THE MECHANISM OF ACTION OF CARBON DIOXIDE ON THE LIMB VESSELS OF THE CAT

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It is generally accepted [4, 7] that carbon dioxide has a dual action on the tone of the blood vessels in skeletal muscles: a central, vasoconstrictor effect and a local (direct), vasodilator effect. However, the information in the literature on this question is contradictory. For instance, Bernthal [3, 4], who studied the changes in the blood flow in the intact and denervated limb by means of a thermoelectric method, showed that during inhalation of a mixture of air with 10% CO_2 the blood flow in both the intact and the denervated limbs decreased, indicating constriction of the vessels. Similar results were obtained by Mercker [8], who conducted experiments under similar conditions. Conversely, Rein and Otto [9], who also used a thermoelectric method, observed under the same conditions an increase in the blood flow in the denervated limb. Rein concluded from these findings [9] that excess of CO_2 has a local constricting action on the vessels of the limb. However, in the experiments conducted by these writers, the increase in the blood flow in the denervated limb took place against the background of an increased arterial pressure, and Rein's conclusion cannot therefore be regarded as justified.

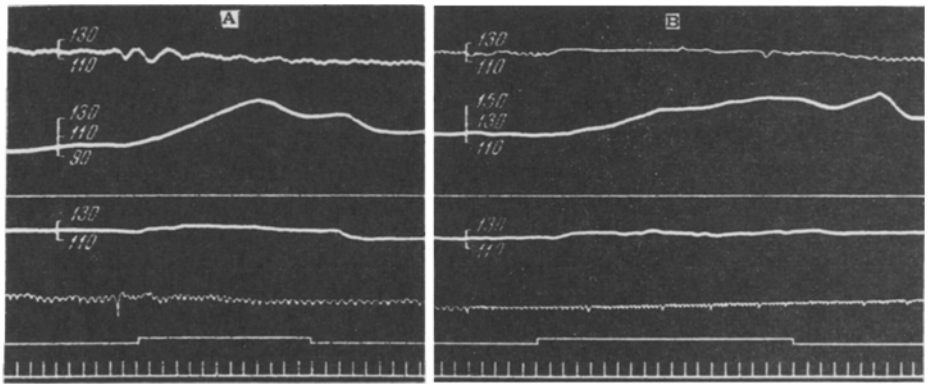

Fig. 1. Inhalation of a mixture of air and 10% CO_2 by the recipient (A) and donor (B). Significance of curves (from above down): donor's arterial pressure; perfusion pressure of limb vessels; recipient's arterial pressure; recipient's respiration; stimulus marker; time marker (5 seconds).

Fleisch, Sibul, and Ponomarew [6] used a different method to investigate the local effect of excess of CO_2 on the limb vessels. The intact hind limb of a cat was perfused by means of a pump with blood to which carbon dioxide was added. The changes in tone were judged from the pressure recorded by a differential manometer. When the arterial blood contained 2-5% CO_2, in one third of the experiments dilation of the limb vessels was observed. Subsequently, however, the results of Fleisch and co-workers were not confirmed by Binet and Burstein [5]. In these workers' experiments the intact hind limb of a recipient dog was perfused with a donor's blood by means of a con-

stant flow pump. When the donor inhaled a mixture of air with 10% CO_2, i.e., in response to the local action of CO_2, these writers observed constriction of the vessels of the perfused limb. The action of excess of CO_2 in the blood on the vessels of the skeletal muscles thus remains unexplained.

Within the framework of the study of the role of the composition of the blood gases in vasomotor regulation, as undertaken systematically in our laboratory, this problem has become of theoretical importance. A special investigation was therefore carried out in order to study the effect of an excessive CO_2 concentration in the blood on the vessels of the skeletal muscles.

