THE EFFECT OF ANAESTHETIC AGENTS UPON CALF MUSCLE BLOOD FLOW IN THE ISCHAEMIC LIMB

BY

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SUMMARY

The effect of anaesthesia using trichloroethylene, halothane, and tubocurarine was studied on the calf blood flow before surgical stimulation using venous occlusion plethysmography. There were twenty-seven patients in the study divided into three groups, each group receiving one of the three anaesthetic agents. All patients had a history of intermittent claudication and were subsequently shown to have abnormal aortograms. There was a decrease in calf blood flow in all three groups. Those patients anaesthetized with halothane showed a considerably smaller decrease in flow compared to the other two groups. It is suggested that halothane might be a more suitable agent for anaesthesia in patients with lower limb ischaemia.

The anaesthetic management of patients with ischaemic disease of the lower limb presents special problems. These patients are likely to have generalized arterial disease affecting in particular the brain, heart and bowel; during anaesthesia, it is important to ensure maximum tissue perfusion. Such patients may be candidates for anaesthesia for urgent, essential or elective surgery, which may be related directly or indirectly to their ischaemic lower limbs. In either case, these patients with borderline viability of their lower limbs may have to be anaesthetized. It is the purpose of the present study to compare the changes in calf blood flow of ischaemic limbs before and during anaesthesia, using one of three commonly used anaesthetic techniques. Apart from a study of the effects of methohexitone on peripheral blood flow (Dormandy and Bullough, 1969), to our knowledge there appear to be no other reports of the effects of anaesthetic agents per se on the calf blood flow of ischaemic limbs prior to surgical stimulation.

METHOD

The patients (21 male, 6 female) selected for study were undergoing translumbar aortography for investigation of symptoms and signs of lower limb ischaemia. They all had intermittent claudication at variable distances in the calf and/or buttock, and absence of peripheral pulses. The following patients were excluded from the 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 patients investigated were randomly allocated into three groups, one receiving halothane, one receiving trichloroethylene, and the other tubocurarine with intermittent positive pressure respiration. Patients were visited on the day before aortography and the nature of the study explained to them. A clinical examination of the cardiorespiratory system and of the lower limbs was made.

The calf blood flow was measured on the limb which had 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 D.C. 2C pre-amplifier; a Devices sub-unit 1C and a Devices pen recorder.

All blood pressure measurements were made in 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).

Pethidine 1 mg/kg and atropine 0.6 mg were given as pre-anaesthetic medication by intramuscular injection approximately 1½ hours prior to anaesthesia.
EFFECT OF ANAESTHETIC AGENTS ON CALF MUSCLE BLOOD FLOW

515

to induction of anaesthesia. The patient lay supine on the X-ray table, and the mercury-in-rubber strain gauge was placed around the widest part of the calf. A pneumatic cuff was placed around the patient's ankle and a collecting cuff was placed around the thigh just above the knee. The leg was elevated to 10 degrees above the horizontal by insertion of a pad under the heel to facilitate the drainage of blood from the calf after the release of the occluding cuff. The time elapsing between the patient being placed on the X-ray table and the first calf blood flow measurement (CBF1) was always longer than 15 minutes, in an endeavour to achieve a basal state. The ankle cuff was inflated to above arterial pressure (approximately 250 mm Hg) 5 minutes before the blood flow measurements. The collecting cuff was inflated to 10 mm Hg below the diastolic blood pressure of the patient. Each blood flow measurement was the mean of approximately eight recordings, and the duration of each recording was 20-30 seconds with intervals of 5 seconds. Room temperature was measured before and after all blood flow measurements and ranged from 19 to 25°C, and was constant for each patient. The lower limb under investigation was exposed to room temperature for at least 15 minutes (average 21 minutes). The studies were all carried out in the same room which had no window and was thermostatically controlled and artificially ventilated.

Anaesthesia was induced with intravenous thiopentone 5 mg/kg body weight. Suxamethonium 100 mg was given to facilitate endotracheal intubation with a cuffed Latex oro-endotracheal tube and the trachea was sprayed with 2 ml of 4 per cent lignocaine solution before intubation. Anaesthesia was maintained with nitrous oxide (6 l./min), oxygen (3 l./min) via a Mapleson A circuit (Mapleson, 1954). Halothane was administered from Fluotec in 1-1.5 per cent concentration. Trichloroethylene was added via a Boyle bottle or Tritec in a 1.5-0.7 per cent concentration (Mapleson, 1957). Tubocurarine was administered in a 30-mg dose after return of spontaneous respiration following the suxamethonium. Ventilation was controlled with a Manley ventilator. The minute volume was set at 9 l./min (nitrous oxide 6 l./min, oxygen 3 l./min).

