Original Article

Effect of dexmedetomidine on emergence agitation in male patients undergoing closed reduction of a nasal bone fracture

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Objective: Emergence agitation (EA) is defined as a transient condition in which emergence from general anesthesia is accompanied by psychomotor agitation. Dexmedetomidine (Dex) is known to reduce EA in children. The objective of this study was to determine the effects of intraoperative Dex on EA undergoing closed reduction of a nasal bone fracture.

Methodology: Thirty-eight male patients, ages 18 to 60 years, were randomized to receive a single intraoperative dose of Dex 1.0 μg/kg (Group D) or the same volume as normal saline (Group N) over 5 minutes before endotracheal intubation. The Richmond agitation sedation scale (RASS) was utilized to assess the intensity of the EA.

Results: EA was observed in 12 patients in group D compared with 18 patients in group N (*P*=0.042). Heart rate was significantly lower one minute after intubation (*P*=0.032), one minute before extubation (*P*=0.023), and upon arrival in the PACU (*P*=0.013). The mean blood pressure was lower one minute after extubation (*P*=0.004). Postoperative pain was significantly less in group D (*P*=0.050).

Conclusion: A single intraoperative dose of Dex was an effective method to reduce EA in adult patients undergoing closed reduction for a nasal bone fracture. (Rawal Med J 201;40: 191-196).

Key Words: Dexmedetomidine, emergence agitation, general anesthesia, nasal bone fracture, Richmond agitation sedation scale.

INTRODUCTION

Closed reduction of a nasal bone fracture is usually performed under general anesthesia however, some characters of this surgery might relate to high incidence of emergence agitation (EA), such as a short time, the location of the surgery, and uncomfortable breathing due to nasal packing, known for risk factors of postoperative agitation in patients who had general anesthesia.[1] EA may lead to serious consequences for the patient, such as increased pain, injury, bleeding, self-extubation, and removal of catheters. It is also disturbing to anesthesiologists and recovery room staff and can lead to increased hospital costs.

Dexmedetomidine (Dex), a specific α 2-adrenergic receptor agonist, has sedative, anxiolytic, and analgesic properties and is considered effective in the reduction of pain and in the prevention of EA in children.[2,3] However, most research regarding EA is conducted on pediatric patients, and there are few data on adults. This study was performed to determine whether Dex was effective to reduce EA in adults undergoing closed reduction for a nasal bone fracture.

METHODOLOGY

This prospective, randomized, double blind study included 38 male patients undergoing closed reduction for a nasal bone fracture. Patients had ages of 18 and 60 years with an ASA classification of I or II. The exclusion criteria were a known allergy to α_2 agonists, an ASA classification of III or more, and the presence of confirmed mental retardation. A random number table was used to assign subjects into 1 of 2 treatment groups: Normal saline infusion (Group N) or Dex infusion (Group D). The anesthesiologists, data collectors, the subjects, and their parents were blinded to the treatment group. An approval from the Institutional Review Board of the hospital was obtained written Informed consent was taken from all patients.

Table 1. Richmond agitation sedation scale.

Score	Term	Description
+4	Combative	Overtly combative or violent; immediate danger to staff.
+3	Very agitated	Pulls on or removes tube(s) or catheter(s) or has aggressive behavior toward staff.
+2	Agitated	Frequent non-purposeful movement or patient-ventilator dyssynchrony.
+1	Restless	Anxious or apprehensive but movements not aggressive or vigorous.
0	Alert and calm	
-1	Drowsy	Not fully alert, but has sustained (more than 10s) awakening, with eye contact, to voice.
-2	Light sedation	Briefly (less than 10s) awakens with eye contact to voice.
-3	Moderate sedation	Any movement (but no eye contact) to voice.
-4	Deep sedation	No response to voice, but any movement to physical stimulation.
-5	Unarousable	No response to voice or physical stimulation.

After a preoperative fasting period of a minimum of 8 hours, while patients were being administered 100% oxygen through a face mask, they received Dex (1 µg/kg over 5 minutes) or normal saline in same volume and propofol 2 mg/kg. Succinylcholine 1 mg/kg was used to facilitate tracheal intubation. Manual ventilation with sevoflurane 3 vol% and 100% oxygen was stopped right after fasciculation, and tracheal intubation was performed. The anesthesia was maintained through 1 minimum alveolar concentration of sevoflurane with 50% oxygen as long as the BIS remained below 60 during surgery.

Table 2. Patients' baseline demographic and clinical characteristics.

