THE EFFECT OF HYPERCAPNIA ON THE BLOOD SUPPLY TO THE HEART

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Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 55, No. 4, pp. 9-14, April, 1963
Original article submitted July 13, 1962

Many investigators have shown that as a rule the blood supply to the heart is increased by influences which evoke varied changes in the blood supply to the different organs. We regard this result as a valuable adaptive response of the coronary arteries which has developed during the course of evolution. However under certain circumstances the effect is reversed, and the coronary arteries contract [1, 3, 4, 9]. It is very important to determine what circumstances evoke this response, because it is closely associated with the mechanism of the regulation of blood supply to the organs, and is directly related to the problem of coronary insufficiency.

The object of the present work has been to study further the conditions under which constriction of the coronary arteries occurs [1, 3, 4]. As stimulus we used carbonic acid gas. The reason for this choice was the observation by Rein as far back as 1931 that vessels of working skeletal muscle show a reversed vascular response under conditions of strong hypercapnia [14]. It remained to find how inspiration of a mixture of gases containing various amounts of carbon dioxide influenced the blood supply of cardiac muscle. Previous investigations on the isolated heart [6, 11, 13], and on a heart-lung preparation [8, 12] have shown that an increased coronary supply results from an increase of CO_2 in the perfusate. However, the results obtained on isolated organs do not give a complete picture of the process occurring in the body with its intact blood supply and nervous connections. Also, insufficient work has been done on the influence of hypercapnia on blood supply in the intact animal. Some authors maintain that this gas exerts mainly a vasoconstrictor influence on the coronary vessels [10], whereas others find that the vessels dilate [7, 15].

In our experiments we investigated the influence of breathing carbon dioxide over a wide range of concentrations on the blood supply of the heart in the intact animal; we studied the effect of inspiration for various times, and under natural conditions.

EXPERIMENTAL METHOD

The experiments were carried out on 28 dogs weighing from 12 to 22 kg under morphine-urethane anesthesia. The changes in the minute volume of the blood in the circumflex branch of the left carotid artery were recorded by a thermoelectric method without dissection of the vessel [2, 5]. Under known conditions a comparison of the changes in blood flow with variations of arterial pressure indicate changes in the tone of the coronary vessels. A reduction of the blood flow during unchanged or raised arterial pressure indicates constriction; an increased flow accompanied by a reduced or unchanged arterial pressure indicates dilation. A simultaneous record was made of respiration and of arterial pressure in the femoral artery. The electrocardiogram was recorded on an ÉKP-4M instrument from three standard leads, recordings being continued during the whole time the gaseous mixture was breathed, and for some time after it; intervals of 15 to 60 sec were left between recordings. Amplification was 1 mv/1 cm. We used 3, 5, 7, 10, 15, 20, and 30% carbon dioxide in the air with the addition of the amount of oxygen required to maintain the normal partial pressure. The time for which the mixture was breathed varied from 30 sec to 60 min. The animal breathed naturally. The gaseous mixture was supplied from a Douglas bag through valves connected with a tracheal cannula.

EXPERIMENTAL RESULTS

Experiments in which various concentrations of carbon dioxide were breathed showed that a 3-5% mixture of carbon dioxide causes no appreciable change in coronary flow, and only in two experiments where the concentration

