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The Effect of I-131 Treatment on Complete Blood Count

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ABSTRACT

Radioactive iodine-131 (RAI) treatment may cause suppression in the bone marrow. In this study, hemoglobin levels, leukocyte, thrombocyte, and lymphocyte counts will be compared before total thyroidectomy and 6 months after RAI treatment. 97 patients (76 females, 21 males) with a diagnosis of well-differentiated thyroid cancer who had undergone total thyroidectomy and received 50-200 mCi RAI treatment were included in the study. Hemoglobin levels, leukocyte, thrombocyte, and lymphocyte counts of the patients in the last month before the treatment and in the sixth month after the treatment were compared retrospectively. When the whole patients were analyzed, hemoglobin levels, leukocyte, thrombocyte, and lymphocyte counts in pretreatment were statistically lower than after-treatment values. While hemoglobin levels of female patients were similar before and after treatment, lymphocyte, thrombocyte, and leukocyte counts were statistically lower before treatment. Hemoglobin levels, leukocyte,and thrombocyte counts were similar before and after treatment, while lymphocytes decreased significantly after RAI treatment. Thyroid cancer patients who received 50-200 mCi RAI treatment after total thyroidectomy, have bone marrow suppression but are still in normal mean value ranges. This mild bone marrow suppression is more prominent in female patients than in male patients.

INTRODUCTION

Thyroid cancer had an increasing incidence in the past 20 years and is the eighth most frequently diagnosed cancer [1]. Thyroid cancers have a longer survival rate compared to other cancer types and generally have well-differentiated histological features [2].

Radioisotopes are used in diagnosis and treatment. Scintigraphies with radioisotopes such as Technetium-99m (^{99m}Tc), Iodine-131 (^{131}I), Iodine-123 (^{123}I), and positron emission tomography/computed tomography imaging with radioisotopes such as Fluorine-18 (^{18}F) and Galium-68 (^{68}Ga) are the most commonly used radioisotopes in diagnosis. Lutetium-177 (^{177}Lu) is used in the treatment of prostate cancer, and ^{131}I is used in thyroid diseases. Radioactive iodine (RAI) is frequently used in hyperthyroidism and well-differentiated thyroid cancers [3]. RAI therapy has been used in the treatment of thyroid gland diseases since the 1940s [4]. The treatment of RAIprovides a unique opportunity in the treatment of well-differentiated thyroid cancers due to the high iodine-retaining properties of thyroid follicle cells.

The most common malignancy of the thyroid gland is differentiated thyroid cancer (DTC). DTC derived from follicular cells of the thyroid gland has an excellent prognosis after treatment [2]. RAI therapy is used for the ablation of the remaining thyroid tissue after surgery in DTC and for the treatment of the remaining malignant tissues and metastases of DTC [5]. RAI therapy can be repeated, especially for metastatic patients. Side effects of RAI therapy may occur after RAI treatment. Although the most common side effect is decreased saliva production, it is not usually a serious problem. Rare side effects may occur in the lacrimal glands, bone marrow, lungs, and reproductive organs [3,6-8].

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A complete blood count is a blood test that evaluates many parameters, such as the hemoglobin level, leukocyte, lymphocyte, and thrombocyte counts of the patients. The decrease in these parameters has effects on the patients,such as their susceptibility to infection or bleeding, cardiac,and metabolic disorders [9]. RAI may decrease these blood parameters by causing bone marrow suppression.

In this study, hemoglobin levels, leukocyte, lymphocyte, and thrombocyte counts of the patients who were diagnosed with well-differentiated thyroid cancer and given RAI treatment were compared before total thyroidectomy and 6 months after RAI treatment to evaluate the effect of RAI on bone marrow suppression.

METHODOLOGY

Patients who received RAI treatment with a diagnosis of well-differentiated thyroid cancer were included. The study was initiated after approval from the local ethics committee. 97 patients (21 male, 76 female) who received RAI treatment between 2013-2020 and whose complete blood counts were checked just before total thyroidectomy and in the 6th month after the treatment were included. All 97 patients were diagnosed with well-differentiated thyroid cancer and had a total thyroidectomy. Patients included in the study received a single dose of RAI treatment. In the case of more than one dose of RAI treatment, only the first treatment was taken into account. The mean age of the patients was 43.27±14.04 (min:13-max:79), the mean age of the male patients was 46.08±14.96 years (min:23-max:79), and the mean age of the female patients was 42.42±13.74 years (min:13-max:79).

The mean RAI treatment dose was 123.71±45.12 mCi (min: 50 mCi-max: 200 mCi). A RAI dose of 50 mCi was given to 7 patients, 75 mCi to 7 patients, 100 mCi to 42 patients, 125 mCi to 5 patients, 150 mCi to 18 patients, and 200 mCi to 18 patients.

