

RESEARCH ARTICLE



Frequency and Relationship between Changes in Some Blood Factors and Acute Radiation-induced Skin Complications among Head and Neck Cancer Patients in Sanandaj in 2017 ”

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Abstract

Background: Head and neck cancers account for 2 to 5% of body cancers and radiotherapy is one of the treatments for these conditions. Destroying cancer cells without damaging healthy cells around the tumor is very difficult. Cancer cells eventually die after repeated injuries by radiation in various treatment sessions, but unlike cancer cells, repair and replacement of normal cells happens between treatment sessions. In these patients, the most important complications are skin and blood complications. The occurrence of these complications may cause interruption of treatment by physicians' order or patients' request. Discontinuation of treatment may result in disturbance of tumor cells destruction that is the main purpose of radiotherapy. The high prevalence of head and neck cancer that are candidate for radiotherapy, and the increase use of electron beam therapy have made the occurrence of acute skin reactions and reduction of blood factors inevitable. In this cross-sectional study, we evaluated 60 patients include 22 female and 38 male patients who underwent neck and head radiotherapy from March 2017 to March 2018 in Sanandaj, west of Iran. For this purpose, by assessing the weekly blood tests, we evaluated blood cells changes. The rate and intensity of acute skin complications were recorded according to the RTOG (radiation therapy oncology group) scoring system. Then, the collected data were entered into SPSS version 20 and ANOVA test was used for analysis. P-value<0.05 was considered statistically significant. **Results:** The evaluation of 60 patients' tests revealed that blood factor changes happen during radiotherapy. Mitotic catastrophes occur in blood cells and bone marrow suppression happens concurrently and without replacement. Regarding the radiation-induced skin complication, there is not a notable complication in the first weeks (first and second weeks), but from the late third week, these complications begin to manifest and continue to the tenth week, then the intensity mitigate and acute complications recover and became mild. In this study, the intensity of complications depends on the total and fractional delivery schedule doses. **Conclusion:** skin complications and blood factor changes occur during radiotherapy frequently. The changes of different blood factors are not the same and some of them can undergo decrease whereas increment happens in others.

Keywords: skin complications, blood cells, radiotherapy, head, and neck cancer

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1 | BACKGROUND:

Head and neck cancer account for 2 to 5 percent of all body cancers and include cancers in the upper gastrointestinal (GI) and respiratory system. For example, paranasal sinuses, nasal and oral cavity, oropharynx, hypopharynx, larynx, and upper esophagus. Radiotherapy is an integral part of therapy for cancer patients that is used alone or in combination with other therapies like surgery or chemotherapy. Half of the cancer patients, experience radiotherapy as a part of their treatment. The effect of radiation on normal cells causes the complications of radiotherapy. [1] Cancerous and normal cells react differently to radiation, but eradicating cancerous cells without damaging normal cells around the tumor is very difficult. The damages of repeated radiation would kill the cancerous cells eventually but recovery and replacement of normal cells, unlike cancerous cells; occur between therapeutic sessions.[2] Although cancer patients do not feel any of these intracellular changes, the radiation effects on cancerous and normal cells would increase gradually that can even cause cessation of the treatment.[3] The intensity of the skin complications correlates with different factors like total radiation dose, technique, and place, the volume of irradiated tissue, chemotherapy, chronic disease, dose parameters, time, and fractional doses.[4] Different scoring systems are used for determining the extent of radiation-induced skin complications (RISC). Scoring skin complications according to clinical manifestation and patient's expression is classified into 4-5 grades. These complications vary from mild erythema to dry desquamation and moist desquamation. [5] The high prevalence of head and neck cancer candidates for radiotherapy, and using low depth electrons are inevitable reasons for acute skin complications. The occurrence of these complications may persuade physicians or patients to cease the treatment. The cessation of treatment may disturb the destruction of the tumor that is the main purpose of radiotherapy. [6]

Bone marrow cells are the main hematogenous tissue in the body are the most sensitive tissue against radiation. Pelvis and vertebra bones account for about 60% of blood-producing tissues, and ribs, skull,

sternum, scapula, proximal femur, and humerus bone account for the 40% remaining. Damaging the hematogenous tissues reduces blood cells number and changes the hemoglobin and hematocrit. [7] Different blood cells have a different sensitivity to radiation, and the first lymphopenia, then granulopenia, thrombocytopenia, and anemia lastly occur. The extent of damages depends on different factors like the amount of received radiation, radiation time, the number of sessions, and the volume of irradiated tissue. [8] The level of hemoglobin and white blood cells can affect the response to radiotherapy, radiotherapy in patients with a high level of hemoglobin and hematocrits is more effective in comparison to patients with anemia. [9]

