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Analyzing Serum Level Changes in Dehydroepiandrosterone Sulfate, Dihydrotestosterone, Progesterone, and Prolactin after Radioactive Iodine Treatment for Papillary Thyroid Carcinoma

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ABSTRACT

Introduction: Effective treatment of papillary thyroid carcinoma (PTC) is total thyroidectomy which is followed by radioactive iodine therapy (RIT) to ablate pathologic thyroid remnants and treat metastatic tumors. However, there are concerns about possible side effects of RIT on different hormones that are important in different aspects including the immune defense system, cardiovascular system, pregnancy, and reproductive health. This study aimed to assess the impact of RIT on reliable hormonal markers levels including dehydroepiandrosterone sulfate (DHEA-S) and dihydrotestosterone (DHT) in men as well as progesterone and prolactin in women undergoing treatment for PTC.

Material and Methods: 60 patients (30 male and 30 female) who underwent total thyroidectomy due to PTC and aged 25-50 were selected using convenient sampling. Blood samples were collected from each PTC patient before and 60 days after RIT. DHEA-S, DHT, progesterone, and prolactin concentrations were quantified using an enzyme-linked immunosorbent assay kit. The paired t-test was conducted to compare hormonal marker levels before and after RIT.

Results: Our data revealed significant decreases in DHEA-S and DHT levels between pre- and post-RIT ($P< 0.001$). In contrast, progesterone and prolactin levels increased significantly after RIT ($P< 0.001$).

Conclusion: The levels of DHEA-S, DHT, progesterone, and prolactin, which reflect testicular and ovarian reserves, were found to change after RIT. The levels of DHEA-S, DHT, progesterone, and prolactin, which reflect testicular and ovarian reserves, were found to change 60 days after RIT. Despite its benefits in treating PTC, RIT can have serious adverse effects including changes in the serum levels of sexual hormones.

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Introduction

The incidence of thyroid cancer, the most common endocrine system malignancy, has been rapidly rising in recent years [1]. Effective treatment of papillary thyroid carcinoma (PTC) is total thyroidectomy which is followed by radioactive iodine therapy (RIT) to ablate pathologic thyroid remnants and treat metastatic tumors [2, 3]. However, there are concerns about possible side effects of RIT on different hormones that are important in different aspects including the immune defense system, cardiovascular system, pregnancy, and reproductive health. For example, during RIT, the gonads, which play a major role in pregnancy, may be exposed to radiation due to their proximity to the urinary bladder and the bowels [4, 5]. Different hormonal markers including anti-mullerian hormone (AMH), follicle-stimulating hormone (FSH), dehydroepiandrosterone sulfate (DHEA-S), dihydrotestosterone (DHT), progesterone, and prolactin can be reliable markers to assess the side effects of radioactive iodine on different aspects of health, especially reproductive health [6-9]. DHEA-S acts as a metabolic intermediate in androgen and estrogen formation [10]. DHEA-S reduction can cause a reduction in the androgen pool, thus leading to a decrease in general well-being, libido, mood, and motivation [11]. DHT, a potent androgen receptor ligand, plays an important role in hair loss, adipose tissue, muscle mass, central nervous system, bone, liver, prostate growth, fertility, spermatogenesis, and virilization [12-14]. Progesterone is a central modulator of successful female reproductive functions [15]. It plays a crucial role in the preparation for lactation and breastfeeding [16]. However, there is a possible relationship between high progesterone levels and breast cancer risk [17]. Prolactin is a type of peptide hormone that is associated with various reproductive disorders that can ultimately lead to infertility when its levels increase [18-20]. Considering the above-mentioned data, this study aimed to assess the impact of RIT on levels of DHEA-S

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and DHT in men and progesterone and prolactin levels in women receiving papillary thyroid carcinoma (PTC) treatment.

