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THE EFFECT OF LUMBAR SYMPATHETIC STIMULATION ON THE VASCULATURE OF BONE

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1 The nutrient artery to the tibia of anaesthetized dogs was perfused at a constant rate by blood from the femoral artery and the perfusion pressure in the artery, the intramedullary pressure of the bone and the pressure in the nutrient vein recorded.

2 Low frequency stimulation (1 to 5 Hz) of the lumbar sympathetic chain always increased the perfusion pressure but the intramedullary pressure sometimes increased, sometimes decreased and sometimes remained unchanged.

3 The α-adrenoceptor blocking agents, phentolamine (1 mg/kg i.v.) and dihydroergotamine (0.5 mg/kg i.v.) reduced or abolished these effects whereas the β-adrenoceptor blocking agent, propranolol (1 mg/kg i.v.) did not modify them.

4 The nutrient vein end pressure did not differ significantly from the intramedullary pressure and underwent similar variations during stimulation of the lumbar sympathetic chain.

Introduction

Numerous investigations have demonstrated the existence of nervous control of bone circulation. Drinker & Drinker (1916), by perfusing the nutrient artery of an isolated tibia of the dog, showed that the blood flow of the nutrient vein decreased during stimulation of nerve fibres arising from the tibial nerve and destined for the bone. Many years later, the effects of sectioning and stimulating the sympathetic nerves were investigated in cats (Herzig & Root, 1959), rabbits (Azuma, 1964; Shim, Hawk & Yu, 1972) and dogs (Shim, Hawk & Yu, 1972; Yu, Shim & Hawk, 1972; Kita, 1974). After stimulation of the lumbar sympathetic chain at high frequencies (30 to 200 Hz), the intramedullary pressure of the tibia and of the femur decreased considerably. In contrast, sympathectomy increased the intra-osseous flow rate and the intramedullary pressure in the dog tibia (Lowenstein, Pauporte, Richards & Davidson, 1958; Yu, Shim & Hawk, 1972; among others). As the frequency of stimulation used in earlier studies greatly exceeds physiological discharges in the sympathetic vasoconstrictor system (2 to 3 Hz: Folkow, 1952) it was decided to investigate (a) the effects of lumbar sympathetic stimulation, at physiological range frequency, on the intramedullary pressure and the nutrient vein end pressure in the dog tibia during constant flow perfusion of the nutrient artery and (b) the effects on these responses of α- and β-adrenoceptor blocking agents.

Methods

Adult dogs (27) weighing between 10 and 30 kg were anaesthetized with chloralose (80 mg/kg i.v.), curarized with gallamine (2 mg/kg i.v.) and artificially respired with an Ideal-Palmer pump. Gallamine does not affect sympathetic nerve function but has vagolytic properties in keeping with which, tachycardia without modification of the carotid arterial pressure was noted in some experiments. Because of the paralysis of the respiratory muscles, variations of the carotid arterial pressure, induced by respiratory irregularities, are suppressed. Furthermore fully adequate anaesthesia was maintained by injection of 10 to 15 mg of pentobarbitone every hour. The nutrient vein and artery of the tibia were dissected out by Tran & Geral's technique (1978) (Figure 1). The anterior tibial artery and vein were isolated after removal of the antero-external chamber muscles of the leg. Their collaterals were all ligated with the exception of the nutrient artery and vein which were isolated and carefully prepared. The femoral artery on the same side was dissected and the deep femoral artery was ligated so that the tibia was only irrigated by the nutrient artery. After sub- and supra-umbilical median laparotomy, the homolateral lumbar sympathetic chain was uncovered at its exit from the diaphragm and along its latero-vertebral path. This chain was dissected, separated from the communicating ramifications,