The high prevalence of acute skin complications and utilizing low depth electrons, reduction of blood cells and RISC is inevitable that cause cessation of treatment. This cessation may disturb the eradicating of the tumor that is the main purpose of radiotherapy. [2] Given the acute skin complications and reduction of blood cells caused by radiotherapy that affect the treatment and patient's quality of life, the present study aimed at evaluating the frequency and relationship between these complications among head and neck cancer patients.

2 | METHODS:

in this cross-sectional study, 67 patients include 42 male and 25 female patients were study from March 2017 to March 2018. This study was conducted on patients who underwent radiotherapy on the head and neck. For this purpose, by evaluating the patients' blood test, blood cell changes were identified. For each patient, the blood cell test was performed and recorded in the patients' files during therapy. The

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extent and intensity of the acute skin complications were scored according to the RTOG system. This evaluation started from the first day and up to the thirteenth week of treatment. Finally, after analyzing the data, the frequency and intensity of complications were evaluated. For evaluating blood cell changes, blood cell counting was performed before, during, and up to the end of radiotherapy using formula. In this evaluation, in addition to red blood cells (RBC), white blood cell (WBC), platelet, and hemoglobin, partial and complete lymphocytes and neutrophils were evaluated too. This evaluation was performed for all the weekly tests. Other information like demographic information, cancer type, treatment type and place, dose, the number of sessions, and duration of treatment were recorded. Finally, the SPSS version 20 was used for analyzing obtained data; an independent t-test was used for analyzing descriptive data. P-value<0.5 was considered statistically significant.

Ethical consideration :

The study protocol was approved and funded by Kurdistan University of Medical Science. Written informed consent for participation was obtained from each participant after full disclosure of the aim of the study.

3 | RESULTS:

out of 67 eligible patients, four male patients (Iraqi patients) and three female patients (death during the study) were excluded from the study and 60 cases (38 male and 22 female) remained. The patients' ages range from 24 to 85 years with a median of 57 years. Treatment period range from 29 to 64 days. The cumulative dose varies from 31.9 to 75.2 Gy (Table 1).

Regarding the cancer type, 46 cases of carcinoma, 4 cases of sarcoma, and 10 cases of lymphoma comprise the patients. Out of this number, 25 patients underwent surgery, and 35 cases did not undergo surgery. Also, 13 patients received chemotherapy before radiotherapy, 47 patients did not receive it, and 31 patients received radiotherapy and chemotherapy concurrently. Radiotherapy type was on fraction schedule and the daily doses were 180, 180-200,

and 200 cGy for 30,20, and 10 cases respectively. The skin complications were evaluated according to the RTOG system weekly for 13 weeks (table 2). Most of the skin complications in these patients were observed in grades two and three (figure 1, table2).

Patients' blood cells including leukocytes, erythrocytes, platelets, neutrophils, and lymphocytes before and after treatment were measured based on the Pearson correlation coefficient. According to this analysis, there was a significant relationship between these blood factor changes and radiotherapy (table3). In the first week, the number of white blood cells decreased, which stimulated the bone marrow, and in the second week, the number of lymphocytes increased, but in the third and fourth weeks, it decreased due to bone marrow intense suppression (figure 2). The rate of decrease in red blood cells during treatment was gradual (figure 3). The platelet size was constant in the first and second weeks and decreased in the third and fourth weeks due to platelet loss after mitotic death due to radiation (figure 4). Neutrophils increased during irradiation (figure5).

Lymphocytes decreased between the first and second week and remain constant in the third week, and decreased again in the last week (figure 6).

