J Bionic Mem 2023; 3(2): 23-28 DOI 10.53545/jbm.2023.26

Journal of Bionic Memory Original article

CRP-lymphocyte ratio as a novel marker of treatment response to hyperthyroidism with radioactive Iodine 131

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ABSTRACT

Aim: To compare CRP/lymphocyte ratio (CLR), a new inflammatory marker, before and after treatment of hyperthyroidism with Radioactive iodine 131 (RAI 131).

Methods: Patients who received RAI 131 treatment for hyperthyroidism in the Department of Nuclear Medicine between January 2020 and May 2023 were included in this retrospective study. Age, gender, WBC, hemoglobin neutrophil, platelet, glucose, AST, ALT and CLR values were compared before and within 1 year of treatment.

Results: There were 59 patients in the current study. 38 were women (64.4%) and 21 were men (33.3%). The mean age was 56.3±15.4 years. There was no statistically significant difference between before and after treatment values of WBC, hemoglobin, neutrophil, platelet, glucose, ALT and AST. However, CLR before treatment (1.74±2.34) was higher than after treatment (1±1.72) and the difference was statistically significant (p=0.048).

Conclusions: CLR, an inflammatory marker, decreased in patients receiving RAI 131 treatment due to hyperthyroidism after treatment. This supports that the presence of an inflammatory burden play an important role in thyroid pathologies. We think that this marker is a simple and useful marker that can be used to monitor the response of CLR to treatment in patients receiving RAI 131 therapy for hyperthyroidism.

Key words: Radioactive Iodine 131, CRP/lymphocyte ratio, hyperthyroidism, inflammation.

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Received: 2023-08-16

Accepted: 2023-08-24 / Published: 2023-09-07

Introduction

Radioactive Iodine 131 therapy which is often referred to as radioiodine therapy or I-131 therapy, is effectively used in the treatment of hyperthyroidism and thyroid cancer. Radioactive iodine 131 is uptaked by thyroid follicle cells. Due to harmful effect of iodine 131 beta ray entering into the cell, it has a limited effect on follicle cells, which is especially active in the thyroid gland. It reduces the functions of follicle cells of the thyroid that produce excessive hormones. Because the effect of beta-ray on thyroid follicle cells remains in a limited area, it does not damage neighboring tissues. With its precision and efficiency, radioactive iodine treatment has revolutionized the approach to thyroid-related medical conditions, offering patients a non-invasive and well-tolerated option for achieving hormonal balance and improved quality of life [1].

The main causes of hyperthyroidism are Graves' disease and toxic multinodular goiter. RAI 131 is an effective, cheap, easily applied

and safe treatment method that has been used for more than 50 years for hyperthyroidism. It is generally preferred in patients over middle age. The risk of complications of RAI is much less than surgical treatments [2].

In the realm of medical diagnostics, the interplay between various blood biomarkers has provided valuable insights into the body's physiological responses to different diseases and conditions. One such intriguing relationship is the C-reactive protein (CRP) to Lymphocyte Count Ratio, a novel metric that has gained attention for its potential as a prognostic indicator and a marker of systemic inflammation. By examining the balance between CRP, an acute-phase protein synthesized in response to inflammation, and the lymphocyte count, a crucial component of the immune system, this ratio offers a comprehensive glimpse into the body's immunologic and inflammatory status. As we delve into the intricacies of the CRP to lymphocyte count ratio (CLR), we will explore its significance in assessing disease severity, predicting outcomes across various medical conditions, and guiding clinical decision-making. This emerging biomarker ratio exemplifies the medical field's continuous pursuit of more nuanced and informative measures, aiming to enhance patient care and refine medical strategies [3,4].

Hence, we aimed to present and compare hematological and biochemical parameters as well as CLR between pre-treatment periods to those in the post-treatment period in hyperthyroid patients receiving RAI 131 treatment.

Materials and methods

A total of 59 patients, 21 men and 38 women, who came to the Nuclear Medicine Department of the Faculty of Medicine Bolu Abant Izzet Baysal University (BAIBU) Training and Research Hospital for Radioactive Iodine 131 treatment of hyperthyroidism between January 2020 and May 2023 were included in our retrospective study. Ethics committee approval was obtained from the local Ethics committee of BAIBU Medical Faculty with the decision dated 20.06.2023 and numbered 2023/207.

Thyroid scintigraphy, thyroid uptake study, thyroid ultrasonography, thyroid function tests and other blood tests of patients who came to our clinic for hyperthyroidism treatment were examined at the Nuclear Medicine Thyroid outpatient clinic and it was decided whether they were suitable for radioactive iodine 131 treatment and the dose of RAI 131 to be given was determined. The time of stopping the patient's antithyroid medications, the necessary precautions and considerations after the iodine-free diet and iodine treatment were explained to the patients. Patients were given an appointment for treatment. On the day of treatment, RAI 131 in oral form was given to patients on an empty stomach. The patients were asked to stay hungry for the next 3 hours. It was recommended that patients to stay away from pregnant women and children for 10 days and to stay as isolated as possible in order to reduce the radiation exposure to the community. The examination and follow-up of the patients were performed before and for 1 year after the treatment. All treatment applications of RAI 131 were made based on the guidelines for the treatment of hyperthyroidism with TNTD, I-131 [5].

Age and gender of the patients, WBC, hemoglobin, neutrophil, platelet, glucose, ALT, AST and CRP/lymphocyte ratio were recorded retrospectively from patient files and records before and after RAI 131 treatment.

