A controlled trial of the effects of esmolol on cardiac function

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SUMMARY
We have examined the effects of two different bolus doses of esmolol hydrochloride (Brevibloc) on haemodynamic variables in a placebo-controlled, double-blind, randomized trial. Sixty healthy adult patients undergoing minor orthopaedic surgery were given a standardized general anaesthetic using a laryngeal mask airway. Heart rate (HR), mean arterial pressure (MAP), stroke volume (SV) and cardiac output (Q) were measured (the latter two by Doppler ultrasonography) every 1 min for 5 min after injection of either placebo or esmolol 100 mg or 200 mg. HR, MAP, SV and Q decreased significantly (P < 0.05) for both esmolol groups compared with placebo and, except for MAP, esmolol 200 mg had a greater effect than esmolol 100 mg (P < 0.05). Depression was maximal at 2 min after which recovery was observed but was still incomplete at 5 min. (Br. J. Anaesth. 1994; 72: 594-595)

KEY WORDS

Esmolol hydrochloride (Brevibloc) is a cardio-selective β1 adrenergic receptor blocking agent. It has a rapid onset and short duration of action with an elimination half-life of only 9 min. A bolus of esmolol 1.5–3 mg kg\(^{-1}\) has been shown to attenuate the increase in heart rate (HR) and mean arterial pressure (MAP) associated with tracheal intubation [1]. Whilst attenuation of this pressor response is desirable, excessive negative chronotropic and inotropic action of a β1 receptor blocker may reduce coronary perfusion and precipitate heart failure in susceptible patients [2].

This study was undertaken to observe the change in haemodynamic variables, including cardiac output (Q) and stroke volume (SV), in healthy anaesthetized patients, after a bolus dose of esmolol 100 or 200 mg.

METHODS AND RESULTS
Hospital Ethics and Research Committee approval was obtained and 60 adult, ASA I patients (33 males) undergoing minor orthopaedic surgery, gave written consent for the study.

Premedication comprised temazepam 0.3 mg kg\(^{-1}\) orally 1 h before operation. On arrival in the anaesthetic room, a suitable vein was cannulated and oxygen saturation, HR, automatic non-invasive MAP and ECG were monitored. After 3 min of preoxygenation, anaesthesia was induced with propofol 2.5 mg kg\(^{-1}\) i.v. at a rate of 120 mg min\(^{-1}\) and maintained with 70% nitrous oxide in oxygen and 1% enflurane. A laryngeal mask was inserted and spontaneous ventilation established. No further stimulation was applied to the patient. HR and MAP were noted every 1 min until a period of stability was observed. Baseline measurements of SV and Q were then obtained using suprasternal Doppler ultrasonography with an ODM 1 machine (Deltex, Chichester). The same clinician recorded all Doppler measurements to reduce operator bias.

The patients were allocated randomly to one of three groups. The trial solution (group A, 0.9% saline 20 ml; group B, esmolol 100 mg in 20 ml; and group C, esmolol 200 mg in 20 ml) was then administered i.v. over 30 s. Readings were obtained 30 s after injection of the trial drug and then at 1-min intervals for 5 min. The anaesthetic then continued as appropriate. The results were calculated as percentage change in the readings before injection (to remove inter-patient variations in baseline readings). Data were analysed using the unpaired Student's t test. Significance was accepted at P < 0.05.

There was no significant difference in height, weight, age, gender or baseline haemodynamic readings between the three groups. Mean age was 38.4 (range 18–60) yr, mean height 170.1 (SEM 1.60) cm and mean weight 71.1 (1.71) kg. Mean values before injection and percentage changes in haemodynamic variables are shown in table I.

There was a statistically significant decrease in HR (P < 0.05) in both esmolol groups compared with placebo every 1 min after injection. There was a significantly greater decrease in the 200-mg group until 4 min, compared with the 100-mg group (P < 0.05). The 100-mg group showed a statistically significant decrease in SV up to 2 min compared with placebo (P < 0.05). There was a statistically significant decrease in the esmolol 200 mg group compared with placebo and the esmolol 100 mg group until 4 min (P < 0.05). The decrease in Q in both esmolol groups was significant (P < 0.05) and...
TABLE 1. Mean (SEM) percentage change in haemodynamic variables after i.v. administration of placebo or esmolol 100 or 200 mg compared with values before injection. Significant difference ($P < 0.05$) compared with: * placebo, † 100 mg group, ‡ 200 mg group, $n = 20$ for each group

<table>
<thead>
<tr>
<th>Time (min)</th>
<th>HR (beat min$^{-1}$)</th>
<th>SV (ml)</th>
<th>Q (litre min$^{-1}$)</th>
<th>MAP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before injection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>65.2 (5.6)</td>
<td>18.6 (1.2)</td>
<td>89.4 (7.1)</td>
<td>67.4 (5.9)</td>
</tr>
<tr>
<td>Esmolol 100 mg</td>
<td>64.7 (6.1)</td>
<td>18.6 (1.2)*</td>
<td>83.8 (7.4)</td>
<td>61.7 (2.4)</td>
</tr>
<tr>
<td>Esmolol 200 mg</td>
<td>69.4 (4.4)</td>
<td>18.6 (1.2)*†</td>
<td>115.5 (5.8)</td>
<td>61.7 (2.4)</td>
</tr>
</tbody>
</table>

was greatest at 1 and 2 min after injection. There was also a significant difference between the two esmolol groups until 4 min after injection ($P < 0.05$), with a maximal difference of 10% at 1 min. Both esmolol groups showed a significant decrease in MAP ($P < 0.05$) with no significant difference between them.

**COMMENT**

Esmolol hydrochloride is a new cardioselective $\beta_1$ blocker. It is a phenoxycyanopropanolamine that is metabolized rapidly by esterases in red blood cell. Its acid metabolite has only 1/1500 the $\beta$ adrenoreceptor blocking activity of esmolol. The rapid onset of action and short elimination half-life of 9 min makes this drug useful in controlling acute increases in HR and MAP. Esmolol is licensed for use as an infusion following a loading dose of 500 $\mu$g kg$^{-1}$ min$^{-1}$ and studies have shown that bolus doses of up to 3 mg kg$^{-1}$ attenuate the increase in the rate-pressure product after tracheal intubation. Laryngoscopy and tracheal intubation are associated with an increase in sympathetic activity [3]. The increase in cardiac workload may precipitate myocardial ischaemia and acute heart failure in susceptible patients [4].

**REFERENCES**