Variable	Overall	Group		P value
		D	N	
All patients	**38 (100.0)**	**19 (50.0)**	**19 (50.0)**	
Age (yrs)	30.3±9.3	31.6±9.2	28.9±9.4	0.380
BMI (kg·m$^{2-1}$)	23.6±3.1	23.0±2.8	24.2±3.3	0.237
PMHx				
Hypertension	4 (10.5)	3 (15.8)	1 (5.3)	0.290
ASA				
1	34 (89.5)	16 (84.2)	18 (94.7)	0.290
2	4 (10.5)	3 (15.8)	1 (5.3)	
Anesthesia time	23.7±3.9	24.7±4.3	22.6±3.1	0.085
Operation time	8.3±2.6	8.6±3.2	7.9±2.0	0.398
Postoperative nausea and vomiting				
Yes	0 (0.0)	0 (0.0)	0 (0.0)	1.000
No	38 (100.0)	19 (100.0)	19 (100.0)	

Values are mean ± SD, *n* and percentage. ASA = American society of anesthesiologist physical status classification system, BMI = body mass index, PMHx = past medical history.

During nasal packing after reduction of the nasal bone, all patients received intravenous ketorolac 0.5 mg/kg, the desflurane was ceased, and 100% oxygen was administered. Two experienced anesthesiologists were always assigned to every case. One observed and graded the recovery state using the RASS (Table 1) until the patient was discharged from post-anesthetic care unit (PACU). The other performed the anesthesia and observed the patient with assistance in evaluation.

After the operation, the patient was transferred to the PACU. The anesthesiologist observed the patient and recorded heart rate, systolic, mean, and diastolic blood pressures, pulse oximetry, BIS, the intensity of pain and RASS every 5 minutes until discharge from the PACU. The degree of pain was assessed using a numeric rating scale (NRS) ranged from 0 to 10. When the patient's NRS was 4 or more, it was considered postoperative pain. Fentanyl 0.5 µg/kg was injected in the PACU when the patient had postoperative pain (NRS ? 4) and wanted to alleviate the pain. In addition, the duration of surgery, the time from induction to extubation, and the time required for the patient to reach 0 on the RASS were noted.

EA was defined as a RASS score 2 or more at any time observed. Continuous EA or any postoperative complications were observed and recorded until the patient left the PACU. When the patient was hemodynamically stable, could maintain their own airway, had a NRS below 4, and had an oxygen saturation that could be maintained at greater than 95% during atmospheric respiration, the patient was transported to the ward, and the duration of the stay in the recovery room was recorded.

Statistical analysis: The calculation of sample size was based on the primary end-point and the

incidence of agitation. In a pilot study, the Dex infusion reduced EA by 40% (α of 0.05 and a power of 80%); 17 subjects were required in each group. We included 19 patients per group to allow for possible dropouts. Data were analyzed using SPSS version 16 and R 2.13.2 (R Foundation for Statistical Computing, Vienna, Austria) statistical software. After descriptive analyses were performed, Fisher's exact test was used to compare categorical variables between groups, whereas an independent t test was used to compare continuous variables between groups. A *P*=0.05 or less was considered statistically significant.

RESULTS

There were no statistically significant differences in the demographic data of the two groups (Table 2). EA was observed in 18 (94.7%) patients in Group N and in 12 (63.2%) patients in Group D (*P*=0.042) (Table 3).

Table 3. Comparison of RASS and NRS between groups.

Variable	Group D (n=19)	Group N (n=19)	P value
RASS			
-2	1 (5.3)	0 (0.0)	
-1	0 (0.0)	0 (0.0)	
0	0 (0.0)	0 (0.0)	
1	6 (31.6)	1 (5.3)	
2	7 (36.8)	8 (42.1)	
3	4 (21.1)	9 (47.4)	
4	1 (5.3)	1 (5.3)	
Emergence agitation			
≥2	12 (63.2)	18 (94.7)	0.042
NRS			
0	0 (0.0%)	1 (5.3%)	
1	2 (10.5%)	1 (5.3%)	
2	2 (10.5%)	1 (5.3%)	
3	9 (47.4%)	3 (15.8%)	
4	4 (21.1%)	6 (31.6%)	
5	1 (5.3%)	6 (31.6%)	
6	1 (5.3%)	1 (5.3%)	
Pain			
NRS ≥4	6 (31.6%)	13 (68.4%)	0.050
RASS zero time	17.37±9.48	7.37±6.95	0.001
PACU stay time (min)	26.58±9.58	24.47±5.24	0.406
Average fentanyl in PACU	3.68±11.16	12.63±19.10	0.088
Patients needed fentanyl	2 (10.5)	6 (31.6)	0.078

Values are mean ± SD, *n*, percentage. Control = control with normal saline, DEX = dexmedetomidine, NRS = numeric rating scale, PACU = post-anesthetic care unit, RASS = Richmond agitation sedation scale, RASS zero time = the time required for the patient to reach 0 on the RASS

There was also significant difference in the RASS during the emergence time period (Figure 1). Additionally, no patient showed being sustained EA over 5 minutes. The number of patients who had postoperative pain (NRS ? 4) was 13 (68.4%) in Group N and 6 (31.6%) in Group D (*P*=0.050). However, there was no difference in the amount of fentanyl used during the recovery period in the PACU. During some of the assessment periods, there were statistically significant differences in heart rate (Figure 2) and mean blood pressure between two groups (Figures 3).

