

# Comparison of recovery after anesthesia with remifentanyl infusion versus halothane in children undergoing strabismus surgery

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## ABSTRACT

**Objective:** To compare recovery after anesthesia with remifentanyl infusion versus halothane for strabismus surgery

**Methods:** This study was performed from September 2004 to March 2005 in Tabriz Nikookary Hospital, Tabriz, Iran on children aged 2-12 years scheduled for strabismus surgery randomized into 2 groups of 25 patients each: the H group in which anesthesia was maintained with halothane and the R group in which anesthesia was maintained with remifentanyl.

**Results:** There was no meaningful difference in extubation time after discontinuing drugs between the 2 groups ( $p=0.14$ ). However, there was a significant difference in the time of purposeful movements, proper oxygenation, consciousness, and discharge from the post anesthetic care unit between the 2 groups, all being shorter in group R. Also in group R, the time to spontaneous breathing return was longer, cases of neuromuscular reversal were fewer and cases of limb movements were more than group H.

**Conclusion:** Maintenance of anesthesia with remifentanyl in children aged 2-12 years undergoing strabismus surgery provided desired hemodynamic status and shorter time of discharge criteria.

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Currently more than 60% of all elective surgeries are performed in the outpatient surgical setting. It is expected that this number will increase to 70% in the near future. However, the growth in ambulatory surgery would have not been possible without developments in anesthetic and surgical techniques.<sup>1</sup> Anesthesiologists should now be able to handle these new techniques with the use of short-acting drugs and methods. Halothane, in proportion to the length of surgery, lengthens the recovery period. Remifentanyl is a new ultra-short acting synthetic opioid, which because of its unique characteristics is considered in ambulatory surgeries, and even in long duration surgeries.<sup>2</sup> The use of anesthetic techniques associated with more rapid recovery will result in lower sedation score in the early postoperative period, decrease the risk of airway obstruction and cardiorespiratory instability, and reduce the number of nursing interventions. Patients will be able to leave the surgical center early after discharge from the post anesthetic care unit (PACU). The ideal outpatient anesthetic should have a rapid and smooth onset of action, produce intraoperative amnesia and analgesia, provide good surgical conditions with a short recovery period, and not have adverse effects. For many ambulatory procedures, general anesthesia remains the most popular technique with both patients and surgeons. Although there is no ideal anesthetic drug or technique for outpatients, a vast array of pharmacologically active drugs, when combined in a rational manner and carefully titrated, can produce the desired anesthetic conditions with an acceptable recovery profile and reasonable cost. The recovery period after ambulatory surgery is divided to 2 stages: In the first stage, when patients emerge from anesthesia, they recover control of their protective reflexes and resume early motor activity. In the second stage, the patient's mental and physical functions return and they become ready for discharge. Compared with traditional anesthetic techniques, the use of new drugs (propofol, alfentanil, remifentanyl, sevoflurane, and desflurane) results in better cognitive function and psychomotor tests during the early and intermediate periods. In the last stage of recovery, patients return to their baseline physical and mental status. Discharge time is important in assessing new anesthetic drugs and techniques, as rapid discharge time is more cost-effective. The modified Aldrete score is usually used to assess the patient's

readiness for transfer to the second stage of recovery.<sup>3</sup> This score is a simple sum of numerical values assigned to activity, respiration, circulation, consciousness, and oxygen saturation.<sup>4</sup> The aim of the current study is to compare recovery after anesthesia with remifentanyl infusion versus halothane for strabismus surgery.