The second calf blood flow measurement (CBF2) was taken at approximately 15 minutes after the addition of the agent. Blood pressure and pulse were also recorded. A third calf blood flow measurement was taken approximately 15 minutes later (CBF3). Pulse and blood pressure were again recorded.

The experiment was then ended and the aortogram was performed. The significance between results was determined by the use of the Student t test.

RESULTS

Calf Blood Flow.

Twenty-seven patients were investigated. All had a history of intermittent claudication, and showed varying degrees of vascular abnormalities on aortography. Tables I, II and III summarize the results of the blood flow measurements.

Calf blood flow and halothane anaesthesia.

The ten patients anaesthetized with halothane had an initial mean calf blood flow (CBF1) of 4.38 ml/100 ml tissue/min; 14-18 minutes (mean 15) after addition of halothane, the calf blood flow (CBF2) fell to a mean of 3.20 ml/100 ml tissue/min. This was not statistically significant (P<0.10). After 20-34 minutes (mean 31) the calf blood flow was 3.23 ml/100 ml tissue/min. The difference between CBF1 and CBF3 was statistically significant (P<0.05). The mean percentage difference between CBF1 and CBF2 reading was 20 per cent and between the CBF1 and CBF3 reading was 21 per cent.

Calf blood flow and trichloroethylene anaesthesia.

The nine patients anaesthetized with trichloroethylene had an initial mean calf blood flow (CBF1) of 4.00 ml/100 ml tissue/min; 14-20 minutes (mean 17) after addition of trichloroethylene the calf blood flow (CBF2) fell to a mean of 2.08 ml/100 ml tissue/min. This was not statistically significant (P<0.10). After 20-34 minutes (mean 31) the calf blood flow was 3.23 ml/100 ml tissue/min. The difference between CBF1 and CBF3 was statistically significant (P<0.025). The mean percentage difference between CBF1 and CBF2 reading was 20 per cent and between the CBF1 and CBF3 reading was 21 per cent.
### TABLE I

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

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<th>Change in flow (%)</th>
<th>CBF2 (ml/100 ml tissue/min)</th>
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### TABLE II

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

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### TABLE III

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

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| SD  |          |          |     | 1.80                        | 0.48               | 0.42                        | 0.42               | 14.50                                 | 26.79               | 20.25                  | 18.11              |
| SE  |          |          |     | 0.64                        | 0.17               | 0.15                        | 0.15               | 5.12                                  | 9.46               | 7.15                   | 6.39               |
EFFECT OF ANAESTHETIC AGENTS ON CALF MUSCLE BLOOD FLOW

Calf blood flow and tubocurarine with intermittent positive pressure respiration anaesthesia.

The eight curarized patients had an initial mean calf blood flow (CBF1) of 2.79 ml/100 ml tissue/min; 15-19 minutes (mean 17) after tubocurarine was given the calf blood flow (CBF2) fell to 1.49 ml/100 ml tissue/min. This was a statistically significant difference (P<0.025). After 24-32 minutes (mean 29) the calf blood flow (CBF3) was 1.34 ml/100 ml tissue/min. This was a statistically significant difference (P<0.025). The mean percentage difference between the CBF1 and CBF2 reading was 42 per cent and between the CBF1 and CBF3 reading was 46 per cent.

Arterial Blood Pressure and Pulse Rate.
The arterial blood pressure fell from the control level in all three groups. The mean value for mean arterial blood pressure fell in the halothane group from 99 to 82 mm Hg (P<0.01) and 99 to 79 mm Hg (P<0.01) between the blood pressure measurement taken at the time of the measurement of CBF1 to CBF2 and CBF1 to CBF3 respectively. These falls were statistically significant. There was no statistically significant change in the pulse rate. The pulse rates were not recorded in patients 1 and 2.

The mean value for mean arterial blood pressure fell in the trichloroethylene group from 106 to 93 mm Hg (P<0.2) and 106 to 90 mm Hg (P<0.1) between the blood pressure measurement taken at the time of the measurement of CBF1 to CBF2 and CBF1 to CBF3 respectively, but the falls were not statistically significant. There was a statistically significant fall in the pulse rate from 92 to 74 beats/min (P<0.02) and 92 to 72 beats/min (P<0.02) between the pulse rate measurement taken at the time of the measurement of CBF1 to CBF2 and CBF1 to CBF3 respectively.

The mean value for mean arterial blood pressure fell in the tubocurarine-IPPV group from 109 to 79 mm Hg (P<0.025) and 109 to 96 mm Hg (P<0.1) between the blood pressure measurement taken at the time of the measurement of CBF1 to CBF2 and CBF1 to CBF3 respectively. The fall between CBF1 and CBF2 was statistically significant but the fall between CBF1 and CBF3 was not statistically significant. There was a statistically significant fall in the pulse rate from 87 to 75 beats/min (P<0.05) and from 87 to 74 beats/min (P<0.02) between the pulse rate measurement taken at the time of the measurement of CBF1 to CBF2 and CBF1 to CBF3 respectively.