Figure 1. The Richmond agitation sedation score change across time. (*means statistically significant differences).

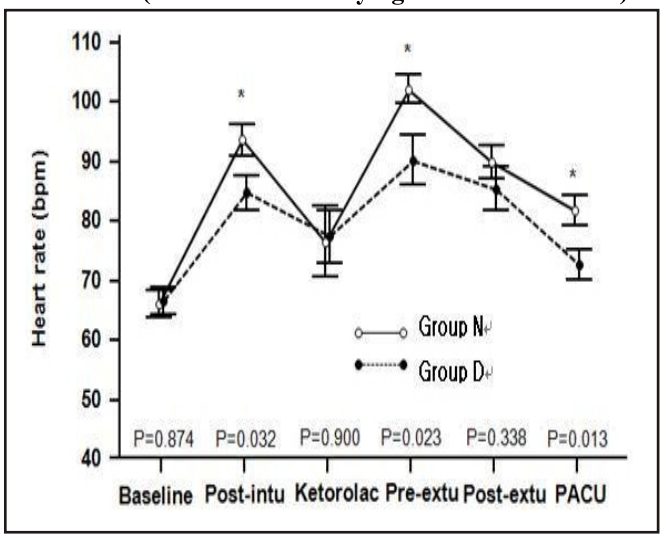


Figure 2. Heart rate change across time. (*means statistically significant differences).

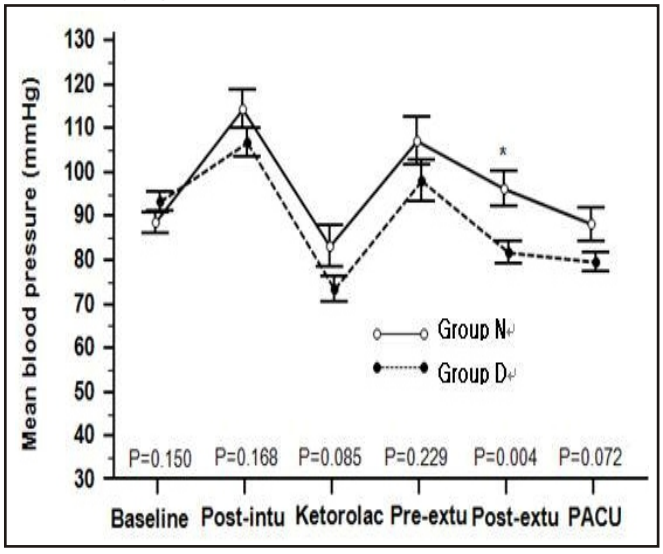
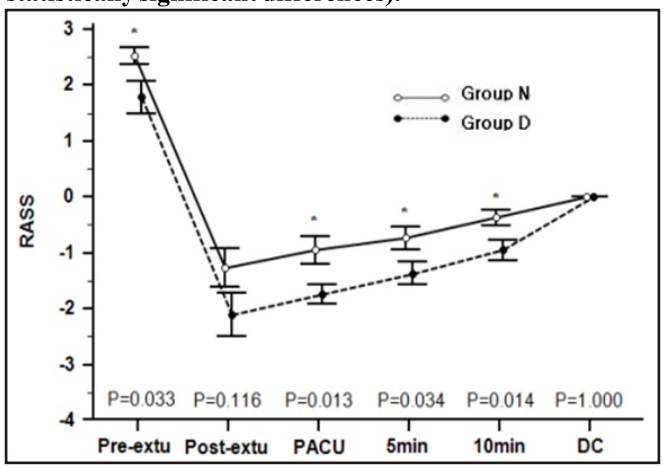


Figure 3. Mean blood pressure across time. (*means statistically significant differences).



There were no differences in the duration of surgery, the time from induction to extubation and the time to discharge from the PACU between two groups. However, the time required for the patient to reach 0 on the RASS was significantly longer in Group D (*P*=0.001). No patients had complications during the perioperative period.

