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LETTER TO THE EDITOR

Normothermic and Hyperthermic Intraperitoneal Chemoperfusions with Cisplatin to Treat Advanced Ovarian Cancer in Experimental Settings

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Cisplatin is commonly used in chemoperfusion treatment of advanced ovarian cancer but only in terms of hyperthermic intraperitoneal chemoperfusion (HIPEC) [1]. Normothermic intraperitoneal chemoperfusion (IPEC) with cisplatin is a potentially safer option of chemoperfusion, however its efficacy remains unstudied. In several experimental studies it was shown that antitumor effects of IPEC with cisplatin or mitomycin C were comparable or even higher compared to HIPEC with the drugs [2]. Despite that results of these few preclinical studies are controversial. The authors carried out experimental study to compare safety and efficacy of normothermic and hyperthermic intraperitoneal chemoperfusions with cisplatin in ovarian cancer model. 61 rats with transplanted ovarian cancer were randomized into 4 groups: I – control, i.p. administration of 0.5 ml of saline (n = 19); II – i.p. administration of cisplatin in MTD – 4 mg/kg (n = 12); III – IPEC with cisplatin in MTD – 40 mg/kg (n = 12); IV – HIPEC with cisplatin in MTD – 20 mg/kg (n = 14). The temperature of the perfusate in the abdomen was maintained between 36.5–37.5°C for IPEC and 40.5–41.5°C for HIPEC.

IPEC with cisplatin was associated with less postoperative morbidity and was better tolerated compared to HIPEC with cisplatin. The only postoperative complication in IPEC group was paresis of the hind limbs registered in 1 rat, while HIPEC with cisplatin was associated with pneumonia (n = 1), bowel adhesions (n = 1); limb paresis (n = 3) and diarrhea (n = 1).

When evaluating antitumor effects of the treatment in each group median survival of rats after IPEC with cisplatin (37.5 days) was significantly higher compared to single i.p. administration of the drug (median survival =19.5 days; p = 0.037). The most interesting was that no advantage in antitumor efficacy was observed for HIPEC with cisplatin over IPEC with cisplatin. Median survival of rats receiving HIPEC with cisplatin (25.5 days) was significantly higher compared to median survival of untreated animals in the control group (9 days; p = 0.003) but didn't differ significantly either from median survival of rats receiving cisplatin i.p. (19.5 days; p = 0.354) or from median survival of rats receiving IPEC with cisplatin (37.5 days; p = 0.256). Several studies have shown that platinum drugs exert significant synergestic effect with moderate hyperthermia (39–41°C) [3]. Despite that in our study antitumor effects of cisplatin were comparable for IPEC and HIPEC because survival of rats with ovarian cancer in these groups didn't differ significantly. Similar results were obtained by Zeamari et al. in their experimental study where authors didn't observe any advantages of HIPEC with cisplatin over IPEC with cisplatin [4]. I.p. chemoperfusions were performed in rats with peritoneal carcinomatosis for 90 min (twice as long as in our research) using temperatures similar to those in our research (37 °C for IPEC and 40 °C for HIPEC). There was no difference in cisplatin concentration in the tumor nodes from the peritoneal cavity of rats after HIPEC and IPEC. Thus authors concluded that hyperthermia doesn't increase cisplatin uptake by tumor cells in the peritoneal cavity compared to normothermic conditions.

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The sum of immediate and long-term experimental results of IPEC and HIPEC with cisplatin could be the basis for reconsidering the rationale of combining hyperthermia with chemoperfusion with cisplatin in clinical settings. It is advisable to conduct clinical trial comparing IPEC and HIPEC with cisplatin in patients with advanced ovarian cancer.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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