Treatment of hypertension following endotracheal intubation

A study comparing the efficacy of labetalol, practolol and placebo

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Summary

Labetalol, a new adrenergic receptor antagonist, has both α- and ß-blocking properties. Intravenous labetalol (0,25 and 0,5 mg/kg), practolol (0,4 mg/kg) and saline (1 ml), injected prior to anaesthesia, were compared with respect to their effect on the haemodynamic consequences of direct laryngoscopy followed by the passage of an endotracheal tube.

When compared with intravenous saline injection, both labetalol and practolol obtunded the tachycardia induced by endotracheal intubation. The higher dose of labetalol was more effective in reducing the hypertensive response than the lower dose of practolol. However, none of the regimens completely abolished the adverse haemodynamic consequences of laryngotracheal manipulations.

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The acute hypertensive effects of laryngoscopy and endotracheal intubation are probably of little consequence in the young, healthy, normotensive patient. However, the sudden rise in systolic blood pressure consequent on endotracheal intubation increases the afterload on the heart and may precipitate acute left ventricular failure or a cerebrovascular accident in susceptible subjects.[1,2] A rise in heart rate reduces left ventricular filling time, and, together with the rise in systolic blood pressure, increases the rate pressure product, thus compromising myocar-

dial contractility and oxygen supply. In patients with pre-existing hypertension, myocardial ischaemia or cerebrovascular disease, these haemodynamic changes are therefore potentially harmful.

The adverse cardiovascular changes induced by routine laryngoscopy and passage of an endotracheal tube are thought to be due to reflex sympatho-adrenal stimulation.[3] Several pharmacological agents have been investigated in an effort to prevent these detrimental responses; the agents include atropine,[4] phentolamine,[4] halothane,[5] adrenergic receptor antagonists,[2] droperidol[6] and topical[7] and intravenous lignocaine.

This study was planned to elucidate the effects of labetalol, a ß-adrenergic antagonist with weak α-adrenergic antagonist properties, on the haemodynamic effects of laryngoscopy and endotracheal intubation. Labetalol was used in two dosages, their efficacy being compared with that of a single dose of practolol and saline placebo.

Patients and methods

Sixty healthy patients (American Society of Anesthesiologists categories I - II) scheduled for elective surgery were studied with their informed consent. The study was approved by the Ethics and Standards Subcommittee of the Faculty of Medicine, University of Natal. All patients received premedication with lorazepam 2 mg given sublingually approximately 2 hours before induction of anaesthesia.

On arrival in the operating theatre, the leads of an ECG monitor (Portascope; Mennen Greatbatch) were attached to each patient. The cuff of an automatic arterial blood pressure recording device (Sentry; Automated Screening Devices) for determination of the systolic, diastolic and mean arterial blood pressures and the heart rate encircled the patient's arm. Baseline recordings of the heart rate and the systolic, diastolic and mean blood pressures were made. If the initial blood pressure reading was higher than that obtained at the pre-anaesthetic examination, the patient was allowed to adjust to the surroundings, and measurements were repeated after 5 minutes. All patients with a mean arterial pressure higher than 100 mmHg or lower than 80 mmHg were excluded from the trial.

The patients then received labetalol 0,5 mg/kg (group I), practolol 0,4 mg/kg (group II), saline (group III) or labetalol 0,25 mg/kg (group IV) intravenously on a random basis.

Arterial blood pressure and heart rate were determined 2 minutes and 5 minutes after injection of the drug or placebo, during which time the patient was pre-oxygenated with a Magill anaesthetic breathing system.

Anaesthesia was induced with a 2,5% solution of thiopentone 4 mg/kg injected at a rate of approximately 5 mg/s. Heart rate and blood pressures were then recorded again. Muscle relaxation was produced by the injection of suxamethonium 1 mg/kg. Further readings were taken before visualization of the larynx and passage of an endotracheal tube via the mouth. Arterial blood pressure and heart rate were recorded at the time of intubation and subsequently every minute for up to 7 minutes. Anaesthesia was maintained with nitrous oxide 60% in oxygen given through the endotracheal tube, using a circle absorber throughout this period. The subsequent anaesthetic management varied according to surgical requirements.

Statistical analysis was performed by computer. Two-tailed probability values equal to or less than 0,05 were regarded as significant.

Results

Although heart rate and blood pressure readings were taken every minute for 7 minutes after intubation, the need to use halogenated inhalation agents to maintain anaesthesia in some patients makes the values obtained after 3 minutes not strictly comparable, as various concentrations of halothane were used. Only measurements obtained up to 3 minutes after intubation were therefore considered comparable for analysis.