![Figure 1](image)

Changes in calf blood flow before and during anaesthesia.

Figure 1 shows the mean value for the calf blood flow measurements plotted against time. Figure 2 shows the relationship between the percentage change in blood pressure and the percentage change in calf blood flow for each patient after approximately 30 minutes anaesthesia.

Patient No. 5 in the tubocurarine group showed a fall in systolic blood pressure to 50 mm Hg, the diastolic being unrecordable, giving a mean arterial pressure of 20 mm Hg. An electrocardiograph was taken immediately which showed no evidence of cardiac abnormality. Methoxamine 10 mg was administered intravenously and the patient's blood pressure rose to 135/90 mm Hg (mean 105). The blood flow at a mean arterial pressure of 20 mm Hg was 1.80 ml/100 ml tissue/min and fell when the blood pressure was restored, to 1.52 ml/100 ml tissue/min 5 minutes after injection of methoxamine.
Patient No. 7 in the halothane group had a typical history of intermittent claudication in the calf muscles after walking 150 yards but he had a high resting calf blood flow. The aortogram showed that he had minimal vascular disease apart from a slight stenosis in the superficial femoral artery in the mid-thigh region on the side investigated but below the stenosis the arterial tree was of a rather wider calibre than usual. This was thought to represent an early case of the arteria magna syndrome (Staple et al., 1966; Lea-Thomas and Andress, 1970). This is of interest since Staple and co-workers showed that the circulation of the contrast medium was much slower than usual in these cases. A further case of arteria magna has been found in a subsequent study, this case also apparently had a high resting blood flow.

Apart from these cases there was a wide variation in resting blood flows in individual patients, and this has also been noted by previous workers (Shepherd, 1963).

Patient No. 2 in the trichloroethylene group had a high resting calf blood flow level. This patient was shown by aortography to have an abnormal tortuosity of the iliac arteries but with no demonstrable block although the history was that of typical intermittent claudication after walking less than 100 yards.

Aortography in all other cases showed localized or generalized arterial disease obstructing the vessels at varying sites in the arterial tree. There was no apparent correlation between the site of the block, the severity of the disease with the resting calf blood flow levels, or the percentage decrease in the calf blood flow measurements after induction of anaesthesia.

**DISCUSSION**

In the present investigation the authors have studied the effects of three commonly used anaesthetic techniques on the calf muscle blood flow of patients with arterial insufficiency of the lower limbs, after pre-anaesthetic medication and before any surgical stimulation. Although there was a statistically significant fall in calf muscle blood flow from the pre-induction levels in all three groups after approximately 30 minutes anaesthesia, the fall in the halothane group was 21 per cent compared with 46 per cent in the other two groups. After 30 minutes anaesthesia there was a fall in mean arterial blood pressure in the halothane group but the fall in mean arterial pressure in the trichloroethylene and tubocurarine groups was not statistically significant.

Previous workers have studied the limb blood flow before and during anaesthesia. Lynn and Shackman (1951) investigated the effects of general anaesthesia and surgery on the peripheral circulation. In one group of patients undergoing short minor surgical operations such as herniorrhaphy, the average resting calf blood flow in the sedated patient prior to induction was 2.3 ml/100 ml tissue/min. The average peak calf blood flow after 15-30 minutes anaesthesia was 7.5 ml/100 ml tissue/min; the anaesthetic agents were various—thiopentone, nitrous oxide and oxygen, trichloroethylene, cyclopropane, ether, gallamine.

Pauca and Sykes (1967) studied the effects of thiopentone-oxygen-halothane anaesthesia on the forearm blood flow in nine unpremedicated patients and found a decrease of 44 per cent in forearm blood flow after 30 minutes anaesthesia. These workers also reported that pre-operative medication, intubation, addition of nitrous oxide, surgical stimulation, had no obvious effect on the decrease of forearm blood flow.

Black and McArdle (1962) investigated the changes in forearm and calf blood flow in unpremedicated patients undergoing thiopentone-nitrous oxide-oxygen-halothane anaesthesia without surgical stimulation. The control blood flow recordings were taken after thiopentone-nitrous oxide-oxygen induction, and after the addition of halothane the forearm blood flow increased from the control value of 2.6 ml/100 ml tissue/min to 4.0 ml/100 ml tissue/min. Calf blood flow
changes were studied in two subjects and a similar increase was found.

McArdle, Unni and Black (1968) reported no significant alteration in forearm blood flow before surgical stimulation in unanaesthetized patients anaesthetized with thiopentone, nitrous oxide, and trichloroethylene.

