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Effect of remifentanil on the haemodynamic response to orotracheal intubation

J. P. THOMPSON, A. P. HALL, J. RUSSELL, B. CAGNEY AND D. J. ROWBOTHAM

Summary

We have examined the effect of remifentanil on the haemodynamic response to orotracheal intubation in a randomized, double-blind study. We studied 40 patients allocated to one of four groups of 10 each, to receive the following immediately before induction of anaesthesia: remifentanil 1 μg kg^{-1} bolus over 30 s, followed by an infusion of 0.5 μg kg^{-1} min^{-1}; saline placebo only; glycopyrrolate 200 μg and remifentanil 1 μg kg^{-1} bolus over 30 s, followed by an infusion of 0.5 μg kg^{-1} min^{-1}; or glycopyrrolate 200 μg only. Anaesthesia was induced with propofol, vecuronium and 1% isoflurane with 66% nitrous oxide in oxygen. The trachea was intubated under direct laryngoscopy 3 min after induction of anaesthesia. Arterial pressure and heart rate were measured non-invasively, immediately before induction of anaesthesia and then at 1-min intervals. Remifentanil was found to effectively attenuate the pressor response to intubation ($P<0.05$ for the increase in mean arterial pressure; $P<0.01$ for the increase in heart rate). In the absence of a concurrent vagolytic agent, remifentanil was associated with bradycardia or hypotension, or both, in five of 10 patients, compared with one patient who received remifentanil and glycopyrrolate. (*Br. J. Anaesth*. 1998; **80**: 467–469)

Keywords: analgesics opioid, remifentanil; premedication, glycopyrrolate; intubation tracheal; intubation tracheal, responses; cardiovascular system, effects

The pressor response to tracheal intubation, resulting in tachycardia and hypertension, is well described.[1] Plasma concentrations of catecholamine are increased[2,3] and there may be associated myocardial ischaemia.[4] Haemodynamic responses may be attenuated by several methods, including administration of i.v. opioids,[5] vasodilators,[6] β-blockers[7] or by deepening of anaesthesia. Remifentanil is a new opioid agent that is structurally unique. An ester bond renders it subject to rapid hydrolysis by non-specific blood and tissue esterases and thus it has a short half-life.[8] Speed of onset of effect is rapid (1–2 min) and similar to that of alfentanil.[9] Therefore, remifentanil may be appropriate for attenuation of the pressor responses to brief but noxious stimuli. The aim of this study was to assess the effect of remifentanil on changes in heart rate and arterial pressure after intubation. In view of the reported association of remifentanil with bradycardia,[10] the effect of concurrent administration of glycopyrrolate was also examined.

Patients and methods

After obtaining approval from the local Research Ethics Committee and informed written consent, we studied 40 ASA I–II female patients, aged 18–48 yr, presenting for elective surgery. Patients were assigned to one of four treatment groups of 10 patients each, to receive the following in a randomized, double-blind manner: remifentanil 1 μg kg^{-1} bolus given over 30 s, followed by an infusion of 0.5 μg kg^{-1} min^{-1}; saline placebo only; glycopyrrolate 200 μg and remifentanil 1 μg kg^{-1} bolus given over 30 s, followed by an infusion of 0.5 μg kg^{-1} min^{-1}; and glycopyrrolate 200 μg only. All treatments were given immediately before induction of anaesthesia. Anaesthesia was induced with a bolus dose of propofol 0.5 mg kg^{-1} followed by 10 mg every 10 s titrated to loss of verbal contact, vecuronium 0.1 mg kg^{-1}, and 1% isoflurane with 66% nitrous oxide in oxygen. We ventilated the patients' lungs manually using a Bain system for 3 min after which the trachea was intubated under direct laryngoscopy. Thereafter the lungs were ventilated mechanically using a Manley ventilator (tidal volume 10 ml kg^{-1}, target end-tidal carbon dioxide partial pressure 4.0–4.5 kPa: Datex Capnomac). Arterial pressure was measured non-invasively using an automatic oscillometric device (Datex Cardiocap), and heart rate recorded from the ECG trace. Observations of heart rate (HR), systolic arterial pressure (SAP), mean arterial pressure (MAP) and diastolic arterial pressure (DAP) were recorded every minute from the start of induction to 5 min after intubation (nine time points). Hypotension (SAP < 80 mm Hg for > 60 s) was treated with ephedrine 3-mg or atropine 300-μg increments i.v. (HR < 50 beat min^{-1}); bradycardia (heart rate < 45 beat min^{-1} for > 60 s) was treated with atropine 300-μg increments i.v.

