THERMORADIOThERAPY AND RADIOCHEMOTHERAPY OF LOCALLY ADVANCED PHARYNX CANCER WITH INVOLVED LYMPH NODES

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Purpose of the study. To prove an expected benefit of simultaneously given radiotherapy or chemoradiotherapy and local hyperthermia for the treatment of stage III and IV unresectable pharynx cancer a prospective non-randomized trial was initiated.

Materials and method. From March 1994 to October 2001, one hundred twenty two patients were enrolled, 111 of them completed the treatment (median age 53 years; 35.1% stage III tumors; 64.9% stage IV tumors; 64% oropharynx; 36% hypopharynx). In the first group, 59 patients underwent a split-course of conventional radiation therapy (RT) up to total dose 68-70 Gy. In the second group (RT+HT), 52 patients were performed RT and 6-9 sessions of local microwave hyperthermia (915 MHz, 45-50 Wt). Heat was delivered for an hour up to 41.50-43° C in the tumor before irradiation. From December 2002 to April 2006, fifty seven patients were included into the study, 46 of them completed the course (median age 57 years; 39.1% stage III tumors; 60.9% stage IV tumors; 71.7% oropharynx; 28.3% hypopharynx). The treatment protocol of chemoradiotherapy (CRT) consisted of three courses of chemotherapy (5-FU+cisplatin) given in the 1st, 5th and 11th week and conventional split radiation therapy (6-9 and 12-14 weeks). In the forth group (CRT+HT), besides, patients were performed 6-8 sessions of local hyperthermia. Adverse events (skin and mucosal toxicity, dysphagia, xerostomia and hematological toxicity) were scored according to RTOG\EORTC criteria.

Results. Patients treated with thermoradiotherapy had significantly better OS than those treated with standard fractionation (p=0.0225). One-year overall survival (OS) was 49.1% and 68.1%, 3-year OS – 15.1% and 34%, 5-year 11.3% и 23.4%, 10-year – 5.7% and 12.7% in RT and RT-HT group, respectively (Fig.1), with median survival 11.9 and 19.1 months. Patients in local hyperthermia group demonstrated non-significant increase of grade 3+4 mucositis, dysphagia, skin and soft tissue toxicity (p=0.067). Hematological toxicity was low and identical in both groups. One-years OS of patients, who underwent chemoradiotherapy, was 85.7%, 3-years – 66.2% with undefined median survival (Fig.2). In CRT-HT group, one- and three-years survival was 87.5% and 30%, respectively, with median survival 23.7 months. There was no significant difference between the groups (p=0.2413). Patients treated with chemoradiotherapy and local hyperthermia more often developed grade 3+4 mucositis (52.9% vs 32.9%, p=0.0347) and dysphagia (28.6% vs 8.8%, p=0.0315) compared to those with chemoradiotherapy alone. Severe myelosuppression (WBC less than 2.500 cells/mkl) was observed in 10.3% of patients in the course of CRT and 29.4% of patients in the course of CRT+HT, p=0.0213. Grade 2-4 anemia developed in 34.5% and 52.9% cases, respectively.

Conclusions. There is an evident benefit for CRT vs RT and RT+HT for the treatment of locally advanced pharynx cancer. Thermoradiochemotherapy doesn’t improve survival, but significantly increases toxicity of the treatment.