Materials and Methods

Study Design and Patient Selection

For this study, 60 patients (30 male and 30 female) undergoing total thyroidectomy due to PTC enrolled in this study. Patients who were referred to the nuclear medicine department to receive 150 millicuries of iodine-131 for the first time and aged 25-50 were selected using convenient sampling. The exclusion criteria were interfering with drug consumption or diseases that could affect the ovarian or testicular reserves. All patients signed the informed consent for inclusion before they participated in the study.

Sampling

Ten milliliters of whole blood were collected from each PTC patient before and 60 days after RIT. Serum levels of DHEA-S and DHT in male patients, and progesterone and prolactin in female patients were measured using an enzyme-linked immunosorbent assay kit (CUSABIO, Cosmo Bio, Carlsbad, CA, USA).

Statistical Analysis

To perform all statistical tests, Graph Pad Prism statistical software, version 8.00 (Graph Pad, San Diego, CA, USA) was utilized. The paired t-test was conducted to compare hormonal marker levels before and after RIT. The results are presented as mean ± standard deviation (SD). For all tests, a P-value of <0.05 was considered statistically significant.

Results

Serum levels of DHEA-S before and after RIT were compared. After 60 days of RIT, DHEA-S levels showed a decrease of 63.04 µg/dL from the initial value of 184.18 µg/dL ($P< 0.001$) (Figure 1).

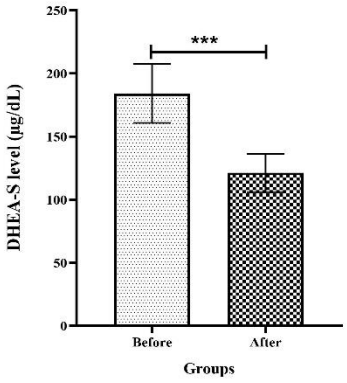

Figure 1. DHEA-S blood levels before and 60 days after RIT.

Changes in the DHT levels are presented in Figure 2, showing a significant decrease from pre- to 60 days post-RIT. The mean of DHT blood levels before RIT was 279.11 ng/dL reduced to 216.10 ng/dL 60 days after RIT ($P< 0.001$). Progesterone blood levels as well as prolactin levels increased significantly after RIT from 0.24 ng/dL to 0.33 ng/dL ($P< 0.001$) and from 14.61 ng/mL to 16.93 ng/mL ($P< 0.001$), respectively (Figures 3 and 4).

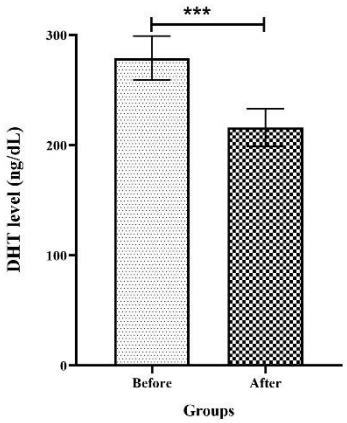

Figure 2. DHT blood levels before and after RIT.

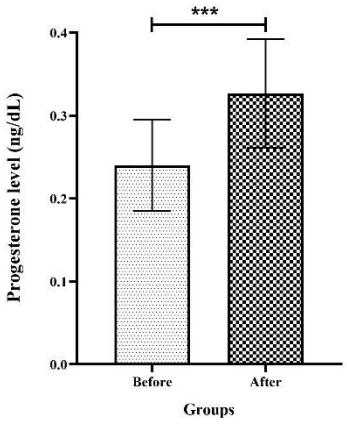

Figure 3. Progesterone blood levels before and after RIT.

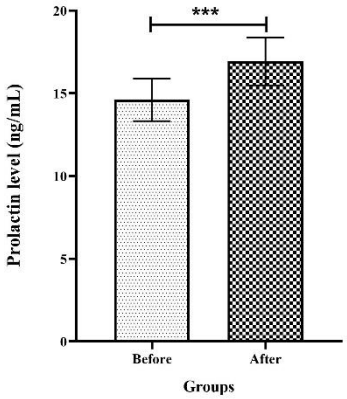

Figure 4. Prolactin blood levels before and after RIT.