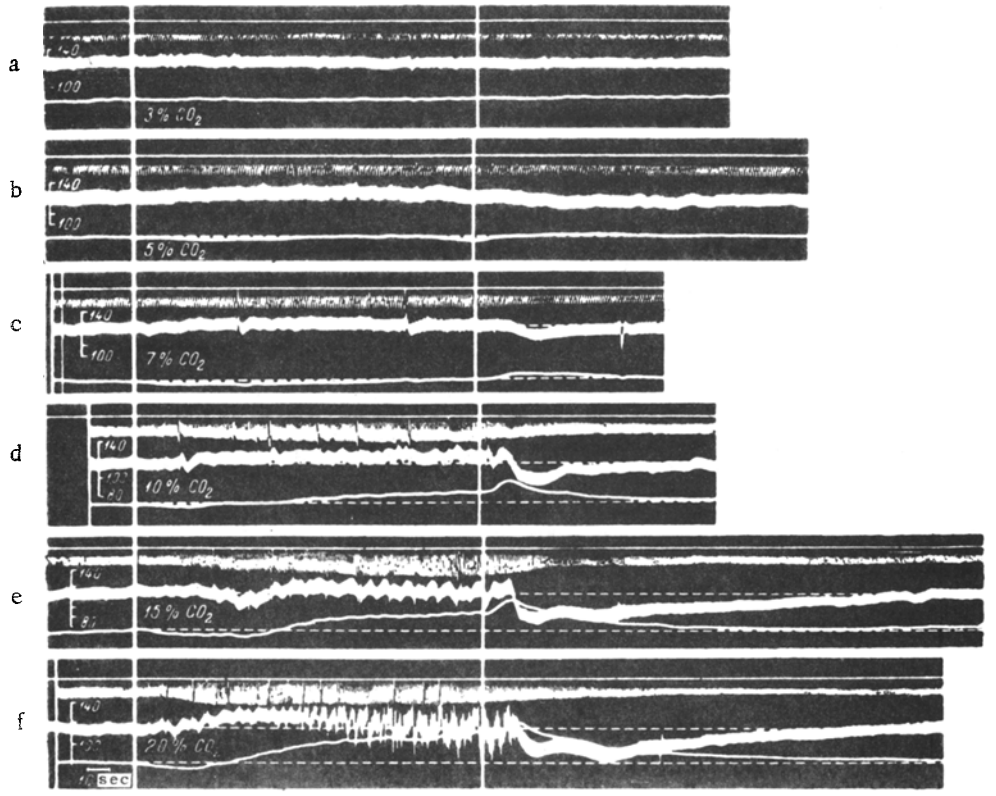

Fig. 1. Change in the minute volume of the blood flow in the coronary arteries during breathing (a) of a 3%, (b) 5%, (c) 7%, (d) 10%, (e) 15%, and (f) 20% carbon dioxide for 3 min in each instance. Curves, from above downwards: respiration, arterial pressure, blood flow. The verticle lines indicate the times at which breathing of the mixture started and stopped.

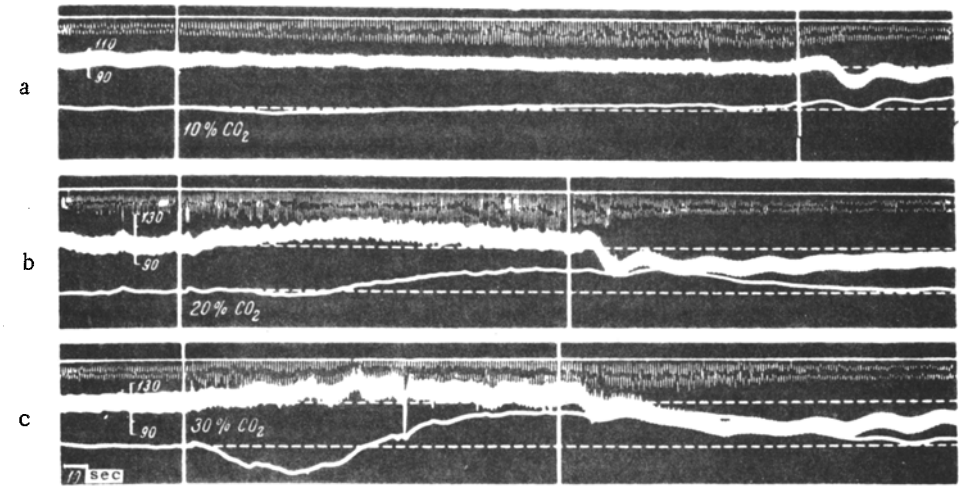

Fig. 2. Change in the rate of blood flow through the coronary arteries when the animal breathes 10%, 20%, and 30% carbon dioxide. Indications as in Fig. 1.

of CO_2 was 5% was there a small increase. Greater concentrations give a greater number of cases where the change in the coronary flow is biphasic (Fig. 1): in the first phase, after the mixture has been breathed for 20-40 sec there is a reduced flow which then returns to the original or to a higher value in the second phase. The maximum increase of coronary flow usually occurs within the first minute after the animal has changed back to breathing air. A compar-

