EFFECTS OF PANCRUORNIUM AND ALCURONIUM ON THE CHANGES IN ARTERIAL PRESSURE AND PLASMA CATECHOLAMINE CONCENTRATIONS DURING TRACHEAL INTUBATION

M. F. CUMMINGS, W. J. RUSSELL AND D. B. FREWİN

The changes in the plasma concentrations of noradrenaline, adrenaline and dopamine, during tracheal intubation, were studied in 17 patients. Nine patients received pancuronium and eight alcuronium to produce neuromuscular blockade. In the patients receiving pancuronium, intubation of the trachea was accompanied by an increase in mean arterial pressure, and in the plasma concentrations of noradrenaline and adrenaline. In the alcuronium group, there were no significant changes in the plasma concentrations of any catecholamine, nor any change in mean arterial pressure in response to intubation of the trachea.

Administration of the various non-depolarizing neuromuscular blocking drugs is associated with a variety of haemodynamic responses. This is well recognized clinically and has been documented. Pancuronium increases mean arterial pressure (MAP), heart rate (HR) and cardiac output (Kelman and Kennedy, 1971; Coleman et al., 1972; Stoelting, 1972). The administration of alcuronium and of tubocurarine is usually followed by a decrease in MAP and an increase in HR (Coleman et al., 1972; Stoelting, 1972).

A previous study demonstrated significant increases in MAP and plasma noradrenaline (NA) concentration after intubation of the trachea in patients who had received pancuronium (Russell et al., 1981). The present study was undertaken to determine whether the changes seen were related specifically to the use of pancuronium. Thus, the responses to tracheal intubation, after the administration of pancuronium, were compared with those after alcuronium.

PATIENTS AND METHODS

Seventeen patients, aged from 21 to 84 yr, undergoing elective surgery, were allocated randomly to one of two groups. The procedure of radial artery cannulation and sampling was explained and consent obtained from each patient. An Allen's test, to assess the patency of the collateral circulation in the hand, was performed. Premedication was not standardized, but was left to the preference of the anaesthetist.

In the operating theatre, a 20-gauge cannula was inserted to the radial artery using 2% lignocaine to anaesthetize the skin. Arterial pressure was recorded continuously using a Statham P23 ID transducer, an amplifier and a standard hot wire recorder. The system was calibrated using a standard mercury column. MAP was calculated from the record of the arterial pressure as diastolic pressure plus one-third of the pulse pressure. As the pressure recording was lost during sampling, MAP at the time of sampling was calculated as the average of the MAP at end-expiration immediately before and after sampling.

Arterial blood was sampled from a three-way tap adjacent to the cannula. Samples (5 ml) were taken before the induction of anaesthesia (thiopentone) and administration of any neuromuscular blocking drug (A1), immediately before tracheal intubation (A2) and at 1, 5 and 10 min after the tracheal tube had been passed (A3, A4, A5, respectively). All samples were immediately placed in heparinized tubes containing glutathione (5 mmol litre⁻¹ final concentration) to prevent oxidation of the catecholamines and stored on ice. The tubes were centrifuged on completion of sampling and the plasma decanted and stored at −20 °C until the assay was performed within 2 weeks.

The assay measured the plasma concentration of adrenaline (AD), NA and dopamine (DA) by a modification of the radio-enzymatic method de-
scribed by Da Prada and Zürcher (1976). Briefly, this uses tritiated-S-adenosyl methionine as a methyl donor for O-methylation of the DA, AD and NA. The products were separated by thin layer chromatography. The lower limit of detection of the assay for each of the three catecholamines was 0.02 pmol ml⁻¹, with an overall coefficient of variation of 11% at very low concentrations to 5% at and above the concentrations found in this study.

Statistical comparison was performed with Student t tests, paired or unpaired, as appropriate. Results are expressed as the mean ± SEM, and probability is given for a single-sided test unless otherwise stated.

RESULTS

Seventeen patients were studied; nine received pancuronium and eight alcuronium. The sex distribution, body weight and ages of the two groups were similar. Approximately equal numbers in each group received oral benzodiazepines or parenteral narcotics as premedication.

Before the induction of anaesthesia (A1) the MAP of both groups were similar (table I), as were the plasma concentrations of all three catecholamines. After induction, MAP decreased in both groups, but for pancuronium this was not significant (Δ mean 7.4 ± 4.5 mm Hg, P = 0.065; alcuronium Δ mean 10.3 ± 1.75 mm Hg, P < 0.0001). During intubation of the trachea MAP in the pancuronium group increased, whereas MAP in the alcuronium group did not change. At 1, 5 and 10 min after intubation MAP was significantly greater in the pancuronium group than the alcuronium group at comparable times. The increase in MAP on intubation in the pancuronium group was significant (Δ mean 29.3 ± 4.2 mm Hg, P < 0.0001) and MAP remained greater than its value immediately after induction for 10 min (5 min Δ mean 19.4 ± 3.8 mm Hg, P = 0.006; 10 min Δ mean 12.1 ± 5.6 mm Hg, P = 0.03). In contrast, in the patients receiving alcuronium MAP remained uniformly low for the 10-min period of observation (table I).

