

## **HIPEC (HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY) FOR PERITONEAL CARCINOMATOSIS – HOW TO ESTABLISH THE APPROPRIATE DOSE OF CYTOSTATICS?**

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There are only few therapeutic options for peritoneal carcinomatosis. Hyperthermic intraperitoneal chemotherapy (HIPEC) was developed as a unique technology combining more modalities. There is only a narrow therapeutic range of current cytostatics. In HIPEC it is influenced by a number of variables - penetration, absorption, concentration, volume of administered fluid, indwelling time, temperature, previous surgery etc., all alternating the risk of both adverse and antitumor effects.

We are the only group in Czech republic performing HIPEC, thus our experience is unique. We use a simple dose calculation of mitomycin C, carboplatinum and adriamycin based on a systemic exposition as an endpoint. It estimates the absorption rate of particular agent into a systemic circulation. It results in at least 80% absorption according to the variables of our methodology (indwelling time 90 mins., temperature 42°C, isotonic solution). The calculated dose may be finally adjusted accordingly to pretreatment status, blood count, number of previous chemotherapy cycles etc.

118 cycles of HIPEC were administered in 104 pts. with advanced peritoneal involvement by various malignancies (peritoneal pseudomyxoma, primary peritoneal, colorectal, ovarian and gastric cancer). The dose resulting of calculation was 18–22 mg for mitomycin, 50–80 mg for adriamycin and 400–500 mg for carboplatinum. The incidence of side effects was compared with the risk rate related to a current systemic chemotherapy as declared in official documents (SPC). It does not significantly differ and remains within the expected range. The predominant side effect gr. III–IV was a reversible myelosuppression. There were 2 toxic deaths after mitomycin C HIPEC, however combined with subsequent 5-FU treatment.

The dose derived of the systemic exposure estimate is safe. Any suitable model of dose calculation is desirable due to a number of insufficiently explored variables influencing the risk of side effects. The use of cytostatics for HIPEC is usually “off-label” and treatment safety remains fully in physician’s responsibility despite HIPEC is a developed methodology. Thus the manufacturers are challenged to include HIPEC into standard indications of their drugs and to declare dosage.

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