

EFFECTS OF HYPERTHERMIA ON THE PERIPHERAL NERVOUS SYSTEM. AN OVERVIEW.

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The present paper overviews the current knowledge about effects of hyperthermia at temperatures used in clinical oncology on the peripheral nervous system.

From the experimental studies it may be concluded that the heat sensitivity of the nerve is determined by the sensitivity of the nerve vasculature. These studies show that in order to avoid induction of severe neuropathy, application of heat to the peripheral nerves should not be in excess of doses of 30 min at 44°C or equivalent.

Using modern equipment for application of loco-regional hyperthermia the incidence of even mild neurological complications is very low. In hyperthermic isolated limb perfusion (HILP) neurotoxicity is an often-mentioned side effect, this in spite of the fact that in all studies a relatively mild hyperthermic temperature is used that, based on the experimental studies, should be well tolerated by the nerves and other normal tissues in the limbs. It seems that the neurotoxicity observed after HILP results from thermal enhancement of drug toxicity, very probably combined with effects of a high tourniquet pressure that is used to isolate the blood flow in the leg. Whole body hyperthermia (WBH), using anaesthesia and appropriate monitoring to avoid cardiovascular stress, is at present considered a safe procedure. However, cases of neuropathy after treatment have been described in the recent past.

When chemotherapy, and notably cisplatin, is administered before or during hyperthermia there are several clinical and experimental observations that indicate a limited tolerance of the peripheral nervous tissue in such case. Also previous radiotherapy may limit the tolerance of nerves to hyperthermia, notably when radiation is applied with a large field size. Experimental studies show that combined treatment with radiation and heat leads to enhancement of effects of radiation (enhancement ratio ~1.5 at 60 min at 44°C).

A clear contraindication for the application of hyperthermia in patients is the presence of a neurodegenerative disease, such as multiple sclerosis. Vigilance is also required in the treatment of diabetic patients with hyperthermia, this based on experimental animal studies, but so far no clear clinical data are available.