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Smoking during radiotherapy for head and neck cancer and acute mucosal reaction



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ABSTRACT

Aim: We compared the incidence of RTOG/EORTC grade III and higher acute mucositis in patients with head and neck cancer who continued to smoke during radiotherapy with those who quit smoking.

Background: There are conflicting data on the relationship between smoking during radiotherapy and the severity of acute mucosal reaction. More studies dealing with this issue are needed.

Materials and methods: Among 136 patients receiving curative radio(chemo)therapy, 37 (27%) declared that they had not quit smoking during radiotherapy. The intensity of mucositis was scored daily by a nurse and weekly by a physician using the RTOG/EORTC scale. The main end-point of the study was the highest observed RTOG/EORTC grade of mucositis.

Results: Patients who smoked during radiotherapy (smokers) were younger than their counterparts who quit smoking (non-smokers), $p=0.06$. There were no other differences in the baseline characteristics between smokers and non-smokers. Grade III/IV acute mucositis was observed in 43.5% of all patients. The percentage of patients with grade III/IV acute mucositis was similar in smokers and non-smokers (46% vs. 42%, $p=0.71$). Nine patients (smokers [13.5%]; non-smokers [4%], $p=0.05$) required prolonged hospitalization to heal mucositis.

Conclusions: In the whole group, smoking during radiotherapy was not related to acute mucosal toxicity evaluated as the rate of the highest observed grade of mucositis.

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1. Background

Head and neck cancers are a very heterogeneous group of tumours, but most are squamous cell cancer associated with

smoking history. In Poland, head and neck cancer accounts for about 6% of all cancer cases.¹ Given the ageing of the population, the incidence of this malignancy is expected to grow.² Treatment options for patients with head and neck cancer comprise surgery, radiotherapy, chemotherapy or some

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combination of those depending on the cancer location, stage of the disease and patient's condition. Head and neck cancer treatment can cause many complications, and acute mucositis is the most common side effect of radiation therapy. The severity of acute mucositis depends mainly on the technique and dose of radiation, but patient-related factors also influence the severity of mucosal reactions.^{3,4}

Because most head and neck cancer patients are former or current smokers, they are asked whether they smoke before receiving radiation therapy, and current smokers receive smoking cessation counselling. Despite this counselling, a proportion of patients continue their habit during radiotherapy. Some studies have reported an inferior outcome of radiotherapy for such patients compared with patients who quit smoking before treatment.^{5–10} There are scarce data on the relationships between smoking during treatment and the incidence and severity of radiotherapy-related complications, but some studies have reported a negative impact of continuous smoking on treatment tolerance.^{11–14}

2. Aim

The aim of this study was to evaluate the relationship between cigarette smoking during radiotherapy or radiochemotherapy and the severity of acute mucosal reactions in head and neck cancer patients. We hypothesized that patients who did not smoke during treatment would experience less severe acute mucositis than their counterparts who continued smoking during treatment, independently of the intensity of the radiation therapy schedule.

3. Materials and methods

One hundred and thirty-six consecutive head and neck cancer patients treated with radiation on an in-patient basis between 2011 and 2012 in our institution were included in the analysis. They all had a history of smoking; i.e., were either current or former smokers. Details of the duration of their smoking and the amount smoked were not available. A list of the included patients was generated from the institutional database, and their case histories were available for the purpose of the study.

It is a departmental policy to ask all patients about their smoking habits during the baseline interviews with the doctor and nurse before treatment and to counsel them to quit smoking. During treatment, patients were also asked about their smoking by doctors and nurses, and their replies, as well as the nurses' observations, were recorded in the medical charts. According to the departmental policy, all patients were evaluated for the severity of acute mucosal reaction according to the Radiation Therapy Oncology Group/European Organisation for Research and Treatment of Cancer (RTOG/EORTC) criteria¹⁵ daily during radio(chemo)therapy by a nurse and once a week by a physician. Nurses evaluated acute mucositis at the level of the oral cavity only. Evaluations performed by doctors were more complex, included evaluation of oral cavity, pharynx and larynx using the mirror indirect laryngoscopy. All our staff had a special training in the scoring of mucosal reaction in the RTOG/EORTC scale. Less experienced nurses were supervised by a senior nurse and all complex

cases were collectively discussed. The highest RTOG/EORTC grade of the acute mucosal reaction during treatment was scored for each patient as the end-point of the study. Grade III and higher acute mucosal toxicity was considered severe. Any breaks in radiotherapy equal or longer than three days and prolongation of treatment time were also recorded.

Departmental policy of management of acute mucositis including pain control, nutritional support, oral decontamination, palliation of dry mouth, prevention of bleeding followed international guidelines.¹⁶ The following variables were analyzed with regard to the incidence of grade III and higher acute mucosal toxicity during radiotherapy: smoking status during treatment (smoker vs. non-smoker), sex (woman vs. man), age (≤ 65 vs. > 65 years), schedule of radiotherapy (accelerated fractionation comprising 63.6–69.96 Gy with 2.12 Gy per fraction vs. conventional fractionation comprising 60–70 Gy with 2 Gy per fraction), technique used to deliver radiotherapy (intensity-modulated radiation therapy [IMRT] vs. three-dimensional conformal radiotherapy [3D-CRT]), the use of combined treatment methods (radiotherapy with surgery vs. without surgery, radiotherapy with chemotherapy vs. without chemotherapy), overall duration of radiotherapy (≤ 43 days vs. > 43 days) and cancer location (oral cavity vs. all other locations, oropharynx vs. all other locations, larynx vs. all other locations).

Ninety-nine patients (73%) who reported that they did not smoke during radiation therapy were classified as non-smokers. Thirty-seven patients (27%), who declared that they had not quit smoking completely during radiotherapy were classified as smokers. The characteristics of the patients and the treatment given are presented in Table 1. All patients were treated with external-beam radiation using a 6 MV photon beam from linear accelerators. All patients who were treated with the accelerated radiotherapy (2.12 Gy per fraction) schedule had IMRT. Seventy patients (52%) received definitive radiotherapy alone or radiochemotherapy, and 68 patients (48%) were treated with adjuvant radiotherapy or radiochemotherapy following curative surgery. Mean radiation doses were 65 Gy (range: 46–70 Gy) and 62 Gy (range: 50–66 Gy) for patients treated with definitive and postoperative radiotherapy, respectively. In patients given combined treatment, chemotherapy comprised cisplatin given concurrently with radiation (100 mg/m² every 3 weeks or 40 mg/m² weekly).

Statistical analysis was performed using STATISTICA software (version 10; 2012). The chi-square test was used to compare the percentage of smokers in relation to treatment and other patient-related factors, and to compare the frequency of severe acute mucositis in relation to the variables analyzed. Possible interactions between smoking status and other variables in relation to the occurrence of grade III and higher acute mucositis were also tested with the correlation Pearson coefficient. To adjust for possible interactions, a multiple regression analysis was carried out to adjust the smoking status to other patient and treatment related parameters. A p -value ≤ 0.05 was considered significant.

4. Results

Sex distribution, cancer location, schedule and radiotherapy technique did not differ significantly between smokers and

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