Plasma DA did not change significantly during induction and intubation in either group. However, the plasma NA increased after intubation in the patients receiving pancuronium, and the concentrations differed significantly between the alcuronium and pancuronium groups at 1 and 5 min after intubation of the trachea. The increase in NA between the post-induction concentration with pancuronium and at 1 and 5 min after intubation was significant (Δ mean 0.56 ± 0.14 pmol ml⁻¹, P = 0.002; Δ mean 0.34 ± 0.17 pmol ml⁻¹, P = 0.04, respectively). With the administration of alcuronium there were no significant changes in NA concentration during the period of observation.

Plasma AD decreased after induction of anaesthesia in the alcuronium group and was unchanged thereafter (Δ mean 0.25 ± 0.11 pmol ml⁻¹, P = 0.03). In the pancuronium group, a similar decrease in AD concentration occurred after induction, but there was a marked increase 1 min after intubation of the trachea (Δ mean 0.14 ± 0.05 pmol ml⁻¹, P = 0.013).

As had been noted in the previous study (Russell et al., 1981), the changes in MAP were associated with changes in NA with the pancuronium group.

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**Table I. Plasma catecholamine concentrations and mean arterial pressures for the pancuronium- (P) and alcuronium- (A) treated groups. All values quoted are mean ± SEM. MAP = mean arterial pressure (mm Hg). Dopamine (DA), adrenaline (AD) and noradrenaline (NA) values are given in pmol ml⁻¹. A1 = pre-induction value; A2 = value after induction but immediately before intubation; A3 = 1 min; A4 = 5 min and A5 = 10 min after intubation. Comparison is between values at the same time of the pancuronium and alcuronium groups. *0.01 < P < 0.05; **P < 0.01 (two tails)**

<table>
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<td>P</td>
<td>0.38 ± 0.03</td>
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<td>AD</td>
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<td>P</td>
<td>0.24 ± 0.05</td>
<td>0.13 ± 0.03</td>
<td>0.27 ± 0.08**</td>
<td>0.14 ± 0.04</td>
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<td>P</td>
<td>1.72 ± 0.23</td>
<td>1.76 ± 0.18</td>
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<td>P</td>
<td>103 ± 5.1</td>
<td>96 ± 5.0</td>
<td>125 ± 5.6**</td>
<td>115 ± 4.4**</td>
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(r = 0.56, for the present study, line of best linear fit, MAP = 13.0 × NA + 84) (fig. 1). In addition, however, a positive correlation was also found between MAP and NA in the alcuronium group (r = 0.64, and for best linear fit, MAP = 11.1 × NA + 75). In the pancuronium group, a weaker but statistically significant linear correlation was found between MAP and AD (r = 0.44, 0.01 < P < 0.05).

DISCUSSION

The differences in MAP which occurred in this study following the administration of pancuronium or alcuronium were similar to those reported by others (Kelman and Kennedy, 1971; Coleman et al., 1972; Stoeltiug, 1972). There was a decrease in MAP after alcuronium and no increase on tracheal intubation. With pancuronium, MAP did not decrease significantly after the drug had been administered and there was a significant increase immediately after intubation of the trachea. The lack of pressor effect with alcuronium would be consistent with a sympathetic ganglion blocking action of the drug, histamine release, or could be caused by direct arteriolar dilatation. However, the low concentration of AD and NA which accompanied the lack of pressor response was more consistent with sympathetic blockade than with any peripheral vasodilator effect.

In the patients receiving pancuronium, the increase in MAP paralleled the increase in plasma NA concentration and these findings were similar to those reported by us on a previous occasion. The similarity of the correlation of MAP with NA in both the alcuronium and pancuronium groups suggests that neither drug was affecting the ability of the vascular system to respond to NA. Indeed, the similar slope of the lines of best fit for the two groups was consistent with an unimpaired receptor re-

![Graph](https://academic.oup.com/bja/article-abstract/55/7/619/298993)

**FIG. 1.** Relationship between MAP (mm Hg) and the concentration of noradrenaline (pmol ml⁻¹) in both the pancuronium and alcuronium groups. ● = pancuronium; ○ = alcuronium.
sponse to NA. The offset may be a chance finding, or it may represent either a slight competitive blocking effect of alcuronium, or an enhancement with pancuronium. Indeed, it has been proposed that pancuronium may act at post-ganglionic nerve endings to release NA (Segarra Domenech et al., 1976).