The mean treatment dose given to female patients was 118.42±43.27 mCi (min: 50 mCi-max: 200 mCi). The mean treatment dose given to male patients was 142.85±47.53 mCi (min: 75 mCi-max: 200 mCi). The dose of RAI treatment depends on the histopathological type and the dissemination of the thyroid cancer. The metastatic disease ratio was higher in male patients, so a mean higher dose was given to male patients.

Hemoglobin levels, leukocyte, thrombocyte, and lymphocyte counts measured in the preoperative period and in the sixth month after RAI treatment were compared retrospectively.

Laboratory analysis

Blood samples were taken from the patients included in the study into hemogram tubes containing EDTA. Hemoglobin, leukocyte, lymphocyte, and platelet levels in the blood samples were studied on Mindray BC 6800 hematology analyzer (Wuhan, China).

Statistical analysis

Hemoglobin level, leukocyte, thrombocyte, and lymphocyte counts in the preoperative period and in the 6th month after RAI were calculated as mean±standard deviation (SD), maximum, and minimum values. A paired t-test was used for comparison of parameters before and after treatment in total patients and only female patients, and the Wilcoxon test was used for male patients. A p-value of <0.05 was considered statistically significant.

RESULTS AND DISCUSSION

The mean hemoglobin levels, leukocyte, platelet, and lymphocyte counts in whole, female, and male patients were shown in Tables 1, 2, and 3, respectively. The decrease in hemoglobin level, leukocyte, platelet, and lymphocyte counts was statistically significant when whole patients were analyzed ($p = 0.044$, $p<0.001$, $p<0.001$, $p<0.001$, respectively), which shows bone marrow suppression in the 6^{th} month after RAI treatment.

The decrease in leukocyte, platelet, and lymphocyte counts was statistically significant, whereas the hemoglobin level was not statistically significant when female patients were analyzed ($p = 0.131$, $p<0.001$, $p<0.001$, $p<0.001$, respectively). The decrease in lymphocyte counts was statistically significant whereas the hemoglobin level, leukocyte, and platelet counts were not statistically significant when male patients were analyzed ($p=0.10$, $p=0.296$, $p = 0.06$, $p = 0.029$, respectively). These results suggested that bone marrow suppression is more prominent in female patients but is still in normal mean value ranges.

Table 1. Preoperative and 6 months after RAI blood parameters of all patients.

	Mean Hemoglobin Level (g/dL) (min-max)	Mean Leukocyte Count (10^3/μL) (min-max)	Mean Thrombocyte Count (10^3/μL) (min-max)	Mean Lymphocyte Count (10^3/μL) (min-max)
Preoperative period	12.90±1.72 (9.60-17.40)	8.38± 2.49 (4.42-17.80)	302.78±87.39 (109-590)	2.36± 0.83 (0.60-4.22)
After RAI treatment	12.65±1.66 (9.10-17.00)	6,94±1,89 (3,27-12,65)	269,15±67,75 (131-471)	1.87±0.64 (0.40-3.65)
p	0.044	<0.001	<0.001	<0.001

Normal reference ranges: Hemoglobin level in females: 11.9-14.8 g/dL, hemoglobin level in males: 13.6-16.9 g/dL, Leukocyte count: 3.8-10.4 10^3/μL, Thrombocyte count: 150-450 10^3/μL, Lymphocyte count: 1-3.2 10^3/μL

Table 2. Preoperative and 6 months after RAI blood parameters of females.

	Mean Hemoglobin Level (g/dL) (min-max)	Mean Leukocyte Count (10^3/μL) (min-max)	Mean Thrombocyte Count (10^3/μL) (min-max)	Mean Lymphocyte Count (10^3/μL) (min-max)
Preoperative period	12.36±1.39 (9.60-15.30)	8.45±2.54 (4.42-17.80)	314,54± 87.92 (109-509)	2.33±0.84 (0.60-4.22)
After RAI treatment	12.16±1.35 (9.10-14.60)	6.78±1.89 (3.27-12.37)	277.58±65.81 (131-471)	1.84±0.64 (0,40-3.44)
p	0.131	<0.001	<0.001	<0.001

Table 3. Preoperative and 6 months after RAI blood parameters of males.

	Mean Hemoglobin Level (g/dL) (min-max)	Mean Leukocyte Count (10^3/μL) (min-max)	Mean Thrombocyte Count (10^3/μL) (min-max)	Mean Lymphocyte Count (10^3/μL) (min-max)
Preoperative period	14.82±1.40 (12.50-17.40)	8,11±2,32 (4,67-12,92)	260.23± 72.40 (154-407)	2.50±0.83 (0.96-3.89)
After RAI treatment	14.41±1.49 (11.70-17.00)	7.53±1.81 (4.57-16.15)	238.67±67.40 (131-367)	2.00±0.63 (0.83-3.65)
p	0.100	0.296	0.06	0.029

Differentiated thyroid cancer is the most common endocrine malignancy, and ^{131}I is used in the treatment of patients. ^{131}I is a cheap and easy treatment method with low side effects. However, bone marrow suppression may occur after RAI treatment [8].