4 | DISCUSSION:

One of the common therapies for head and neck cancers is radiotherapy. In this method, a radiation source (internal or external) is used for irradiation of the tumor-bearing tissues. In radiotherapy, especially the external one, in addition to tumor, the normal cells around the tumor-bearing tissue are irradiated too. Radiation would damage the cells that eventually kill them. The more multipliable, the more sensitive to radiation. [8] Radiation would affect bone marrow that is the hematogenous tissue in the body. Blood cells have different sensitivity to radiation in a way that first lymphocyte, then granulocytes, thrombocytes, and lastly anemia occurs. The cumulative dose, the number of sessions, the dose, and the volume of irradiated tissue are among the factors that influence the blood cell changes.[7] In a study

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entitled the impact of white blood cell count and hemoglobin level on the response to radiotherapy in patients with colorectal cancer “, chiao and colleagues revealed that patients with a high level of WBC and hemoglobin respond better to radiotherapy.[9] In line with our study, Faraji and colleagues reported that the decline of WBC correlates with the cumulative dose of radiation, and the decline of hemoglobin and platelet correlates with the length of the radiation period.[10] The intensity of skin reactions depend on factors like radiation type, therapeutic technique, irradiated tissue position, dose, and period length. According to clinical manifestation and patient’s description, radiation-induced skin reactions are classified into 4 to 5 grades. These complications vary from mild dry desquamation to moist desquamation[5] that may persuade the physician or patient to cease the treatment, and disturb the purposeful therapy.[6] The result of a study conducted by Yungjing Wang on 47 anaplastic thyroid carcinoma patients in 2002 revealed that patients who received higher fractional dose manifest acute dermatitis grade III whilst patients who received palliative care and lower dose did not manifest dermatitis that is in line with our report.[11] The result of another study by Tejpal and colleagues on 264 patients inflicted with advanced squamous cell carcinoma of the head and neck that treated with cisplatin and radiotherapy (CRT) concurrently showed that the mean age was 54 years, and dermatitis grade III (RTOG-3) occurred in 35 percent of patients.[12] In a systemic review by Langendijk and colleagues on the efficacy of radiotherapy and Cetuximab (CRT) on head and neck squamous cell carcinoma patients revealed that skin reactions correlate with radiation dose and therapeutic technique, and response-dose relationship applied for the occurrence of RISC.[13] In this report, we concluded that blood cells undergo changes during therapy. During radiation, the WBC would reduce at the first week that triggers bone marrow that causes lymphocytosis at the second week, but at the third and fourth weeks of radiation, due to suppression of bone marrow, a large reduction of lymphocyte would occur. Regarding RBC, there was a gradual reduction in its number that can be explained by the longer lifespan of a red blood cell. The size of the platelet remained unchanged during

the first and second weeks, but from the third and fourth weeks, it would decline that is due to the destruction of platelets and mitosis death due to radiation. Radiation has a different effect on neutrophils, and a growing trend was observed during therapy. Regarding RISR, no notable complication was noted at the first and second weeks, but gradually from the late third week, the skin complications would start to manifest as dry desquamation and sweat reduction. This trend would continue until the tenth week. The intensity of reactions varies from a mild reaction to moist desquamation and generalized moderate edema, and even wound, bleeding, and necrosis was observed in four patients. From the tenth week on, the intensity of complications decreased, and the acute ones recovered and became mild. In this study, the intensity of complications correlates with the cumulative and fractional scheduled doses.

It worth mentioning that for preventing these complications during radiotherapy, from the first week until the thirteen weeks we evaluate the skin complications and refer patients to dermatologist weekly. Arranging these appointments made some difficulties, especially for patients from other cities that made us exclude foreign patients.

The limitation of our study was the low number of participants. It is recommended to perform this study on a larger number of patients to obtain more accurate results.

5 | CONCLUSION:

Skin complications and blood factor changes are the most frequent complications of radiotherapy. Our study revealed the different blood factor changes and its relationship with the stage of the radiotherapy.

Declaration: Ethical approval and consent to participate: this study was approved and funded by deputy of research of Kurdistan university of medical science (IR.MUK.REC.1395/324), the written consent was taken from the patients before participating in the study.

Consent for publication: he written informed consent was obtained from all research participants after a full explanation of the study.

Availability of data and materials: all of the data and materials are available for sharing. **Competing interest:** The authors declare no conflict of interest.

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Authors' contributions: All authors (KA, SHN, KM, MH, JA, NS, FGH, and FE) participated in the design of the study and helped to draft or revise the manuscript. JA, KM and SHN participated in the acquisition of data. FE and NS performed the statistical analyses. KA and FGH profred the final version of the manuscript. All authors have read and approved the final manuscript

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Abbreviations:

RTOG: radiation therapy oncology group

ANOVA: analysis of variance

RISC: radiation-induced skin complications

GI: Gastrointestinal

WBC: white blood cell

CRT: cisplatin and radiotherapy

CGY: centi-gray

6 | REFERENCE

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