DISCUSSION

EA is a transient confusional state that is mostly associated with the early stage of emergence from general anesthesia and is interchangeably described in the literature as post-anesthetic excitement and delirium. The majority of studies for EA have been on children due to the high incidence of up to 67% in this population.[4] However, EA in adult patients with high risks might occur as frequently as in children,[5] and Kim et al reported that the incidence of EA in adults was 45.0% after sevoflurane anesthesia for closed reduction of a nasal bone fracture.[6]

When EA occurs in an adult patient, it is usually aggressive and uncontrollable, causing a greater possibility of injury, such as increased pain, hemorrhage, and self-extubatio.[5] Furthermore, in this situation, it is difficult to assure the safety of both the patient and the staff. Treatment of EA is usually not required because the condition is self-limiting. If unremitting, however, treatment with fentanyl,[7] midazolam, ketamine[8] or clonidine[9] may be required.

The risk factors and cause of EA remain unclear, especially in adults. Yu et al described several predisposing factors in adults.[1] Those were male gender, inhalational anesthetics, otolaryngological surgery, use of doxapram, pain, and the presence of a tracheal tube and/or a urinary catheter.[1] Several predisposing factors existed in our patients resulting in incidence of 94.7% in control group. We assume that the uncomfortable breathing caused by nasal packing in both nasal cavities definitely contributed to the high incidence of EA.

The mechanism of agitation is still unclear. In Sachdev and Kruk's model, agitation is explained as the consequence of decreased inhibitory signals from the substantia nigra and the globus pallidus interna containing gamma-aminobutyric acid (GABA) and/or disinhibition of the thalamocortical and brain stem neurons.[10] Lindenmayer reported that multiple pathophysiologic abnormalities were found in the dopaminergic, serotonergic, noradrenergic, and GABAergic systems, and although there may be a final common pathway, there is no unifying etiologic pathophysiology.[11]

Though EA is not a new problem in clinical practice, it has become more of a concern because its incidence appears to be increasing with the widespread use of less-soluble vapors, sevoflurane and desflurane.[12] A variety of ways to reduce EA have been studied, including the use of propofol, fentanyl, clonidine, and Dex.[6,9] A large number of studies have demonstrated that the use of Dex is a reasonable way to prevent EA in children.[13,14]

Dex is a highly selective α_2 agonist with a 1600:1 preference for α_2 receptors relative to α_1 receptors and it reduces peripheral norepinephrine release by stimulation of prejunctional inhibitory α_2 adrenoceptors.[15] The half-life of Dex is 2.3 hours, although its distribution half-life is less than 5 minutes, thus making its clinical effect quite short.[16] Due to this, there was no difference in the anesthetic time between both groups in this study. Its primary effect is sympatholytic, and it is used for sedative, anxiolytic, and analgesic purposes as an adjunct to several anesthetics. These complex properties of Dex led patients to experience less EA and pain during the postoperative period in this study. Furthermore, it helps attenuate the hemodynamic lability during perioperative and intraoperative periods; this study showed that heart rate was lower

1 minute after intubation, 1 minute before extubation, and upon arrival time in the PACU, and mean blood pressure was lower 1 minute after extubation. Kim et al recently reported that continuous infusion of Dex was effective for hemodynamic stability and quality of recovery after nasal surgery.[17] However, they included various type of nasal surgery with relatively longer duration of surgery than our study (mean 54 min vs 8.3 ± 2.6 min) (17).

Studies have demonstrated that both the Ricker and the Richmond scales have an excellent inter-rater reliability.[18,19] Although all of these scales were created for adults in intensive care, we are of the opinion that patients staying in the PACU are comparable to patients admitted to the intensive care unit. However, various variables in these scales may have caused the observed difference in the incidence of EA across several studies.[1,5,6] Unification of the numerous scales is needed to facilitate precise comparisons across studies. An example of such a scale is the Pediatric Anesthesia Emergence Delirium Scale.[2,20]

A limitation of this study is an absence of preoperative anxiety in the patients. However, there is no relationship between preoperative anxiety and EA in adults,[5] although the relationship is known to be important in children.[21] Second, the incidence of EA is 78.9% on average for the participants in both groups. However, it is a difficult to generalize this result in a high-risk patient for EA because of the small number of subjects.

CONCLUSION

The infusion of Dex is a satisfactory method for preventing EA in male adults, who are undergoing closed reduction for a nasal bone fracture. Although Dex had no analgesic-sparing effect, it contributed to having less pain in the PACU. Moreover, it induced a steady mean blood pressure 1 minute after extubation and a lower heart rate 1 minute after intubation, 1 minute before extubation, and upon arrival in the PACU. We suggest that in adult patients at high risk for EA, Dex may be an alternative method to reduce EA. Further studies are needed to find effective options to prevent EA in high-risk adult patients.

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