Cerebral Blood Flow Changes Induced by Electrical Stimulation of the Gasserian Ganglion After Experimentally Induced Subarachnoid Haemorrhage in Pigs

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Summary

The effect of trigeminal electrical stimulation on cerebral blood flow has been studied in conditions of normal or reduced cerebral blood flow (CBF).

Autologous blood was injected into the subarachnoid space of ten Pittmann-Moore pigs to induce subarachnoid haemorrhage (SAH) accompanied by cerebral blood flow (CBF) reduction. One week later, in six of ten animals, a considerable decrease of CBF was noted as evaluated by means of a recording-system monitoring over the right parieto-temporal calvarium the washout of ¹³³Xenon injected into the internal carotid artery after the external carotid had been clamped. Continuous electrical stimulation of the Gasserian ganglion performed in the six animals with severely induced CBF reduction produced a remarkable cerebrovascular dilation and increase of CBF lasting over 3 h.

Electric stimulation of the Gasserian ganglion produced a similar pattern of vasodilation in six pigs in which no blood was injected and no reduction of CBF was evident.

The mechanisms and the anatomical pathways which underlie these results are discussed.

Keywords: Cerebral blood flow; electrical stimulation; Gasserian ganglion; trigeminal nerve.

Introduction

Ipsilateral flushing of the face has been reported during and after attacks of trigeminal neuralgia. Flushing has also been noticed after stimulation of the trigeminal ganglion by injection of alcohol or thermocoagulation. Extension of this phenomenon has always been reported as being limited to the cutaneous distribution of the involved trigeminal root, occasionally of an adjacent ipsilateral root. Among the current theories credited for this phenomenon, support must be given to the existence of an active vasodilator system originating in the facial nerve and influenced by stimulation of the Gasserian ganglion; also to the destruction of a tonic vasoconstrictor system which is normally active on cutaneous circulation, and finally to the antidromic release of vaso-active substances from the terminal endings of the trigeminal nerve.

It should be stressed, however, that following electrical stimulation of the trigeminal ganglion in cats, vasodilation has been observed also in the internal carotid artery distribution. This result is supported also by the anatomical evidence of a trigeminal-cerebrovascular system of fibers which plays an important role in cerebrovascular regulation and is supposed to restore the diameter of the vessels when excessive vasoconstruction occurs, for example during the vasospasm which follows a subarachnoid haemorrhage (SAH).

The vasodilation in the internal carotid artery distribution as a result of stimulation of the Gasserian ganglion might be possible both in physiological conditions and in situations in which CBF is reduced to ischaemic levels, as for example after subarachnoid haemorrhage.

The present study has been designed to investigate the vasodilation induced by trigeminal stimulation in Pittman-Moore pigs both in physiological conditions and after induced CBF reduction caused by experimental SAH.

Material and Method

The experimental protocol was thoroughly examined and then approved by the Intramural Research Animal Welfare Committee according to the directions given by the Animal Welfare Act.
Sixteen female, 16–18 month old Pittman-Moore pigs, weighing approximately 90 kg, were employed. The animals were fed in a conventional manner before and during the entire investigation. All over this period, the vital signs were monitored and any variation was recorded. Also the neurological status was monitored with particular care for motor and impairment of consciousness.

The entire investigation consisted in two separate procedures. During the first procedure, the animals were surgically prepared and the CBF was determined in basal conditions. The animals were divided in two groups: in ten animals, autologous blood was injected into the subarachnoid space to induce SAH (treated), while six were sham-treated, i.e. they were similarly prepared but blood was not injected. In the second procedure, one week later, electrostimulation of the Gasserian ganglion was performed and the resulting effects on CBF evaluated in sham-treated animals and in six out of ten animals injected with blood, in which a considerable decrease of CBF was noted.

**Anaesthetic Management**

The anaesthetic management was identical in both procedures. Anaesthesia was induced by intramuscular injection of 6–8 mg/kg of ketamine followed by 7 mg/kg of i.v. thiopentine. Muscular relaxation was obtained with pancuronium bromide (0.1 mg/kg); an endotracheal tube was then inserted and mechanical ventilation regulated to keep PaCO₂ between 35 and 40 mmHg and PaO₂ above 100 mmHg. Anaesthesia was maintained by fentanyl and nitrous oxide 50–70%.

