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PLASMA CATECHOLAMINE RESPONSES TO TRACHEAL INTUBATION

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SUMMARY

Plasma adrenaline and noradrenaline concentrations were measured in 24 patients during the induction of anaesthesia and the subsequent tracheal intubation. The patients received either suxamethonium 1 mg kg^{-1} or pancuronium 0.1 mg kg^{-1} to facilitate tracheal intubation. Mean arterial pressure (MAP) increased in both groups following laryngoscopy and tracheal intubation and there were concomitant increases in the plasma catecholamine concentrations, the changes being more marked in the suxamethonium group. There was a significant correlation between MAP and plasma catecholamine concentrations in the suxamethonium group. Measurement of plasma catecholamine concentrations in samples obtained simultaneously from central venous, peripheral venous and arterial sites were in broad agreement; the greatest changes occurred in central venous samples.

There have been many studies on the cardiovascular responses to laryngoscopy and tracheal intubation (Siedlecki, 1975), but few in which sympathoadrenal activity has been assessed by measurement of plasma catecholamine concentrations.

A significant increase in plasma concentration of noradrenaline (but not adrenaline) in response to tracheal intubation and in association with a significant pressor response was reported by Russell and colleagues (1981). However, no change in catecholamine concentrations was observed by Zsigmond and Kumar (1980), despite the presence of a significant pressor response. In both these studies conventional, although differing, anaesthetic techniques were used.

With high-dose opiate techniques, both Stanley and colleagues (1980) and Hoar and co-workers (1981) failed, in different categories of patients, to demonstrate either a significant pressor or catecholamine response to laryngoscopy and tracheal intubation.

The present study was designed, first, to replicate that of Russell and colleagues in an attempt to confirm their findings in respect of noradrenaline and to observe any changes in plasma adrenaline concentration (preliminary results: Fell et al., 1982). In the second place, we have compared changes following tracheal intubation facilitated with suxamethonium (SUX) with those following pancuronium (PCB), since the latter has been shown to decrease the uptake of noradrenaline at adrenergic nerve endings *in vitro* (Salt, Barnes and Conway, 1980). Third, noradrenaline has been shown *in vitro* to be taken up selectively by the lungs (Ginn and Vane, 1968) and, as a result, we have compared the noradrenaline concentrations in samples of blood obtained from different sites.

PATIENTS AND METHODS

Twenty-four patients scheduled for elective major surgery (in whom radial arterial and central venous cannulation would be undertaken as a routine) gave informed consent for the study which was approved by the District Ethics Committee. The patients were allocated to receive either SUX or PCB to facilitate tracheal intubation.

Premedication comprised diazepam 10 mg and droperidol 5 mg given orally 1–1.5 h before surgery. In the anaesthetic room, under local analgesia (without vasopressor), cannulae were inserted to a radial artery and a peripheral vein; a catheter was inserted via the ante-cubital fossa to a central vein. The ECG was monitored continuously with either a standard lead II or CM5 configuration.

After a period of stabilization a recording of arterial pressure was obtained and at the same time blood samples (10 ml) were obtained from each of the three sites (*viz.* radial artery, central vein and peripheral vein) for measurement of plasma noradrenaline and adrenaline concentrations.

Following preoxygenation, anaesthesia was in-

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duced with thiopentone 5 mg kg^{-1} and when the eyelash reflex was abolished, either suxamethonium 1 mg kg^{-1} or pancuronium 0.1 mg kg^{-1} was administered. Ventilation was maintained with 33% oxygen in nitrous oxide using a face-mask, and during this period blood samples were removed simultaneously from the three sampling sites (after induction – before intubation). Laryngoscopy and tracheal intubation were performed; 1 min later further samples were taken (immediately after intubation). Five minutes after intubation a further set of samples was obtained (5 min after intubation). Systemic arterial pressure was measured continuously using an appropriate transducer. In the SUX group, neuromuscular blockade was maintained by the administration of tubocurarine 30 mg 2–3 min after the trachea had been intubated.

