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BIOPHARMS

Research department

Dear colleagues,

Kindly given the combined antioxidant drug SOD roused definite interest, because potentiation of free-radical processes and decrease of SOD activity is important pathogenetic link of many diseases including such serious process as acute cerebral ischemia.

"EFFECT OF ORAL ANTIOXIDANT ENZYME SUPPLEMENTATION UPON TRANSIENT ISCHAEMIC ATTACKS (TIA)."

A summary of Clinical research.

Introduction.

In many investigators opinion the use of SOD in therapeutic aims is complicated by two circumstances: First, this enzyme is quickly demolished during injection into organism and has few time of semilife (T 1/2 = about 6 minutes) (Beckman at all, 1988), second - SOD penetrates badly through cellular membranes and hematoencephalic barrier (Michelson, Ruget, 1980).

At the same time SOD impenetrated into cells and being in blood, prevents injuring action of free radicals on enphotelis and vascular wall of smooth muscle cells (Kontos, 1985), as well as showing its defending action, especially in pathologic conditions, accompanied by violation of hemocirculation (McCord, 1985). SOD effect in experimental organal ischemia and lack of information

about negative consequences, SOD-therapy is a theoretical basis for drug use in angioneurological branch of our institute.

Materials

For appraisal of antioxidental therapy influence on biochemical models dynamics (maintenance of lipid peroxidation (LPO) products and antioxidental enzyme activity in erythrocytes) a group of patients (10 men) with TIA was picked out and information received was compared with biochemical models in group of TIA patients, in which only symptomatic therapy was carried out (hypotensive, cardiac drugs).

Insufficient quantity of drug and peroral from of given antioxidant SOD/CAT deprived us the possibility of its clinic approbation in heavier ischemia forms.

The first group of patients with symptomatic therapy.

The second group of patients given antioxidant drug in addition. A minimum of 6 tablets were given once daily. First thing in the morning upon rising, 1 hour before eating.

Dates of observation - 1-2 days, 7-8, 14-15 days.

Analysis were carried out on the biochemical analyzer "Spectrum".

Methods:

1. Definition of SOD by Nishikini N., Rao N.A., Jagi K. with use of nitroblue tetrazolil.

2. Definition of glutathione reductase (GR) activity by kinetic of oxidation HADQH2.

3. Definition of glutation peroxidaza (GPO) activity carried out in a system combined with GR activity added in medium incubation.

4. Definition catalaza activity by the quantity of disintegrated H202.

5. Malondialdegid (MDA) and dienocongugats (DK) content determination by Stelov U.D., Garishvili T.G.

The lack of biochemical analyzer at our institute forced us to

carry out the investigations in one of the Moscow clinical laboratories.

Findings

DK content doesn't increase in the first group of patients during the whole process of observation. This parameter remains unaltered also in the second group included in the scheme of antioxidant drug therapy, that is to say the preparation doesn't decrease DK content of erythrocyte below the control level.

MDA content of the first group is increased quiet enough at 1-2 days of observation and only at 14-15th day comes back to the control level. MDA content in the second group of patients during the whole period of observation doesn't differ from the control level, that is to say reliable MDA decrease takes place.

SOD activity in the first group of patients is decreased during the first week of observation, but in the second group the former is increased up to the control level.

Catalase, GPO and GR activity in erythrocytes of both groups is unaltered. That is to say against the background of antioxidant drug distinct decrease of second products content takes place in the TIA patients. This effect is probably connected with the normalization of the first antioxidant protection element - SOD.

The fact that the given antioxidant doesn't influence the DK content, catalase, GPO and GR activity, that is to say the unaltered indexes in TIA patient attracts attention. It shows that the former plays a positive effect on weakened antioxidant system links and suppressing lipid peroxidation (LPO) activity caused by ischemia at the same time doesn't decrease LPO intensity below the control level.

Conclusion

That means that the antioxidant therapy is effective in TIA patients, and gets back to normal LPO and erythrocytes antioxidant enzyme activity. As the LPO activation in erythrocytes reflects the metabolic shifts, which takes place in ischemic areas,

positive dynamics of biochemical indexes shows the intensification of antioxidant protection system in brain, caused by the usage of given drug and gives base to wait for positive dynamics in neurologic status in case of more acute ischemia forms.

We consider the use of given injectable antioxidant form the most effective in case of more acute ischemia forms.

Yours sincerely,

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