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# RADIOTHERAPY OF NASOPHARYNGEAL CARCINOMA (NPC). IS PROPHYLACTIC NECK IRRADIATION NECESSARY?

M. MESTRE, MD AND H. MODIG, MD

Department of Oncology, University Hospital, S-901 85, Umeå, Sweden.

During the period 1959-1987, 132 pts. with histopathologically confirmed NPC received radiotherapy with curative intent. Prophylactic neck node irradiation was with a few exceptions not given. In 100 pts. in which one side or both sides of the neck was not irradiated the clinical course was as follows. Twentythree pts. are living free of disease, 17 pts. died from intercurrent diseases, 7 pts died from generalized disease without local and regional recurrence, 37 pts. had recurrence within the irradiated volume and only 16 pts. had node recurrence outside the irradiated volume. Out of these 16 pts. 8 are living free of disease after retreatment, 3 are dead of intercurrent disease and only 5 of the pts. are dead with disease and could theoretically have been cured by prophylactic neck irradiation. It seems that in countries with a good surveillance of treated pts. prophylactic irradiation of cervical nodes is not necessary.

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# CARBOPLATIN, 5-FLUOROURACIL AND FOLINIC ACID IN ADVANCED AND RECURRENT SQUAMOUS CARCINOMA OF THE HEAD AND NECK.

Juncor EJ, Canney PA, Symonds RP.

Beatson Oncology Centre, Glasgow, Scotland.

22 patients with locally advanced and recurrent squamous carcinoma of the head and neck have been entered into a study using a two day, inpatient, intravenous regimen of Folinic Acid 200mg/M<sup>2</sup>, 5-FU 500mg/M<sup>2</sup> bolus followed by 5-FU 500mg/M<sup>2</sup> in 22 hours days 1+2. Carboplatin 300mg/M<sup>2</sup> day 2 repeated every 21 days.

M:F 15:7, median age 61(31-74) years, 7 patients recurrent after radical radiotherapy +/- surgery, 15 had no prior treatment. Performance status 0x3 patients, 1x15 patients, 2x4 patients.

61 cycles assessable for W.H.O. toxicity. WBC grade 1x4, grade 3x1. Platelets grade 2x1, grade 3x1. Nausea grade 2x4, grade 1x6. Vomiting grade 2x5, grade 1x1. Alopecia grade 1x3, grade 3x1. One patient died of toxicity.

19 patients assessable for response. RR in previously untreated patients was 83.3% (10/12) and 40% (2/5) in previously treated patients.

Trial continues to ascertain if good response rate and minor toxicity is maintained with larger numbers of patients.

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# PHASE II STUDY OF FOUR-DRUG CONCOMITANT CHEMORADIOTHERAPY IN ADVANCED HEAD AND NECK CARCINOMA (AH&NC): PRELIMINARY RESULTS.

P. Michel-Janglet<sup>1</sup>, C.S. Wang<sup>1</sup>, P. Brunel<sup>1</sup>, C. Peytral<sup>2</sup> - Departments of radiotherapy<sup>1</sup> and ORL surgery<sup>2</sup> - Intercommunal Hospital, 93370 Montfermeil, France.

Locoregional control remains a major challenge in AH&NC. This prospective ongoing trial evaluates the toxicity and efficacy of a four-drug chemo-sensitized radiotherapy (RT) conserving conventional fractionation. Patients (pts): from Dec-88, 33 pts with AH&NC, IK ≥ 70, Mo. were included. 28 pts are eligible for analysis. Median age = 59. Oropharynx = 13, pharyngo-larynx = 10, Oral cavity = 1, Sinus cavity = 2, Cervical metastatic Adenopathy = 2. All pts had bulky tumours: T3T4 = 86%, N2N3 = 79%, T3T4-N2N3 = 68%. Methods: Chemotherapy included cisplatin (C) 10 mg/m<sup>2</sup> x 4d at d1+36, fluorouracil (F) 400 mg/m<sup>2</sup> x 4d at d1+36, mitomycin (M) 6 mg/m<sup>2</sup> d8+43 and hydroxyurea (H) 1 gr/m<sup>2</sup> x 5d at d8+43. RT started d1 and delivered 72 Gy in 8wks. Toxicity (Tox): No pt died from Tox. Grade 3-4 hematological Tox: Neutropenia = 43%, thrombopenia = 25%; Grade 3-4 mucositis occurred in 71% of pts, responsible of a median weight loss of 7% (0-19%). Nausea, anemia, cutaneous and renal Tox were mild. Only 22% of pts received the whole protocol without interruption. 39% stopped 1wk, 32% 2wks, 7% ≥ 2wks. The planned dose has been delivered in 96% of pts for RT and H, 89% for C and M, 86% for F. Results: After treatment, 14/28 pts (50%) were in CR. 7/14 pts in CR relapsed (local: 3, regional: 3, systemic: 3), 1 salvaged by surgery. Currently (2-93) 9/28 pts (32%) are still NED for a median time of 13 months following onset of treatment. 2 yr actuarial overall survival is 44% (27-63). Conclusions: 1/ Mucositis remains the major limiting factor, making a 1-2 wk interruption often compulsory. Hematotoxicity has always been easily manageable. 2/ locoregional control compares favorably with RT alone, given the high rate of advanced stages, but results are still preliminary.

