

SHORT COMMUNICATION

Effects of remifentanyl and alfentanil on the cardiovascular responses to induction of anaesthesia and tracheal intubation in the elderly

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Background. We compared the effects of remifentanyl and alfentanil on arterial pressure and heart rate at induction of anaesthesia and tracheal intubation in 40 ASA I–III patients aged greater than 65 yr, in a randomized double-blind study.

Methods. Patients received either remifentanyl $0.5 \mu\text{g kg}^{-1}$ over 30 s, followed by an infusion of $0.1 \mu\text{g kg min}^{-1}$ (group R) or alfentanil $10 \mu\text{g kg}^{-1}$ over 30 s, followed by an infusion of saline (group A). Anaesthesia was then induced with propofol, rocuronium, and 1% isoflurane with 66% nitrous oxide in oxygen.

Results. Systolic arterial pressure (SAP) and mean arterial pressure (MAP) decreased after the induction of anaesthesia ($P < 0.05$) and increased for 3 min after intubation in both groups ($P < 0.05$), but remained below baseline values throughout. Heart rate remained stable after induction of anaesthesia but increased significantly from baseline after intubation for 1 and 4 min in groups R and A, respectively ($P < 0.05$). There were no significant between-group differences in SAP, MAP, and heart rate. Diastolic pressure was significantly higher in group A than group R at 4 and 5 min after intubation ($P < 0.05$). Hypotension (SAP < 100 mm Hg) occurred in four patients in group R and three patients in group A.

Conclusions. Remifentanyl and alfentanil similarly attenuate the pressor response to laryngoscopy and intubation, but the incidence of hypotension confirms that both drugs should be used with caution in elderly patients.

Br J Anaesth 2002; **88**: 430–3

Keywords: age factors, cardiovascular responses; analgesics opioid, remifentanyl; analgesics opoid, alfentanil; intubation tracheal, responses; heart, heart rate; arterial pressure

Accepted for publication: November 13, 2001

The cardiovascular responses to laryngoscopy and tracheal intubation have been well documented, and a number of methods may be used to modify them, including alfentanil and remifentanyl.^{1,2} The elderly, who comprise an increasing proportion of patients presenting for surgery, have a diminished physiological reserve, alterations in autonomic function, an increased incidence of coexisting cardiovascular disease,³ and increased sensitivity to opioids and anaesthetic drugs.^{4,5} These factors may combine to increase cardiovascular lability during induction of anaesthesia, with the attendant risks of myocardial ischaemia, stroke, cardiac arrhythmias, or sudden death.⁶

Few studies of the haemodynamic responses to intubation have been performed in the elderly, and none have used remifentanyl. The aim of this study was to compare the effects of remifentanyl and alfentanil in modifying the haemodynamic response to intubation in elderly patients.

Methods and results

With hospital ethics committee approval and informed consent, we recruited 40 normotensive, non-premedicated ASA I–III patients aged 65–85 yr undergoing elective

surgery and requiring tracheal intubation. Exclusions were: concurrent vasoactive medication, risk of gastroesophageal reflux, obesity (BMI >30), anticipated difficult airway, or evidence of cardiac disease. Patients were randomized to two groups (group R=remifentanyl, group A=alfentanil) in a double-blind manner by the sealed envelope technique.

All patients received i.v. Hartmann's solution 5 ml kg⁻¹ over 5–10 min before the induction of anaesthesia. Routine monitoring was instigated and heart rate and arterial pressure were recorded at 1 min intervals throughout the study. Arterial pressure was measured non-invasively using an automatic oscillometer (Datex Cardiocap II) and ECG was monitored with electrodes in the CM5 position. Three readings of heart rate and arterial pressure were taken before the start of the study and the mean of these three values defined as each individual's baseline data. All patients received i.v. glycopyrrolate 0.2 mg immediately followed by a bolus of either remifentanyl (0.5 µg kg⁻¹ in 10 ml saline over 30 s) followed by a remifentanyl infusion at 0.1 µg kg⁻¹ min⁻¹ (group R), or a bolus of alfentanil (10 µg kg⁻¹ in 20 ml saline over 30 s) followed by an infusion of saline (group A). Immediately after the study drug, anaesthesia was induced with propofol (0.5 mg kg⁻¹ followed by 10 mg every 10 s until loss of verbal contact) and rocuronium 0.6 mg kg⁻¹ was administered to produce neuromuscular block. Patients' lungs were ventilated manually with 1% isoflurane

and 66% nitrous oxide in oxygen, to an end-tidal carbon dioxide tension of 4.0–4.5 kPa. Neuromuscular block was confirmed with a nerve stimulator and laryngoscopy, and tracheal intubation were then performed 3 min after loss of verbal contact.