In the present study, there was a significant increase in the plasma AD concentration after intubation of the trachea in the patients receiving pancuronium. In our previous study, there was also an increase in plasma AD concentration at this time, but the difference did not achieve statistical significance. No significant increase in the plasma concentrations of AD could be demonstrated in the patients given alcuronium and this would also be consistent with a sympathetic ganglion blocking effect.

The increase in plasma AD concentration at 10 min (A5) in the pancuronium group may relate to the onset of surgery in some patients and did not appear to be related to the administration of the drug itself.

Most of the NA circulating in the plasma is released from sympathetic nerves and approximately 25% of the NA in pulmonary artery blood is extracted during passage through the lungs (Sole et al., 1979; Russell, Frewin and Jonsson, 1982). Consequently, samples from a central vein may contain greater concentrations than blood from the radial artery (Fell et al., 1982). The radial artery was chosen because sampling was facilitated by the indwelling cannula, which was used for MAP recording; the site is also easy to standardize. However, it does mean that the values for changes in the concentrations of NA and AD are probably underestimated of the amount of catecholamine released.

Intubation of the trachea is a potent sympathetic stimulus and can cause major haemodynamic changes. Several methods of attenuating the pressor response have been suggested (Föex and Prys Roberts, 1974). It appears that pancuronium is associated with an increase in the plasma concentrations of NA and AD, which in turn may account for the increase in MAP, HR and cardiac output seen on intubation (Segarra Domenech et al., 1976). The lack of pressor response to intubation in the patients receiving alcuronium is noteworthy. It was not associated with an increase in the concentrations of NA and AD and suggests that alcuronium in normal doses may be a clinically effective sympathetic ganglion blocker. On the other hand, it has been postulated that pancuronium acts on post-ganglionic nerve endings to cause the release of NA (Segarra Domenech et al., 1976). Certainly, the increase in the plasma concentration of NA in patients receiving pancuronium is a consistent finding (Nana, Cardan and Domokos, 1973; Russell et al., 1981; Fell et al., 1982) and this may mean that pancuronium magnifies the sympathetic response to intubation.

The importance of attenuating the pressor response to intubation is most obvious in patients with cardiovascular disease. From the results of the present study, we conclude that patients who are likely to have high circulating catecholamine concentrations, or those in whom the pressor response to intubation is undesirable, should receive alcuronium as the neuromuscular blocking drug of choice.

ACKNOWLEDGEMENTS

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REFERENCES


**LES EFFETS DU PANCURONIUM ET DE L’ALCURONIUM SUR LES MODIFICATIONS DE LA PRESSION ARTÉRIELLE ET DES CONCENTRATIONS PLASMATIQUES DE CATECHOLAMINES AU COURS DE L’INTUBATION TRACHEALE**

**RESUME**

Les variations des concentrations plasmatiques de noradrénaline, d’adrénaline et de dopamine, au cours de l’intubation trachéale, ont été étudiées chez 17 patients. Neuf patients ont reçu du pancuronium et huit de l’alcuronium pour inclure le relâchement musculaire. Chez les patients qui recevaient du pancuronium, l’intubation trachéale s’accompagnait d’une augmentation de la pression artérielle moyenne et des concentrations plasmatiques de noradrénaline et d’adrénaline. Dans le groupe alcuronium, il n’y a pas eu de variation significative des concentrations plasmatiques des catecholamines quelles qu’elles soient, ni aucune variation de la pression artérielle moyenne en réponse à l’intubation trachéale.

**EFFEKTE VON PANCURONIUM UND ALCURONIUM AUF VERÄNDERUNGEN VON ARTERIELLEM BLUTDRUCK UND KATECHOLAMIN-PLASMAKONZENTRATIONEN WÄHREND TRACHEALER INTUBATION**

**ZUSAMMENFASSUNG**


**EFECTOS DEL PANCURONIO Y DEL ALCURONIO SOBRE LOS CAMBIOS DE LA PRESION ARTERIAL Y DE LAS CONCENTRACIONES DE CATECOLAMINA EN EL PLASMA DURANTE LA INTUBACION TRAQUEAL**

**SUMARIO**

Se estudiaron en 17 pacientes los cambios de las concentraciones de noradrenalina, adrenalina y dopamina en el plasma durante la intubación traqueal. Nueve de los pacientes recibieron pancuronio y los ocho restantes recibieron alcuronio con el fin de producir bloqueo neuromuscular. En el caso de los pacientes que recibieron pancuronio, la intubación de la tráquea vino acompañada por un incremento de la presión arterial, así como de la concentración de adrenalina y de noradrenalina en el plasma. No se presentó cambio significativo alguno en las concentraciones de ninguna de las catecolaminas en el plasma, ni tampoco se observó cambio alguno en la presión arterial media, como respuesta a la intubación de la tráquea en el grupo del alcuronio.