EFFECTS OF PINDOLOL ON THE CARDIOVASCULAR RESPONSE TO TRACHEAL INTUBATION


SUMMARY
Laryngoscopy and tracheal intubation often cause hypertension, tachycardia and arrhythmias, which may be exaggerated during rapid-sequence induction of anaesthesia. We have studied the efficacy of pindolol in attenuating the cardiovascular responses to laryngoscopy and intubation in patients receiving pindolol 2 µg kg\(^{-1}\) or 4 µg kg\(^{-1}\) 3 min before induction of anaesthesia in a double-blind design. The data were compared with those in a control group receiving saline. Each group consisted of 10 patients undergoing elective surgery. Anaesthesia was induced with thiopentone 5 mg kg\(^{-1}\) i.v. and tracheal intubation was facilitated with vecuronium 0.2 mg kg\(^{-1}\). Patients receiving saline showed a significant increase in mean arterial pressure and heart rate associated with tracheal intubation. These increases after tracheal intubation were reduced in pindolol 4 µg kg\(^{-1}\) treated patients compared with those in the control group (\(P < 0.05\)). Pindolol 2 µg kg\(^{-1}\) attenuated tachycardia in response to intubation but did not affect hypertension. These data suggest that a bolus injection of pindolol 4 µg kg\(^{-1}\) is a simple, practical and effective method for attenuating cardiovascular responses to laryngoscopy and tracheal intubation.

KEY WORDS

Laryngoscopy and tracheal intubation often provoke a marked sympathetic response, resulting in hypertension and tachycardia [1–4]. Although transient, this response may be deleterious. In patients with coronary artery disease (CAD) or those with risk factors for CAD, myocardial ischaemia may occur during the...
TABLE 1. Patient data (mean (range or SEM)). No significant differences (P > 0.05)

<table>
<thead>
<tr>
<th></th>
<th>Control (saline)</th>
<th>Pindolol 2 µg kg⁻¹</th>
<th>Pindolol 4 µg kg⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. patients</td>
<td>10</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>3:7</td>
<td>3:7</td>
<td>4:6</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>43.4 (25-57)</td>
<td>44.7 (26-58)</td>
<td>45.1 (24-57)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>57.6 (3.6)</td>
<td>59.5 (3.8)</td>
<td>56.7 (3.6)</td>
</tr>
</tbody>
</table>

Pindolol is a non-selective β-adrenergic antagonist exhibiting prominent intrinsic sympathomimetic activity (ISA). The ISA causes mild vasodilating properties, making this drug useful in the treatment of hypertension [14]. Compared with β-adrenergic antagonists devoid of ISA, such as propranolol and practolol, pindolol is less likely to cause myocardial depression, resting severe bradycardia, or a reduction in cardiac output. Thus pindolol is usually preferred for individuals with diminished cardiac reserve or a propensity for bradycardia [14]. The agent blocks exercise-induced increases in heart rate (HR) [14].

The rationale for administration of pindolol 5 min before the stimulus of laryngoscopy and intubation was based on data from a preliminary study and other laboratories. In our preliminary study, in which patients (ASA physical status I) were anaesthetized with 1% enflurane and 50% nitrous oxide in oxygen to determine the time courses and magnitudes of decreases in HR and MAP after administration of various doses of pindolol in the absence of surgery, the effect of pindolol peaked 5–6 min after injection. Miyazaki and Fujita reported that the peak effect of i.v. pindolol on HR and AP changes and tachyarrhythmia, determined mainly in ASA I patients, occurred approximately 5 min after administration [15, 16]; their data are consistent with those of several studies mainly of ASA I patients that the anti-arrhythmic effect of this drug is apparent 1–7 min after injection [17, 18]. All investigators used pindolol 1–4 µg kg⁻¹ in their studies [15–18]. Furthermore, the β-adrenergic blocking effect of pindolol is 5–20 times as potent as that of propranolol [1, 16]; because propranolol in a dose of 40 µg kg⁻¹ has been confirmed to be useful in reducing haemodynamic changes after intubation [1], we used pindolol 2 and 4 µg kg⁻¹ for this purpose. Thus it was predicted that the peak of action of pindolol 2 or 4 µg kg⁻¹ administered 5 min before laryngoscopy would occur at the same time as the peak of hypertension and tachycardia produced by laryngoscopy and tracheal intubation.