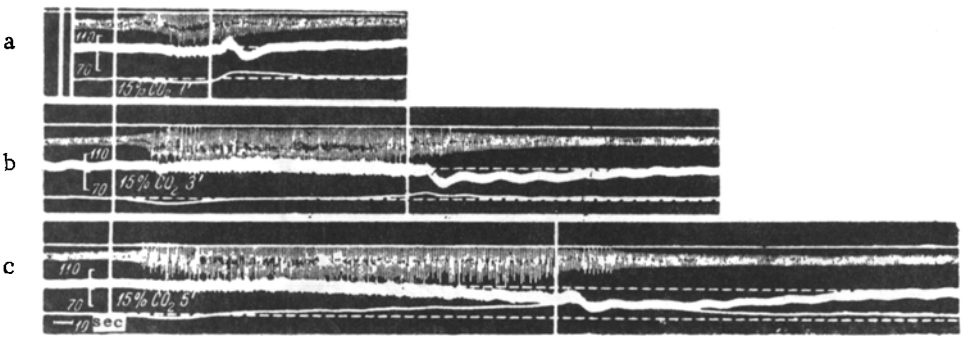

Fig. 3. Change in the coronary artery flow during respiration of 15% carbon dioxide for (a) 1 minute, (b) 3 minutes, and (c) 5 minutes. Indication as in Fig. 1.

ison of the curves of arterial pressure and blood flow revealed a constriction of the coronary arteries in the first phase and their dilatation in the second, particularly after the change back to air breathing, when the increase was accompanied by a marked hypotension.

The first phase of constriction began when the concentration reached 7% (or sometimes 10%) CO_2, and was very small. At higher concentrations of 15-20% there was a marked reduction in the coronary flow, and at a 30% concentration it was associated with an increased arterial pressure (Fig. 2).

The second phase of dilatation of the vessels was also directly related to the concentration of carbon dioxide: the higher the concentration of the inspired mixture the greater was the increase of flow.

The appearance of both phases depended upon the time for which the mixture was breathed. If the time was only one or two minutes, then only the first phase occurred, but if the mixture was breathed for 3-5 min, the second phase was marked (Fig. 3).

For 3% carbon dioxide concentration there was practically no change in the pneumogram. Starting at 5% concentration, the respiration became deeper and more frequent as the concentration increased.

At a 3-5% CO_2 concentration, (and sometimes at 7%) there was no change of arterial pressure; on occassions it rose slightly and then returned to the original value. At concentrations between 10 and 30% the pressure was proportional to the increase of concentration. As the animal continued to breathe the mixture the arterial pressure frequently returned to the original value. At concentrations bet ween 10 and 30% the pressure was proportional to the increase of concentration. As the animal continued to breathe the mixture the arterial pressure frequently returned to the original value or even fell somewhat below it (at a concentration of 20-30%). In other cases an increased arterial pressure was maintained throughout, and masked the response of the coronary vessels. When the gaseous mixture was withdrawn and the animal once more breathed air there was a marked fall in arterial pressure to below the original value, the fall being proportional to the time for which the mixture was breathed and to the CO_2 concentration (see Figs. 1 and 2).

The ECG showed various degrees of bradycardia; 30-40 sec after the return from 10-30% CO_2 to air a tachycardia occurred. At low concentrations of 3-7% CO_2 there was no observed change in the pulse rate. The T wave of the ECG was increased in all three leads, especially in leads II and III. When the T wave was initially negative or biphasic it became less negative or might even change to positive. There was a linear relationship between these changes and the concentration of CO_2 breathed; the changes were more marked the higher the concentration. A comparison of the ECG and coronary flow showed that in the first phase there was no change in the ECG, and not until a concentration of 30% CO_2 was reached was there some small reduction of the positive or a deepening of the negative T waves in some of the experiments.

As the coronary flow increased in the second phase marked changes occurred which were maintained; usually they became more marked in the first or second minute after the hypercapnia and then gradually returned to normal values together with reestablishment of normal coronary flow.

