

THE INFLUENCE OF THE GAP IN POSTOPERATIVE RADIOTHERAPY PATIENTS WITH CARCINOMA OF THE LARYNX

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ABSTRACT

The aim of study was to evaluate the influence of gap in postoperative irradiation on the outcome. For this purpose the retrospective review the cases histories of 311 patients after total laryngectomy and postoperative radiotherapy between 1986 and 1990 was performed. All patients were divided into 3 groups : A- without gap (160 patients), B- with short gap up to 7 days (94 patients) and C- with long gap over 7 days (57 patients). The endpoint in analysis was loco regional rate control. All patients had a minimum follow up 3 years. Based on our data it was calculated that the prolongation of treatment resulted in decrease in loco regional control. The correlation between length the gap and decrease the outcome of treatment was very strong ($p < 0,001$). It is very important to avoid any gaps during course of radiotherapy.

key words: cancer of the larynx, gap, postoperative radiotherapy.

INTRODUCTION

Carcinoma of the larynx is predominantly a local/regional disease and the primary treatment is consequently directed towards achieving loco regional control. Most of the patients with carcinoma of the larynx in Poland have been treated in advanced stages of the disease. It requires a surgical operation and postoperative irradiation. The radiotherapy after surgery is essential to prevent any recurrence of the disease [Fletcher, 1977]. During such treatment gaps occur mainly due to acute irradiation reaction of mucosa. Mucositis is extremely uncomfortable for the patient and may limit oral intake. At present, there are no satisfactory medications for local treatment of oral mucositis. Other causes of treatment interruptions are: public holidays, machine breakdowns, intercurrent diseases. Reactions which occur during gaps affect not only at local area treated (irradiation volume), but also general affect (a loss of weight, psychological disorder immunodeficiency). It has an undoubted influence on the outcome of treatment. Prolongation of treatment due to a gap in irradiation favours to diminish acute irradiation reaction [Acht et al, 1989].

In literature we can examine many papers about the prolongation of irradiation on the outcome of treatment when only radiotherapy was performed [Barton et al, 1992; Maciejewski et al, 1983; Overgaard et al, 1988; Putten et al, 1994; Skladowski et al, 1994].

There are a lack of well proven works concerning the influence of a gap in postoperative radiotherapy. For this reason we have made our own investigation on patients after total laryngectomy due to cancer of the larynx.

MATERIALS AND METHODS

The aim of our work was to evaluate any differences in the outcome of treatment caused by gap in postoperative radiotherapy patients after total laryngectomy. The retrospective analysis was performed on 311 patients who were irradiated between January 1986 and December 1990 in Wielkopolskie Centrum Onkologii in Poznań. All surgical procedures were performed in a uniform method (school). Criteria for inclusion in this study were as follow:

- no distant metastasi,
 - histologically proven squamous cell carcinoma,
 - macroscopic radical surgery,
 - performance status in Karnofsky scale over 70,
 - complete documentation of treatment, follow up and blood count.
- The qualification for the postoperative radiotherapy treatment was based on the following rules
- invasive cancer at margin in pathology examination,
 - cervical lymph nodes metastases (N1-N3),

-extension of the primary tumour (T3-T4). All patients were treated with orthovoltage radiotherapy (250 kV X-ray). For all cases the dose was calculated at midline. Daily fractionation was 200 R per day, five fractions per week to total dose 6000R. The spinal cord was excluded at 4500R from the treatment field. The two lateral opposite treatment fields comprised the tumour bed after total laryngectomy with margins and cervical lymph nodes. The average, planning time of treatment was about 6 weeks. Time of follow up examination was from 3 to 8 years. During treatment there were observed gaps in irradiation, which were defined as any days without irradiation with exclusion of week-ends. The analysed data was divided, in order of dependence according to the length of the gap, into the following groups: - A without gap, B with a gap up to 7 days and C with a gap over 7 days. The duration of the gap during irradiation is presented in general terms. All patients without gaps (group A) were taken as the control group. The analysed group 311 patients consisted of 290 (93%) men and 21 (7%) women. The patients ranged in age from 35 to 70 years, with a median of 55,9 years. The estimation of the extent of the disease was based on the TNM system according to the UICC-Geneva 1987. In 115 (37%) patients it was noted as the IV stage of disease and in 137 (44%) patients pathological examination indicated metastases to the regional lymph nodes. The group of patients without gap in irradiation numbered 160 (52%). There occurred gaps in 151 (48%) cases.

