Comparison between Alfentanil and dexmetomidine to reduce agitation in adults undergoing septorhinplasty after sevoflurane anaesthesia

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Background and objectives: Emergence agitation frequently occurs with sevoflurane anesthesia. This study was designed to compare the effect of alfentanil versus dexmedetomidine on the emergence agitation after sevoflurane anesthesia in adult patients scheduled for septorhinoplasty.

Methods: This randomized, double-blinded study enrolled 72 patients scheduled for septorhinoplasty. Patients were randomly categorized into 3 groups. Group A: received alfentanil 10μg/kg. Group D: received dexmedetomidine 0.3μg/kg. Group S: received 10 ml normal saline 10 min before the end of operation. Time to emergence, time of first postoperative analgesic dose, duration of surgery, behavior during emergence according to Riker sedation-agitated scale, time to meet discharge criteria (min), all are recorded.

Results: The behavior during emergence, incidence of agitation was significantly higher in group S (P < .001) (36%) in comparison with groups A & D (16% and 12% respectively) while comparison between groups A & D was insignificant.

Conclusion: Adding alfentanil or dexmedetomidine to adults undergoing septorhinoplasty surgery reduces sevoflurane-related emergence agitation, without delaying discharge and decreasing the need of analgesia in PACU.

Sevoflurane is currently the most popular inhaled anaesthetic especially in pediatric patients. It is characterized by a safe, smooth and pleasant mask induction. Sevoflurane provides fast recovery with less cardiovascular affection. Dexmedetomidine, a more selective α-2 adrenoceptor agonist than clonidine, has been used as an adjuvant in general anesthesia and for postoperative sedation and analgesia. Agitation is simply excessive motor activity, common in the postoperative period in children as well as in adults. It is a non-specific symptom resulting from any type of internal discomfort including pain and anxiety. Agitation resulting from pain or anxiety is relatively easily treated with reassurance and the appropriate use of analgesics and benzodiazepines. However, emergence agitation frequently occurs with sevoflurane, particularly pediatric patients are known to have a high incidence of emergence agitation with sevoflurane. Emergence agitation (EA) can often occur after anesthesia and can increase the risk of falling, bleeding, self-extubation, and removal of endotracheal tubes, and there is the need for continuous monitoring of patients by recovery room staffs and treatments such as drug administration or physical restraint of the patient. The reason for postoperative agitation or delirium is unclear but factors such as pain, rapid recovery, gender, and age have been suggested. However, emergence agitation occurs even if sufficient analgesia is present.

AIM OF THE WORK
The aim of this study was to compare the effect of alfentanil versus dexmedetomidine on the emergence agitation after sevoflurane anesthesia in adult patients scheduled for septorhinoplasty.

Patients and Methods
After ethics committee approval and written informed consent, the study was conducted on 72 adult patients aged 18-45 years ASA physical status I-II scheduled for septorhinoplasty under general anesthesia. This study was a prospective, randomized, placebo controlled, double blind, single center study that was carried out in the Armed Forces Hospital-Dhahran from 1st October 2011 till 30 April 2012. The patients scheduled were randomly assigned by using a computer-generated code into three groups alfentanil (group A) or dexmetomidine (group D) and saline (group S).

Exclusion criteria included known allergy to the study medications, bronchial asthma, patients with acute infection in the upper respiratory tract, history of sleep apnea, administered medication for psychiatric diseases, chronic or acute intake of sedative or analgesic drugs.

Patients were randomly categorized into 3 groups. Group A: received alfentanil 10μg/kg diluted in 10 ml normal saline 10 min before the end of operation. Group D: received dexmedetomidine 0.3μg/kg diluted in 10 ml normal saline 10 min before the end of operation. Group S: received 10 ml normal saline 10 min before the end of operation.

