CHANGES IN THE DOPAMINE CONCENTRATION IN ORGANS OF RATS WITH EXPERIMENTAL PNEUMOCOCCAL INFECTION

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During the development of pneumococcal infection in rats changes are found in the dopamine content in the organs. These changes occur as a series of phases. At the beginning of the disease the increase in the dopamine level in the adrenals, hypothalamus, heart, liver, intestine, and brain is caused by the need to intensify catecholamine synthesis. With the development of poisoning by the bacterial endotoxin dopamine accumulates in the brain tissues and its concentration in the lungs and kidneys of the rats falls. The absence of precise correlation between the dynamic changes in the dopamine, noradrenalin and adrenalin concentrations in various organs suggests not only that dopamine is a precursor of the catecholamines, but also that it performs a hypothetical physiological role of its own.

The role of dopamine in the pathogenesis of bacterial infection has not yet received sufficient study. Nevertheless investigation of the dopamine content concurrently with that of adrenalin and noradrenalin would provide a more complete picture of the character of the part played by the sympathico-adrenal system in the regulation of body functions during infection.

The object of the present investigation was to examine the changes in the dopamine level in animals during experimental pneumococcal infection, bearing in mind that the writers have previously [1, 2] found marked disturbances in the content of noradrenalin and adrenalin (of which dopamine is the precursor in the chain of biosynthesis) in the blood, urine, and organs, and of vanillin-mandelic acid in the urine of rats with this infection.

EXPERIMENTAL METHOD

Experiments were carried out on 108 male albino rats weighing 180-200 g. An intradermal injection of type I pneumococci was given into the right flank of the experimental animals in a dose of 0.1 ml of an 18-h culture diluted 1:100. The rats were decapitated 30 min and 1, 3, 5, 12, 24, 48 and 72 h after infection and the organs removed. The dopamine content was determined in the adrenals, liver, kidneys, heart, lungs, intestine, brain, and hypothalamus. The corresponding organs of intact rats acted as the control. The improved method of Matlina et al. [3] was used for the quantitative fluorometric estimation of dopamine. The dopamine fluorescence was recorded on a spectrofluorometer (Hitachi No. 203) at the Moscow Research Institute of Psychiatry, Ministry of Health of the RSFSR. The standard was 3-hydroxytryptamine hydrochloride (Ferak, Berlin). Statistical analysis of the results was carried out by the constant method of Montsevichyute-Éringene [4] and curves were plotted. Differences were regarded as significant when $P \leq 0.05$.

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EXPERIMENTAL RESULTS

The results of investigation of the dopamine content in the rats showed that the changes in its level in the organs during the development of pneumococcal infection passed through several phases. Disturbances of the dopamine level were found during the first 30 min after infection of the rats with pneumococci. During this period of the disease a sharp rise was found in the dopamine content in the adrenals (by 1.6 times over the normal 4.281 ± 0.676 μg/g), the hypothalamus (by 1.6 times over the normal of 1.192 ± 0.159 μg/g), the heart (by 2.6 times over the normal of 0.075 ± 0.009 μg/g), the liver (by 1.7 times over the normal of 0.142 ± 0.012 μg/g), the intestine (by 3.8 times over the normal of 0.071 ± 0.009 μg/g), and in the brain (by 1.8 times over the normal of 0.123 ± 0.020 μg/g). The dopamine level in the lung tissue was reduced by 1.3 times from the normal of 0.267 ± 0.005 μg/g). Statistical analysis showed the significance of the changes in the dopamine content during the first 30 min after pneumococcal infection ($P \leq 0.05$). The transient increase in the dopamine concentration in response to injection of pneumococci was followed during the next 30 min by a return to the normal values in the adrenals, hypothalamus, liver, and intestine of the rats.

After 1 h a further increase in the dopamine concentration (by 2.4 times; $P = 0.03$) was observed in the brain, but a marked decrease in the lungs (by 2.6 times; $P < 0.001$) and in the kidneys (by 2.0 times; $P = 0.05$).

The short course of the first phase (until the first hour) and the rapid onset and long duration of the second phase (3-12 h) must be emphasized. The second phase is marked by a sharp increase in the dopamine concentration in the infected animal, but at different times in different organs. The highest values of the dopamine concentration in the adrenals (7.752 ± 1.037 μg/g), hypothalamus (2.263 ± 0.191 μg/g) and heart (0.162 ± 0.012 μg/g) were observed 5 h after infection of the animals, but in the liver (0.282 ± 0.018 μg/g), intestine (0.446 ± 0.039 μg/g), kidneys (0.269 ± 0.013 μg/g), and brain (0.704 ± 0.034 μg/g) they were observed later during the development of the disease, in the kidneys and brain after 12 and 24 h respectively. In the lung tissues 12 h after infection there was a small increase in the dopamine concentration (0.131 ± 0.020 μg/g) compared with the previous marked decrease (0.037 ± 0.007 μg/g).

The later period of development of pneumococcal infection, 24-72 h after administration of the pneumococci when the state of the rats had worsened (temperature raised by 1-2°C, absence of appetite, apathy, adynamia, pneumonia, inflammatory focus around the site of injection of the pneumococci), was accompanied by the third phase – by the accumulation of dopamine in the brain tissue (to a maximum increase of 5.7 times after 24 h; $P < 0.001$), by a sharp fall in the dopamine level in the lungs (by 10.2 times; $P < 0.001$), kidneys (by 3.5 times; $P < 0.001$), and liver (by 4.3 times; $P < 0.001$) and by the absence of any significant change in its content (within normal limits or even slightly below) in the adrenals, hypothalamus, heart, and intestine.

Analysis of the results of determination of the dopamine concentration in the organs thus showed a series of phases of change in the dopamine level in the various organs, not coinciding in time. Probably the appearance of the first phase – a simultaneous but transient rise in the dopamine level in the hypothalamus, adrenals, heart, liver and intestine – must be regarded as a nonspecific response to stress, in this case to injection of the infectious material, based on neurohumoral reflex mechanisms leading to compensatory activation of synthetic processes in the body [1, 2].

The subsequent dynamics of the dopamine concentration in most of the investigated organs was largely dependent on its role as the precursor of noradrenalin and adrenalin, as shown by comparison of the results with the changes previously discovered by the writers in the noradrenalin and adrenalin concentrations in the corresponding organs during pneumococcal infection. However, other workers [5-8] have shown the biological importance of dopamine itself as a motor mediator controlling skeletal muscle tone. In this connection the absence of definite correlation between the levels of dopamine, noradrenalin, and adrenalin in the liver, as well as its dissimilar changes in the brain, lungs and intestine in the last stage of the infection imply not only that dopamine is the precursor of noradrenalin, but that it may also have an independent biological role.

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