THE CHANGE IN CALF MUSCLE BLOOD FLOW IN
THE ISCHAEMIC LIMB DURING ANAESTHESIA
WITH PANCURONIUM BROMIDE

BY
G. J. J. FUZZEY AND J. C. EDWARDS

SUMMARY

Calf muscle blood flow was measured in eight patients with confirmed ischaemic disease of their lower limbs, before and during general anaesthesia which included pancuronium bromide and intermittent positive pressure ventilation. Anaesthesia was associated with a decrease in limb blood flow. Comparison of these results with those of a similar study in which tubocurarine was employed in a place of pancuronium suggest that tubocurarine causes a greater reduction in limb blood flow. Possible mechanisms for this are discussed.

Patients with ischaemic lower limbs who are undergoing surgery present problems to the anaesthetist. One of these is the choice of anaesthetic drugs and techniques which have the least detrimental effect on the blood flow to ischaemic limbs. Recent work suggests that limb blood flow in patients with ischaemic lower limbs may depend on the type of anaesthetic used (Dormandy and Bullough, 1969; Edwards and Fuzzey, 1970).

Pancuronium has been shown to have little effect on the stability of the cardiovascular system (Crul, 1963) and it has been suggested that it may be the drug of choice in "poor risk" cases (Sellick, 1968). We considered it of interest to compare the calf muscle blood flow in the ischaemic limb before and during anaesthesia using pancuronium. The design of this investigation is essentially similar to that of a previous study using other anaesthetic agents (Edwards and Fuzzey, 1970).

METHOD

Venous occlusion plethysmography involves the inflation of a cuff (collecting cuff) placed around the lower part of the thigh to above venous pressure. The change in volume of the lower limb can be measured and is proportional over a short period of time to the blood flow into the limb. The circulation to the foot is arrested before calf blood flow measurements are made, using an ankle occluding cuff inflated to above arterial pressure. The change in volume of the limb is related to the change in circumference, which may be measured by stretching a column of mercury in sialastic rubber tubing wrapped around the limb and thereby altering its resistance. This strain gauge is incorporated as one of the resistances in a Wheatstone bridge circuit. The output of the bridge is suitably amplified and recorded. The rate of change in circumference may be measured and from these recordings the blood flow calculated.

The patients selected for study were undergoing translumbar aortography to investigate symptoms of intermittent claudication. The following patients were excluded from this study:

(1) Those with gangrene or ulceration of the lower limb.
(2) Those with cyanosis and/or dyspnoea at rest due to either cardiac or respiratory disease.
(3) Those who had had previous surgical treatment for vascular disease of the lower limb.

The cardiorespiratory systems and the lower limbs of the patients were examined on the day before aortography and the investigation was explained to the patient. The patients were premedicated with pethidine 1 mg/kg body weight and atropine 0.6 mg approximately 1½ hours before the control blood flow measurement. The patient rested supine on the X-ray table for at least 15 minutes before the investigation began, in an endeavour to attain a basal state. The

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mercury-in-rubber strain gauge was temperature-compensated and the heating of the room in which the investigation was carried out was thermostatically controlled and was kept constant for each investigation. The range of temperature was between 19 and 26°C.

The calf blood flow was measured on the limb which was associated with the more severe symptoms. Blood flow measurements were made using a temperature-compensated mercury-in-rubber strain gauge (Whitney, 1953), a Devices S7 coupling unit, a Devices DC 2C pre-amplifier, a Devices sub-unit 1C and a Devices pen recorder. Pneumatic cuffs were placed around the ankle and just above the knee, and the mercury-in-rubber strain gauge was placed around the widest part of the calf. The foot was elevated 10 degrees above the horizontal by a supporting heel pad, in order to facilitate venous drainage between measurements. The ankle cuff (occluding cuff) was inflated to above arterial pressure, approximately 250 mm Hg, for 5 minutes before the blood flow measurements were taken. The venous cuff (collecting cuff) was inflated to 10 mm Hg below diastolic blood pressure. The duration of each blood flow measurement was 20–30 sec with intervals of 5 sec between each measurement. Each calf blood flow measurement was the mean of eight readings.