Statistical analyses: SPSS software (SPSS version 15 for Windows; IBM, Chicago,

Illinois) was used for statistical analysis. The normality of the data was assessed using the Kolmogorov-Smirnov test. Variables showing normal distribution were expressed as a mean±standard deviation and compared with ANOVA test. Variables not showing normal distribution were expressed as median and interquartile range (IQR) and compared with Kruskal–Wallis test. Paired samples t-test was used to determine whether there is a difference between pre-treatment and post-treatment parameters. Correlation analysis was conducted using Pearson's correlation. A *p* value of less than 0.05 was considered statistically significant.

Results

The mean age of the 59 patients in our study was 56.3±15.4 years, 38 of them were women (64.4%) and 21 of them (33.3) were men. The CLR rate of patients before treatment (1.74±2.34) was higher than after treatment (1±1.72). The decrease in CLR rate after treatment was found to be statistically significant (*p*=0.048).

The WBC, hemoglobin, neutrophil, platelet, glucose, ALT and AST values of the patients before treatment were 7.30±2.03 (k/mm3), 13.85±1.52 (g/dL), 4.14±1.89 (k/mm3), 257±61 (k/mm3), 115±50 (mg/dl), 18±7.42 (U/L), 19±4.70 respectively. While the same were 7.04±2.56(k/mm3), 13.92±3.85(g/dL), 4.29±1.92(k/mm3), 246±79 (k/mm3), 108±35 (mg/dl), 19±10 (U/L), 21±8.32 (U/L) after treatment, respectively.

There were no significant changes in the WBC, hemoglobin, neutrophil, platelet, glucose, ALT and AST values of the patients ($p>0.05$ for all). Comparison of parameters before and after treatment were given in Table1.

Discussion

According to the results of our study, the post-treatment CLR was lower in patients receiving RAI 131 treatment due to hyperthyroidism than before treatment. This situation supports the presence of inflammation at the origin of thyroid disorders such as Graves' disease and Toxic nodules which cause hyperthyroidism. A decrease in CLR after

Table 1. Comparison of parameters before and after treatment.

Parameters	Before treatment (mean ± SD)	After treatment (mean ± SD)	*p* value
CLR rate (%)	1.74±2.34	1±1.72	0,048
WBC (k/mm3)	7.30±2.03	7.04±2.56	0,41
Hemoglobin (g/dL)	13.85±1.52	13.92±3.85	0,9
Neutrophil (k/mm3)	4.14±1.89	4.29±1.92	0,6
Thrombocyte (k/mm3)	257±61	246±79	0.2
Glucose (mg/dl)	115±50	108±35	0,29
ALT (U/L)	18.±7.42	19±10	0,59
AST (U/L)	19±±4.70	21±8.32	0,16

treatment in patients with hyperthyroidism indicates that the inflammatory load is reduced in patients with RAI 131 treatment.

In a study conducted on CRP and lymphocyte counts in heart failure, the authors found that the CLR value increased compared to healthy people [6]. In another study, it was reported that increased CRP and decreased lymphocyte count were associated with intestinal ischemia in patients with incarcerated hernias {7]. In another recent study, it was found that a high CLR rate was an effective marker for determining fibrosis in chronic hepatitis C patients [8]. Therefore, diseases such as intestinal ischemia, heart failure and chronic hepatitis C are associated with an inflammatory burden. Similar to these diseases, we found that the CLR rate was found to be lower in our study after iodine therapy in relation to the inflammation in thyroid pathologies that cause hyperthyroidism.

The relationship between inflammatory conditions and CLR is well-known. In a study investigating the contribution of CLR to the prognosis in patients undergoing esophageal resection due to esophageal cancer, it was determined that CLR is a useful marker for predicting major morbidity at the end of surgery [9]. In a current study, CLR was investigated in patients with pancreatic cancer and it was shown that CLR is more successful than all other prognostic markers in predicting survival [10]. Another study by the same authors also supported that pancreatic cancer, as with other cancers, triggers inflammation so that CLR is a useful marker for predicting survival [11]. Since inflammation is the basis of thyroid disorders that cause hyperthyroidism, a decrease in CLR level was found in patients after treatment in a similar way in our study.

The authors looked at the importance of preoperative CLR in patients with oral squamous cell carcinoma. It was shown that high CRL level, which indicates disease-free survival and poor prognosis, has a superior prognostic value than other inflammatory markers in this patient population [12].

Similarly, a recent study examined the importance of CLR in colorectal cancers and showed that patients with elevated CLR had less survival than patients with diminished CLR [13]. Findings of Mungan and colleagues were consistent with a previous study conducted on colorectal cancers [14]. Moreover, the prognostic importance of high CLR has been reported in lung cancers [15], osteosarcoma [16], and colangiocarcinoma [17].

The fact that our study is retrospective, conducted in a small study population and centered on abandonment constitutes our limitations. Only addition could be the single center nature of the work could be listed as another limitation. In addition, according to our knowledge, this is the first study in the literature investigating CLR in patients receiving RAI 131 treatment for hyperthyroidism.

Conclusion

We think that CLR is a simple and useful marker that can be used to monitor the response to treatment in patients who have been treated with RAI due to hyperthyroidism. Our study should be supported by prospective studies involving a larger number of patients.

Funding: *The author(s) received no financial support for the research, authorship, and/or publication of this article.*

Conflict of Interest: *The author(s) declare that they have no conflict of interest.*

Ethical statement: *Ethics committee approval was obtained from the local Ethics committee of BAIBU Medical Faculty with the decision dated 20.06.2023 and numbered 2023/207.*

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