When carbon dioxide was breathed for up to one hour the arterial pressure, coronary flow, and ECG became stable after 4-5 min and remained at this level for some time. After 5-20 min (according to the concentration of CO_2) the coronary flow fell progressively as did the arterial pressure also, but remained above the initial values. When the animal once more breathed air the coronary flow again increased while the arterial pressure showed a marked fall followed by a return to the initial level (after 5-10 min), indicating a considerable reduction of coronary tone. The ECG changes were correlated with changes of coronary flow.

From our observations we have established that a biphasic change of coronary flow is induced by increased carbon dioxide concentrations. The disagreement between published reports may have arisen either because relatively low concentrations of carbon dioxide were used or because the gas was used for a very short time, or again because respiration was maintained artificially.

It is known that carbon dioxide exerts a central vasoconstrictor action as well as a local vasodilator influence on the coronary vessels. We may suppose that coronary tone also depends on the interaction of central and local effects exerted by carbon dioxide. As a result coronary tone increases in the first phase (due mainly to the central effect) and falls in the second. The latter phase is probably due to the peripheral vasoconstrictor influence preponderating over the nervous vasodilator influences.

As far as the blood supply to the heart is concerned it is determined not only by the tone of the vessels but also by the arterial pressure in the aorta. Because the first phase usually occurs during a period of raised arterial pressure there is no impairment of the supply to the heart despite the increased coronary tone. However, at carbon dioxide concentrations as high as 30% the increased tone is so strong that even when the pressure in the aorta is raised the supply to the heart suffers. Therefore with vigorous hypercapnia there may be a reduced blood flow to both cardiac and the skeletal muscle, contrary to the demands of the organ.

SUMMARY

Experiments were carried out on dogs under morphine-urethane anesthesia. A thermoelectric method was used to study the coronary circulation. Simultaneous records were made of the respiration, blood pressure, and ECG while 3, 5, 7, 10, 15, 20, and 30% CO_2 and oxygen were added to the air breathed. Breathing was maintained for from 30 sec to one hour. It was found that in most cases the change of coronary flow was biphasic: in the first phase it was reduced and in the second increased. For a given CO_2 concentration the extent to which the second phase was manifested depended on the time for which the mixture was breathed, there being no effect for periods for less than three minutes. From the curves of the blood pressure and coronary circulation it could be seen that the coronary vessels were constricted in the first and dilated in the second phase.

LITERATURE CITED

1. G. N. Aronova, Byull. éksper. biol., 1953, No. 4, p. 20.
2. G. N. Aronova, Fiziol. zh. SSSR, 1956, No. 10, p. 898.
3. G. N. Aronova, Transactions of the Institute of Clinical and Experimental Cardiology, AN Georgian SSR. Tbilisi, 1958, Vol. 5, p. 423.
4. G. N. Aronova and T. A. Maeva. In the book: Problems of the Physiology and Pathology of the Coronary Circulation. [in Russian] Kiev, 1960, p. 22.
5. M. E. Marshak and G. N. Aronova, Fiziol. zh. SSSR, 1958, No. 8, p. 770.
6. Dixoi Bareroft and M. Hochrein. Ch. J. Keller.
7. H. Feinberg, A. Gerola, and L. N. Katz, Fed. Proc., 1958, Vol. 17, p. 45.
8. R. Hilton and F. Eichholtz, J. Physiol. (Lond.), 1925, Vol. 59, p. 413.
9. J. Hinrichsen and A. C. Ivy, Arch. intern. Med., 1933, Vol. 51, p. 932.
10. M. Hochrein, Keller Ch. J., Arch. exp. Path. Pharmak., 1931, Vol. 159, S. 312.
11. M. Iwai, Pflüg. Arch. ges. Physiol., 1924, Bd. 202, S. 356.
12. J. Markwalder and E. H. Starling, J. Physiol. (Lond.), 1913, Vol. 48, p. 275.
13. W. T. McElroy, Jr., A. J. Gerdes, and E. B. Brown, Jr., Am. J. Physiol., 1958, Vol. 195, p. 412.
14. H. Rein, Ergebn. Physiol., 1931, Bd. 32, S. 63.
15. H. Rein, Z. Biol., 1932, Bd. 92, S. 115.