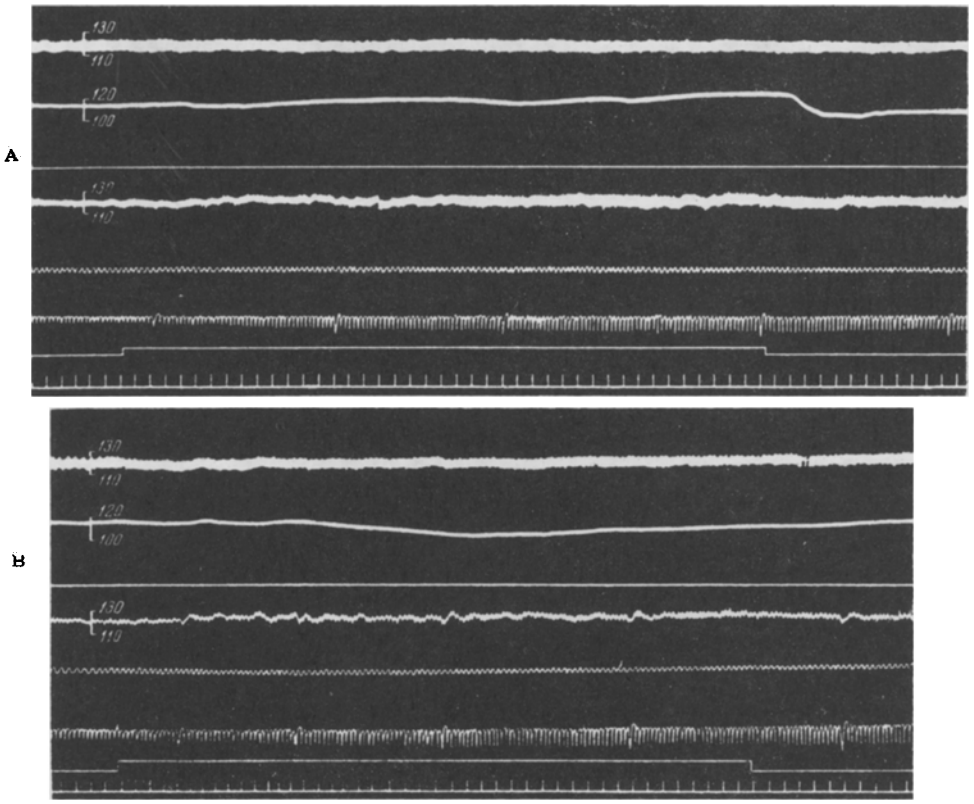

Fig. 2. Inhalation of a mixture of air with 7% CO_2 before (A) and after (B) denervation of the limb. Significance of the curves (from above down): donor's arterial pressure; perfusion pressure of the limb vessels; recipient's arterial pressure; donor's respiration; stimulus marker; time marker (5 seconds).

EXPERIMENTAL METHOD

The reflex, central, and also the local (direct) action of excess of CO_2 in the arterial blood on the vascular tone in the hind limbs was recorded in cats anesthetized with urethane (1 g/kg). For this purpose the hind limb of a recipient cat, isolated humorally from the rest of the body, was perfused with the blood of a second animal (donor) by means of a pump providing a constant flow of blood [1]. The volume of blood injected into an organ by this pump is unchanged during fluctuations in the arterial or perfusion pressure. In these conditions an increase in the perfusion pressure takes place only as a result of vasoconstriction in the organ, and a decrease in the perfusion pressure, on the other hand, as a result of vasodilatation. To prevent coagulation of the blood heparin (0.15 ml/kg) was injected into the donor animal. The aspirating tube of the pump was connected to the central end of the donor's femoral artery, and the injecting tube to the peripheral end of the recipient's femoral artery. Venous blood flowing from the recipient's limb was directed towards the central end of the donor's femoral vein.

When the experiment was conducted in this way, and the recipient inhaled a mixture of air and an increased concentration of CO_2 (7-10%), only the central action of CO_2 was brought into play, and when the donor inhaled the mixture, only the local action of excess of CO_2 was seen. The inhalation of the mixture of air with excess of CO_2

was carried out from a Douglas bag, through a valve and a tracheal tube. The arterial pressure of both donor and recipient was recorded by a mercury manometer, and their respiration by the pneumograph. Altogether 26 experiments were conducted.

EXPERIMENTAL RESULTS

When the recipient animal inhaled a mixture of air with 7-10% CO_2, and only the central action of the CO_2 was brought into play, constriction of the blood vessels of the perfused limb was observed (Fig. 1A). This constriction usually began after 2-8 seconds, reached its maximum after 20-35 seconds, and in most experiments amounted to 30-40 mm Hg.

When the same mixture was inhaled by the donor, and blood containing excess of CO_2 bathed only the vessels of the recipient's limb, constriction of the vessels of the perfused limb was also observed in all experiments. The constriction began after 10-40 seconds and reached its maximum after $1\frac{1}{2}$-2 minutes (Figs. 1B and 2A).