Immediately after the control calf blood flow measurement (CBF I) anaesthesia was induced intravenously with thiopentone 5 mg/kg body weight. A cuffed latex oro-endotracheal tube was passed after suxamethonium 100 mg had been given intravenously and the trachea had been sprayed with 2 ml 4 per cent lignocaine. Anaesthesia was maintained with nitrous oxide 6 l./min and oxygen 3 l./min. After the return of spontaneous ventilation a paralyzing dose of pancuronium (6 mg) was given intravenously, and ventilation controlled with a Manley ventilator (tidal volume 500–600 ml). Approximately 20 minutes after administration of pancuronium the second calf blood flow measurement was taken. In a previous study (Edwards and Fuzzey, 1970) using tubocurarine and intermittent positive pressure ventilation, calf blood flow measurements were taken at 15 and 30 minutes after the addition of tubocurarine. However, as the changes in blood flow measured between the 15-minute measurement and 30-minute measurement were slight, it was considered reasonable to shorten the duration of anaesthesia and take one blood flow measurement at 20 minutes.

All blood pressure measurements were made on each patient in the same arm by the same observer, using conventional sphygmomanometry. A random zero sphygmomanometer was used in some cases (Wright and Dore, 1970; Rose, Holland and Crowley, 1964).

Student's t test was used to determine the significance between the results.

RESULTS
All of the eight patients studied were shown by aortography to have varying degrees of arterial block. The results are shown in table I. There was no apparent correlation between the percentage fall in calf blood flow and the severity of the arterial disease in individual patients.

In eight patients studied the initial mean calf blood flow (CBF I) was 3.52 ml/100 ml tissue/min. Nineteen–28 minutes later, after intravenous injection of pancuronium and intermittent positive pressure ventilation, the mean calf blood flow fell to 2.54 ml/100 ml tissue/min. This represented a statistically significant fall (P<0.02). The mean percentage difference was a 25 per cent fall in calf blood flow. There was no statistically significant change in mean arterial blood pressure and pulse rate between the measurements taken at the time of measuring CBF I and CBF II.

DISCUSSION
Venous occlusion plethysmography using a mercury-in-rubber strain gauge is an accepted and well- tried technique for measuring limb blood flow, and compares well with the direct technique of water plethysmography (Clarke and Hellon, 1957; Pauca and Sykes, 1967). There has previously been a number of studies on the effect of general anaesthesia on limb blood flow in normal subjects (Lynn and Shackman, 1951; Prime and Gray, 1952; Black and McArdle, 1962; Pauca and Sykes, 1967; McArdle, Unni and Black, 1968). There appears at first sight to be considerable discrepancy between the findings of various authors. However, their studies were not strictly comparable in design, because the control readings were taken at different times and in
TABLE I

Effect of thiopentone, suxamethonium, nitrous oxide, oxygen, pancuronium and endotracheal intubation with IPPV on the blood flow to the ischaemic lower limb.

<table>
<thead>
<tr>
<th>No.</th>
<th>Wt. (kg)</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>CBF I (ml/100 ml tissue/min)</th>
<th>CBF II (ml/100 ml tissue/min)</th>
<th>% change in flow</th>
<th>Mean arterial blood pressure (mm Hg)</th>
<th>CBF I</th>
<th>CBF II</th>
<th>% change in pressure</th>
<th>Pulse rate (beat/min)</th>
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<td>64</td>
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<td>92</td>
<td>-8</td>
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<td>64</td>
<td>F</td>
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<td>133</td>
<td>111</td>
<td>-17</td>
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<td>96</td>
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<tr>
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<td>59</td>
<td>M</td>
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<td>1.71</td>
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<td>111</td>
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<td>67</td>
<td>F</td>
<td>5.24</td>
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<td>123</td>
<td>103</td>
<td>-16</td>
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Mean: 3.52 2.54 -25 111.5 108.2 91 94
SD: 1.45 1.15 11.55 20.17 14.45 19.59
SE: 0.51 0.41 4.08 7.12 5.10 6.92

r=3.17
P<0.02

t=0.78
P<0.50

CBF I=Pre-induction calf muscle blood flow.
CBF II=Flow 19-28 min (mean 23) after injection of pancuronium.