All the physiological parameters (EKG, blood pressure, blood gases, body temperature) were continuously monitored. Body temperature was monitored with a rectal probe and maintained at 37 ± 0.5 °C by external heating. Blood pressure was monitored through a polyethylene catheter (PE 160) inserted into the femoral artery and connected with a transducer. From the same catheter, samples of blood were drawn for analysis of blood gases, pH, hematocrit, and haemoglobin concentration. A PE 160 catheter was inserted into the femoral vein for the administration of drugs and plasma expanders. No blood transfusion was necessary.

At the end of the first of the two surgical interventions, nitrous oxide was suspended and the specific opioid antagonist naloxone administered, when necessary. Muscular relaxation was reversed by neostigmine.

At the end of the second intervention, the animals were killed with an overdose of thiopentine.

**Animal Preparation**

After femoral vessel cannulation, the animals were positioned laterally, to expose the right side of the head and neck. The common carotid artery was exposed and isolated up to its bifurcation into external and internal carotid arteries. A 22 G cannula was inserted in the internal carotid for injection of 133Xenon. On the external carotid, 5 mm beyond its origin from the common carotid, a clamp was placed to be locked at every injection of the radiotracer. Then, a skin incision was made over the temporal region and a small craniectomy performed to approach extradurally the Gasserian ganglion. The incision was then enlarged to expose the parieto-temporal bones. The landmarks for detection of the radiotracer were fixed just above and behind the small craniectomy and care was taken to remove completely all the soft tissues to avoid any interference with the monitoring of inert gas clearance. The surgical procedure required 2.5 h approximately.

SAH was produced by exchanging 5 ml of CSF with 5 ml of autologous blood. The CSF was drawn from the cisterna magna through a needle inserted 4 cm behind the trigeminal ganglion. Once the CBF measurements were completed, the wound was accurately closed in layers to prevent any leakage of CSF. In sham-treated animals, the procedure was identical but no blood was injected.

After the second procedure, the animals were sacrificed as mentioned above.

**Measurement of CBF**

For determination of CBF a 1 ml bolus of saline solution of the emitting isotope 133Xenon (5 mCi/ml; Amersham International, London, UK) was injected into the internal carotid artery after the external carotid was clamped. The washout of the radiotracer was evaluated by means of a collimated sodium iodide (thallium-activated) scintillation crystal, contained in a cylindrical lead collimator 5 cm in diameter, 5 cm deep, placed over the exposed parieto-temporal region. The detector was coupled to a photomultiplier and a ratemeter and the output recorded on chart paper (1 cm/sec speed). The pulse-height analyzer was set to the photopeak of 133Xe (81 keV). CBF was calculated by the initial slope of a semilog plot of the clearance curve using the formula given by Olesen et al. A steady state period of 10–15 sec has been adequate to obtain the initial slope of the 133Xe clearance curve.

**Stimulation of the Gasserian Ganglion**

During the second experimental procedure, stimulation of the Gasserian ganglion was performed in sham-treated animals and in treated animals, when a significant decrease of CBF had been obtained. The animals, in which blood was injected into the subarachnoid space but no CBF reduction was noticed, were excluded from the study.

A stimulating electrode (1 mm in diameter and an active surface area of 3 mm²) was tightly applied to the intact dura above the trigeminal ganglion. The electrode was connected to a Medtronic electrostimulator (Model 3522 A Transmitter and Antenna) regulated to deliver a stimulation of frequency (R: rate) equal to 45 pulses per second, of intensity (strength) equal to 2.5 “volts control” and 75 “A (amplitude) control”, and of pulse width (PW) equal to 0.2 msec. The transmitter was provided with a 9 volts battery. The stimulation was maintained for 3 h. During this time, vital signs were carefully monitored mostly to rule out significant variations of systemic arterial pressure influencing CBF.

**Determination of CBF in the Two Experimental Procedures**

During the first procedure, several determinations of CBF were performed both in treated (Table 1) and sham-treated animals (Table 2). The first one was made once the surgical preparation had been completed (#1 a). The second was carried out just after the subarachnoid injection of blood (#2 a) or, in sham-treated animals, at the corresponding time. Further determinations were made 1, 2, and 3 h after the injection of blood (#3 a, #4 a and #5 a respectively), or the corresponding time for sham-treated animals, to verify the effect in due course of blood and anaesthesia. During the second procedure, one week later, the first CBF determination was made once again after the surgical preparation was completed (#1 b). As previously stated, treated animals in which no significant reduction