All patients underwent thorough preoperative evaluation, which included history, physical examination and relevant laboratory investigations. All patients were NPO at midnight, transported to the operating room without preoperative medication, and the patients were reminded that there could be discomfort from nasal packing following the surgery and...
would be mouth breather postoperative. All patients had the following monitoring devices attached: electrocardiography, noninvasive blood pressure and pulse oximetry monitor. While patients were being administered 100% oxygen through a face mask, they received tramadol 1.5 mg/kg by IV injection, thiopental 5 mg/kg by IV injection and atracurium 0.5 mg/kg by IV injection. Patients were intubated with suitable size of ETT and after sealing the tube a pack was inserted in hypopharynx. Respiration rate and tidal volume were controlled so end-tidal CO2 concentration was maintained at 30-36 mmHg, and a total of 3 L/min of nitrous oxide and oxygen was administered in a 7:3 ratio as inhalation gas. Sevoflurane were measured continuously during anaesthesia and maintained at 1.5-2% using multigas analyzer (Primus-Drager).

Additional opioids were not used during surgery in any of the patients, and when blood pressure showed a difference of more than ± 20% from basal levels, labetalol or ephedrine was injected IV for adjustment. All patients received bilateral nasal packs. After the completion of surgery when the operating surgeon attached the nasal splint, all anaesthesia was ceased and 100% oxygen was administered to all patients.

A medical attendant who was unaware of the grouping of the patients evaluated each patient’s in the recovery room.

At the end of surgery the anaesthetics were discontinued, the pack in hypopharynx was removed, the oropharynx was suctioned and when spontaneous respiration and muscle strength of the patient recovered sufficiently to allow the patient to respond to verbal stimulation and after the patient’s eyes had opened, the endotracheal tube was removed and the patient was transported to the recovery room. In addition, anaesthesia time, surgery time, time from end of surgery to extubation, and duration of emergence agitation were investigated. When emergence agitation more than 4 and continued for more than 2 minutes, pethidine was administered IV, the total amount of pethidine administered was recorded.

The patients were observed for the occurrence of complications or side effects of medications, while being observed for nausea and vomiting. If a patient experienced nausea or vomiting, the patient received 4 mg Zofran by IV route. When the patient was haemodynamically stable, could maintain their own airway, and oxygen saturation was maintained at greater than 95% during atmospheric respiration, the patient was transported to the ward, and the duration of stay in the recovery room was recorded. Discharge criteria included being fully awake, stable vital signs for 40 min, no bleeding, no pain, no nausea or vomiting.

Table 1: Riker sedation-agitated scale. (7)

| 7 | Agitated | Pulling at ET tube, trying to remove catheters, climbing over bed rail, striking at staff, thrashing side-to-side
|   | Dangerous agitation | Does not calm, despite frequent verbal reminding of limits; requires physical restraints, biting ET tube
|   | Very agitated | Anxious or mildly agitated, attempting to sit up, calms down to verbal instructions
|   | Agitated | Calm, awakens easily, follows commands
|   | Non-agitated | Difficult to arouse, awakens to verbal stimuli or gentle shaking but drifts off again, follows simple commands
| 4 | Calm and cooperative | Arouses to physical stimuli but does not communicate or follow commands may move spontaneously
| 3 | Sedated | Minimal or no response to noxious stimuli, does not communicate or follow commands
| 2 | Very sedated | Calm, awakens easily, follows commands
| 1 | Unarousable | Difficult to arouse, awakens to verbal stimuli or gentle shaking but drifts off again, follows simple commands
Demographic data such as age and weight are presented as mean ± SD. The following parameters were recorded: duration of anaesthesia (time from the start of induction till discontinuation of anaesthetics in min), duration of surgery (from the skin incision to end of operation in min), time of emergence (time from termination of anaesthesia to eye opening on command in min), behavior during emergence according to Riker sedation-agitated scale, time to meet discharge criteria (min), and rescue analgesic requirement all are recorded and presented as mean ± SD.

For all patients, pain was assessed and treated so as to obtain a pain level <3 on the visual analogue scale (8). Total amount of pethidine in the PACU (mg) calculated.

