Comparison of remifentanil and alfentanil during anaesthesia for 
patients undergoing direct laryngoscopy without intubation

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Background. Remifentanil and alfentanil are opioids often used during direct laryngoscopy (DL). This prospective, randomized study compared these agents with respect to haemodynamic and Bispectral Index (BIS) responses, glottic visualization, and rapidity of recovery (spontaneous ventilation, eye opening) in DL without intubation.

Methods. A total of 60 patients undergoing DL were randomized into two groups: remifentanil (R) and alfentanil (A). Anaesthesia was induced with propofol 2.5 mg kg⁻¹ and the opioid was administered 1 min later (R=2 µg kg⁻¹ or A=30 µg kg⁻¹ over 30 s). DL was commenced 1 min after (corresponding to 3 min after the beginning of induction). Glottic visualization, opioid and/or propofol re-injection, spontaneous ventilation recovery, and eye opening were recorded.

Results. During DL, mean arterial pressure (MAP) increased by 6% in the R group vs 20% in the A group (P<0.05) when compared with post-induction values without affecting heart rate or BIS. No significant difference was observed between groups with respect to glottic exposure, opioid and/or propofol re-injection, and spontaneous ventilation recovery (mean (SEM) 3.8 (0.6) min, R group vs 3.2 (0.7) min, A group, NS) or eye opening (7.1 (1.1) min, R group vs 7.4 (0.9) min, A group, NS). Thirty minutes after postanaesthesia care unit (PACU) admission, MAP returned to its pre-induction value in the R group (104 (3) vs 109 (3) at baseline, NS), whereas in the A group MAP remained significantly lower at this time point (96 (4) vs 106 (3) at baseline, P<0.05).

Conclusion. This study showed that only remifentanil prevented MAP increase without adverse effects such as bradycardia during DL, and prevented MAP decrease 30 min after PACU admission.

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Direct laryngoscopy (DL) is a brief surgical procedure which can be performed safely under general anaesthesia with intense analgesic without intubation.¹ Two opioids which may provide analgesia with rapid onset are available: remifentanil and alfentanil. Because of its unique pharmacokinetic characteristics, remifentanil seems to be ideal; it offers rapid recovery, whereas alfentanil displays considerable variability because of its liver metabolism. Remifentanil has been proven to be more effective than alfentanil with respect to haemodynamic response to intubation, allowing faster recovery and tracheal extubation.²–6

Numerous studies have compared remifentanil with alfentanil, but none has attempted to compare them in a brief surgical procedure performed without intubation associated with intense stimulation. The aim of this study was to compare the effects of remifentanil vs alfentanil during DL on haemodynamic and Bispectral Index (BIS) responses, glottic visualization, and rapidity of recovery (spontaneous ventilation, eye opening).
Methods and results

After obtaining local institutional Research Ethical Committee approval and informed consent, we studied 60 patients, aged more than 18 yr, undergoing DL without intubation. Exclusion criteria included pregnant women, patients under juridical protection, or with known adverse reactions to the study drugs and, during the procedure, patients where mask ventilation was deficient, long procedure more than 10 min, or more than two ENT surgeons performing the DL. Four Board Certified surgeons participated in the study. One patient in each group was withdrawn because of long procedure duration.

Patients were allocated randomly to receive i.v. injection over 30 s of either remifentanil (2 μg kg⁻¹) (R group) or alfentanil (30 μg kg⁻¹) (A group). These dosages were based on a potency ratio of remifentanil 1 μg kg⁻¹ to alfentanil 15 μg kg⁻¹, and that remifentanil 2 μg kg⁻¹ was shown to block haemodynamic responses following intubation. Speed of onset of remifentanil effect has been shown to be as rapid as alfentanil (90 s). No pre-medication was given. Continuous heart rate (HR) and pulse oximetry, non-invasive arterial pressure, and BIS were recorded at baseline, 3-min after induction, DL and after opioid or propofol re-injection. After a 3-min pre-oxygenation we injected propofol (2.5 mg kg⁻¹, over 1 min), and either remifentanil or alfentanil. No muscle relaxant was used. Mean (SEM) total doses of propofol were similar in both groups (206 (15) vs 204 (12) mg in R and A groups; Mann–Whitney U-test). Three minutes later (90 s after the opioid injection), all patients were ventilated with a facemask before DL started. During laryngoscopy mean arterial pressure (MAP) increased by 6 (R group) vs 20% (A group) (P<0.05), and HR decreased by 8 and 4% in the R and A groups, when compared with post-induction values (NS) (Fig. 1). BIS decreased by 60 (R group) and 58% (A group), 3 min after induction (ANOVA, NS vs baseline values), and increased by 20 and 19% at DL (NS vs post-induction values).

