

Combined application of cisplatin, vindesine, hyaluronidase and radiation for treatment of advanced squamous cell carcinoma of the head and neck

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Forty eight patients with advanced head and neck tumours were treated with irradiation and concomitant chemotherapy with cisplatin, vindesine and hyaluronidase. The disease-free survival rate at 5 years was 47%. The toxic effects were mucositis (48 patients), nausea (25 patients - in 6 patients vomiting), bone marrow depression (15 patients), and peripheral neuropathy (14 patients). The results warrant a randomised trial.

Key words: head and neck neoplasms-therapy; radiotherapy; cisplatin; vindesine; hyaluronidase; treatment outcome

Introduction

Advanced, unresectable epithelial cancer of the head and neck is a challenging problem in oncology. Standard radiation therapy is suboptimal because of a comparatively high risk of recurrence and long term survival is only achieved in less than 10% of the cases. Recent studies have shown that simultaneous radiochemotherapy can prolong the recurrence-free interval as well as the patient's survival time.¹ Also, the radiosensitizing effect of Cisplatin has been observed.^{2,3,4} The tumor-cell synchronizing effect of vinca alkaloids is well known.⁵ The combination of Vindesine and Cisplatin was tested in several clinical studies.^{6,7} The sensitizing effect of Hyaluronidase on polychemotherapy has already been demonstrated in separate studies, also as additive to the regimen with Cisplatin and Vindesine.^{8,9}

The purpose of the present study is to evaluate the effect of radiation therapy in combination with

chemotherapy consisting of Vindesine, Cisplatin and additional Hyaluronidase.

Material and methods

The chemotherapy scheme was as follows: on day 1 (5 mg Vindesine) and day 2 (80 mg/sqm Cisplatin), with 200.000 IU Hyaluronidase administered i.v. over 20 min. on each of these two days before initiation of chemotherapy, and on 12 radiation days 3 - 5, 8 - 12 and 15 - 18. Renal function was protected by infusions before and after chemotherapy. This therapy regimen was repeated twice starting with chemotherapy on days 22 and 43.

The irradiation treatment was given by 6 MeV photon beam unit, 5 x 2 Gy per week, to the mid-plane tumour dose 72 Gy with shrinking field technique. If the radiomucositis was severe, the irradiation treatment was interrupted for a week.

The response to the treatment was evaluated after each cycle and after every month and finally three months after completion of treatment (according to WHO-guidelines). Mean observation time was 62 months (range: 32 - 85 months).

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Results

To date, 48 patients were treated. No one was lost to follow-up. The survival of patients at 5 years was 47%. Sixteen patients are still in complete remission without relapse. The complete and partial remission was achieved in 40/48 patients and 3/48, respectively; in 1 patient, the condition remained unchanged. In 4 patients, tumor progression was evident under therapy and they died 3, 5, 6 and 8 months after therapy. In 12 cases relapses occurred after complete remission and all died because of cancer. Those who did not achieve complete remission died as well. Nine patients with stage T4 N2 and T4 N3 tumor died from tumor progression or recurrent disease. One patient died of pneumonia 5 months after achieving complete remission; another died of sudden heart failure 25 months after achieving complete remission. One patient died from secondary liver carcinoma.

Toxic effects: nausea occurred in 25 cases (WHO-grade 1 - 2); only 6 patients suffered from vomiting (WHO-grade 1 - 2). In 15 patients, signs of myelotoxicity (in 13 patients with WHO-grade 1, and in 2 patients with WHO-grade 2) and in 14 cases peripheral neuropathy (WHO-grade 1) developed. Twenty seven patients suffered from moderate/severe mucositis (WHO-grade 1 - 2) caused by radiation, and 12 patients experienced mucositis WHO-grade 3. Nine patients developed mucositis WHO-grade 4 and at this point radiation therapy was stopped for about a week. However, chemotherapy was administered according to the protocol in these patients as well.

Conclusion

Encouraged by the promising results of the presented trial, a randomized trial is being made

with unchanged combined radiochemotherapy plus or minus additional hyaluronidase to evaluate the impact of this enzyme on the effectiveness of the therapy.

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