Systolic arterial blood pressure (Fig. 1). The systolic blood pressure in all four groups were similar until endotracheal intubation. In the group which received the higher dose of labetalol the rise was similar to that in the other three groups. At 1, 2 and 3 minutes, the patients receiving practolol had a higher systolic pressure than the other three groups. The maximum arterial pressure on intubation was highest in the control group. The difference between the high-dose labetalol group and the placebo group was significant ($P < 0,04$) 1 minute after intubation. The same P value applied to the mean arterial pressure.

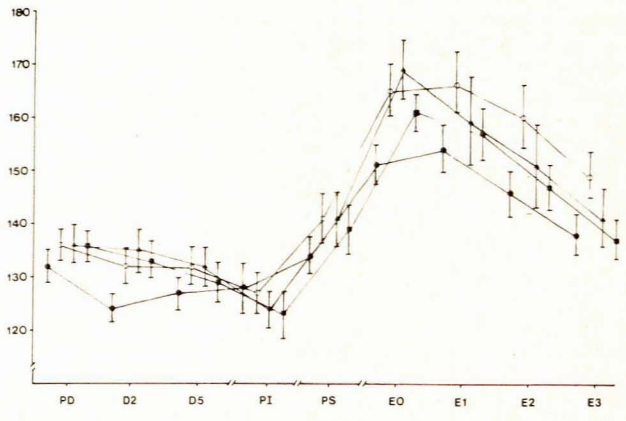

Fig. 1. Changes in systolic blood pressure. Key (same for Figs 1-4): ○ = practolol 0,4 mg/kg; ▲ = saline 1 ml; ■ = labetalol 0,25 mg/kg; ● = labetalol 0,5 mg/kg; PD = pre-drug; D2 = 2 minutes after injecting drug; D5 = 5 minutes after injecting drug; PI = post-induction; PS = post-suxamethonium; EO = at intubation; E1 = 1 minute after intubation; E2 = 2 minutes after intubation; E3 = 3 minutes after intubation.

Diastolic pressure (Fig. 2). Similar diastolic pressures were recorded before induction of anaesthesia, with a tendency for the high-dose labetalol group to have a lower diastolic blood pressure than the placebo group at injection of suxamethonium. On endotracheal intubation, the diastolic pressure was highest in the placebo group; it was significantly higher than that in the high-dose labetalol group ($P = 0,05$). At 1, 2 and 3 minutes the diastolic pressure was higher in the practolol group than in the other groups, the difference at 2 minutes proving significantly higher ($P = 0,03$).

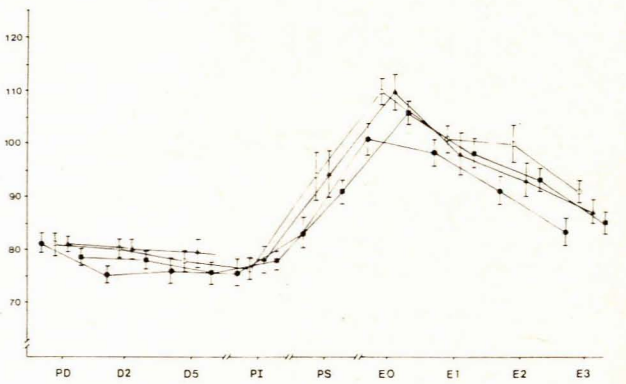

Fig. 2. Changes in diastolic blood pressure.

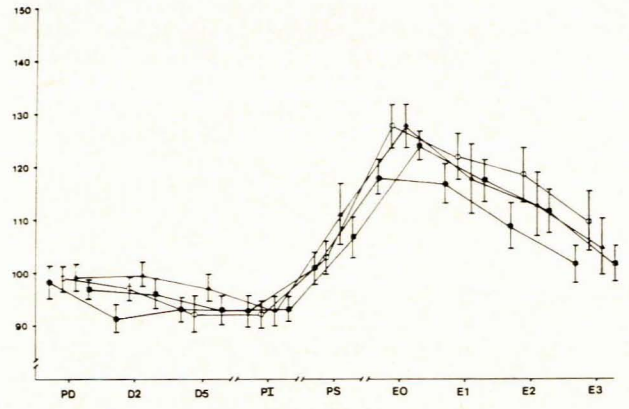

Fig. 3. Changes in mean blood pressure.

Mean blood pressure (Fig. 3). Changes in mean blood pressure are shown in Fig. 3.

Heart rate (Fig. 4). In all four groups, the heart rate increased initially to the same level following induction and after the administration of suxamethonium. However, after laryngoscopy and endotracheal intubation the placebo group had a higher heart rate than either the patients who received practolol (group II) or those who received labetalol (groups I and IV), the difference attaining statistical significance at the $P = 0{,}04$ and $P = 0{,}001$ levels respectively. No statistically important differences were noted between groups I, II and III.