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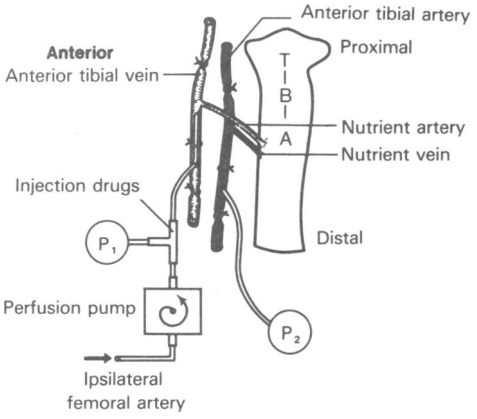

Figure 1 Cannulation technique for nutrient vein and artery. P_1 and P_2 denote electromanometers for measuring perfusion pressure and end nutrient vein pressure respectively.

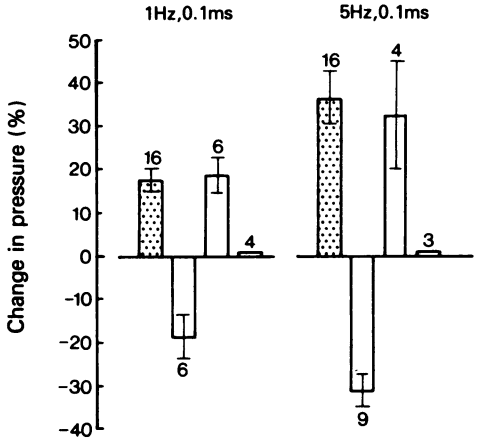

Figure 2 Mean percentage change of the perfusion pressure (stippled columns) and the intramedullary pressure (open columns) induced by stimulation of the lumbar sympathetic chain at 1 and 5 Hz. Sympathetic stimulation always increased the perfusion pressure (16 cases): Simultaneously, the intramedullary pressure changed variably: at a stimulation frequency of 1 Hz it increased in 6 cases, decreased in 6 cases and remained unchanged in 4 cases; at a frequency of 5 Hz, it increased in 4 cases, decreased in 9 cases and remained unchanged in 3 cases.

exposed to electrodes with a 7.5 mm gap and maintained in a liquid paraffin bath. The animals were heparinized (500 iu/kg every 2 h) and controlled-flow perfusion of the nutrient artery was then started with femoral arterial blood. The perfusion rate (0.4 to 0.6 ml/min) was different for each experiment. It was regulated at the beginning of each experiment so as to obtain a perfusion pressure approximatively equal to carotid arterial pressure; it was then kept constant. The pump was associated with a debit-meter in order to check constant blood flow continuously. With Beckman pressure transducers linked to a chart recorder, the following were measured: the nutrient artery perfusion pressure, the intramedullary pressure (by insertion of a 0.8 mm diameter needle into the diaphyseal marrow), the vein end pressure (by insertion of a catheter into the anterior tibial vein up to the junction with the nutrient vein), and the carotid arterial pressure.

The stimulation applied to the sympathetic chain had the following parameters: frequency, 1 to 10 Hz; pulse width 0.1 ms; intensity, supramaximal; duration, 2 min. The stimulation was always applied 10 min after the last gallamine injection. The α and β adrenoceptor blocking agents: phentolamine (Ciba), dihydroergotamine (Sandoz), (±)-propranolol hydrochloride (ICI) were administered intravenously.

Results

Effects of lumbar sympathetic stimulation on perfusion pressure and intramedullary pressure (Figures 2 and 3)

Nineteen dogs were used for the experiments. Stimulation of the sympathetic chain was never accompanied by changes in the carotid arterial pressure but always caused (55 cases) an increase in the nutrient artery perfusion pressure. The magnitude of the response to a given frequency varied from dog to dog. However, during any one experiment, the effects were proportional to the frequency of stimulation. The mean percentage increase in the perfusion pressure was 17.3 ± 2.3 at 1 Hz and 36.6 ± 5.7 for a frequency of 5 Hz (16 cases). Simultaneous sympathetic chain stimulation had a variable effect on the intramedullary pressure. It usually fell but sometimes rose or remained the same (Figure 2).