Statistical analysis was performed using two-way and multivariate analysis of variance for repeated measures (ANOVA, MANOVA with treatment group and time as the between- and within-group factors) and paired and unpaired *t* tests with Bonferroni post-test analysis, as appropriate, using SPSS for Windows computer software (release 6.0., 1993).

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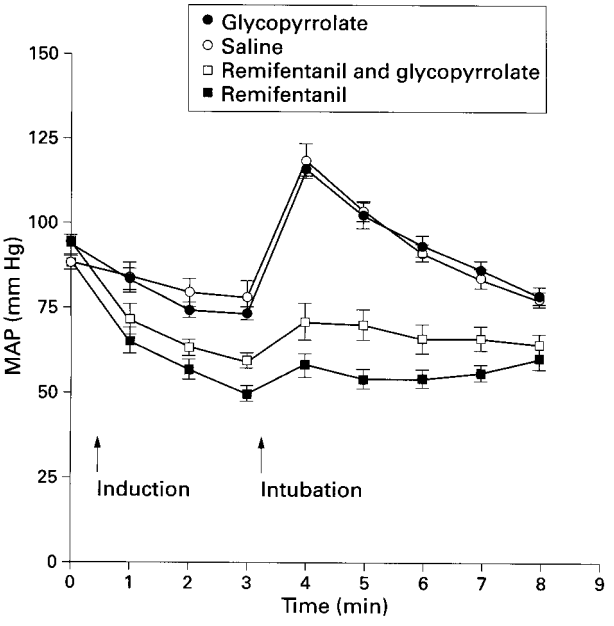

Figure 1 Mean (SEM) mean arterial pressure (MAP) in the glycopyrrolate, saline, remifentanil–glycopyrrolate and remifentanil groups. Preinduction MAP is represented by $t=0$; induction and intubation are indicated by arrows.

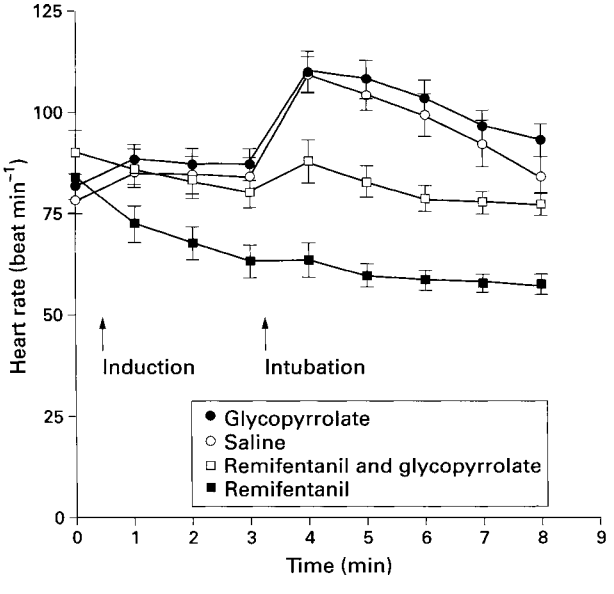

Figure 2 Mean (SEM) heart rate in the glycopyrrolate, saline, remifentanil–glycopyrrolate and remifentanil groups. Preinduction HR is represented by $t=0$; induction and intubation are indicated by arrows.

Results

Patient characteristics were similar in all four groups. Patients who received remifentanil required less propofol to produce loss of consciousness than those in the non-remifentanil groups (mean 1.66 (SEM 0.12) mg kg^{-1} *vs* 2.23 (0.17) mg kg^{-1}; $P=0.01$). MAP and HR over the nine times are shown in figures 1 and 2, respectively. SAP and DAP changed in parallel with MAP and therefore have not been reported. There were no differences in MAP or HR before induction of anaesthesia between the groups.

MAP and HR decreased in all groups after induction of anaesthesia ($P<0.01$). MAP was lower in the remifentanil groups than in the non-remifentanil groups 1 min before intubation ($P<0.01$). MAP increased significantly in all groups after laryngoscopy and tracheal intubation ($P<0.01$) but was significantly greater in the non-remifentanil groups than in the remifentanil groups ($P<0.05$). Mean increases in MAP at intubation were 39.9 mm Hg, 42.0 mm Hg, 8.1 mm Hg and 11.3 mm Hg in the saline, saline–glycopyrrolate, remifentanil and remifentanil–glycopyrrolate groups, respectively; MAP remained below pre-induction values in the remifentanil groups. There were no significant differences in MAP between the remifentanil and remifentanil–glycopyrrolate groups and the saline and glycopyrrolate groups before and after tracheal intubation.