Blood for measurement of the catecholamine concentrations was collected into pre-cooled "Vacutainer" tubes containing lithium heparin and stored immediately in ice. The samples were centrifuged as soon as possible in a refrigerated centrifuge at 0 °C. The separated plasma was stored at −70 °C until analysis was performed. Plasma catecholamine concentrations were assayed using a technique of reverse phase high-pressure liquid chromatography as described by Hallman and colleagues (1978) and modified slightly in our laboratory (Fell, Achola and Smith, 1982). The inter-assay coefficient of variation within our laboratory was 6–9% and the intra-assay coefficient was 4% using pooled plasma which had a mean plasma noradrenaline concentration of 1.9 pmol ml^{-1} (±0.3) and adrenaline of 0.8 pmol ml^{-1} (± 0.09).

Data were analysed utilizing analysis of variance and paired Student's *t* tests within groups. Correlation comparisons were undertaken utilizing one-way analysis of covariance.

RESULTS

Because patients in this study were drawn from two different surgical units, with differing anaesthetists

TABLE I. *Details of patients studied*

Age (yr)	Sex	Concomitant medication	Operation
Suxamethonium (SUX)			
52	M	—	Femoro–popliteal bypass
52	M	—	Bifurcation graft
60	M	—	Bifurcation graft
59	F	Nifedipine, GTN	Bifurcation graft
69	M	—	Bifurcation graft
62	M	Methyldopa	Bifurcation graft
62	M	—	Axillo–femoral graft
62	M	Propranolol	Aortic aneurysm repair
72	M	—	Aortic aneurysm repair
46	F	Inositol nicotinate	Bifurcation graft
57	M	—	Femoro–popliteal bypass
64	M	—	Bifurcation graft
Pancuronium bromide (PCB)			
71	F	—	Carotid endarterectomy
74	M	—	Femoro–popliteal bypass
47	M	Oxprenolol, hydrallazine	Aortic aneurysm resection
71	M	Digoxin, chlorothiazide	Aortic aneurysm resection
71	M	Frusemide, prednisolone	Pan proctocolectomy
80	M	GTN, oxprenolol	Axillo–femoral bypass
61	M	Metoprolol, chlorothiazide	Femoro–popliteal bypass
70	M	Digoxin	Aortic aneurysm resection
69	F	Oxprenolol, methyldopa prochlorperazine, bendrofluazide	Femoro–popliteal bypass
52	F	—	Thoraco–abdominal gastrectomy
52	M	—	Oesophago–gastrectomy
61	M	—	Whipple's procedure

TABLE II. *Changes in mean arterial pressure and the concentrations of the catecholamines in arterial blood (mean ± SEM).* n = *12.* *P < *0.05 (compared with control, before induction, values)*

	Control Before induction		After induction Before intubation		1 min after intubation		5 min after intubation	
	PCB	SUX	PCB	SUX	PCB	SUX	PCB	SUX
MAP (mm Hg)	96.6±6.1	93.2±4.0	99.8±7.5	108.3±8.5	121.0±9.5*	141.7±9.2*	96.2±7.9	85.2±6.5
Adrenaline (pmol ml^{-1})	0.5±0.1	0.6±0.2	0.5±0.1	0.6±0.1	0.8±0.2	1.9±0.5*	0.6±0.2	0.6±0.1
Noradren. (pmol ml^{-1})	2.0±0.3	1.7±0.2	1.8±0.4	1.7±0.2	3.5±0.6*	4.0±0.6*	2.9±0.5*	2.6±0.4*

and a different selection of patients, the two groups were not strictly comparable (table I), although the mean ages of the two groups were similar (PCB 64.9 yr; SUX 59.7 yr).

Following tracheal intubation there was a significant increase in mean arterial pressure (MAP) of 52% in the SUX group and 25% in the PCB group (table II). A few patients received small increments of thiopentone because of a larger pressor response, but no patient revealed ECG evidence of myocardial ischaemia.

Plasma noradrenaline concentrations increased significantly following tracheal intubation (141% in the SUX group and 74% in the PCB group). Plasma adrenaline increased significantly by 189% in the SUX group, but the 39% change in the PCB group was not statistically significant.