Ephedrine (3 mg increments) was administered for hypotension (systolic arterial pressure (SAP) <100 mm Hg, or a decrease of >30% from baseline values for >60 s) and atropine, in 300 µg increments, for bradycardia (heart rate <45 beats min⁻¹). For hypertension (SAP >200 mm Hg, or an increase of >30% above baseline for >60 s) or tachycardia (heart rate >130 beats min⁻¹ for >60 s), the inspired isoflurane concentration was increased in increments of 0.5%. Power calculations based on previous data,⁷ suggested that 20 patients per group would detect a 15% difference in SAP or heart rate between the groups after intubation ($\alpha=0.05$, $\beta=0.2$).

Statistical analysis was performed using a general linear model analysis of variance for repeated measures for continuous variables (with treatment group and time as between- and within-group factors, and Bonferroni adjustment for multiple comparisons). All analyses were performed using SPSS for Windows computer software (release 9.0).

One patient in the remifentanyl group was excluded because of a procedural violation (unanticipated difficult tracheal intubation with duration of laryngoscopy >2 min). Patient characteristics are given in Table 1. Baseline arterial pressure and heart rate were similar in both groups (Table 2). Mean arterial pressure (MAP) decreased significantly after induction of anaesthesia in both groups ($P<0.05$ compared with baseline values) and increased for 3 min after intubation ($P<0.05$ compared with pre-intubation), but remained below baseline throughout the study period. It was significantly lower than baseline at 4–5 min after intubation in both groups ($P<0.05$). Changes in SAP and diastolic arterial pressure (DAP) followed a similar pattern but DAP was significantly higher in group A at 4 and 5 min post-intubation ($P<0.05$). However, there were no differences between groups in MAP or SAP at any time point.

Table 1 Patient characteristics, view and duration of laryngoscopy: mean (SD, or range), or number. There were no significant differences between groups

	Group R (n=19)	Group A (n=20)
Age (yr)	73.1 (65–83)	74.0 (65–85)
Sex (M:F)	9/10	11/9
Weight (kg)	68.8 (15.3)	69.8 (13.5)
ASA grade (I/II/III)	6/11/2	7/12/1
Propofol dose (mg)	76.7 (25.0)	76.1 (23.9)
Grade of anaesthetist intubating (SHO/SpR/Consultant)	3/12/4	2/16/2
Duration of laryngoscopy (s)	14.7 (9.8)	13.4 (8.7)
View at laryngoscopy (1/2/3)	12/6/1	17/2/1

Table 2 Mean (SD) SAP, DAP, and MAP and heart rate at baseline, after induction of anaesthesia (Ind) and after tracheal intubation (Int) in groups R and A. * $P<0.05$ compared with baseline, ** $P<0.05$ compared with pre-intubation (Ind+3 min), *** $P<0.05$ between groups. Baseline values are the mean of three readings

	Baseline	Ind+1 min	Ind+2 min	Ind+3 min	Int+1 min	Int+2 min	Int+3 min	Int+4 min	Int+5 min
Group R									
SAP (mm Hg)	159 (17)	134 (30)*	121 (29)*	104 (23)*	133 (27)**	141 (26)**	129 (30)**	118 (21)*	109 (19)*
DAP (mm Hg)	79 (11)	68 (17)	63 (20)	54 (15)*	77 (18)**	77 (22)**	69 (18)**	60 (15)*, ***	57 (11)*, **
MAP (mm Hg)	103 (11)	82 (21)*	79 (21)*	68 (19)*	96 (18)**	97 (25)**	88 (21)**	78 (20)*	73 (14)*
Heart rate (beats min ⁻¹)	77 (14)	75 (19)	74 (20)	74 (20)	92 (18)*, **	89 (18)**	82 (19)	79 (18)	77 (17)
Group A									
SAP (mm Hg)	153 (23)	130 (28)*	115 (24)*	105 (19)*	132 (28)**	143 (34)**	135 (32)**	127 (29)*	119 (25)*
DAP (mm Hg)	83 (11)	73 (15)	65 (13)	60 (10)*	84 (16)**	86 (20)**	80 (19)**	74 (17)*, ***	69 (13)*, **
MAP (mm Hg)	106 (15)	90 (18)*	82 (17)*	74 (12)*	101 (23)**	105 (24)**	98 (24)**	89 (20)*	83 (17)*
HR (min ⁻¹)	77 (10)	78 (10)	77 (12)	77 (12)	97 (15)*, **	94 (15)*, **	91 (17)*, **	88 (16)*, **	86 (15)**