In a previous study of the effects of tubocurarine (Table II) on the blood flow to the lower limb.

TABLE II

Effect of thiopentone, suxamethonium, nitrous oxide, oxygen, tubocurarine, and endotracheal intubation with IPPV on the blood flow to the ischaemic lower limb.

<table>
<thead>
<tr>
<th>No.</th>
<th>Wt. (kg)</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>CBF I (ml/100 ml tissue/min)</th>
<th>CBF II (ml/100 ml tissue/min)</th>
<th>% change in flow</th>
<th>Mean arterial blood pressure (mm Hg)</th>
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<th>Pulse rate (beat/min)</th>
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<td>111</td>
<td>72</td>
<td>-35</td>
<td>84</td>
<td>72</td>
</tr>
</tbody>
</table>

Mean: 2.79 1.34 -46 109 96 87 74
SD: 1.80 0.42 14.50 20.25 18.11 8.80
SE: 0.64 0.15 5.12 7.15 6.39 3.11

t=2.98
P<0.025

t=1.94
P<0.1

t=3.06
P<0.02

CBF I=Pre-induction calf muscle blood flow.
CBF II=Flow 24-32 min (mean 29) after injection of tubocurarine.

Table II modified from a previous study (Brit. J. Anaesth. (1970), 42, 516).
in patients with lower limb ischaemia, a considerable fall in calf blood flow from pre-induction levels was found compared with halothane anaesthesia. However, it may be desirable in many cases to administer a muscle relaxant and, because of the reported stability of the cardiovascular system during anaesthesia using pancuronium, an investigation similar to that using tubocurarine was carried out. Figure 1 shows the fall in calf muscle blood flow following the administration of pancuronium and tubocurarine respectively.

Our results show that the mean percentage change in calf muscle blood flow following the administration of pancuronium was 25 per cent and following tubocurarine, 46 per cent. All the patients studied had proven arterial disease but it is seen that there is a wide variation in the control flow readings. This variation is common in patients with lower limb ischaemia and in comparing the change in flow following the administration of muscle relaxants in these two groups of patients we have used Student's t test to determine the significance of the difference of the means of the percentage change in calf muscle blood flow, \( t = 1.819 \) and \( P < 0.5 \).

The possible mechanism for the difference between the change in calf muscle blood flow from pre-induction levels between pancuronium and tubocurarine is that the arterial blood pressure does not fall to the same extent with pancuronium as with tubocurarine. It can be seen in tables I and II that there is no apparent correlation between the change in mean arterial blood pressure and the change in calf muscle blood flow. Another possible mechanism is that pancuronium has a vagolytic effect (Baird and Reid, 1967; Kelman and Kennedy, 1970) but there was no clinically significant change in pulse rate taken at the time of recording CBF I and CBF II.

It has been found in man that the cardiac output is increased after injection of pancuronium and the peripheral resistance remains unchanged (Kelman and Kennedy, 1970). There is evidence that in perfused isolated digitalized rabbits' hearts the addition of tubocurarine to the perfusate has a depressant action on myocardial muscle which is proportional to the amount of tubocurarine added (Dowdy, Duggar and Fabian, 1965). Recently, however, it has been suggested that the apparent myocardial depressant action of commercially available tubocurarine may be due to substances used as preservatives (Carrier and Murphy, 1970). The peripheral resistance after tubocurarine might be expected to fall because of autonomic ganglionic blockade and histamine release (Guyton and Reeder, 1950; Westgate and Van Bergen, 1962; Thomas, 1957; Hewer, 1957), but if this were the case a decrease in peripheral resistance would be associated with an expected increase in muscle blood flow.

Both groups of patients were ventilated with a Manley ventilator at a constant minute volume. It has been shown that there is a fall in cardiac output associated with hypocapnia which was independent of the type of ventilation (Prys-Roberts et al., 1967). In studies on the conscious man, changes in Pco\(_2\) had little effect on limb blood flow in the presence of an intact autonomic nervous system. However, in the presence of sympathetic blockade, hypo- and hypercapnia had the effect of increasing the limb blood flow (Richardson, Wasserman and Patterson, 1967). Therefore it might be expected with tubocurarine that a smaller fall in blood flow would
result compared with pancuronium. Since this has not been found in our investigation the fall in blood flow with tubocurarine may be due to the effect of the drug and hypocapnia on the myocardium.

