

THE MECHANISMS INVOLVED IN THE THERAPEUTIC EFFECT OF HYPERTHERMIA ON TUMOR TISSUE

N. Mitagvaria, I. Lazrishvili, M. Devdariani, M. Nebieridze, L. Davlianidze, T. Bikashvili, T. Lortkipanidze, N. Sikharulidze

I. Beritashvili Center of Experimental Biomedicine

Accepted 11.11.2011

On the basis of the analysis of own experimental data and data published in literature the attempt is made to reveal the main mechanisms for the explanation of therapeutic effect of hyperthermic exposure in the cancer clinic. The leading role of iNOS expression is not in doubt.

We mean: caused by hyperthermia upregulation of iNOS expression, the formation of peroxynitrite, platelet aggregation, the deterioration of the rheological properties of blood and, finally – thrombosing of vessels with all well-known consequences for tumor tissue.

Key words: hyperthermia, tumor, nitric oxide, mechanisms

The high efficiency of hyperthermia in cancer patients is no longer in doubt, although the mechanisms of conditioning its effectiveness are still being debate [2].

It is established that after 20-30 minutes of exposure 43°C hyperthermia can cause the thrombosis and arteriolar constriction [5]. The microcirculation in its turn in many aspects is conditioned by rheological properties of blood. Increased blood viscosity results in a slowing down of blood flow, stagnation of its constituents and in ischemia [9].

It has also been hypothesized that hyperthermia promotes oxygen-centered free radicals formation in cells. By means of electron paramagnetic resonance spin trapping direct evidence for free radicals generation during hyperthermia in intact functioning cells was received [6]. This findings indicate that heat increases the flux of cellular free radicals and support the hypothesis that increased generation of oxygen-centered free radicals and the resultant oxidative stress may mediate in heat-induced cellular damage [6].

We know as well that hyperthermia causes activation of Nitric Oxide Synthases (NOS) [1]. Nitric oxide (NO) is a vasoactive molecule produced by the activation of at least three NOS: neuronal (nNOS), inducible (iNOS) and endothelial NOS (eNOS). Activation of iNOS causes prolonged increase in nitric oxide production and it may be 1,000 times greater than the amount of NO produced by eNOS activation. In this case we have observed a sharp vasodilation, increased vascular permeability, edema and the subsequent development of an inflammatory response [12]. Nitric oxide combines with