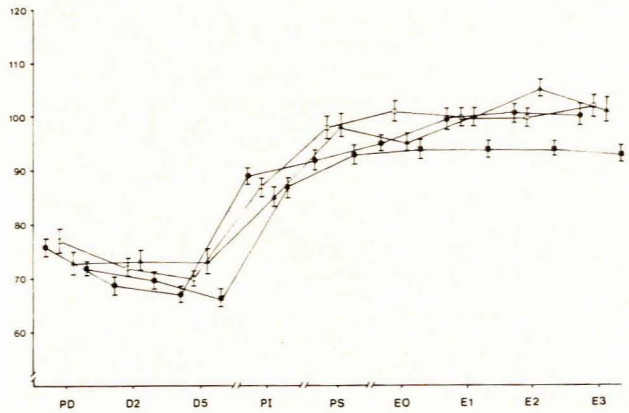

Fig. 4. Changes in heart rate.

Percentage changes in blood pressure from baseline values (Figs 5, 6 and 7). In its higher dose (0,5 mg/kg) labetalol produced a significant decrease in blood pressure 2 minutes after injection of the drug. While there is an impression that blood pressure in those patients pretreated with the higher dose of labetalol tended to have a lower pressor response to intubation, these values failed to achieve statistical significance when compared with the placebo group. An interesting finding is that those patients pretreated with practolol had a slower rate of decline in blood pressure towards normal than the other groups.

Percentage changes from baseline heart rate (Fig. 8). The high-dose labetalol group had a significantly greater reduction in heart rate 2 minutes after injection of the drug ($P = 0{,}01$). This effect persisted at the 5th minute after injection. At this stage the low-dose labetalol group also had a significantly lower pulse rate ($P = 0{,}01$). Immediately after intubation the rise in heart rate was lowest in the two groups pretreated with labetalol. The practolol group also had a lower heart rate at this point, but the values failed to reach statistical significance ($P = 0{,}08$). The maximal rise in all three treated groups was lower than that in the

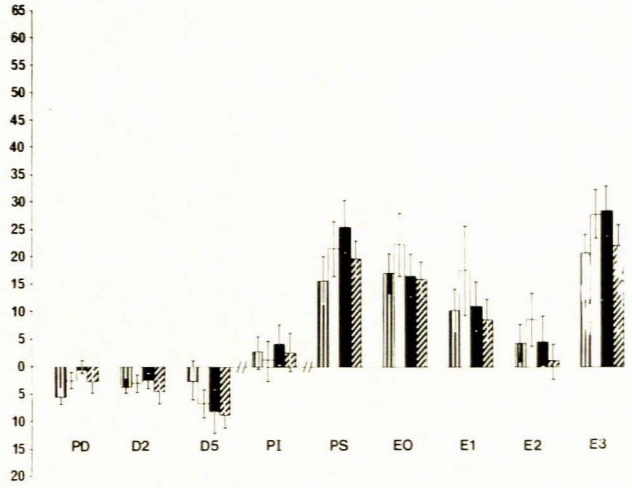

Fig. 5. Changes in systolic blood pressure expressed as percentage change from pre-drug baseline value. Key (same for Figs 5-8): □ = practolol 0,4 mg/kg; ■ = saline 1 ml; ▨ = labetalol 0,25 mg/kg; ▩ = labetalol 0,5 mg/kg; abbreviations as for Figs 1-4.

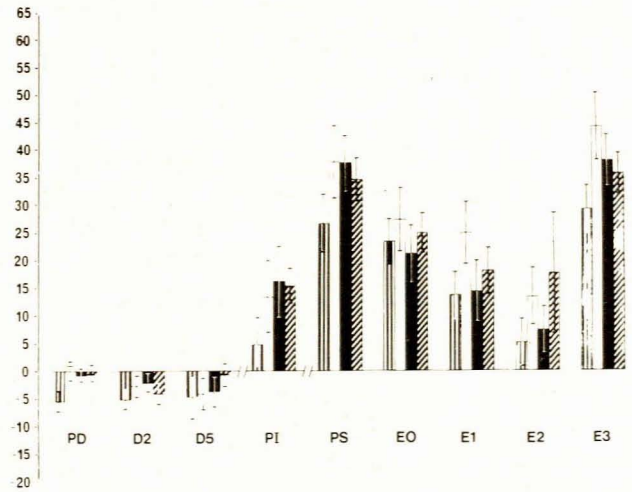

Fig. 6. Changes in diastolic blood pressure expressed as percentage change from pre-drug baseline value.

