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Bolus dose remifentanil for control of haemodynamic response to tracheal intubation during rapid sequence induction of anaesthesia

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The effect of three bolus doses of remifentanil on the pressor response to laryngoscopy and tracheal intubation during rapid sequence induction of anaesthesia was assessed in a randomized, double-blind, placebo-controlled study in four groups of 20 patients each. After preoxygenation, anaesthesia was induced with thiopental 5–7 mg kg^{-1} followed immediately by saline (placebo) or remifentanil 0.5, 1.0 or 1.25 μg kg^{-1} given as a bolus over 30 s. Cricoid pressure was applied just after loss of consciousness. Succinylcholine 1 mg kg^{-1} was given for neuromuscular block. Laryngoscopy and tracheal intubation were performed 1 min later. Arterial pressure and heart rate were recorded at intervals until 5 min after intubation. Remifentanil 0.5 μg kg^{-1} was ineffective in controlling the increase in heart rate and arterial pressure after intubation but the 1.0 and 1.25 μg kg^{-1} doses were effective in controlling the response. The use of the 1.25 μg kg^{-1} dose was however, associated with a decrease in systolic arterial pressure to less than 90 mm Hg in seven of 20 patients.

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Rapid sequence induction of anaesthesia is often associated with significant haemodynamic changes which are potentially harmful.[1] This response may be attenuated by opioid drugs, such as fentanyl and alfentanil.[2 3] However, these drugs are relatively slow in onset and their effective doses may result in prolonged effects. An effective drug with a shorter duration of action would be desirable for cases of short duration requiring rapid sequence induction of anaesthesia. Remifentanil is a new synthetic opioid providing intense analgesia of rapid onset and short duration.[4 5] A bolus dose of 1 μg kg^{-1} followed by an infusion of 0.5 μg kg^{-1} min^{-1} was shown to attenuate the haemodynamic response to laryngoscopy and tracheal intubation during routine induction of anaesthesia.[6] We have investigated the effectiveness of using only a bolus dose of remifentanil in controlling the haemodynamic response to intubation during rapid sequence induction of anaesthesia.

Methods and results

After obtaining approval from the Ethics Committee and written informed consent, we studied 80 patients presenting for elective surgery requiring tracheal intubation. Patients were aged 18–60 yr, weighing 75–125% of ideal for height, and were not receiving any medication with significant cardiovascular effects. No premedication was given. After preoxygenation for 3 min, anaesthesia was induced with thiopental 5–7 mg kg^{-1} followed by remifentanil 0.5, 1.0 or 1.25 μg kg^{-1}, or placebo, administered double-blind and by random allocation. The highest dose of 1.25 μg kg^{-1} was chosen in an attempt to compensate for the absence of infusion. Each treatment was made up to 15 ml with 0.9% saline and injected over 30 s. Cricoid pressure was applied as consciousness was being lost. Succinylcholine 1.0 mg kg^{-1} was given over 5 s soon after administration of the study drug, and laryngoscopy and tracheal intubation were performed 1 min later. Patients' lungs were ventilated with 0.5% isoflurane and 50% nitrous oxide in oxygen after intubation. Arterial pressures and heart rate (HR) were recorded before and after preoxygenation (averaged to give baseline values), after injection of the induction agent, just before laryngoscopy and intubation, and at 1-min intervals for 5 min after intubation.

Data within each group were subjected to repeated measures analysis of variance and between groups to one-way analysis of variance. The power calculation for including 20 patients was based on being able to show a

Table 1 Patient characteristics (age (yr), height (cm) and weight (kg)), systolic (SAP mm Hg) and diastolic (DAP mm Hg) arterial pressures, and heart rate (HR beat min^{-1}) during and after induction and intubation (mean (SD)) in the saline and remifentanil 0.5, 1.0 and 1.25 μg kg^{-1} groups. *$P<0.05$, **$P<0.01$ compared with baseline; †$P<0.05$, ††$P<0.01$ compared with saline group