There was a significant correlation between plasma catecholamine concentrations and MAP in the SUX group ($P < 0.001$ for noradrenaline; $P < 0.01$ for adrenaline), although the correlation between catecholamines and MAP in the PCB group did not reach statistical significance.

Comparison of samples obtained from different sites revealed that the greatest values for the plasma concentrations were noted most commonly in the central venous samples, although parallel changes occurred during the study in samples from all three sites. Although there was no significant difference in the values obtained from different sites before and

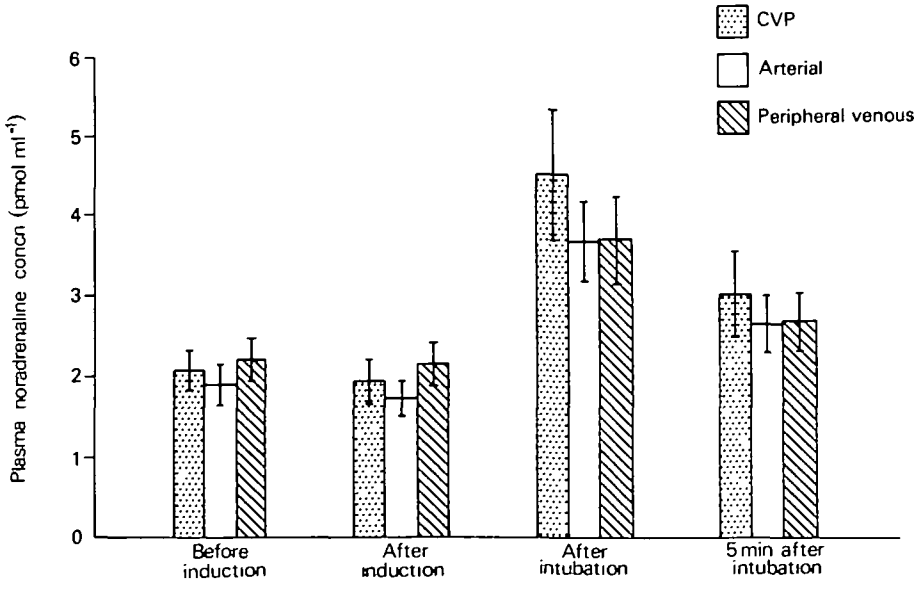

FIG. 1. Plasma noradrenaline concentrations in samples obtained from three different sites at each stage of the study. Patients from both groups are combined. (Mean ± SEM; $n = 24$.)

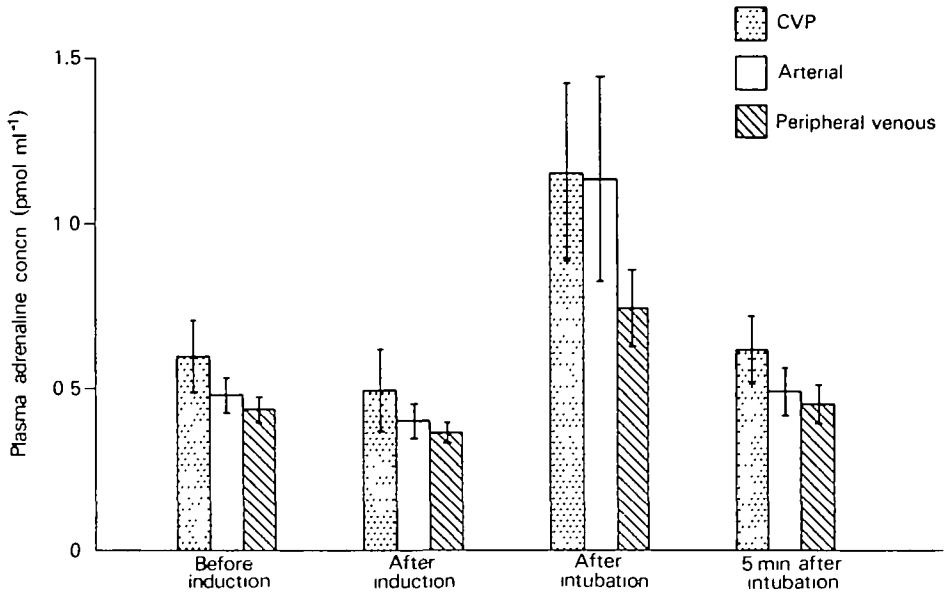

FIG. 2 Plasma adrenaline concentrations in samples obtained from three different sites at each stage of the study. Patients from both groups are combined. (Mean ± SEM; $n = 24$.)