Discussion

One of the important factors in the success of RIT is the meticulous planning and precision provided by proficient medical physicists who play a crucial role in optimizing treatment outcomes [21]. However, to ensure a favorable therapeutic outcome while minimizing potential side effects and enhancing the overall quality

of life for patients undergoing RIT, it is essential to have a comprehensive understanding of its impact on hormonal markers in both males and females. In the present study, the impact of RIT on DHEA-S, DHT, progesterone, and prolactin blood levels was evaluated in patients undergoing treatment for PTC. Different studies have been done to estimate the effects of RIT on different hormonal markers; however, they did not evaluate the levels of the mentioned hormonal markers as we did. According to Yaish et al., AMH levels significantly decreased 3 months after RIT [22]. In a study by Evranos et al., AMH levels reduced after RIT, stabilizing after 3 months. Additionally, they showed that there is no relationship between RIT and alterations in AMH levels [5]. Rezaeyan et al., have found that γ-irradiation decreased superoxide dismutase (SOD) and Glutathione (GSH) levels and increased the levels of malondialdehyde (MDA) significantly [23]. Aymond et al., have indicated elevated serum gonadotropin levels and temporary amenorrhea during the first year after RIT [24]. In a study by Eftekhari et al., evaluating the effects of RIT on gonadal function, FSH values increased significantly in both men and women after RIT and sperm count decreased significantly from 124000000 to 62000000 [25]. Wichers et al., have indicated that 3 and 6 months after radioiodine therapy FSH, luteinizing hormone (LH), and testosterone levels are elevated and inhibin B levels decreased significantly. However, there was a recovery in gonadal function levels 18 months after RIT [26].

Our results showed that DHEA-S levels decreased 60 days after RIT. Low levels of DHEA-S can have different side effects. Researchers have reported that low levels of DHEA-S can increase the risk of diabetes, cardiovascular disease, insulin resistance, obesity, reduction of the immune defense system, impaired glucose tolerance, and fracture risk in women [27-29].

We observed lower serum levels of DHT 60 days after RIT. It has been well documented that DHT levels play a significant role in health status. Joyce et al., have reported that there is an inverse relationship between DHT levels and the risk of insulin resistance and diabetes [30]. Yeap et al, have found a clear relationship between higher DHT levels and lower ischemic heart disease mortality [31].

Regarding progesterone, it had an increase after RIT. Despite the advantages that progesterone has in fertilization and pregnancy, high levels of progesterone can lead to negative mood symptoms including stress, depression, and anxiety, and can also increase the risk of breast cancer [17, 32].

The findings also indicated that prolactin levels increased after RIT. Prolactin level imbalances can cause adverse impacts on the menstrual cycle [33]. In females, high levels of prolactin lead to amenorrhea, infertility, and galactorrhea [34]. Too much prolactin in males results in a reduction in libido and headaches [33]. Although low levels of prolactin are essential for progesterone production, high levels of prolactin can inhibit progesterone production [35].

Conclusion

The present study, conducted as a prospective pilot study, aimed to investigate the specific impacts of RIT on patients undergoing treatment for PTC. The levels of DHEA-S, DHT, progesterone, and prolactin, which reflect testicular and ovarian reserves, were found to change after RIT. These changes appeared to be irreversible after 60 days of RIT. However, despite these changes, due to limitations and a lack of long-term follow-up, we cannot speculate about the aforementioned side effects. To determine whether these changes are permanent or temporary, further research with a larger sample size and longer follow-up is required. Considering the findings of this study and similar studies, medical physicists must employ their knowledge in treatment planning, dosimetry, and quality assurance to ensure that patients receive safe, accurate, and personalized RIT. Accurate treatment planning plays a crucial role in achieving favorable treatment outcomes and reducing the potential for adverse effects.

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