Results
Table 2: Demographic and Anaesthetic Data

<table>
<thead>
<tr>
<th></th>
<th>Group A</th>
<th>Group D</th>
<th>Group S</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>29.23 ± 8.13</td>
<td>29.5 ± 7.14</td>
<td>28.85 ± 7.82</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>78.88 ± 14.35</td>
<td>78.13 ± 13.92</td>
<td>80.21 ± 12.39</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>167.62 ± 11.82</td>
<td>171.7 ± 10.84</td>
<td>170.3 ± 8.93</td>
</tr>
<tr>
<td>Gender (Male/Female)</td>
<td>15/8</td>
<td>17/6</td>
<td>16/7</td>
</tr>
<tr>
<td>ASA (I/II)</td>
<td>17/6</td>
<td>18/5</td>
<td>16/7</td>
</tr>
<tr>
<td>Duration of anaesthesia (min)</td>
<td>128.85 ± 7.82</td>
<td>127.8 ± 8.34</td>
<td>125.9 ± 7.71</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>102±6.56</td>
<td>108±7.36</td>
<td>103±7.7</td>
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</tbody>
</table>

There were no statistically significant differences in the demographic and perioperative data of the 3 groups.

Table 3: Time to emergence (time of eye opening on command or first response to commands after endotracheal extubation).

<table>
<thead>
<tr>
<th></th>
<th>Group A (n=23)</th>
<th>Group D (n=23)</th>
<th>Group S (n=24)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to emergence (min)</td>
<td>9.45±2.02</td>
<td>8.86±2.35</td>
<td>6.92±1.82</td>
<td>Group A versus Group D NS P &gt;0.05 Group A versus Group S P***&lt;0.001 Group D versus Group S P**&lt;0.01</td>
</tr>
</tbody>
</table>

Time to emergence (time of eye opening) was significantly shorter in group S in comparison of group A & D.

Criteria for transfer to the ward included a patient with no pain, calm and with a Modified Aldrete Score (9) > 10. All syringes with study drugs or placebo were prepared by the same investigator. Administration of anaesthesia study drugs and intraoperative data collection were done by 2 investigators blinded to the study drugs.

Data were expressed as mean ± standard deviation and were analyzed using student t test and analysis of variance ANOVA. P 0.05 was considered significant. Chi-square /Fischer exact test was applied for categorical variables. For continuous variables, ANOVA/non-parametric Kruskall-Wallis test was applied. Two-sample t-test/non-parametric Wisconsin Mann Whitney test was applied.
Figure 1: Time to emergence.

Table 4: Time of first postoperative analgesic dose.

<table>
<thead>
<tr>
<th>TIME/SCORE</th>
<th>Group A (n=23) mean ±SD</th>
<th>Group D (n=23) mean ±SD</th>
<th>Group S (n=24) mean ±SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time of first postoperative analgesic</td>
<td>34.61±15.25</td>
<td>38.75±18.35</td>
<td>15.63±14.62</td>
<td>Group A versus Group D NS P &gt;0.05</td>
</tr>
<tr>
<td>dose (min)</td>
<td></td>
<td></td>
<td></td>
<td>Group A &amp; D versus Group S***P&lt;0.001</td>
</tr>
</tbody>
</table>

Time of first postoperative analgesic dose was significantly shorter in group S compared with group A & D with P < 0.001 and no significant difference between group A & D P >0.05.

Table 5: Agitation score according Riker sedation-agitated scale.

<table>
<thead>
<tr>
<th>TIME/SCORE</th>
<th>Group A (n=23) mean ±SD</th>
<th>Group D (n=23) mean ±SD</th>
<th>Group S (n=24) mean ±SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>During and immediately after extubation</td>
<td>3.6±1.03</td>
<td>3.26±1.21</td>
<td>4.5±1.38</td>
<td>Group A versus Group D NS P &gt;0.05</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Group A versus Group S *P &lt;0.05</td>
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<td></td>
<td>Group D versus Group S ** P &lt; 0.01</td>
</tr>
<tr>
<td>5 min after transfer to PACU</td>
<td>3.7±1.4</td>
<td>3.41±1.34</td>
<td>4.7±1.29</td>
<td>Group A versus Group D NS P &gt;0.05</td>
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<td></td>
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<td></td>
<td>Group A versus Group S * P &gt;0.05</td>
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<td></td>
<td>Group D versus Group S ** P &lt; 0.01</td>
</tr>
<tr>
<td>15 min after transfer to PACU</td>
<td>3.4±1.28</td>
<td>3.1±1.02</td>
<td>5.1±1.56</td>
<td>Group A versus Group D NS P &gt;0.05</td>
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<td></td>
<td>Group A versus Group S * P &lt;0.05</td>
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<td></td>
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<td></td>
<td>Group D versus Group S ** P &lt; 0.01</td>
</tr>
</tbody>
</table>

As regard the behavior during emergence, incidence of agitation was significantly higher in group S ( P<0.001) (36%) in comparison with groups A & D (16% and 12% respectively) while comparison between groups A&D was insignificant.
Figure 2: Agitation score according Riker sedation-agitated scale.