Comparison of the results obtained in response to the central and direct action of carbon dioxide on the limb vessels shows that there was no essential difference between these reactions. The only observation was that in the second case, in the majority of experiments the vasoconstriction reached its maximum more slowly than as a result of the central action (Figs. 1A and 1B).

It may be concluded from these experiments that excess of carbon dioxide does not dilate the limb vessels when it acts directly.

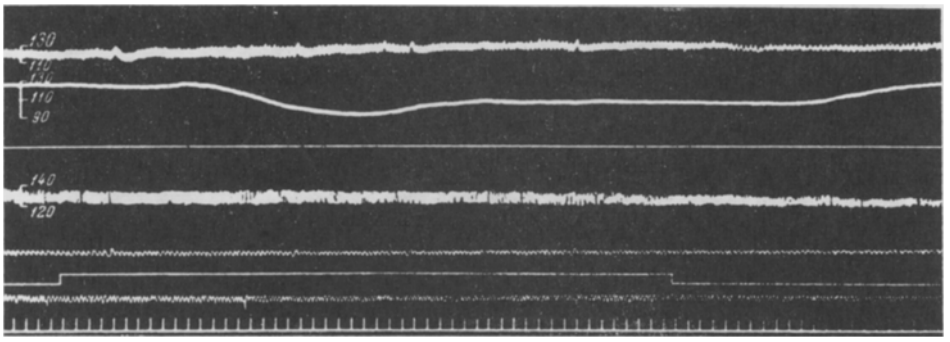

Fig. 3. Inhalation of a mixture of air with 10% CO_2 by the donor after denervation of the recipient's limb. Significance of the curves (from above down): donor's arterial pressure; perfusion pressure of the limb vessels; recipient's arterial pressure; recipient's respiration; stimulus marker; donor's respiration; time marker (5 seconds).

Subsequent experiments showed, however, that if the perfused limb was first denervated by division of the sciatic and femoral nerves, as a result of the direct action of carbon dioxide an obvious dilatation of the limb vessels took place (Fig. 2B and Fig. 3). The fall in perfusion pressure amounted to 10-40 mm Hg. The vascular tone of the limb was restored after 15-30 seconds in the majority of experiments. In these conditions inhalation by the donor of a mixture of air with 7-10% CO_2 vasodilatation of the perfused, denervated limb of the recipient.

The degree of dilatation of the vessels of the denervated limb in response to inhalation of the mixture by the donor was largely dependent on when the denervation was performed. For instance, if the nerves were divided 1-2 hours before the beginning of the experiment the reaction was more marked (a fall of 30-40 mm Hg in the perfusion pressure; see Fig. 3). If the denervation was carried out 15-30 minutes before the action of CO_2, the vasodilatation was only slight (see Fig. 2B), and sometimes it was hardly noticeable.

The direct action of CO_2 on the limb vessels thus differed on the intact and denervated limbs. The vasodilator effect of excess of CO_2 was shown only on the vessels of the denervated limb.

The question arises, how can the constriction of the vessels of the intact limb be explained in cases when blood with an increased CO_2 concentration bathes this limb alone and does not act on the vasomotor center. The vasoconstriction arising in these conditions can be understood if it is remembered that during perfusion of the intact limb with donor's blood containing excess of CO_2 the vascular receptors of this limb are stimulated. It may therefore be postulated that the ensuing flow of afferent impulses causes a reflex constriction of the limb vessels.

The direct vasodilator action of excess of CO_2 in the blood is thus not shown in the limb because the reflex vasoconstrictor influences arising from the chemoreceptors of the carotid body and the arch of the aorta, and also from the receptors of the limb itself, are stronger.

SUMMARY

A study was made of the reflex and direct action of the arterial blood CO_2 surplus on the vascular tone of the posterior extremity in a cat perfused with donor's blood by means of a pump, providing a constant blood inflow. During inhalation of the air mixture containing 7-10% CO_2 by the recipient vascular constriction was noted in the perfused extremity. When inhaled the same mixture is inhaled by the donor (direct action) the constriction effect is also observed. Following denervation of the extremity, the same mixture inhaled by the donor caused vascular dilatation.

It is suggested that the direct vasoconstricting effect of the CO_2 blood surplus is not manifested in the extremity because of the prevalence of the vasoconstricting reflex effect from the chemoreceptors of the carotid bodies and the aorta arc as well as from the receptors of the extremity itself.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.
