

Correction of metabolic disorders of heart tissues and vascular walls during experimental hypertension of various geneses

Usage of various intermediates of tricarboxylic acid cycle in experimental pharmacotherapy and medical practice concerns their important role in metabolism, because they can be as energy source and substrates for synthesis; they can change direction of metabolic flows within the cell and at the extent of organism.

The basis of usage of Amber Acid and their salts includes:

- succinate-CoA deficit;
- increase of permeability of cellular and mitochondrial membranes for intermediates of tricarboxylic acid cycle;
- increase of resistance of oxidative systems of mitochondrion "charged" with substrates of tricarboxylic acid cycle towards alteration of hypoxia.

Oral injection of sodium succinate for normotensive rabbits with the dose of 100mg/kg during the period of 7 days leads to significant accumulation of pyruvate within tissues of blood - vessels under absence of significant changes of lactate content within walls of arteria and vena cava. Appropriate increase of pyruvate content gets ahead of lactate content. More feasible explanation of increase of concentration of pyruvate under injection of sodium succinate enables formation of phosphoenole pyruvate within quick cluster tricarboxylic acid cycle. Increase of pyruvate content is accompanied with reduction of relation lactate/pyruvate within cytoplasm of myocytes. Under the influence of sodium succinate the amount of lactate within tissue of heart of rats is likely to drop. Lactate content within the wall of aorta was not accompanied by changes of pyruvate level. The same as with rabbits' intensity of oxidative metabolism within tissues of rats was subject to changes under the influence of the preparation. Significant changes of balance of metabolites under the influence of sodium succinate may be conditioned by differences of formation of phosphoenole pyruvate within tissues of rabbits and rats.

Monitoring of changes of balance of catecholamines for rats under the influence of sodium succinate were as follows: accumulation of adrenaline in the wall of major arterial blood vessels for rabbits, accumulation of noradrenaline by the tissues of carotid artery and aorta of thorax; accumulation of adrenaline by the heart and renal. The present facts may be conditioned by the syntheses of catecholamines within chromaffin tissue due to direct energizing impact of sodium succinate towards cellular mitochondrion. Increase of content of catecholamines is an important link of mediated metabolic influence of sodium succinate. Sodium succinate evokes significant accumulation of pyruvate within tissues of blood vessels of rabbits with pyruvate hypertension, glucose within wall of aorta, reduction of lactate level within all except femoral artery and vascular segments. Shift of cytoplasmic relation lactate/pyruvate has been observed.

Increase of pyruvate content is typical test of impact of sodium succinate under metabolic acidosis. Similar impact of the preparation although expressed in other level is being observed for rats with pituitrin hypertension who has increased level of pyruvate in heart tissues due to impact of sodium succinate. Rats contrary to rabbits had had significantly increased lactate level within heart tissues and aorta. The preparation is likely to normalize redox system of pyridine nucleotides within cardiac and kvazi - myocytes. Adenyl energy charge within cells of heart is likely to restore till control level.

Sodium succinate for rats with pituitrin hypertension acts the more favourably towards cardiac metabolism compared with aorta. If level of adrenaline normalizes, wall of aorta will contain increase of catecholamine content on the basis of increase of adrenaline and noradrenaline within the tissues of renal gland. The preparation has no "pyruvatogenic" effect on the basis of initial accumulation of pyruvate by vascular tissue of rabbits. Despite of aerobic shift within cytoplasm of myocytes of rabbits with reno-vascular hypertension, significant drop of inorganic phosphate and pool of adenyl within vascular wall stops consideration about high energy state of the system.

Increase of pyruvate content for rats with reno-vascular hypertension under their treatment with sodium succinate has been observed in line with drop of lactate level within vascular wall. Under the treatment of rats with salt hypertension level of pyruvate dropped within aorta in line with increase of the amount of lactate within the heart and blood. Balance of noradrenaline within wall of aorta disturbed as a result of pathology was not likely to restore after intake of sodium succinate. Increase of adrenaline and noradrenaline content within renal gland is not the result of accumulation of adrenaline within the heart and aorta. But level of noradrenaline within the heart is likely to increase. In the event of stress-inducing hypertension for rats sodium succinate influenced reduction of pyruvate and lactate content within heart and aorta tissues. For rats with pituitrin hypertension sodium succinate was likely to restore level of intracellular and total Na on the basis of preservation of low level of K at the extent of cells. By normalizing Na level at the extent of cell and plasma, the preparation strengthens cellular fixation of Na for rats with salt hypertension. Combination of papaverine and sodium succinate for rabbits with pituitrin hypertension (1 mg/kg of weight 7 days subcutaneously) significantly changed character of metabolic processes within vascular tissue of animals with hypertension. Level of pyruvate and lactate was likely to increase within vascular wall under normalization of content of inorganic phosphate and aerobic shift of redox-system. Impact of sodium succinate occurs under its combination with papaverine. Evaluation of metabolic effectiveness of sodium succinate has confirmed capability of new preparation to eliminate metabolic acidosis, occurring within vascular system under experimental hypertension of various geneses. Achieved results on increase of pyruvate content within tissues of animals after injection of sodium succinate should be used for involving of the present preparation into complex treatment under conditions of hypertension.

Authors

Ratchkov A.K. Ratchkova M.A.