Remifentanil 1 μg kg⁻¹ or alfentanil 15 μg kg⁻¹ was re-injected if the BIS value was greater than 60 or 40–60 with patient movement, if MAP or HR increase was greater than 20% vs preoperative values, or if the vocal cords were not relaxed. If these criteria were unchanged after 90 s, propofol 1 mg kg⁻¹ was re-injected. Eleven (R group) and nine (A group) patients did not require opioid re-injection (χ²-test, NS). Re-injection criteria were similar in both groups. Vocal cords were in abduction in 24 (R group) and 20 patients (A group) (χ²-test, NS).

In the A group, two episodes of bradycardia were observed: one less than 40 beats min⁻¹ responded well to 0.5 mg atropine and two sternal thumps, and one resolved when DL was suspended. In the R group, two cases of mild bradycardia did not require any treatment. Ten (R group) and eight patients (A group) presented with desaturation episodes (SpO₂ <90%) requiring oxygen administration only via facemask (NS). No tracheal intubation was required.

Mean (SEM) procedure duration was 6.1 (0.4) (R group) vs 5.6 (0.4) min (A group) (Mann–Whitney U-test, NS). No difference was noted in time to eye opening (7.1 (1.1) vs 7.4 (0.9) min, R and A groups, Mann–Whitney U-test, NS) and return of adequate spontaneous ventilation (3.8 (0.6) vs 3.2 (0.7) min, R and A groups, Mann–Whitney U-test, NS).

Thirty minutes after postanaesthesia care unit (PACU) admission, MAP returned to pre-induction value only in the R group, HR was not different between groups (Fig. 1) nor was the Aldrete score at 15 min (score=10 in 79.3% of patients in both groups, χ²-test, NS), and at 30 min (score=10 in 93% of patients in R group vs 82.7% in A group, NS).

Comment

In this study, we found that remifentanil administration resulted in a lower increase in MAP during DL when compared with alfentanil. MAP, HR, and BIS decreased.
significantly 3 min after induction, but with no difference between the groups. These results suggest that remifentanil did not induce more cardiovascular depression than alfentanil, whereas previous studies concluded the opposite.\textsuperscript{4,5} Comparison of these former results with ours is difficult as remifentanil was compared with saline, or premedication was used. We decided to avoid premedication in our patients to exclude a bias. During laryngoscopy HR decreased similarly in both groups. Opioid was injected over 30 s eliminating the effect of a bolus. These results are in agreement with a previous study\textsuperscript{2} even if one demonstrated bradycardia after remifentanil administration in a patient treated with a $\beta$-blocker.\textsuperscript{9} In contrast, we observed a severe bradycardia in one A group patient. In our study, MAP significantly increased during laryngoscopy in the alfentanil group, whereas no difference between remifentanil and alfentanil was found in a previous study on haemodynamic responses to orotracheal intubation.\textsuperscript{2}

Whereas MAP significantly increased in the alfentanil group during laryngoscopy, BIS increase was not different between the groups. Our results did not confirm those of Guignard and colleagues who demonstrated that a BIS change was as sensitive as haemodynamic responses after a painful stimulus for detecting deficits in the analgesic component of anaesthesia.\textsuperscript{10}

There was no difference in vocal cord abduction between groups. However, previous studies are conflicting. Alexander and colleagues concluded that alfentanil was the best opioid for intubating conditions in patients receiving premedication.\textsuperscript{4} However, Klemola and colleagues demonstrated that remifentanil provided better intubating conditions than alfentanil. In the latter study the opioid was injected 30 s before the hypnotic.\textsuperscript{3} In our study, we chose to administer the hypnotic before the opioid because its onset of action is twice less rapid than the opioid one. This difference in the protocol probably explains, at least in part, the absence of differences between our groups.

In our study, no difference was shown in recovery including time for eye opening and return of adequate spontaneous ventilation. Our results are not consistent with Wuesten’s study in which an Aldrete’s score at 10 was more rapidly obtained by the use of remifentanil.\textsuperscript{2} As Egan and colleagues suggested, these results can be because of the absence of pharmacokinetic differences between remifentanil and alfentanil for procedures less than 10 min.\textsuperscript{8} Indeed, in the previously mentioned study, procedure duration was longer than 10 min whereas in our study, it was an exclusion criterion.

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