after the induction of anaesthesia, following tracheal intubation, there were significant differences between the central and peripheral venous samples for adrenaline and between the central venous and radial arterial samples for noradrenaline (figs 1, 2).

DISCUSSION

This study demonstrated significant increases in plasma noradrenaline concentration in association with a significant pressor response following intubation. In the SUX group, in which the pressor response was greater in comparison with the pancuronium group (54% *v.* 25%), there were, additionally, significant increases in plasma adrenaline concentration after intubation.

Our results in the PCB group are in broad agreement with the change reported by Russell and colleagues (1981), who also utilized an anaesthetic technique comprising thiopentone and pancuronium. Whilst these workers noted a 22% increase in mean arterial pressure in comparison with our 21% change, the plasma noradrenaline concentration increased by 34% in comparison with the 74% increase in samples obtained from the radial artery in this study. Five minutes after intubation, the noradrenergic response had diminished in Russell's study, although it was still detectable in the present study, as noted by the significant 45% increase in noradrenaline concentration. This small difference between the studies may be accounted for by patient variation, differences in premedication, and differences in handling techniques, since the half-life of the catecholamines *in vivo* is known to be very short (2–3 min).

In contrast, when intubation was performed under suxamethonium, there was not only a more marked pressor and noradrenergic response in comparison with PCB (table I), but also a significant adrenergic response. These results suggest that tracheal intubation is accompanied not only by increased sympathetic activity, but also increased sympathoadrenal activity. Changes in plasma adrenaline activity are probably only demonstrable when there is a particularly marked response to intubation, as may occur under light anaesthesia, or for some reason under the particular conditions of this study following suxamethonium.

Our results, and those of Russell and associates, are at variance with the findings of Zsigmond and Kumar (1980), who did not observe any sympathoadrenal response to tracheal intubation despite the presence of a significant pressor response. This discrepancy may arise from marginal differences in anaesthetic techniques, or more probably from the relative insensitivity of the fluorimetric assay of catecholamines used by Zsigmond and Kumar.

The failure to demonstrate changes in plasma catecholamine concentrations in cardiac surgical patients following intubation in the studies of Stanley and co-workers (1980) and Hoar and colleagues (1981) is undoubtedly related to the much greater depth of anaesthesia produced on induction by high-dose opiates. This was supported by the absence of a pressor response.

Salt, Barnes and Conway (1980), using an *in vitro* preparation of rat heart, showed that high concentrations of PCB inhibited neuronal uptake of noradrenaline. If this were so in man, with clinical doses of the drugs, one would expect to observe greater concentrations of noradrenaline in the present study following PCB in comparison with suxamethonium. However, we did not observe such a difference, suggesting that this effect is unimportant in clinical practice, or that the effect was masked by the larger pressor response following suxamethonium as a result of the non-homogeneity and lack of close similarity between the two groups.

The absolute values of the pre-intubation plasma catecholamine concentrations reported in our study are almost identical to those noted by Russell and colleagues (1981) in radial arterial blood, providing confidence in the accuracy of the measurement techniques. Although there were no significant differences in the plasma noradrenaline concentrations before induction of anaesthesia in samples drawn from the radial artery, peripheral vein or central vein, following intubation, the absolute value of the hormone in central venous blood was significantly greater than that from the other two sites (fig. 1). These results are in agreement with the studies of Ginn and Vane (1968), who showed *in vitro* that 7–30% of noradrenaline was taken up in a single passage through the lungs.