During course of treatment it was confirmed there had been only one gap. The gaps due to acute mucositis were observed in 94 (30%) patients. It was the biggest group of the patients with a gap in treatment. Practically all patients who undergo radiotherapy to the head and neck develop acute oropharyngeal reactions. Mucositis is the result of atrophic changes in the epithelium because of decreased cell renewal and usually is seen at a dose level of 2000 cGy, when radiotherapy is given at a rate of 200 cGy per day. Others causes of gaps were: public holidays (11%), breakdown of machines (2,5%), intercurrent diseases (4%) and problems with transport (0,5%). Failure in treatment was defined as any local recurrence in the bed tumour, metastases to the lymph nodes of neck or death due to cancer of the larynx.

RESULTS

A significant effect of gap on local control was found in this a retrospective review of 311 patients postoperative irradiated. It was calculated that prolongation of the gap in irradiation resulted in an increased chance of failure in treatment. This correlation was very strong ($p < 0,001$). In group A (without gap) failure occurred in only 48% of patients, in group B (with short gap) in 62% of patients, and in group C (with long gap) in 78% of patients. It means that the increase of failure in irradiation between group A and group C was about 30 % (Table 1).

Table I. The results of treatment in groups A, B and C

Group	Patients with		total
	complete remission	failure	
A	83 (51,9%)	77 (48,1%)	160 (100,0%)
B	36 (38,3%)	58 (61,7%)	94 (100,0%)
C	12 (21,1%)	45 (78,9%)	57 (100,0%)
total	131 (42,1%)	180 (57,9%)	311 (100,0%)

DISCUSSION

Postoperative radiotherapy is an important factor in the treatment of patients with advanced carcinoma of the larynx. We are still searching for the most effective method of irradiation which also results in minimal side effects. For this reason the differing fractionation of the daily dose, the total dose and the treatment volume is

worth considerable further investigation [Trott and Kummermehr, 1985]. Radiotherapy in Wielkopolskie Centrum Onkologii in Poznan, the patients after total laryngectomy due to cancer of the larynx were postoperative irradiated with the orthovoltage radiotherapy 250 kV X-ray. The evaluation of the influence of the length of any

gap on the outcome was made. For this purpose group A (no gap) was taken as the reference group. Patients with a gap in treatment were divided according to the length of the gap into two groups: B- with short gap- up to 7 days, C- with long gap- over 7 days. There were no statistical differences in age, stage of the tumour and nodes, between groups A, B and C. The analysis of this work showed that any prolongation of the gap (treatment time) during postoperative irradiation resulted in a decrease in the effectiveness of the treatment. These observations are convergence with data from others works [Amdur et al, 1991; Arriagada et al, 1983; Zelewsky et al, 1992]. The increase in the failure of treatment in group C, with a long gap was about 30%. The same results were noted in many investigations of irradiation without previous surgery [Maciejewski et al, 1992; Overgaard et al, 1988; Putten et al, 1994; Skladowski et al, 1994]. From clinical and experimental investigations we can conclude that the lengthening of any gap in irradiation treatment allows to influence the greater accelerated repopulation of clonogenic cells of tumour. According to many data concerning the radiotherapy of the head and neck carcinoma, the prolongation of the treatment beyond 35-40 days caused an increase in failure [Maciejewski et al, 1992; Putten et al, 1994; Trott and Kummermehr, 1985]. The disadvantageous influence of the gap in the postoperative radiotherapy is probably due to that after surgery some tumour cells are left in the loco regional area. It is known that the greater the advance of the disease the less effective, surgical intervention is. During gaps in irradiation the accelerated repopulation of the clonogenic tumour cells which were left causes faster regrowth. Clinical data on larynx cancer suggested that in some human carcinomas repopulation rates are similar to the potential doubling rate. Between the 3rd and 7th week of conventional radiotherapy of head and neck cancers, an average 0,5 to 0,7 Gy are lost per day by repopulation [Maciejewski et al, 1992; Overgaard et al, 1988; Skladowski et al, 1994]. As this represents an average value, repopulation may be even more efficient in subgroups of faster tumours. Further irradiation has to take into consideration an increment in the number of tumour cells which have occurred during the gap. The interesting question is: why the gap in the postoperative radiotherapy has the same influence on the outcome like in an alone irradiation? The answer is probably simple: because only the one clonogenic tumour

cell is sufficient to give the recurrence in the tumour bed or in regional nodes. Time in this case for disclosing of the clinical recurrence is much longer, but the effect is the same - the failure. In conclusion, the study has shown that parameter such gap during postoperative radiotherapy strongly influences the success of treatment for laryngeal carcinoma. Future studies aiming at a better characterisation of the prognostic parameters are therefore strongly recommended.

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