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 vasodilators 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; Rhyanen et al., 1977; Kopriva, Brown and Pappas, 1978; Fassoulaki, Kaniaris and Kotsanis, 1980; Werner et al., 1980; McCommon, 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 inducti-
on of anaesthesia with phenoperidine 2 mg and
thiopentone 5–7 mg kg\(^{-1}\). Suxamethonium 1 mg
kg\(^{-1}\) was administered and naso-trachea intubation
undertaken following ventilation with oxygen via a
face mask. Anaesthesia was maintained with nitrous
oxide in oxygen (\(F_{102} = 0.4\)) 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, sys-
temic 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 pres-
sure \(\times\) heart rate).

All these haemodynamic measurements were per-
formed before the infusion of labetalol, 1 h after the
beginning of the infusion, before the induction of
anaesthesia, immediately following tracheal intub-
ation, 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 sig-
nificance 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 \(\pm\) SD.

The characteristics of the patients are shown in
table I. Age, weight, sex, number of previous infarc-
tions, number of hypertensive patients and left ven-
tricular ejection fraction were identical in both
groups (table I). The haemodynamic data are sum-
marized in figure 1.

Both groups were identical as far as baseline val-
ues 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 \(\pm\) 4300) and in three patients in the treated
group (mean value: 10.150 \(\pm\) 3200) the rate–pres-
sure product was greater than 10 000 during intuba-
tion \((P < 0.01)\).

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 intu-
bation were similar to those measured before induc-
tion of anaesthesia.

ST segment depression was observed
immediately after intubation in three patients in the
placebo group, but disappeared after the adminis-
tration 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-hyperten-
sive properties as other beta-adrenergic blocking
agents (Wallin and O'Neill, 1983); in acute studies

<table>
<thead>
<tr>
<th>Placebo (n=16)</th>
<th>Treated (n=14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>52</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>15/1</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>71.7</td>
</tr>
<tr>
<td>Hypertensive patients (%)</td>
<td>25</td>
</tr>
<tr>
<td>Previous infarction (%)</td>
<td>44</td>
</tr>
<tr>
<td>EF (%)</td>
<td>83</td>
</tr>
</tbody>
</table>

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LABETALOL AND RESPONSES TO INTUBATION

Heart rate
Systolic arterial pressure
Diastolic arterial pressure
Pulmonary capillary wedge pressure
Cardiac output
Systemic resistance vascular index

FIG. 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 Rhyanen 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 (Kopriova, 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