There appear to be few reports in the literature of the effects of muscle relaxants on limb blood flow. Prime and Gray (1952) using a thiopentone-nitrous oxide and oxygen-tubocurarine technique showed an immediate rise in flow followed by a fall 10 minutes after induction. This was attributed to the effect of thiopentone.

The importance of maintaining the blood pressure to near normal levels during the operative and postoperative periods is stressed by many vascular surgeons (Cockett and Maurice, 1963; Martin, 1963). In the trichloroethylene group the mean arterial blood pressure did not fall significantly but there was a mean decrease in calf blood flow of 46 per cent. It was our clinical impression that the foot was less adequately perfused, as judged by skin colour and filling of superficial veins in this group compared with the cases in the halothane group. The data of Case No. 5 in the tubocurarine group are particularly interesting as this patient showed a further decrease in calf blood flow when the blood pressure was restored with a vasopressor, presumably due to peripheral vasoconstriction. Thus elevation of the blood pressure at the expense of tissue perfusion may be unwise.

In this study the arterial carbon dioxide tension was not measured. It is probable that it would have risen in the halothane and trichloroethylene groups due to the respiratory depressant action of pethidine and thiopentone. The arterial carbon dioxide tension of the patients in the tubocurarine group would probably have fallen, due to hyperventilation (Nunn, 1962).

The effect of a raised arterial carbon dioxide tension on limb blood flow was shown by Lennox and Gibbs (1932) to be small and inconsistent. A lowering of tension is associated with a fall in cardiac output which is independent of the method of ventilation (Prys-Roberts et al., 1967). This may be an important factor in the production of the fall in calf muscle blood flow found in the tubocurarine group in this study.

With regard to vascular grafts, Little and associates (1968) have shown that the intraoperative graft flow is important for the survival of the graft. An intra-operative graft flow of less than 60 ml/min carries an 80 per cent chance of early thrombosis and a flow of 60 ml/min or more carries an 80 per cent chance of patency for 3 months or more.

Our results suggest that halothane might be a preferable agent for anaesthesia in patients who have vascular disease since there are less marked changes in flow from pre-induction levels.

APPENDIX

Principle of the Method.

The change in volume of a limb below a cuff inflated to above venous pressure is equal over a short period of time to the amount of blood entering the limb. A limb may be considered to be a cylinder and a change in the circumference of this cylinder is proportional to the change in volume as the length remains constant. This relationship between circumference and volume applies to any transverse segment of the limb. The strain gauge is a narrow-bore silicone tube filled with mercury which is wrapped around the limb. The terminals are connected to an adjustable perspex block adjusted with a micrometer screw; a temperature-compensating mechanism is incorporated. The gauge forms part of a Wheatstone bridge with two fixed resistances, and a variable resistance for balancing. The signal from the bridge is fed into a suitable pre-amplifier and pen recorder (see text). When the circumference of the limb changes, the rubber is stretched and there is a change in resistance of the mercury column. From the known speed of the paper the slope of the trace may be obtained which is proportional to the blood flow into the segment of limb measured. The strain gauge is calibrated by stretching 1 millimetre, and recording the height to the deflection obtained on the paper trace. Knowing the original circumference of the limb, the deflection obtained from 1 millimetre increase in circumference, and slope of the line obtained, the blood flow may be calculated in millilitres per 100 millilitres of tissue per minute.

Comparisons have been made between the mercury-in-rubber strain gauge and water plethysmography (water plethysmography is a direct measurement of limb blood flow). Pauca and Sykes (1967) and Clarke and Hellon (1957) found that the blood flow measurements were approximately 10 per cent higher using water plethysmography, compared to strain-gauge plethysmography.

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L'EFFET D'AGENTS ANESTHESIANTS SUR LE FLUX SANGUIN DU MUSCLE DU MOLLET DANS UN MEMBRE ISCHEMIQUE

SUMMARY

On a etude, a l'aide de la plethysmographic par occlusion veineuse, l'effet de l'anesthesie au trichloroethyle, halothane et tubocurarine sur le flux sanguin dans le mollet avant la chirurgie. Les vingt-sept patients dans l'etude ont ete partages en trois groupes, dont chacun recevait un des trois agents d'anesthesie. Tous les malades avaient une anamnee de claudication intermittente et on observa ultérieurement chez tous un aortogramme abnormal. Il y eut une reduction dans les trois groupes du flux sanguin dans le mollet, mais cette reduction fut considérablement moins grande chez les patients, anesthesies a l'halothane. Ceci suggere que l'halothane pourrait etre un agent plus adquat pour l'anesthesie de patients avec ischémie du membre inferieur.

DIE WIRKUNG VON NARKOTIKA AUF DEN BLUTSTROM DES WADENMUSKELS IM ISCHAMISCHEN GLIED

ZUSAMMENFASSUNG