	P
Age (years)	38.4±10.97	36.3±12.66	0.441
Weight(kg)	62±7.4	59.77±9.29	0.137
Height (cm)	161.73±8.2	159.03±6.81	0.17
Sex (Male/Female)	20/10	16/14	0.292
Duration of surgery (minutes)	66.83±16.43	66±15.78	0.97
Duration of infusion (minutes)	76.17±16.7	76±15.78	0.875
Duration of inhalational (minutes)	76±16.84	76±16.18	0.84
Eye Opening (min) median±SEM	8.27±0.78	9.77±0.77	<.0001
Emergence agitation (%)	7(23.33%)	13(43.33%)	0.110
Drowsiness	5(16.67%)	7(23.335)	0.110

Table 2. Emergence Agitation Score

Emergence agitation Score	Group D (n=30)	Group M (n=30)	Total	P value
2	2 (6.67%)	3 (10%)	5 (8.33%)	0.270
3	3 (10%)	4 (13.33%)	7 (11.67%)	
4	18 (60%)	10 (33.33%)	28 (46.67%)	
5	5 (16.67%)	6 (20%)	11 (18.33%)	
6	2 (6.67%)	4 (13.33%)	6 (10%)	
7	0 (0%)	3 (10%)	3 (5%)	
Mean ± SD	4.07 ± 0.91	4.43 ± 1.43	4.25 ± 1.2	0.3
Median(IQR)	4(4-4)	4(4-5)	4(4-5)	
Range	2-6	2-7	2-7	

Table 3. Hemodynamic Characteristics

Parameter (median±SEM)	Group D	Group M	P
MAP baseline	85.8±9.31	87±10.6	0.643
MAP 5 min	83.37±8.86	86.33±11.54	0.268
MAP 15 min	82.4±9.32	86.03±11.09	0.174
MAP 30 min	81.63±9.43	84.9±10.15	0.201

Score 2 -Very Sedated, responds to painful Stimuli but not to verbal commands

Score 3 -Sedated, awakens with commands or gentle touch but drifts off again,

Score 4 -Calm and quiet, easily arouses with verbal commands and communicates,

Score 5 - Anxious with mild agitation but calms down on verbal commands,

Score 6 - Very agitated and requires physical restraint,

Score 7 -Dangerous agitation, pulling of intravenous cannula, thrashing side to side.

Score at emergence was noted and then was monitored for every 5 min upto 30 min and then every 15 min for next 90 min.

Score of 5 and above was taken as agitation.

Score of 3 and below was taken as drowsiness.

Score of 4 was taken as ideal with no agitation and drowsiness.

All the observations made in the study were recorded at different time periods and compared for each parameter in the group.

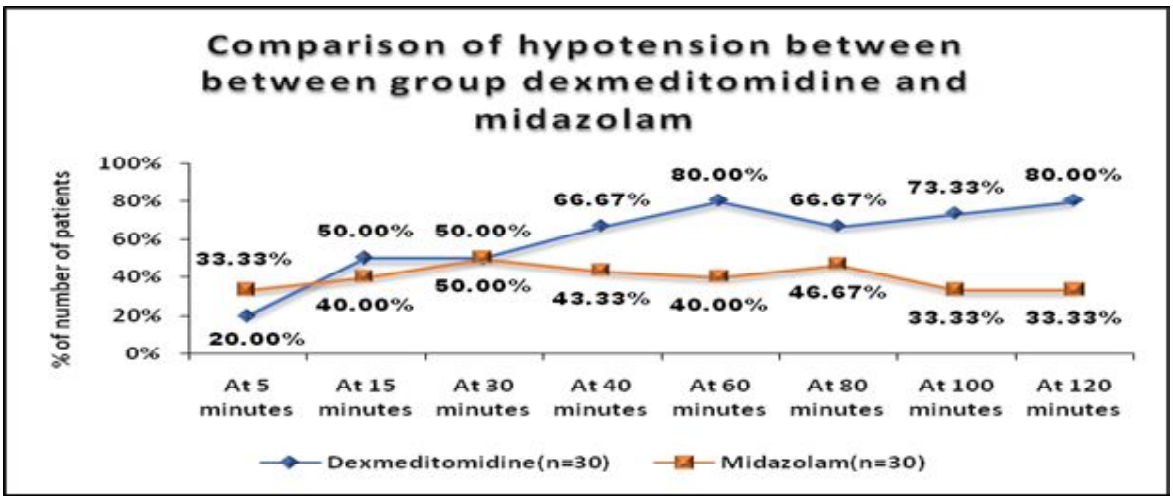
Results

The statistical analysis was done using statistical package for social sciences (SPSS) for Windows, version 23, Armonk, NY: IBM corporation and its licensors 2015. The distribution of data was analyzed with Shapiro-Wilk test. Normally distributed data such as patient's characteristics and duration of infusion were analyzed

with independent t-test and data were expressed as mean ± standard deviation. Abnormally distributed parameters such as recovery time, agitation scores, MAP, and HR at different times were analyzed using Mann-Whitney U-test and were expressed as median ± standard error of mean (SEM). Incidence of agitation between two groups was compared with Chi-square test and data were expressed as frequency and percentage. p value <0.05 was considered statistically significant for two-sided test.