Table 6: Total dose of pethidine (mg) in PACU.

<table>
<thead>
<tr>
<th></th>
<th>Group A (n=23) (mean ±SD)</th>
<th>Group D (n=23) (mean ±SD)</th>
<th>Group S (n=24) (mean ±SD)</th>
<th>P value</th>
</tr>
</thead>
</table>
| Pethidine dose   | 31.08±16.58               | 28.9±17.73                | 48.12±15.93               | Group A versus Group D   NS P > 0.05  
|                  |                           |                           |                           | Group A versus Group S ** P >0.01 
|                  |                           |                           |                           | Group D versus Group S *** P < 0.001 |

According to pethidine consumption, there was statistically significant decrease in groups A & D in comparison to group S.
Vomiting was recorded in two patients in group S and treated with 4 mg of Zofran by direct IV injection. None of patients had suffered from significant itching, shivering, hypotension or bradycardia.

**DISCUSSION**

Emergence agitation is a state of aggressive agitation that occurs temporarily in the process of emerging from anaesthesia, and occurs most often during the early stages of emergence. The incidence of emergence agitation in adults is less frequent compared to paediatric patients, so little research has been done on adults.

However, the occurrence of emergence agitation in adults results in a greater possibility of injury, and medical staff may not be able to restrain the agitation. Thus, there could be the need for more medical staff available compared to paediatric patients, as problems can arise in the safety of both the patient and the medical staff. In the case of closed reduction of nasal bone fracture, in our study, there could be discomfort from the nasal packing performed to prevent post-operative bleeding.

There is no well-established prophylaxis or treatment, although the incidence of this excitatory behavior seems to be reduced by preoperative use of sedative and analgesic drugs. Alfentanil and dexmedetomidine were expected to decrease emergence agitation.

Emergence agitation is a frequent side effect of sevoflurane anaesthesia particularly in children with a reported incidence of up to 80%, and remain a significant post-anaesthetic problem that interferes with children's recovery, and challenges the PACU staff in terms of assessment and treatment.¹⁰⁰

In this study IV alfentanil as a bolus of 10 μg/kg or a bolus of dexmedetomidine 0.3μg/kg improved emergence conditions and decreased incidence of agitation (16% and 12% respectively) compared to group S (36%).

Multiple factors may be the causes of postoperative EA as shorter time for awakening ,young age , sevoflurane anaesthesia, waking up in a strange environment, and psychological immaturity, all have been considered possible risk factors.¹¹

In our study the incidence of agitation was 36 % in group S in adult patients in contrary to the study done by Daihua et al. where the incidence was (21.3%).¹²

The incidence of emergence agitation in adults differs according to the researcher. Lepouse et al.¹⁸ reported it as 3%. Daihua et al.¹₂ as 21.3%. Radtke et al.¹₃ as 5%, and in our study it was 27.3%. There are no clearly fixed criteria used to evaluate the occurrence of emergence agitation and its intensity in existing studies, but the Aono’s four-point scale, Riker Sedation-Agitation Scale, Richmond Agitation-Sedation Scale, or personally categorized criteria have been used; the Riker Sedation-Agitation Scale was used in assessment of agitation in this study.

A limitation of this study is that we did not measure the patient’s degree of anxiety before surgery. Lepouse et al.¹⁵ reported that preoperative anxiety was a risk factor for emergence agitation, and in the research of Kain et al.¹⁴, preoperative anxiety was related to delirium or changes in behavior after surgery.

**CONCLUSION**

Adding alfentanil or dexmedetomidine to adults undergoing septorhinoplasty surgery reduces sevoflurane-related emergence agitation, without delaying discharge and decreasing the need of analgesia in PACU.
REFERENCES


