THE ACTION OF CALCIUM ON BLOOD VESSELS AND ITS RELATION TO HYPERTENSION

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Received October 8, 1955

Calcium has not been assigned any role in hypertension or arterial disease, except that it is deposited in degenerated tissue. There is a natural increase of lime salts in the arteries of the aged. Calcification is frequently found in the arterial system. A striking variety of the condition is that which occurs in the media, as a not uncommon lesion in old people and known as Mönckeberg's sclerosis. Lime salts are deposited in the direction of the muscle fibres, and in the elastic tissue. All this does not show that calcium deposition affects healthy muscle of the arterioles, but it suggests that the medium surrounding them may be rich in calcium, which may penetrate the muscle fibres and thus increase their calcium content.

Calcium acts on the contractile system of muscle and causes contraction. It acts on the contractile system of striated muscle (Heilbrunn, 1952), and that of unstriated muscle (Singh and Singh, 1949 *a*, 1950). In the present research, these experiments have been extended to blood vessels, in order to elucidate the possible role of calcium in hypertension.

Experimental

The action of calcium on the contractile mechanism of unstriated muscle has been studied by prolonged immersion in unoxygenated solutions, the muscle being allowed to die in these solutions, so that calcium then enters the muscle fibres and acts on the contractile mechanism (Singh and Singh, 1949 *a*, 1950). The same technique was used with arterioles. Dog's hind limbs were perfused with solutions of calcium chloride, and the rate of perfusion flow was recorded before and after immersion for 24 hours, as described previously (Singh and Singh, 1955). The reaction of dying arteriole was thus obtained. Direct microscopic observation of arterioles in dog's mesentery was also made before and after immersion in calcium chloride for a similar period.

Results

Direct microscopic observation of small arterioles and venules in dog's mesentrey shows that they contract strongly in isotonic solution of calcium

chloride (0·103 *M*). In dog's hind limbs, the rate of perfusion is immediately retarded and this persists permanently. Thus in 6 experiments, the initial rate of flow was 1 to 5 minutes for 50 c.c. of mammalian saline. When an isotonic solution of calcium chloride was substituted for this, it took from 2 to 3 hours, so that there was an extreme contraction of the arterioles. This spasm of the arterioles was permanent, though after 24 hours slight relaxation might occur (Fig. 1).

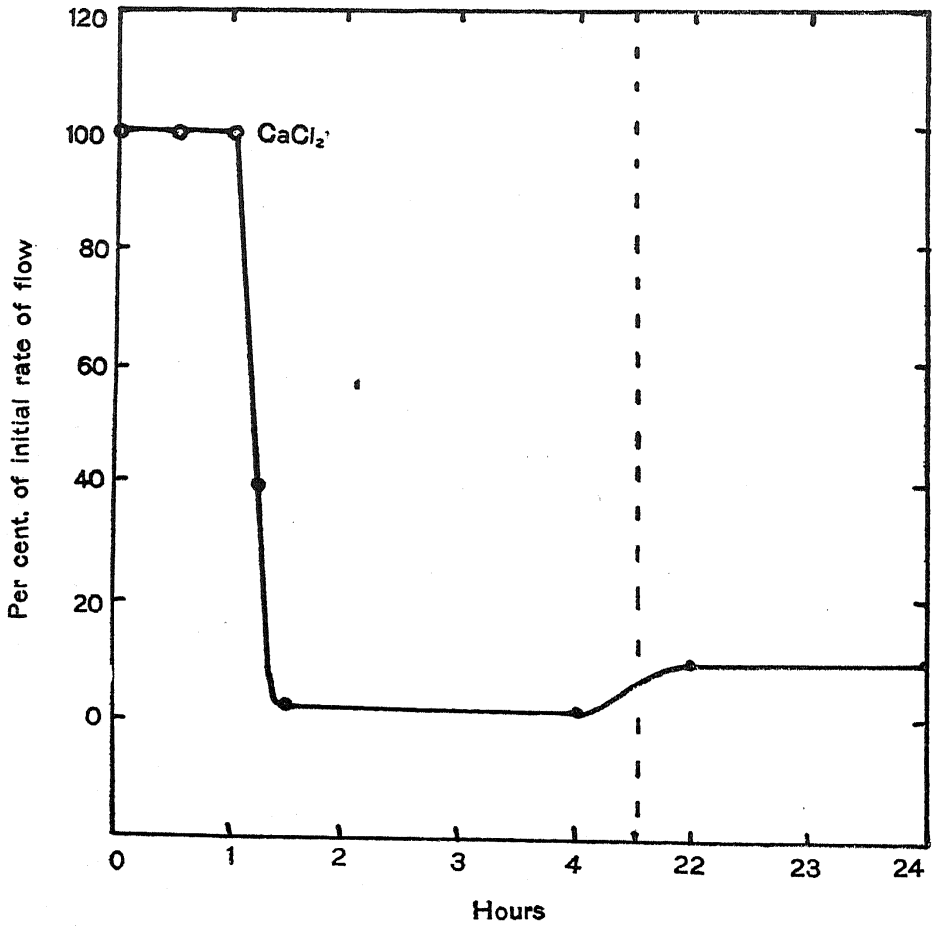

FIG. 1. Dog's hind limbs perfused with 0–103 *M* calcium chloride. At first constant rate of perfusion was obtained with mammalian saline. Perfusion with calcium chloride was then started. Note immediate retardation of flow.