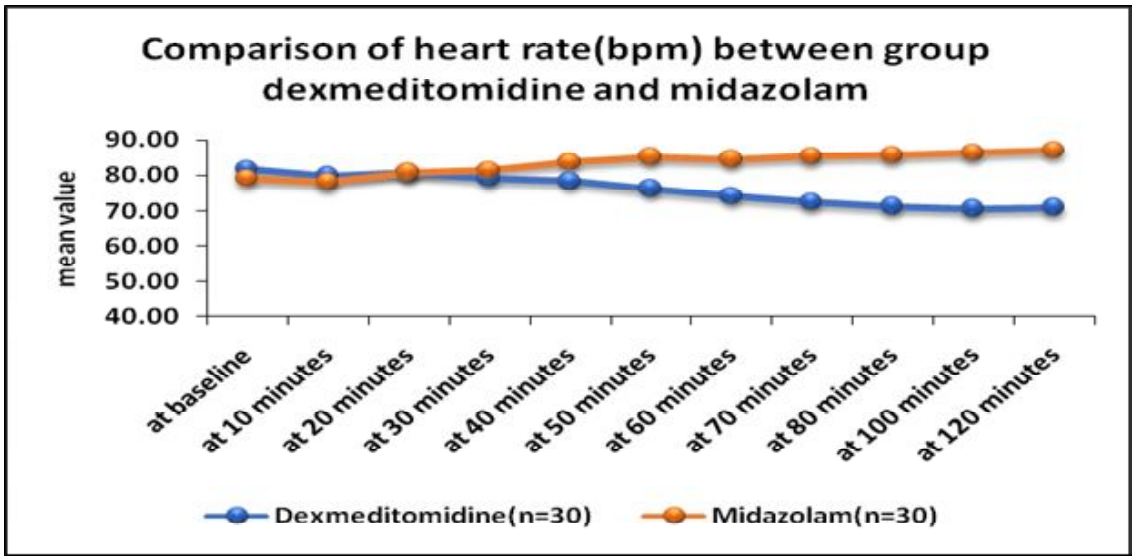
The patient's criteria were comparable. Total duration of surgery (p=0.97), duration of infusion (p=0.875), and inhalational agent (p= 0.84) were comparable between two groups. Time taken for eye opening after discontinuation of infusion was similar in both groups (p= <.0001). Incidence of agitation was more in group M (43.33%) as compared to group D (23.33%) , Incidence of drowsiness was also more in group M (23.33%) than group D (16.67%). However, this difference was statistically insignificant (p = 0.110).

Fig 1. Incidence of hypotension



Maximum number of patients in Group D had scored 4 and in Group M score of 5 at emergence. Score of 7 was noted in three patients in Group M while no patient in Group D had score of 7.

Fig. 2: Heart Rate.



There was no significant difference between MAP median values during 30 min of infusion in both groups. The numbers of hypotensive episodes were more in Group D. The percent of patients going for hypotensive episodes at different time intervals was significantly higher with dexmedetomidine than midazolam.

The fall in HR was more in Group D than Group M but difference was not statistically significant. However, there

was no episode of bradycardia in either group.

Discussion

According to Lee *et al* [10] Emergence agitation is especially common after ENT surgery, where 55.4% of patients experienced agitations as nasal operative procedures are stressful and involved severe sympathetic stimulation. According to Kim *et al* [11] agitation may be related to various risks including self extubation or removal of catheters, which can cause serious complications, such as hypoxia, aspiration pneumonia, bleeding and reoperation. Although pain is not the only factor creating agitation it is one of the major factors that increases the severity and frequency of agitation. High incidence of emergence agitation after ENT surgery may be attributable to a sense of suffocation which is caused by procedures such as nasal packing. In our study, we only included patients who were expected to have a higher risk of emergence agitation for the following reasons: the patient required each side nasal packing, a tracheal intubation was done and inhalation anaesthetics were administered.