Keywords: Chemo-radiotherapy, conventional fractionation.

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# SHORT COURSE INTENSIVE CHEMOTHERAPY USING CISPLATIN AND 5-FU FOLLOWED BY RADIOTHERAPY IN ADVANCED HEAD AND NECK CANCER

J Zidan, E Robinson, A Kuten, N Haim.

The Northern Israel Oncology Center, Rambam Medical Center, Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel.

Thirty two patients with locally advanced stage III and IV squamous cell carcinoma of the head and neck were treated with short induction chemotherapy followed by radical radiotherapy. Chemotherapy consisted of Cisplatin 100mg/m<sup>2</sup> iv on days 1 and 16, and 5-FU 1000mg/m<sup>2</sup> over 24 hours on days 2-5 and 17-20. Radiation therapy was started on day 31. A tumor dose of 60-70Gy was administered. Patient characteristics: 25 males/7 females, median age 52 years (range 15 to 82). Tumor site: 17 nasopharynx, 4 larynx, 3 oropharynx, 3 oral cavity, 3 maxillary sinus, 1 hypopharynx and 1 metastases of unknown primary. After chemotherapy 9 (28%) patients had complete response (CR), 18 (56%) had partial response (PR) and 5 (16%) had no change (NC) of their disease. After radiation 24 (75%) pts had CR, 6 (19%) had PR and 2 (6%) had NC. Patients with nasopharyngeal carcinoma had the highest CR rate after chemotherapy (41%) and radiotherapy (88%). With a median follow up of 38 months (range 6-71), 19 of 24 pts (79%) in CR are alive with no evidence of disease (59% of the whole group). Toxicities have included mild to moderate myelosuppression and moderate to severe mucositis. Our strategy was to give intensive chemotherapy during a short period to achieve maximal effect and not to delay the standard radiation therapy for more than one month. This combined modality treatment appears effective, with high complete response rate and disease free survival.

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# A COMPARISON OF THE INHIBITORY EFFECTS ON DNA-SYNTHESIS OF CISPLATIN, DOXORUBICIN AND 4-HYDROPEROXYCYCLOPHOSPHAMIDE IN CULTURED HUMAN LIP CARCINOMA CELLS AND NORMAL ORAL KERATINOCYTES

Langkjer S. T., Ebbelhøj E., and Jepsen A.

Dept. of Oncology, Aarhus University Hospital, and Institute of Pharmacology, University of Aarhus, DK 8000 Aarhus, Denmark.

Several reports suggest that an intraarterially administered drug may have greater activity in head and neck cancer patients than an intravenously administered drug, but nothing much is gained if the drugs used are just as toxic to the normal tissue in the region as to the neoplastic tumor. In this study we wanted to compare the effect of 3 drugs on normal mucosa epithelial cells to the drug effects on lip carcinoma cells.

Dose effect relationship of cisplatin, doxorubicin, and 4-hydroperoxycyclophosphamide with respect to rates of DNA synthesis, using 3H-Thymidine incorporation, were studied in a human lip carcinoma cell line and in normal keratinocytes subcultured from biopsies of human oral buccal mucosa (Arenholt-Bindslev et al. Invest. Dermatol., 88: 314-319, 1987). The lip cancer cells had a higher uptake of 3H-Thymidine than the normal cells probably because the lip cancer cells had a higher growth rate than the normal cells. The three drugs tested had a direct effect on the DNA synthesis of the cancer cells and the normal cells. The drug dose relationship showed that the cancer cells were significantly more sensitive to cisplatin than the normal cells. For doxorubicin and 4-hydroperoxycyclophosphamide no difference in the drug sensitivity between the two cell types was found.

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# THE USE OF IMMOBILISATION DEVICES IMPROVES LOCAL CONTROL AND OVERALL SURVIVAL IN HEAD AND NECK CANCER PATIENTS TREATED WITH RADIATIONS.

Belderbos J., Van den Weyngaert D., Scalliet P. Radiotherapy, AZ Middelheim, Antwerp, Belgium

The aim of this study was to determine retrospectively whether the introduction of immobilisation masks within our department has improved the local control and overall survival rates in head and neck cancer patients.

We studied 354 patients treated for head and neck cancer during the period of Jan. 81 - Jul. 91. No exclusions were made. All patients were examined and staged by the same person. Prior to this period there was uncertainty about the staging procedures. The use of a mask, total dose, overall time and stage was recorded for each patient. Endpoints of our study were local control and overall survival. A strong positive influence on local control and overall survival was found for patients using a mask. This positive influence remained after correction for stage. At the end of the radiation treatment, a complete remission of almost 82% was found for patients using a mask as compared to 72% of the patients treated prior to the introduction of the mask. When a mask was used the local control remained longer. Overall time and total dose were not found to have a significant influence on local control and overall survival but there were relatively little variations amongst patients.