The initial contraction was due to extracellular calcium, and the later contraction to the action of calcium on the contractile mechanism. The arterioles are capable of dilatation under such conditions, as shown by the action of potassium chloride in which the arterioles contract strongly at first, and then dilate after prolonged immersion (Singh and Singh, 1955). The initial contraction is due to extracellular potassium, and the dilatation

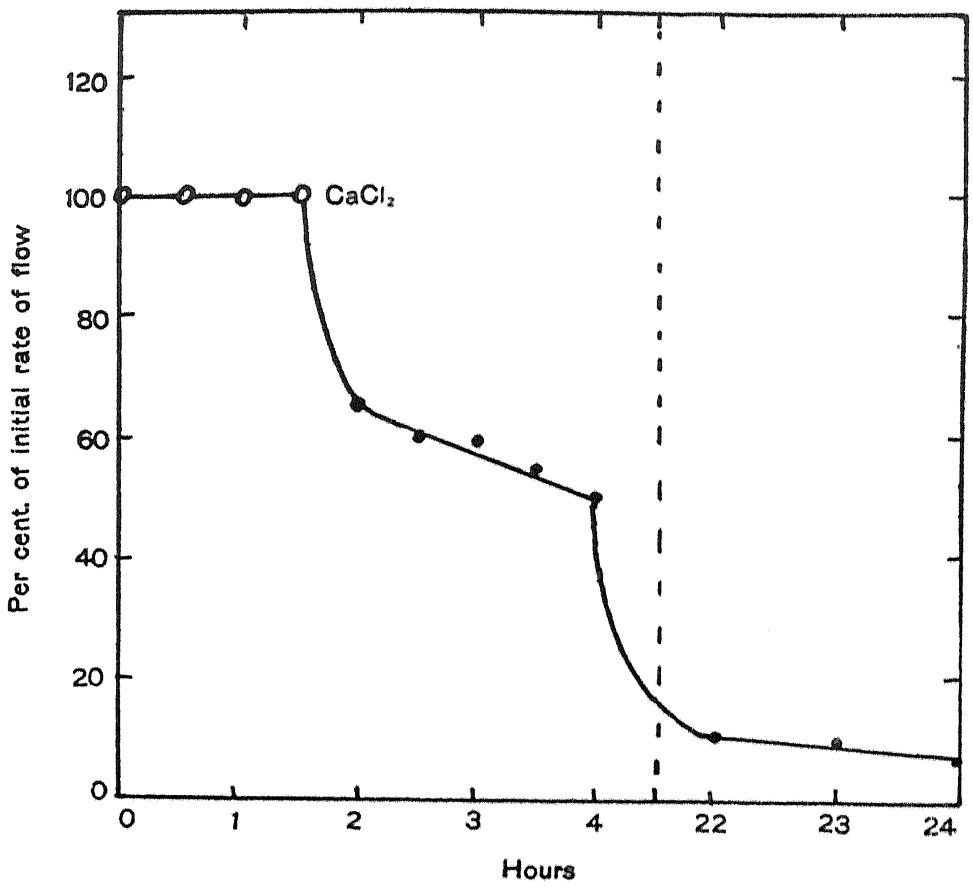

FIG. 2. Dog's hind limbs perfused with 0·01 *M* calcium chloride in saline. At first constant rate of perfusion was obtained with mammalian saline. Perfusion with calcium chloride was then started. Note immediate retardation of flow.

to the action of potassium on the contractile mechanism. Thus sodium and calcium have a contractile effect on the contractile system of the arterioles, and potassium has the opposite action.

Small concentrations of calcium, normally present in the blood, have a dilatory effect on the arterioles, as sodium has a constricting action. This action is both extracellular as shown by immediate effect, and intracellular as shown by delayed effect. Higher concentrations (0·01 *M*) have the opposite action (Fig. 2). Excess of calcium antagonises active relaxation of unstriated muscle (Singh and Singh, 1949 *b*), so this will also tend to produce a tonic and irreversible contraction of the arterioles.

DISCUSSION

It is unlikely that calcium has anything to do initially with hypertension, though later on it may modify the action of the arterioles. If the arterioles

are stimulated to contract by any other agency, such as chemical or nervous, the permeability of their muscle would increase, and sodium or calcium would then enter the cells and produce an irreversible contraction. Excitation increases the permeability of unstriated muscle to other ions (Singh and Singh, 1952).

There is experimental evidence for the above possibility. In rabbits, calcification of the aorta may be produced by injections of adrenaline which raises the blood pressure (Cappell, 1951). The initial action of calcium, when its intracellular concentration is small, will be antagonistic to that of sodium, so that the contractile effect of the latter would be prevented. As the concentration of calcium inside the cells increases, a tonic and irreversible contraction would be produced.

SUMMARY

1. The action of calcium on the contractile mechanism of the unstriated muscle of the arterioles has been studied by prolonged immersion of dog's hind limbs in solutions of calcium chloride and recording the rate of flow before and after immersion for 24 hours.

2. Isotonic solutions of calcium chloride produce a strong irreversible contraction of the arterioles. This is due to the action of calcium on the contractile mechanism.

3. The possible role of calcium in hypertension has been discussed.

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1276-55. Printed at the Bangalore Press, Bangalore City, by C. Vasudeva Rao, Superintendent, and Published by The Indian Academy of Sciences, Bangalore.