In the operating room, a radial arterial catheter was inserted under local anaesthesia for continuous monitoring of MAP. HR was calculated from a 15-s portion of lead II of the ECG. After a 10-min stabilization period, the patients breathed 100% oxygen via a mask for 3 min. Subsequently, pindolol 2 µg kg⁻¹ or 4 µg kg⁻¹ or saline (control) was injected 5 min before starting direct laryngoscopy (3 min before administration of thiopentone-vecuronium). Immediately before administration of pindolol or placebo and induction of anaesthesia, AP and HR were recorded simultaneously by an independent observer. Anaesthesia was induced with thiopentone 5 mg kg⁻¹ followed by vecuronium 0.2 mg kg⁻¹ to facilitate tracheal intubation. Direct laryngoscopy was attempted 2 min after administration of thiopentone-vecuronium, and tracheal intubation was completed within 30 s in all patients, with the aid of a standard Macintosh laryngoscope blade. All intubations were performed by one of the authors (K.M.). The investigator and the patients were blinded to the identity of the experimental treatment. During anaesthesia, ventilation was assisted as required or controlled with 1% enflurane and 50% nitrous oxide in oxygen, and \( P_{\text{CO}_2} \) was maintained at 4.2–4.9 kPa, measured with a Datex Capnometer by means of a catheter placed in the nostril until after the insertion of the
Fig. 2. Changes in mean arterial pressure (mean, SEM) after thiopentone–vecuronium and in response to laryngoscopy and tracheal intubation with pindolol 2 μg kg⁻¹ (●), 4 μg kg⁻¹ (○) or saline control (□), administered i.v. 5 min before starting laryngoscopy. The stippled area indicates duration of laryngoscopy and tracheal intubation. P < 0.05: * vs control; † vs basal value (3 min before induction) within group.

RESULTS

The three groups were comparable in age, weight and gender (table I).

There were no significant differences among the three groups in MAP immediately before the start of the laryngoscopy and at preinduction time (fig. 2). In response to laryngoscopy and intubation, MAP increased significantly in the control group. The increases in MAP 15 s and 30 s after intubation were reduced in patients who received pindolol 4 μg kg⁻¹ compared with those in the control group. However, administration of pindolol 2 μg kg⁻¹ failed to attenuate hypertension. There was no significant difference in HR among the three groups immediately before the start of laryngoscopy and preinduction (fig. 3). The HR increased significantly after intubation in the control group, while the increase was significantly less in the pindolol-treated groups (fig. 3). RPP was significantly smaller in pindolol 2 or 4 μg kg⁻¹ groups compared with control after laryngoscopy and intubation. There was no difference in RPP between the two pindolol-treated groups at any time.

No abnormal changes in ECG were observed in any patient who received pindolol, although two patients in the control group had transient ventricular premature contractions. During this study, no patients had bradycardia severe enough (HR < 50 beat min⁻¹) to require treatment and neither profound hypotension nor adverse respiratory effects were observed.

DISCUSSION

The present study has confirmed previous reports that tracheal intubation following thiopentone and a neuromuscular blocking agent causes significant increases in MAP, HR and RPP.
Pindolol 4 μg kg⁻¹ attenuated increases in these three variables after tracheal intubation compared with those of the control, whereas pindolol 2 μg kg⁻¹ attenuated the increases in HR and RPP but not in MAP.

The use of i.v. β-adrenergic antagonists before induction of anaesthesia in patients not previously receiving these drugs is controversial [1]. In one report it was noted that practolol 12 mg, given to attenuate the pressor response to intubation, caused circulatory collapse and cardiac arrest in an 80-kg patient who was probably hypovolaemic [18]. In this situation, pindolol may be safer than other β-adrenergic blockers without ISA. Furthermore pindolol, which has been used in the management of angina pectoris [19], dilates renal arteries, resulting in increased renal blood flow [20] and this may be an advantage over other β-blockers which lack ISA.

RPP was attenuated after pindolol, mainly because of a decrease in the HR response. The maximum mean RPP after intubation in the pindolol 4 μg kg⁻¹ group was 14263 mm Hg beat min⁻¹. This value compares favourably with the RPP of 15 187 and 15 868 mm Hg beat min⁻¹ in response to intubation in patients given prostaglandin E₁ [8] and buprenorphine [21] before induction, respectively.

In conclusion, we have shown that a single bolus i.v. administration of pindolol is a practical and effective method of attenuating hypertension and tachycardia in response to tracheal intubation. On the basis of changes in MAP, HR and RPP, we recommend the use of a dose of pindolol 4 μg kg⁻¹ as a supplement at the time of induction, for reducing the cardiovascular responses associated with intubation.

REFERENCES