HR decreased in all groups after induction of anaesthesia ($P<0.01$), and was significantly lower in the remifentanil group immediately before intubation compared with the three other groups ($P<0.01$) and compared with pre-induction values ($P<0.001$). HR increased after intubation in the non-remifentanil groups ($P<0.001$) and was significantly greater 1 min after intubation in the non-remifentanil groups compared with the remifentanil groups ($P<0.01$). There were no significant differences in HR immediately before and after intubation in the remifentanil and remifentanil–glycopyrrolate groups.

Five patients in the remifentanil group and one in the remifentanil–glycopyrrolate group had bradycardia (HR <45 beat min^{-1}) or hypotension (SAP <80 mm Hg), or both, requiring rescue medication.

Discussion

We have found that a bolus dose of remifentanil 1 μg kg^{-1} given over 30 s, followed by an infusion of 0.5 μg kg^{-1} min^{-1} at induction of anaesthesia, attenuated the haemodynamic responses to orotracheal intubation. MAP decreased in all four groups after induction of anaesthesia. This decrease was greatest in the remifentanil group and was associated with bradycardia. Glycopyrrolate 200 μg given immediately before remifentanil produced no increase in heart rate but attenuated the bradycardia caused by remifentanil. The decrease in MAP after induction of anaesthesia was less in the remifentanil–glycopyrrolate group, although this was not statistically significant. However, clinically relevant hypotension requiring rescue medication was required in five of the remifentanil patients, but in only one patient in the remifentanil–glycopyrrolate group. Intubation had no significant effect on HR in the remifentanil or remifentanil–glycopyrrolate groups. MAP increased significantly in all four groups, but in the remifentanil groups this increase was quantitatively less and did not exceed baseline preinduction values.

Other workers have reported hypotension and bradycardia associated with remifentanil using similar regimens. Schüttler and colleagues, in a large multicentre study, compared remifentanil with alfentanil using an induction drug combination and dosage similar to ours for their remifentanil group.[11] However, all patients received either atropine or glycopyrrolate and prehydration with a crystalloid solution (5 ml kg^{-1}) before induction of anaesthesia. They reported that 53% of patients had a significant hypotensive episode during operation and 4% had a

significant bradycardia. However, patients were undergoing major abdominal surgery and no distinction was made in respect of timing of the episode or whether or not the aetiology was in fact surgical or drug-related.

Two multicentre studies have reported on the use of remifentanil as part of a total i.v. anaesthesia regimen.[12 13] Both studies used prehydration with a crystalloid solution but a vagolytic agent was not given. Hogue and colleagues[12] reported an incidence of hypotension on induction of anaesthesia of 10% with a dose of remifentanil identical to that used in our study. In a second group who received a higher infusion rate of 1 $\mu g\ kg^{-1}\ min^{-1}$, the incidence of hypotension was 15% although this difference was not found to be statistically significant. Bradycardia occurred in 7% and 19% of patients, respectively, but this difference was not significant. Philip and colleagues[13] also used a remifentanil bolus dose of 1 $\mu g\ kg^{-1}$ and an infusion of 0.5 $\mu g\ kg^{-1}\ min^{-1}$ after induction of anaesthesia with propofol 2 $mg\ kg^{-1}$. In patients undergoing gynaecological laparoscopic surgery, they reported a 17% incidence of hypotension/bradycardia throughout the operative period, but no distinction was made between the induction and intubation phases. It is possible that prehydration or the absence of a volatile anaesthetic agent, or both, are protective against the development of bradycardia and hypotension.

The size of the pressor response observed in those patients who did not receive remifentanil in our study was similar to that reported previously.[1–7] All patients in this study were healthy, of ASA grade I-II, and in the absence of data relating to the effect of remifentanil in this setting, the inclusion of these control groups was felt to be justified. We appreciate that this approach would be inappropriate in patients at risk of myocardial ischaemia,[7] particularly as the effect of remifentanil has now been quantified.

In our study 50% of patients who received remifentanil without glycopyrrolate exhibited hypotension and bradycardia that required rescue medication. One of the patients in the glycopyrrolate–remifentanil group was similarly affected; mean MAP in this group reached a nadir of 59 mm Hg immediately before intubation.

In summary, these results suggest that remifentanil attenuated the haemodynamic response to laryngoscopy and orotracheal intubation but pretreatment with a vagolytic agent may be required if the incidence of bradycardia and hypotension is to be minimized. It is possible that a lower dose of remifentanil may be effective while producing less hypotension, and further studies are required to investigate the optimal regimen.

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