In the current study, we examined the complete blood counts of patients in the preoperative period and 6 months after treatment. Although there was generally a decrease in different parameters in male and female patients, when all patients were evaluated together, a decrease was observed in hemoglobin level, leukocyte, platelet, and lymphocyte numbers at the 6th month that showed bone marrow suppression. But the mean values were still within normal reference values. When female patients were examined separately, a statistically significant decrease was found in other parameters except hemoglobin level. Although the lymphocyte count decreased statistically significantly in male patients, no significant difference was detected in hemoglobin level, leukocyte, or platelet counts. A higher dose of RAI was given to male patients, and more parameters in females decreased after RAI treatment, which may show the sensitivity of females against radiation.

Compared to the literature, a significant decrease in hemoglobin level, leukocyte, and platelet counts in the 6th month was also seen in the study of Bitan et al [10] in the 3rd month. All of the components of white blood cells were not evaluated in the current study, but the decrease in lymphocyte count is similar to the previous studies [8,10]. In another study by Molinaro et al [11], leukocyte and platelet values showed a statistically significant decrease, but no significant change was detected in the hemoglobin level. Despite the decrease in hemoglobin counts in all patients, the hemoglobin decrease was not significant when the genders were separately evaluated in the current study. Tianpeng Hu et al [12] also found an increase in hemoglobin levels compared to baseline in the 6th month after the decrease in the 1st month. The decrease in thrombocyte count is significant in females, but not in males. Tianpeng Hu et al [12] also found that the decrease in platelet count in females was greater than in male patients.

Prinsen et al [13] followed the patients' complete blood counts for 3 months, 5 months, 1, and 5 years after RAI treatment. Posttreatment platelets decreased significantly at 6 months and 1 year compared to baseline. It was found that leukocyte counts decreased between 3 and 6 months and 1 year after treatment, but there was no decrease in hemoglobin level. They showed that posttreatment platelets and leukocytes decreased temporarily compared to pretreatment values, and platelets and leukocytes returned to baseline values 5 years after treatment. However, they concluded that the clinical effects of bone marrow toxicity were limited in most patients. Sönmez et al [14] also followed the hemoglobin, leukocyte, and platelet levels of the patients at the 1st month, 6th month, and 12th month. A significant reduction was observed in hemoglobin, leukocyte, and platelet values 1 month after the ablation treatment. While the platelet count improved in the 6th month, it decreased again in the 1st year. On the other hand, the decrease observed in hemoglobin and leukocyte values in the first month was not observed in the 6th month and 1st year. However, these observed changes were within normal limits, except for patients with low pretreatment values, and they concluded that RAI treatment was a reliable treatment method for patients with thyroid cancer

without causing serious hematological side effects. Both of these studies [13,14] showed mild or limited bone marrow suppression without serious hematological changes, as in our study, because the decreased mean values after RAI treatment were still between the normal reference ranges.

Although the studies are generally compared with the one week before RAI and the 3-12 month period after RAI, in our study, the effect of a high TSH level before RAI on the complete blood count was excluded by looking at the preoperative complete blood count as the baseline. The limitation of our study is that the complete blood count changes over time were not monitored by examining the complete blood count parameters in the earlier period such as the 1st or 3rd month, or later periods, such as the 1st and 2nd year. A complete blood count after the 6th month could tell whether the findings were temporary or not. Although it is known that the patients did not receive additional cytotoxic treatment that could affect the complete blood count until the complete blood count at the 6th month after RAI treatment, as they were monitored in our department, the limitation of our study is that the drugs or supplements used that could affect the complete blood count were not questioned in detail.

CONCLUSION

Though a decrease was observed in different parameters in male and female patients with thyroid cancer who received 50-200 mCi RAI treatment after total thyroidectomy, when all patients were evaluated together, a statistically significant decrease was observed in hemoglobin level, leukocyte, platelet, and lymphocyte numbers at the 6th month. This decrease may differ when evaluated separately by gender. Despite the decrease in the parameters, the mean values were still in normal reference ranges, showing that the bone marrow suppression is mild. A high dose of RAI can be used without severe hematological effects. Male patients had higher doses of RAI, but female patients had significantly reduced parameters, which may be due to the sensitivity of females to radiation, but prospective studies are needed.

While various findings are found in the literature, more comprehensive prospective studies should be conducted on this subject.

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AUTHOR CONTRIBUTION

Gokhan Sahutoglu, Selda Kilic Cetin, and Hasan Ikbal Atilgan participated sufficiently in the design, analysis, interpretation, literature review, and writing. All authors read and approved the final version of the paper.

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