As might be expected, the changes in plasma adrenaline concentrations were greater in central venous and radial arterial samples than in the samples of peripheral venous blood (there being no difference between the first two sites) (fig. 2).

The conclusions to be derived from this study of relevance to clinical practice are that the use of β-blockade alone as a means of inhibiting the pressor response to tracheal intubation is illogical without the concomitant use of α-blockade. In addition, where only small changes in the catecholamine concentrations may be expected to occur in response to differing interventions, it is preferable to obtain blood samples from central venous sites rather than the radial artery. Where large changes in the concentrations of the catecholamines occur, or when it is not ethically justified to cannulate either radial artery or a central vein, sampling of blood from a large cannula in the antecubital fossa will provide useful information. Furthermore, the use of peripheral venous sampling will ethically permit studies on healthy groups of patients, thereby enabling studies in a more homogenous population than that examined here.

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REPONSES DES CATECHOLAMINES PLASMATIQUES A L'INTUBATION TRACHEALE

RESUME

Des concentrations plasmatiques d'adrénaline et de noradrénaline ont été mesurées chez 24 patients pendant l'induction de l'anesthésie et l'intubation trachéale consécutive. Les patients avaient reçu soit du suxaméthonium 1 mg kg^{-1}, soit du pan-

curonium 0,1 mg kg^{-1} pour faciliter l'intubation trachéale. La pression artérielle moyenne (PAM) s'est élevée dans les deux groupes après la laryngoscopie et l'intubation trachéale et il y a eu une augmentation concomittante des concentrations plasmatiques de catécholamines, les modifications étant plus marquées dans le groupe suxaméthonium. Les mesures des concentrations de catécholamines plasmatiques dans des échantillons obtenus simultanément à partir de sang veineux mêlé et périphérique et de sang artériel étaient largement concordantes, les modifications les plus importantes ont été trouvées dans le sang veineux mêlé.

PLASMAKATECHOLAMIN-REAKTION AUF TRACHEALE INTUBATION

ZUSAMMENFASSUNG

Bei 24 Patienten wurde während Narkoseeinleitung und trachealer Intubation die Plasmakonzentration von Adrenalin und Noradrenalin gemessen. Zur Erleichterung der Intubation erhielten die Patienten entweder Suxamethonium 1 mg kg^{-1} oder Pancuronium 0,1 mg kg^{-1}. Nach Laryngoskopie und trachealer Intubation stieg in beiden Gruppen der mittlere arterielle Druck (MAP) an, ebenso stiegen die Plasmakatecholaminkonzentrationen an, wobei diese Veränderungen in der Suxamethonium-Gruppe ausgeprägter waren. Bei der Suxamethonium-Gruppe zeigte sich eine signifikante Korrelation zwischen MAP und Plasmakatecholaminspiegel. Messungen der Plasmakatecholaminspiegel aus Proben von zentralvenösen, peripher-venösen und arteriellen Zugängen wiesen eine breite Übereinstimmung auf. Die größten Abwichungen zeigten sich bei den zentralvenösen Proben.

CONCENTRACIONES DE CATECOLAMINA EN EL PLASMA A RAIZ DE LA INTUBACION TRAQUEAL

SUMARIO

Se midieron las concentraciones de adrenalina y de noradrenalina en el plama en 24 pacientes, durante la inducción de anestesia y la subsiguiente intubación traqueal. Los pacientes recibieron 1 mg kg^{-1} de suxametonio o bien, 0,1 mg kg^{-1} de pancuronio, para facilitar la intubación traqueal. La presión arterial media aumentó en ambos grupos a raiz de la laringoscopia y de la intubación traqueal y hubo incrementos concomitantes en las concentraciones de catecolamina del plasma, siendo los cambios más notorios en el grupo del suxametonio. Hubo una correlación significativa en el grupo de suxametonio, entre la presión arterial media y las concentraciones de catecolamina del plasma. La medición de estas últimas concentraciones en las muestras obtenidas simultáneamente de zonas arteriales y de zonas venosas centrales y periféricas coincidían en términos generales; los cambios más significativos tuvieron lugar en las muestras de las zonas venosas centrales.