The reported increase in cardiac output during anaesthesia with pancuronium (Kelman and Kennedy, 1970) may explain the smaller reduction in calf blood flow with this drug compared with tubocurarine.

ACKNOWLEDGEMENTS

We would like to thank Professor J. B. Kinmonth, Mr F. B. Cockett and Mr N. L. Browse for allowing us to study patients under their care, and Dr H. C. Churchill-Davidson for his encouragement.

We are grateful to Dr M. Lea Thomas for reporting the aortographic findings.

REFERENCES


LES MODIFICATIONS DU FLUX SANGUIN MUSCULAIRE DANS LE MEMBRE ISCHEMIQUE DURANT L’ANESTHESIE AU BROMURE DE PANCURONIUM

SOMMAIRE

Le flux sanguin musculaire dans le mollet était mesuré chez huit patients avec maladie ischémique confirmée des membres inférieurs, avant et durant l’anesthésie générale qui comprenait le bromure de pancuronium et la ventilation à pression positive intermittente. L’anesthésie s’accompagne d’une réduction du flux sanguin dans le membre. Une comparaison de ces résultats avec ceux d’une étude semblable, qui utilisait tubocurarine au lieu de pancuronium, suggère que la tubocurarine cause une plus forte réduction du flux sanguin dans le membre. Les mécanismes possibles en sont discutés.

DURCHBLUTUNGSÄNDERUNGEN AN DER UNTERSCHENKELMUSKULATUR BEI ISCHÄMIERISCHER EXTREMITÄT UNTER PANCURONIUM-BROMID-NARKOSE

ZUSAMMENFASSUNG

An acht Patienten mit gesicherten peripheren Durchblutungsstörungen der unteren Extremitäten wurde vor und während einer Vollnarkose mit Pancuronium-Bromid und mechanischer Beatmung die Durchblutung der Unterschenkelmuskulatur gemessen. Während der Narkose nahm die Durchblutung der Extremität ab. Ein Vergleich dieser Ergebnisse mit denen einer ähnlichen Untersuchung, bei der anstelle von Pancuronium Tubocurarin verwendet worden war,
The material itself is presented in readily identifiable sections aided by a good and reasonably comprehensive subject index. It covers most aspects of the subject from basic science to clinical complications and the large section on pharmacology is further divided; although why the effects of anaesthetics on the eye should merit a separate heading when only one rather circumscribed paper is discussed is not immediately obvious. Similarly it is often difficult to see the value of some of the editorial comments. The short pithy statement which can be so effective in open debate is much less impressive in cold print when the authors have no opportunity to reply. It might be better to confine editorial comment to those more obviously controversial issues where the reader would welcome guidance. Under these circumstances more detailed and lengthy criticism in the form of an annotation could be very useful. In this respect the rather full commentary in the present volume on the papers on hepatic necrosis after halothane anaesthesia is an example of the type of presentation that many readers might welcome. Similar commentaries on other controversial matters such as nurse anaesthetists or neuroleptanalgesia could prove infinitely more useful than the present rather superficial approach.

The book itself is very nicely produced; it is a convenient size and the print and selected illustrations are easy to follow. Although rather dear by British standards, this is a worthwhile investment for all anaesthetists and is an essential requirement for every medical library.

J. P. Payne


The fact that a third edition of this book is already required only three years after publication of its predecessor is testimonial enough to its popularity and usefulness. This new edition contains no major alteration. It is a few pages longer and contains another half dozen figures. None the less the whole text has been most carefully revised and the increase in length of the book is due to the addition of sentences here and there or to the inclusion of the odd additional paragraph to cover recent advances in the specialty of anaesthesia; for example pharmacology has been extended to take in topics like neuroleptic drugs, diazepam and ketamine. Comparable alterations have been made throughout the extent of the book which fully maintains the high standard of its predecessors.

Once more we commend it unreservedly.

A. R. Hunter