Stimulation of the sympathetic trunk was carried out before and after administration of the α-adrenoceptor blocking agents, phentolamine (1 mg/kg) or dihydroergotamine (0.5 mg/kg). In 5 experiments phentolamine caused a persistent decrease of the carotid arterial pressure of 38.8 ± 7.8 mmHg, attributable to its known action of decreasing peripheral resistances. The nutrient artery perfusion pressure, the intramedullary and the vein end pressures decreased simultaneously. Furthermore, phentolamine reduced or abolished the perfusion pressure increase induced by sympathetic stimulation as exemplified in Figure 3. The mean percentage increase in perfusion pressure caused by stimulation at 5 Hz was 52.7 ± 8.4 before and 14.6 ± 4.3 after phentolamine. Dihydroergotamine was used in two other experiments. Its hypotensive effect was less pronounced than that of phen-

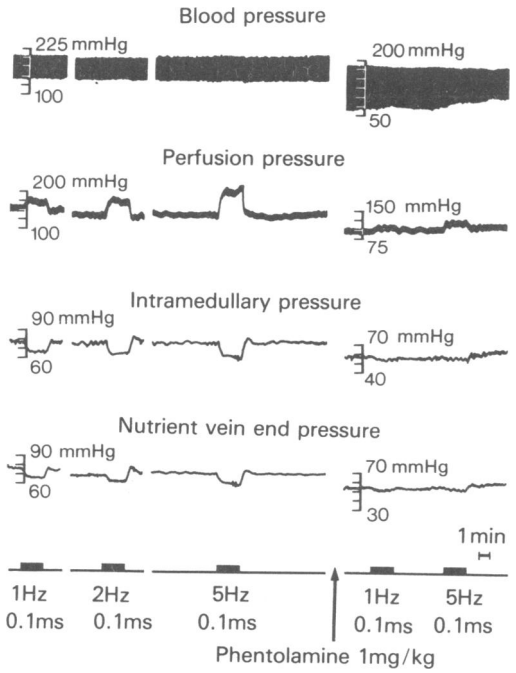

Figure 3 An example of the effect in an anaesthetized dog of sympathetic stimulation, at 1, 2 and 5 Hz, on the perfusion pressure in the nutrient artery perfused at constant flow and on the intramedullary pressure and the vein end pressure before and after administration of phentolamine (1 mg/kg i.v.). Phentolamine decreased the pressures in the carotid artery, the nutrient artery, and reduced intramedullary pressure and the vein end pressure. Before phentolamine, sympathetic stimulation increased the perfusion pressure, the effect obtained being proportional to the frequency of stimulation, and decreased the intramedullary and vein end pressures; 15 min after phentolamine administration the effects of sympathetic stimulation on the perfusion pressure, intramedullary pressure, and vein end pressure were much reduced.

tolamine but similarly it abolished the response to sympathetic nerve stimulation in one of the experiments and greatly reduced it in the other (35 mmHg before; 9.4 after). When the arterial response was blocked, stimulation of the lumbar sympathetic chain did not cause any significant variation in the intramedullary and vein end pressures (Figure 3).

In 5 experiments, the sympathetic trunk was stimulated before and after administration of the β-adrenoceptor blocking agent, propranolol, 1 mg/kg. This did not appreciably modify the perfusion pressure, the intramedullary or the vein end pressure, but in one experiment carotid arterial pressure fell by 12 mmHg. This treatment did not significantly modify the effects of sympathetic stimulation on the perfusion pressure, the intramedullary pressure or the vein end pressure. The percentage increase in perfusion pressure caused by stimulation at 5 Hz was 31.8 ± 3.8 before and 27.1 ± 3.2 after propranolol; with stimulation at 1 Hz the corresponding values were 12.4 ± 2.5 and 14.2 ± 4.8 respectively.