Heart rate increased significantly after intubation in both groups to exceed baseline values. Heart rate remained elevated, compared with pre-intubation values, for 2 min in group R ($P < 0.05$) and for 5 min in group A ($P < 0.05$). Values after intubation were significantly higher than baseline for 1 min in group R and for 4 min in group A ($P < 0.05$). However, there were no between-group differences in heart rate throughout the study.

One patient in group R and two patients in group A experienced marked hypotension (SAP < 80 mm Hg for > 1 min). Four patients in group R and three in group A required ephedrine for hypotension. However, nine patients in group R and eight in group A had transient hypotension (SAP < 100 mm Hg for < 1 min) which did not require ephedrine. One patient in group R and two in group A received an increased inspired concentration of isoflurane to treat hypertension. There were no incidences of bradycardia, tachycardia, arrhythmias, ST segment, or other ECG changes observed during the study.

Comment

In this study, the cardiovascular effects of remifentanyl and alfentanil at induction of anaesthesia and intubation were similar. Although observed increases in MAP and heart rate at intubation were statistically significant, they were modest and clinically acceptable. MAP remained below baseline values throughout the study, whereas HR exceeded baseline values for 1 (group R) and 4 min (group A) after intubation. DAP was significantly higher in group A than group R at 4 and 5 min after intubation, probably because an infusion of remifentanyl was used (group R), whereas the effects of alfentanil would be diminishing by this time (group A).

Mild hypotension (SAP < 100 mm Hg for < 1 min) after induction of anaesthesia occurred in almost 50% of patients despite i.v. fluid pre-loading and glycopyrrolate pre-treatment, but marked hypotension (SAP < 80 mm Hg for > 1 min) occurred in only three patients. There was also large variation in response to laryngoscopy and tracheal intubation, with the maximum mean heart rate and arterial pressure occurring 2 min after intubation. Mean SAP, 2 min after tracheal intubation, was 140.6 (range 100–193) and 143.5 (range 92–196) mm Hg in groups R and A, respectively.

These findings suggest that the elderly are susceptible to marked fluctuations in arterial pressure and heart rate at induction of anaesthesia and that attenuation of cardiovascular responses was sometimes incomplete, with large variations between individual patients. However, the overall incidence and degree of hypotension in this study is likely to have been greater, had higher doses of remifentanyl or alfentanil been used. Although studies in younger adults have used higher doses of alfentanil, $10 \mu\text{g kg}^{-1}$ was found to be optimal in elderly patients.⁷ The potency of remifentanyl compared with alfentanil is approximately

20:1,⁸ which corresponds to the remifentanyl dose of $0.5 \mu\text{g kg}^{-1}$ used here. A previous study showed these dose regimens to have similar cardiovascular effects in hypertensive patients.⁹

In another study in elderly patients, the cardiovascular response to tracheal intubation was attenuated by fentanyl $3 \mu\text{g kg}^{-1}$ but with a 35% incidence of marked hypotension (SAP < 80 mm Hg).¹⁰ The incidence of hypotension in the present study may also have stemmed from the use of propofol, despite careful titration of dose to effect. The elderly are known to be sensitive to the effects of propofol,¹¹ but it has been suggested to be the preferred i.v. anaesthetic agent to attenuate the cardiovascular response to intubation.¹² However, severe hypotension was rare in this study.

Although the drug combinations and doses were reasonable in this group of elderly patients, no patients in this study had significant cardiovascular disease. Few data are available on the effects of remifentanyl in patients with impaired cardiac function, although hypotension is more likely to occur, and further studies should investigate the optimum dose of remifentanyl in these high-risk patients.

In summary, remifentanyl $0.5 \mu\text{g kg}^{-1}$ over 30 s followed by an infusion of $0.1 \mu\text{g kg}^{-1} \text{ min}^{-1}$ was as effective as alfentanil $10 \mu\text{g kg}^{-1}$ in attenuating the pressor response to tracheal intubation in elderly patients. It is an acceptable alternative to alfentanil at induction of anaesthesia when a remifentanyl infusion is used during surgery.

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