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POSSIBLE ROLE OF MUSCLE RECEPTORS IN REGULATION OF ARTERIAL BLOOD PRESSURE DURING DISTURBANCES OF THE ACID–BASE BALANCE IN THE MUSCLE

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KEY WORDS: muscle receptors; acid–base balance; arterial blood pressure; metabolic acidosis.

One of the main problems in the physiology of muscular work is the nature of the stimulus responsible for the cardiovascular and respiratory changes observed during muscular activity. Investigations have shown [9, 12, 13] that these changes can be induced by a reflex mechanism from receptors transmitting information about the working muscles along afferent fibers of groups III and IV. There is also evidence that chemical substances liberated in the muscle during its work are among the principal factors stimulating these receptors. In other words, these receptors can be regarded as metabolic [7-10, 14, 16]. However, to confirm these ideas data are needed on the nature of the adequate chemical stimuli for perception of which muscle receptors are adapted. It has been shown that during changes in the concentration of potassium ions, lactic acid, and phosphate in the solution perfusing a muscle, activity of the muscle afferents is increased [16]. Meanwhile, during intensive muscular work not only do the concentrations of the above-mentioned agents change, but considerable disturbances of the acid–base balance also arise in the blood and tissues, and are reflected chiefly as a fall in the bicarbonate concentration and pH [11, 15]. Previously [1, 4] the writer showed that the interoceptors of the small intestine are sensitive to physiological changes in bicarbonate concentration and pH.

The object of this investigation was to study the sensitivity of skeletal muscle receptors to changes in acid–base balance of metabolic acidosis type.

EXPERIMENTAL METHOD

Experiments were carried out on 26 cats anesthetized by intravenous injection of chloralose (50 mg/kg) and urethane (500 mg/kg). The gastrocnemius muscle was isolated from the systemic circulation, while maintaining its innervation intact, by the method in [5] and perfused through the popliteal artery with Ringer's bicarbonate solution of the following composition (in mM): NaCl 125.0, KCl 4.3, $CaCl_2$ 2.5, $MgCl_2$ 1.0, $NaHCO_3$ 25.0, glucose 5.5; pH 7.4. The value of pCO_2, calculated by the Henderson–Hasselbalch equation, was 38 mm Hg. Solutions with reduced pH but constant pCO_2 were used for stimulation. Changes in pH of the solutions were obtained by reducing the bicarbonate concentration. The surface of the solutions was covered with a thin layer of mineral oil to prevent possible diffusion of CO_2 into the atmosphere. The technique of perfusion and preparation of the solutions was described in more detail previously [1, 4]. The arterial blood pressure was recorded in the right common carotid artery by means of a bridge circuit, with the mercury manometer connected into one arm of the bridge.

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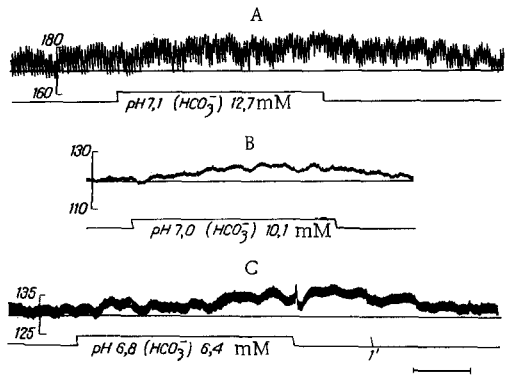

Fig. 1

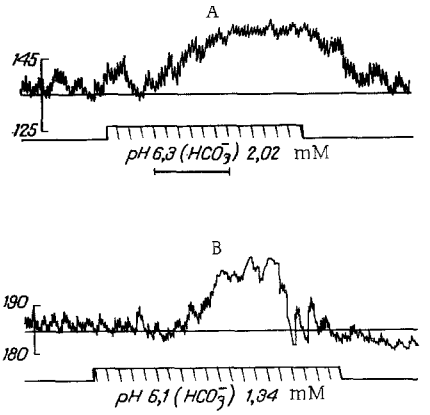

Fig. 2

Fig. 1. Reflex changes in arterial pressure evoked by perfusion of gastrocnemius muscle with solutions with bicarbonate concentration of 12.7 mM and pH 7.1 (A), 10.1 mM and pH 7.0 (B), and 6.4 mM and pH 6.8 (C). From top to bottom: arterial pressure, line of original level of arterial pressure (its value is indicated on the scale on the left), marker of injection of test solution; line below figure is time marker, 1 min.

Fig. 2. Reflex changes in arterial pressure evoked by perfusion of gastrocnemius muscle by solutions with bicarbonate concentration of 2.02 mM and pH 6.3 (A) and 1.34 mM and pH 6.1 (B). Legend as to Fig. 1.

EXPERIMENTAL RESULTS

Investigation of the sensitivity of the muscle receptors to changes in acid–base balance of the metabolic acidosis type showed that to evoke threshold reflex changes in the systemic arterial pressure it was necessary to reduce pH in the perfusion solution to 7.1 and the bicarbonate concentration to 12.7 mM. In five of 10 cases of injection of a solution of this composition the blood pressure was seen to be raised by 2-6 mm Hg (Fig. 1A), and in the other five cases there was no effect.