Dexmedetomidine induces sedation and analgesia without respiratory depression. Therefore, it has been used for preventing emergence agitation. Kim S Y *et al*.[11] found that intraoperative administration of dexmedetomidine reduced emergence agitation in children by 57-70% compared with control groups. Consistent with our results, dexmedetomidine was also effective in reducing emergence agitation in adults.

Kurhekar *et al* [12] stated that Dexmedetomidine is highly selective alpha 2 agonist which is proven effective in prevention of emergence agitation due to its analgesic and sedative properties which result from effect of dexmedetomidine on central alpha 2 receptors in locus coeruleus where as Midazolam acts on gamma-aminobutyric acid receptors and this inhibition is the reason for its role in prevention and treatment of emergence agitation.

Study done by Kim *et al* [13] in adult nasal surgeries has proved that dexmedetomidine infusion reduces incidence of emergence agitation by 50% as compared to placebo. Whereas in study done by Kurhekar *et al* [12] the incidence of emergence agitation in dexmedetomidine group was 28%, but there was no difference in number of patients having RSAS score 7 between groups and in our study, incidence of emergence agitation in dexmedetomidine group was similar, however no patient in dexmedetomidine group had RSAS score 7 as compare to 3 patients in midazolam group.

In a study done by KIM *et al*.[11] the protocols for dexmedetomidine administration were diverse e.g. only loading of 0.5 mcg/kg was given or only infusionof 0.2 mg/kg/ hour was given, or loading of 2mcg/kg was given which was followed by infusion of 0.7 mg/kg/hour. In our study we administered a loading dose of 0.5 mcg/ kg slowly over 15 min followed by continuous infusion of 0.1 mcg/ kg/hour. Intraoperative MAP and HR tended to be lower in Group D compared to Group M but difference was not statistically significant. Furthermore, incidence of hypotension that required mephenteramine treatment was not different between the groups and none of the patients in both groups had bradycardia. Where as, when dexmedetomidine was compared to midazolam, in study done by Kurhekar *et al.* [12] found that there was a significant fall in HR and MAP with dexmedetomidine at infusion rate of 0.1 mcg/kg. Our results are similar to them with more number of hypotensive episodes with dexmedetomidine.

Riker *et al* [14] noted that there was fall in HR with both midazolam and dexmedetomidine but more with dexmedetomidine which is similar to our findings. In our study, fewer patients developed emergence agitation and the severity of agitation was also significantly lower in the dexmedetomidine group as compared to that in midazolam group.

We feel that in the present study dexmedetomidine group was clinically better in many ways in prevention of emergence agitation. First, the maximum number of patient in dexmedetomidine had ideal score of 4. Second, no patient in dexmedetomidine group reached level of dangerous agitation score 7. Third, no patient had agitation in PACU after emergence was over. In our study, fewer patients developed emergence agitation and the severity of agitation was also significantly lower in the dexmedetomidine group as compared to midazolam.

The incidence of emergence agitation varies in different studies according to the researcher and the criteria used. In our study we used the Ricker sedation-agitation scale the criteria used by Khurshid *et al*.[15] the incidence of emergence agitation in the Midazolam group in our study is 43.33%, which is almost similar to the study done by Khurshid *et al* [15]. Kim HJ *et al.* [13] studied several risk factors for emergence agitation including age, sex, use of inhalational anaesthetics, type of surgery, postoperative pain, presence of tracheal tube, presence of a urinary catheter. To remove any bias in our study, we have taken adult patients with statistically insignificant gender ratio, used the same inducing agents,

maintenance agents (except for the study drug), analgesia in all patients in both the groups. All patients underwent nasal surgery with bilateral nasal packing in the postoperative period, all patients were intubated.

The incidence of emergence agitation was lower in the dexmeditomidine group than midazolam group (23.33% vs 43.33%, p=0.110). In agreement with these results, the results of our study suggest that intraoperative continuous dexmeditomidine infusion until extubation was effective in reducing the incidence of emergence agitation after nasal surgery without delay of extubation or increasing the incidence of other complications as compared to Midazolam infusion.

Conclusion

Both Dexmeditomidine and Midazolam are effective in reducing emergence agitation after nasal surgeries. The maintenance of infusion until extubation provides lower incidence of emergence agitation, smooth and hemodynamically stable emergence without complications. Also perioperative analgesia and anaesthesia requirement was reduced. In our study risk of emergence agitation in dexmeditomidine was 23.33% as compared to Midazolam 43.33%, but difference was statistically insignificant. There was no significant difference between two groups comparing MAP median values during 30 min of infusion, heart rate and emergence agitation score. Hence we concluded that Midazolam given as infusion is comparable to Dexmedetomidine for prevention of emergence agitation after nasal surgeries.

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Conflicts of Interest

There are no conflicts of interest.

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