CIRCULATORY RESPONSES TO THIOPENTONE AND TRACHEAL INTUBATION IN PATIENTS WITH CORONARY ARTERY DISEASE

Effects of Pretreatment with Labetalol


Laryngoscopy and tracheal intubation are often accompanied by increases in heart rate and arterial pressure (Wycoff, 1960; Prys-Roberts et al., 1971) which may lead, in patients with coronary artery disease, to myocardial ischaemia. Several methods have been proposed to suppress the circulatory responses to intubation: topical anaesthesia or the use of parenteral lignocaine, induction of anaesthesia using high dose of fentanyl, the supplementation of thiopentone with smaller doses of fentanyl, the use of vaso-dilators or beta-adrenoceptor blocking agents.

Although it is customary to maintain patients with coronary artery disease on their preoperative beta-adrenergic blocking regimen, conflicting results have been published on the haemodynamic responses to intubation in such patients (Prys-Roberts et al., 1973; Siedlecki, 1975; Rhyanan et al., 1977; Koprina, Brown and Pappas, 1978; Fassoulaki, Kaniaris and Kotsanis, 1980; Werner et al., 1980; McCammon, Hilgenberg and Stoelting, 1981; Safwat et al., 1981; Magnusson et al., 1983).

This study, on patients with coronary artery disease, investigated the efficacy of an infusion of labetalol in decreasing the circulatory responses to intubation. Labetalol (Wallin and O'Neill, 1983) is the prototype of a new class of antihypertensive agents that blocks competitively both beta- and alpha-adrenergic receptors. Although a central action has been demonstrated (Devoto et al., 1980), labetalol does not readily cross the blood–brain barrier (Martin, Hopkins and Bland, 1976).

SUMMARY

The haemodynamic responses to induction and tracheal intubation have been studied in patients with coronary artery disease randomly assigned to a labetalol pretreatment group (n = 14) or to a placebo group (n = 16). Twelve hour before operation, treated patients received a bolus dose of labetalol 0.5 mg kg⁻¹ followed by a constant infusion of 0.1 mg kg⁻¹ h⁻¹ i.v. Anaesthesia was induced with thiopentone and phenoperidine, and intubation performed following the administration of suxamethonium. At intubation, the changes in heart rate (P < 0.01), mean arterial pressure (P < 0.05) and rate–pressure product (P < 0.01) were significantly smaller in the labetalol group compared with the placebo group. Labetalol pretreatment appears satisfactory and may be useful in patients with coronary artery disease who have a normal left ventricular ejection fraction.

PATIENTS AND METHODS

Thirty patients scheduled for major surgery were studied and allocated randomly to placebo (n = 16) or labetalol (n = 14) groups in a double-blind study. All patients had a history of stable angina (N.Y.H.A. classes 2 and 3). Patients with a left ventricular ejection fraction < 0.55 were excluded, as were patients already receiving beta blocking drugs. Long-acting nitrates or calcium antagonists, or both, were administered up to the evening before surgery, then the patients remained at rest. The study was approved by the hospital Ethics Committee and informed consent was obtained from each patient.

Twelve hour before surgery a triple-lumen pulmonary artery catheter and a radial artery catheter were inserted under local anaesthesia, after which an
infusion of placebo or of labetalol 0.5 mg kg$^{-1}$ as a bolus dose followed by a constant infusion of 0.1 mg kg$^{-1}$ h$^{-1}$ was started via a peripheral vein. ECG lead V5 was monitored throughout the study.

Premedication consisted of flunitrazepam 1 mg i.m. and atropine 0.5 mg i.m., 1 h before the induction of anaesthesia with phenoperidine 2 mg and thiopentone 5–7 mg kg$^{-1}$. Suxamethonium 1 mg kg$^{-1}$ was administered and nasorotachea intubation undertaken following ventilation with oxygen via a face mask. Anaesthesia was maintained with nitrous oxide in oxygen ($F_{\text{O}_2} = 0.4$) plus additional phenoperidine as required.

The following haemodynamic indices were recorded: heart rate, arterial pressure, pulmonary capillary wedge pressure, and cardiac output using the thermodilution technique. Cardiac index, systemic vascular resistance index and rate-pressure product were calculated using standard formulae (cardiac index = cardiac output/body surface area; systemic vascular resistance index = mean arterial pressure – mean right atrial pressure/cardiac index; rate-pressure product = systolic arterial pressure $\times$ heart rate).

All these haemodynamic measurements were performed before the infusion of labetalol, 1 h after the beginning of the infusion, before the induction of anaesthesia, immediately following tracheal intubation, and 5 min later; heart rate and arterial pressure were recorded every hour following the bolus dose of labetalol.

Clinical differences between groups were evaluated using the chi-square analysis. The Mann-Whitney (two-sided) rank sum test for unpaired data was used for between-group comparisons. The significance of changes within groups was analysed with the Wilcoxon (two-sided) rank sum test for paired data. Probability values less than 0.05 were considered to indicate statistical significance.