Similarity of intramedullary pressure and vein end pressure

A total of 36 simultaneous measurements from 8 experiments gave resting mean values for the intramedullary and vein end pressure of 42.5 ± 2.6 and 39.9 ± 2.5 respectively. The values changed in parallel when sympathetic nerve stimulation was applied at 1, 2, 5 or 10 Hz. For example in each of 16 experiments (9 stimulated at 1 Hz, 7 at 5 Hz), stimulation of the sympathetic chain caused a decrease of both intramedullary pressure ($21.2 \pm 2.9\%$) and vein end pressure ($18.9 \pm 2.3\%$), whereas in 6 other experiments (2 at 1 Hz, 4 at 5 Hz) the two pressures rose together (intramedullary, $23.3 \pm 4.3\%$; vein end pressure, $21.9 \pm 2.8\%$).

Discussion

These experiments on the dog, show that stimulation of the lumbar sympathetic chain, at physiological frequencies, always caused a frequency-dependent increase in the tibia nutrient artery pressure during perfusion at constant flow. Simultaneously, the intramedullary pressure often fell but sometimes increased or remained unchanged. In contrast in earlier studies, lumbar sympathetic stimulation in cats, rabbits and dogs always decreased the intramedullary pressure of the tibia and femur (see Introduction) but the stimulation frequency was always high (Herzig & Root: 30 Hz; Kita: 30 Hz; Azuma: 50 Hz; Shim, Hawk & Yu: 200 Hz; Yu, Shim & Hawk: 200 Hz). Under these experimental conditions the decrease of the intramedullary pressure has been attributed to strong vasoconstriction of the intra-osseous arteries. This causes (a) a reduction of the intra-osseous vascular volume which is accompanied by an expansion of the medullary tissue enclosed in the rigid bone cavity and (b) a simultaneous decrease in the intra-osseous arterial flow rate which increases with the intensity of the vasoconstriction. These two factors act together in decreasing the intramedullary pressure.

It is suggested that in the present studies using lower stimulation frequencies, it is likely that less intense increases in the intra-osseous arterial resistances were produced and that the decreases in the intramedullary pressure observed represent just the expansion of the medullary tissue occurring as a result of intra-osseous arterial vaso-constriction. In

some instances, however, it was observed that the intramedullary pressure nevertheless increased, indicating that the effect of vasoconstriction was masked by the intervention of other factors controlling the intramedullary pressure such as the nutrient artery perfusion pressure. This is in agreement with Held & Thron (1962a, b), Michelsen (1967, 1968) and Wilkes & Visscher (1975) who showed that there was a close correlation between the intramedullary pressure and the changes of the nutrient artery perfusion pressure induced by flow alterations. Among the various factors which determine intramedullary pressure there may be two antagonistic components: nutrient artery perfusion pressure and intra-osseous vasomotor tone. Their relative importance may vary in different animals.

In the study of Kita (1974), intravenous administration of phentolamine (2 $\mu g\ kg^{-1}\ min^{-1}$ for 30 min) to dogs did not suppress the intramedullary pressure decrease of the tibia induced by stimulation of the sympathetic chain. This amount was inadequate to block the adrenergic innervation of the bone; 1 mg/kg phentolamine or 0.5 mg/kg dihydroergotamine reduced or abolished the effects of stimulating the sympathetic chain on the nutrient artery perfusion pressure and so on the intramedullary and vein end pressures. There is no indication that β-adrenoceptors are involved in the adrenergic innervation of the bone; 1 mg/kg phentolamine or 0.5 mg/kg dihydroergotamine reduced stimulation.

The intramedullary and vein end pressures were similar and varied in parallel during stimulation of the lumbar sympathetic chain. These results support those of Wilkes & Visscher (1975) and of Michelsen (1967, 1968) showing parallel modifications under the action of various substances and it can be concluded that the intramedullary pressure is equal to the central venous sinus pressure of the bone.

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