**Methods.** This double blind prospective study was performed in Tabriz Nikookary Hospital (Ophthalmic Surgery Center) from September 2004 to March 2005. Fifty children, aged 2-12 years, with ASA class I, suffering from strabismus were enrolled in this study. The patients were randomized into 2 groups of 25 patients, group H in which anesthesia was maintained with halothane, and group R in which anesthesia was maintained with remifentanyl. Children with systemic or severe illness were excluded from the study. After institutional review board approval and obtaining informed consent from their parents, all patients received 0.3 mg/kg oral midazolam 30 minutes before coming to the operating room. Induction was performed by propofol 2.5mg/kg, following which atracurium 0.4 mg/kg and atropine 0.02 mg/kg were administered. After tracheal intubation, in group H anesthesia was continued with halothane 1.5%, N<sub>2</sub>O and O<sub>2</sub> (in ratio proportion of 50:50), and in group R (remifentanyl), a bolus dose of remifentanyl (1 µg/kg) for 30-60 seconds was administered, and maintenance of anesthesia was performed with infusion of remifentanyl (1 µg/kg/min), O<sub>2</sub> and N<sub>2</sub>O. In both groups, signs and symptoms of insufficient anesthesia such as tearing, sweating, hemodynamic changes, muscle movement, and bucking were recorded during surgery. In those cases of group R where signs of light anesthesia and muscle movement were seen (despite receiving 4 bolus doses), remifentanyl infusion was discontinued and these cases were excluded from the study. Five minutes before the end of surgery, the infusion of remifentanyl was reduced to 50% and halothane to 25%. At the end of surgery, all patients were assessed by a nerve stimulator for residual muscle relaxation. In cases with train-of-four (TOF) ratio less than one, a reversal drug (neostigmine 0.04 mg/kg + atropine 0.02 mg/kg) was given. In cases with TOF equal to one with spontaneous breathing, N<sub>2</sub>O and anesthetic drugs were discontinued. No stimulation (for example, suction) was carried out until 10 minutes after ceasing the drugs. After 10 minutes, if the patient was unready, stimulation and then tracheal extubation was performed. The time of extubation and purposeful movements was recorded by another person blinded to the study. Patients were transferred to the PACU where the nurse recorded the time taken to reach the discharge criteria every 5 minutes. When the sum of discharge

criteria was 8 or more, the patient was discharged from that PACU.

Qualitative variables were compared by chi square test or Fisher's exact test, and quantitative variables by independent sample t-test. A *p*-value <0.05 was considered statistically significant. We used SPSS 13 statistical package for analysis of data.

**Results.** In this clinical trial, 50 children aged 2-12 years with strabismus were randomized into 2 groups of 25 patients each: group H (halothane) and group R (remifentanyl). Two patients from group R had frequent limb movements during the operation despite receiving 4 bolus doses of remifentanyl. Considering the probability of insufficient anesthesia, remifentanyl infusion was discontinued and anesthesia was continued with halothane, therefore 23 cases remained in group R. There was no significant difference in failure rate between the 2 groups (*p*=0.24). The patients demographic data are shown in Table 1, and quantitative respiratory variables are listed in Table 2. Correlation between time of spontaneous breathing return and duration of anesthesia was meaningful and direct (*p*<0.001), namely, while duration of surgery was prolonged, time of spontaneous breathing return significantly increased. Recovery variables are listed in Table 3. Correlation between time of recovery stay, and duration of surgery was not meaningful (*p*=0.41). Patients were assessed for light anesthetic symptoms such as tearing, sweating, bucking, increase in heart rate (more than 20% of baseline values) and muscle movements during surgery. Tearing, sweating, and bucking was not seen in any of the patients. One patient in group R, and 2 patients in group H had an increase in heart rate more than 20% of baseline values (*p*=0.53). Nine patients in group R, and 2 patients in group H had muscle movements during the surgery (*p*=0.012). Bradycardia was seen in 3 cases of group H, and 7 cases of group R at the time of extraocular muscle tension, which resolved immediately after discontinuation of traction. Correlation between age and weight with light anesthesia symptoms and time to reach discharge criteria was not meaningful (*p*>0.05).

**Discussion.** There was no significant difference between the 2 groups regarding gender. As in similar articles, gender was not mentioned, and genetic and pharmacodynamic differences did not affect the results of our study. There was no statistically significant difference between the 2 groups regarding weight. Since the distribution of greater amounts of anesthetic vapor in fat tissue makes recovery longer,<sup>5</sup> obesity and its influence on duration of recovery did not affect our study. There was a significant difference between the 2

**Table 1** - Patient's demographic characteristics (mean ± SD).

Characteristics	Group R (n=23)	Group H (n=25)	P-value
Age (year)	6±2.7	4.6±1.9	p=0.04
Weight (kg)	19.6±7.5	18.6±4.4	p=0.58
Gender (M/F)	11/12	14/11	p=0.08

**Table 2** - Quantitative respiratory variables (mean ± SD).

Variable	Group R (n=23)	Group H (n=25)	P-value
Duration of anesthesia (minutes)	55.9±27.86	49.4±14.86	0.31
Return of spontaneous breathing (minutes)	56.0±28.60	32.7±14.0	0.001
Neuromuscular reversal TOF<1	30.4%	64%	<0.001
Duration of surgery (minutes)	41.1±27.30	36.7±15.1	0.58
TOF - Train-of-four			