**RESULTS**

Results are expressed as mean ± SD.

The characteristics of the patients are shown in Table I. Age, weight, sex, number of previous infarctions, number of hypertensive patients and left ventricular ejection fraction were identical in both groups (table I). The haemodynamic data are summarized in figure 1.

Both groups were identical as far as baseline values were concerned, and there were no changes in the haemodynamic variables during the 12 h of preoperative surveillance in both groups.

At the time of intubation, the heart rate, arterial pressure and systemic vascular resistance index, were significantly different ($P < 0.01$) from the pre-induction value in the placebo group. In the labetalol group, systemic vascular resistance index was increased compared with preinduction values ($P < 0.05$).

At the time of intubation, rate-pressure product increased significantly in both groups ($P < 0.01$ in the placebo group; $P < 0.05$ in the labetalol group). In 13 patients in the placebo group (mean value: 14.900 ± 4300) and in three patients in the treated group (mean value: 10.100 ± 3200) the rate–pressure product was greater than 11 000 during intubation ($P <0.01$).

At the time of intubation, differences between the groups could be documented only for heart rate ($P < 0.01$), mean arterial pressure ($P < 0.05$) and rate–pressure product ($P < 0.05$).

In both groups haemodynamic values after intubation were similar to those measured before induction of anaesthesia.

ST segment depression was observed immediately after intubation in three patients in the placebo group, but disappeared after the administration i.v. of nitroglycerine and phenoperidine. Although no changes were noted in the ECG in the labetalol group, the difference between the groups was not significant.

**DISCUSSION**

Labetalol appears to have the same anti-hypertensive properties as other beta-adrenergic blocking agents (Wallin and O'Neill, 1983); in acute studies

<table>
<thead>
<tr>
<th>Table I. Preoperative values in control and treated patients (mean ± SD). EF = left ventricular ejection fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Age (yr)</td>
</tr>
<tr>
<td>Placebo</td>
</tr>
<tr>
<td>(n=16)</td>
</tr>
<tr>
<td>Treated</td>
</tr>
<tr>
<td>(n=14)</td>
</tr>
</tbody>
</table>
LABETALOL AND RESPONSES TO INTUBATION

Figure 1. Haemodynamic variables recorded before pretreatment, 1 h after its beginning, before induction, just after intubation and 5 min later (mean ± SD). ••• = Placebo group (n = 16); ○○○ = Labetalol-pretreated group (n = 14).

(Bahlmann et al., 1979; Koch, 1976) it does not seem to induce any increase in systemic vascular resistance as has been demonstrated following the administration of several beta-adrenergic blocking agents (Taylor, Silke and Lee, 1982). Labetalol has been shown to be effective in the management of hypertension following coronary artery surgery (Morel, Forster and Suter, 1982).

In patients with coronary artery disease, we believe that pretreatment must begin long before the induction of anaesthesia so as to detect possible complications such as hypotension or low cardiac output. Thus, an initial loading dose of labetalol, which was smaller than that usually recommended for hypertensive patients (Pearson and Harvard, 1976), was followed by a constant infusion.

In the placebo group, the results were consistent with those obtained previously by a number of authors: intubation was frequently associated with tachycardia and hypertension (as a consequence of an increase in systemic vascular resistance).

In the test group, the infusion of labetalol did not modify the haemodynamic variables—probably as a result of the small number of hypertensive patients in this group, and of the absence of patients with poor left ventricular ejection fraction. However, a large percentage of the patients, in both groups, had had a previous myocardial infarction. In the pretreated group there was an increase in systemic vascular resistance at the time of intubation but without significant increase in arterial pressure; heart rate also remained unchanged. Rate-pressure product did increase significantly, but it exceeded 11 000 in only 21% of the labetalol-pretreated patients.

The results obtained in the labetalol group are consistent with those of Prys-Roberts and co-workers (1971) and Ryhanen and colleagues, (1977) who noted the efficacy of pretreatment with practolol, and with those of Safwat and associates (1981). However, many other investigators have reported negative results with practolol (Siedlecki, 1975; Werner et al., 1980), propranolol (Kopriwa, Brown and Pappas, 1978; McCammon et al., 1981) and metoprolol (Magnusson et al., 1983). These conflicting results can be accounted for by the different anaesthetic techniques used (especially...
halothane-nitrous oxide anaesthesia) and the different methods of administration of the beta-adrenergic blocking agents.

The part played by the alpha-adrenergic blocking properties of labetalol is not easy to demonstrate in this study; systemic vascular resistance index appeared to increase to a lesser extent in the labetalol group than in the placebo group, but the difference was not significant. Kopriva, Brown and Pappas (1978) studied haemodynamics during intubation in patients receiving propranolol and found a similar increase in systemic vascular resistance in treated and untreated patients.

The method of administration used in this study enabled us to define a standard rate of infusion of labetalol which appeared to suppress the haemodynamic response to intubation and may be useful in patients with coronary artery disease but with normal ventricular function, when a rapid induction of anaesthesia is contemplated.

REFERENCES