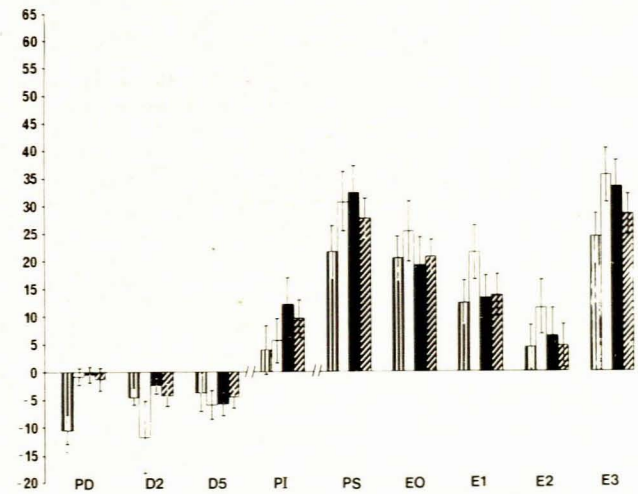

Fig. 7. Changes in mean blood pressure expressed as percentage change from pre-drug baseline value.

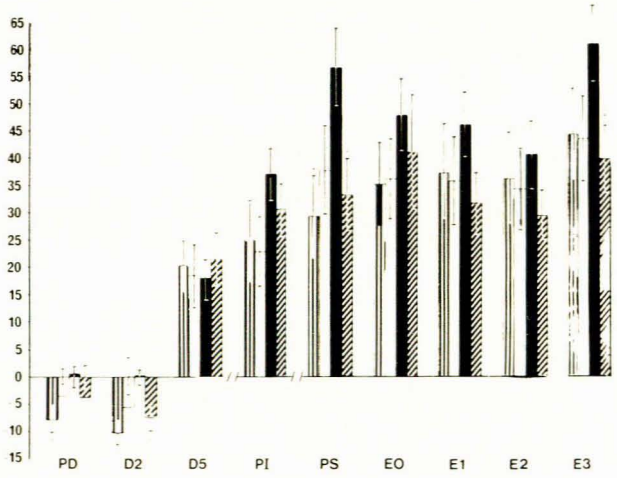

Fig. 8. Changes in heart rate expressed as percentage change from pre-drug baseline value.

untreated group. Values in the low-dose labetalol group attained statistical significance ($P = 0,03$) when compared with those in the placebo group.

No cardiac dysrhythmias were encountered in this series, and anaesthesia was uneventful in all the patients.

Discussion

Significant rises in arterial blood pressure and heart rate have been reported following induction of light general anaesthesia and administration of muscle relaxants.[8] Further increases may follow laryngoscopy and endotracheal intubation, even in the absence of coughing, hypoxia and hypocarbia.[3,9] Hypertension during induction of anaesthesia in critically ill patients may be harmful, causing cerebral haemorrhage,[10] left ventricular failure and serious cardiac dysrhythmias.[11,12] Hypertension is also hazardous to patients with coronary artery disease, since myocardial ischaemia may develop because of the increase in cardiac work. None of the several methods that have been investigated in an effort to attenuate the cardiovascular changes which occur during endotracheal intubation have proved to be satisfactory.[3-7] The use of topical lignocaine has shown that arterial blood pressure increases significantly after application of a topical anaesthetic to the larynx.[3,5]

The adverse cardiovascular responses to endotracheal intubation which have been described are allegedly mediated through the sympathetic nervous system and therefore may in theory be suppressed by adrenergic receptor blockade. The commonest theoretical objection to adrenergic receptor blockade before anaesthesia is that it impairs cardiac performance, and a number of mechanisms have been implicated.

Labetalol, a recently developed adrenergic receptor antagonist, is unique in that it has the properties of a ß-adrenergic blocking drug while possessing weak α-blocking potential as well. These properties suggest that it would be the ideal agent to attenuate the cardiovascular changes occurring on endotracheal intubation.

While neither of the two drugs tested succeeded in abolishing the cardiovascular changes that follow direct laryngoscopy and intubation, the study has demonstrated some benefit in attenuating detrimental increases in heart rate by the use of labetalol (in both dosage ranges) and practolol.

It is more difficult to draw conclusions from the changes in blood pressure that were observed. It would appear that labetalol in the higher dosage range (0,5 mg/kg) exerted the most beneficial effects on the peak values of mean blood pressure ($P = 0,14$). The lack of efficacy of practolol in attenuating the pressor changes is probably due to the fact that the drug has partial agonist activity at the ß-adrenergic receptor site.

Of the three pretreatment regimens tested, we believe that labetalol 0,5 mg/kg has been demonstrated to be of some benefit in attenuating detrimental rises in heart rate and blood pressure. However, this dosage regimen, practolol (0,4 mg/kg) and low-dose labetalol (0,25 mg/kg) do not seem to be the answer to the problem of acute hypertension following endotracheal intubation. Studies of a larger number of patients should be performed to resolve the question of statistical significance.

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