**Table 3** - Recovery variables of patients (mean ± SD).

Variable	Group R (n=23)	Group H (n=25)	P-value
Extubation time after discontinuing of drugs (minutes)	3.13±2.34	2.1±2.1	0.14
Time of purposeful movement after extubation (minutes)	3.8±4.2	17.9±11	<0.001
Time of purposeful movement after entrance to PACU (minutes)	0.86±4.87	15.8±10.7	<0.001
Time of appropriate Sp <sub>o</sub> <sub>2</sub> after entrance to PACU (minutes)	6.1±8.2 (3.4-11.6)	-0.65±3 (-1.2-0.65) <sup>†</sup>	0.001
Time of awaking after entrance to PACU (minutes)	13.4±23.8 (8.2-18.3)	0.42±8.4 (-1.23-3.2)	0.016
Recovery stay (minutes)	19.5±11.7	7.6±6.2	<0.001
<sup>†</sup> 25-75%, PACU – post anesthetic care unit			

groups regarding age, however, the effect of remifentanyl and its recovery was considered unrelated to age in previous studies.<sup>6-8</sup> There was no significant difference in duration of anesthesia between the 2 groups, however, there was a significant difference in time of spontaneous breathing return. The correlation between duration of anesthesia and time of spontaneous breath returning was direct and meaningful ( $p<0.001$ ), illustrating the inhibitory effect of remifentanyl on the respiratory center. The correlation between duration of recovery stay, and anesthesia was not meaningful, therefore, there is not a relationship between duration of recovery and remifentanyl infusion, highlighting remifentanyl's short duration of action. The difference in extubation time was not significant between the 2 groups, but patients of group R reached appropriate SpO<sub>2</sub> sooner, and this time difference was significant between the 2 groups.

Davis et al<sup>9</sup> showed that extubation time, appropriate SpO<sub>2</sub> time, and respiratory rate did not have a significant difference between halothane and remifentanyl groups in newborns.<sup>9</sup> Billard et al<sup>10</sup> showed that remifentanyl significantly reduced extubation time compared to sufentanyl in neurosurgery patients. In order to not influence the extubation time by other factors, we did not stimulate patients (orotracheal suctioning) for 10 minutes after discontinuing of drugs. In our study, the number of cases with neuromuscular reversal in group R was less than group H, and was statistically different ( $p<0.001$ ), which correlates with other studies. Respiratory depression and spontaneous breathing return is dependent on 2 factors: drugs and controlled ventilation. Respiratory depression of drugs can be due to anesthetic vapor, opiate,<sup>9</sup> and atracurium. Controlled ventilation can delay spontaneous breathing return because of the non-stimulation of the respiratory center by CO<sub>2</sub>. Davis et al<sup>8</sup> showed that recovery from remifentanyl is similar to recovery of short-acting drugs such as propofol and isoflurane in patients with strabismus.

In our study, the difference in recovery discharge criteria between the 2 groups was due to remifentanyl's short duration of action. Billard et al<sup>10</sup> showed that remifentanyl was associated with more hemodynamic stability during surgery. Gargiulo et al<sup>11</sup> showed the same results in endoscopic pituitary surgery. In our study, there was no significant difference in more than 20% increase of heart rate between the 2 groups, which could be due to the following factors: sufficient depth of anesthesia, adequate doses of drugs and use of atropine, which counteracts the bradycardia of remifentanyl. In 2 studies performed to highlight the reasons for bradycardia after remifentanyl, Fattorini et al<sup>12</sup> showed that this was due to an increase in parasympathetic activity, and atropine can reverse its effect on heart

rate, and Tirel et al<sup>13</sup> showed that atropine can not completely prevent bradycardia of remifentanyl, because of remifentanyl's direct negative chronotropic effect.<sup>13</sup> In all cases, bradycardia resolved after discontinuing of traction, mostly related to surgery technique and oculocardiac reflex than drug effect.

There was a significant difference in limb movements between the 2 groups, more in group R. This could be due to the following factors: inadequate depth of anesthesia,<sup>14</sup> opioids, which have a ceiling effect and do not have complete anesthetic effects, vapor anesthetics disturbing neuromuscular transmission and enhancing effect of relaxants,<sup>15</sup> and the person who has different thresholds for stimulants.<sup>2</sup>

In conclusion, remifentanyl provides hemodynamic stability, short recovery duration and better recovery discharge criteria. Therefore, it is an appropriate drug for maintenance of anesthesia in children aged 2-12 years undergoing strabismus surgery.

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