			Baseline	After induction	Before laryngoscopy	+1 min	+2 min	+3 min	+4 min	+5 min
Saline										
Age	33 (9)	SAP	121 (16)	115 (13)	124 (20)	152 (19)**	145 (14)**	136 (17)*	132 (14)	124 (13)
Height	167 (9)	DAP	65 (8)	63 (9)	78 (13)	93 (15)**	85 (13)**	76 (13)	73 (12)	71 (13)
Weight	62 (9)	HR	79 (16)	90 (14)*	96 (15)**	101 (10)**	99 (13)**	95 (13)**	93 (15)*	89 (13)*
0.5 μg kg^{-1}										
Age	36 (10)	SAP	130 (18)	128 (23)	128 (23)	150 (18)**	140 (21)	126 (17)	117 (14)**†	116 (14)**
Height	162 (7)	DAP	75 (12)†	74 (17)†	79 (11)	98 (14)**	82 (14)	73 (10)	68 (10)*	64 (12)**
Weight	63 (6)	HR	83 (19)	90 (11)	87 (12)	94 (10)*	90 (11)†	84 (10)††	81 (10)†	79 (12)
1.0 μg kg^{-1}										
Age	33 (7)	SAP	128 (18)	121 (18)*	118 (16)**	130 (17)††	125 (18)††	114 (16)**††	110 (16)**††	110 (17)**†
Height	163 (7)	DAP	75 (11)†	71 (13)	70 (15)	82 (15)*	73 (14)†	66 (11)**†	63 (13)**†	63 (16)**
Weight	65 (9)	HR	84 (17)	95 (11)**	85 (12)†	89 (11)††	87 (12)††	83 (12)††	81 (16)†	76 (15)†
1.25 μg kg^{-1}										
Age	35 (7)	SAP	128 (19)	121 (20)	111 (17)**	122 (19)††	114 (18)**††	109 (17)**††	104 (16)**††	102 (13)**††
Height	165 (10)	DAP	73 (14)	75 (15)†	68 (15)	75 (14)††	66 (11)††	60 (10)**††	59 (11)**††	56 (12)**††
Weight	65 (10)	HR	71 (14)	89 (13)**	78 (13)*††	79 (14)*††	75 (10)††	72 (10)††	69 (10)††	67 (9)††

difference of 20 beat min^{-1} in HR after intubation between the highest remifentanil dose group and the placebo group (16 patients per group for 80% power with $P<0.05$).

The groups were comparable in age, weight, height, mean dose of thiopental and intubating conditions. Mean doses of thiopental for induction were 383 (SD 59), 382 (40), 390 (47) and 390 (64) mg in the saline, and remifentanil 0.5, 1.0 and 1.25 μg kg^{-1} groups, respectively.

Arterial pressures and HR are shown in Table 1. Baseline values did not differ significantly between groups, except for a small but significantly greater diastolic arterial pressure (DAP) in the remifentanil 0.5 and 1.0 μg kg^{-1} groups compared with the saline group. There was a small but significant ($P<0.01$) reduction in systolic arterial pressure (SAP) before laryngoscopy in the groups receiving the two higher doses of remifentanil. Tracheal intubation was associated with a significant increase in SAP in the saline and remifentanil 0.5 μg kg^{-1} groups ($P<0.01$). SAP was significantly lower in the remifentanil 1.0 and 1.25 μg kg^{-1} groups compared with the saline group ($P<0.01$) from 1 min after intubation, and in the lowest dose group in the later part of the study. SAP was less than 90 mm Hg in one, two and seven patients at some time during the study in the remifentanil 0.5, 1.0 and 1.25 μg kg^{-1} groups, respectively. There was a short lasting but significant increase in DAP after tracheal intubation in all but the remifentanil 1.25 μg kg^{-1} group.

HR increased in all groups after induction of anaesthesia. Mean HR just before laryngoscopy was significantly lower in the remifentanil 1.0 and 1.25 μg kg^{-1} groups ($P<0.05$) compared with the saline group. There was an increase in HR in all groups after tracheal intubation which was significant in the saline group ($P<0.05$) for the whole 5-min period after tracheal intubation. HR in the remifentanil groups was significantly higher than baseline ($P<0.01$) for only 1 min after tracheal intubation, with no significant increase in the 1 μg kg^{-1} group. In the remifentanil 1 and 1.25 μg kg^{-1} groups, the increase in HR was significantly lower than in the control group ($P<0.05$). In the remifentanil 1.25 μg kg^{-1} group, mean HR was consistently lower than in the other groups; one patient in this group had a HR <50 beat min^{-1} during the study.

Comment

This study was designed to determine if a single bolus dose of remifentanil could prevent the pressor response to laryngoscopy and tracheal intubation during rapid sequence induction of anaesthesia. This would be useful for any operation of short duration, or when a prolonged opioid effect is undesirable (e.g. Caesarean section). We have shown that remifentanil 1.0 and 1.25 μg kg^{-1} were effective in controlling this response. However, the higher dose was associated with a decrease in arterial pressure in a significant proportion of patients.

A recent study in small groups of patients showed that remifentanil 1.0 μg kg^{-1} was effective in preventing the pressor response.[6] Patients in this study also received an infusion of remifentanil 0.5 μg kg^{-1} min^{-1} for several min, and 1% isoflurane and 66% nitrous oxide. The total dose of remifentanil would therefore have been much greater, in addition to the other agents used. Therefore, it is not surprising that almost 50% of patients showed bradycardia, although this could have been related in part to the use of propofol and vecuronium. Our study using only a bolus dose showed that remifentanil 1.0 μg kg^{-1} was sufficient when using thiopental and succinylcholine as part of a rapid sequence induction.

In summary, when used as part of a rapid sequence induction with thiopental and succinylcholine, remifentanil 1.0 μg kg^{-1}, administered as a bolus after induction of anaesthesia, generally prevented the pressor response after intubation, except for a small increase in DAP. Increasing the dose to 1.25 μg kg^{-1} conferred only minimal additional

advantage (completely preventing the increase in DAP) but was associated with hypotension and occasional bradycardia.

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