A further decrease in the bicarbonate concentration to 10.1 and 6.4 mM and in pH to 7.0 and 6.8 (Fig. 1B, C) led to the appearance of reflexes of about the same magnitude. Comparison of the mean values of amplitude of the pressor reflexes for this range of pH changes (from 7.1 to 6.6), obtained after statistical analysis of the experimental results, revealed only a certain tendency for them to rise. For instance, the mean value of the reflexes was 1.9 ± 0.6 mm Hg at pH 7.1, 2.5 ± 0.7 mm Hg at pH 7.0, 2.7 ± 0.8 mm Hg at pH 6.8, and 2.8 ± 0.3 mm Hg at pH 6.6. When the pH of the solutions subsequently changed to 6.5-6.3, the reflexes increased significantly to reach a mean value of 8.4 ± 1.5 mm Hg and, in some cases, 13-16 mm Hg (Fig. 2).

The biphasic character of the change in amplitude of the pressor reflexes depending on bicarbonate concentration and pH will be seen more clearly in the graph in Fig. 3. Curves of this type were obtained by the writers previously when studying the sensitivity of receptors of the small intestine to changes in acid–base balance of respiratory and metabolic acidosis type [4]. The similarity between the curve given in Fig. 3 and those obtained previously is seen in the fact that all these curves consist of two regions with different angles of slope to the abscissa: An initial portion with a gradual rise of blood pressure is followed after the point of inflection by a sharp increase in intensity of the pressor reflexes. Characteristically, for receptors both of the small intestine and of skeletal muscle, the point of inflection lies in about the same pH region (6.6-6.4). The presence of an inflection indicates inclusion of a new mechanism, triggered when the pH reaches a certain value, in the response. This mechanism is evidently the same for interoceptors of different organs. In view of ideas regarding the existence of two types of pressor reflexes (interoceptive and nociceptive) [6], it can be tentatively suggested that the initial region of the curves reflects the response of the receptors to physiologically adequate changes in the acid–base balance, whereas the second region is linked with direct excitation of nerve fibers and constitutes the vascular component of the nociceptive response of the individual to the action of substances in algogenic concentrations. Significant differences also exist in the response of receptors of the small intestine and gastrocnemius muscle to metabolic acidosis. According to our own observations [1, 4], receptors of the small intestine are more sensitive to changes in pH and bicarbonate concentration. Their threshold lies within the region of pH 7.3 and a bicarbonate concentration of 20.2 mM, and a further decrease in pH to 7.1 and in the bicarbonate concentration to 12.7 mM, i.e., to values characterizing the state

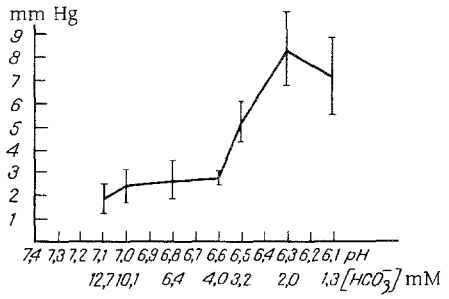

Fig. 3. Dependence of amplitude of pressor reflexes on pH and bicarbonate concentration in perfusion solutions (abscissa). Ordinate, arterial pressure, in mm Hg. Each point on curve is mean of 8-12 determinations.

of the acid–base balance of arterial blood during muscular exertion [11, 15], leads to a significant increase in the intensity of the pressor reflexes. It could be concluded from these data that receptors informing the CNS about the intensity of metabolic processes taking place in the individual or animal concerned, are present in the tissues of the small intestine. As regards the gastrocnemius muscle, this conclusion is premature, for although the threshold of sensation of muscle receptors lies within the physiological region of changes in pH and bicarbonate concentration, the change in pH from the threshold value (7.1) to the point of inflection (6.6) does not lead to a significant increase in amplitude of the reflexes. The possibility cannot be ruled out that the cause of this may be the inadequate sensitivity of a parameter such as the systemic arterial pressure, because of the small mass of the gastrocnemius muscle, rather than the low threshold of sensitivity of the muscle receptors themselves to changes in the acid–base balance. Under natural conditions, not one single muscle but a whole group of muscles takes part in muscular activity, and for that reason the global effect in such cases will be greater. Support for this suggestion is given by data in the literature on the amplitude of pressor reflexes evoked by contraction either of all the limb muscles of a cat [2, 9] or of the gastrocnemius muscle alone [3]. In the first case the blood pressure rose by 10-35 mm Hg, but in the second case by only 6-7 mm Hg. Reflexes arising during perfusion of the gastrocnemius muscle by solutions simulating metabolic acidosis are thus close in amplitude to reflexes observed during stretching of the gastrocnemius muscle or in response to its direct electrical stimulation.

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