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## Changes in Serum Alkaline Phosphatase, Calcium, and Parathyroid Hormone with Different Doses of Iodine Therapy

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### Abstract

**Background:** Despite the benefits of radioactive iodine (RAI) therapy as an adjunctive treatment for thyroid cancer, it can be associated with several side effects. The main purpose of this study was to determine the changes in serum alkaline phosphatase (ALP), calcium (Ca), and parathyroid hormone (PTH) at different doses of RAI therapy among patients who were referred to the nuclear medicine department of Namazi Hospital, Shiraz. **Materials and Methods:** This cross-sectional study was conducted on 60 patients with papillary thyroid cancer who underwent RAI therapy at different doses of 100, 150, and 200 mCi. The ALP, Ca, and PTH levels of patients were measured before and 60 days after RAI therapy. **Results:** Our study revealed that RAI therapy at all doses significantly increased ALP level in comparison with baseline amounts ( $P \leq 0.05$ ). However, changes in PTH and Ca levels were not significant among patients who received different doses of RAI ( $P > 0.05$ ). **Conclusion:** RAI therapy could affect important hormones and enzymes such as ALP and PTH. This issue can be considered in diagnostic and therapeutic prescriptions of RAI for the treatment of thyroid cancer.

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**Keywords:** Nuclear Medicine; Thyroid Cancer, Radioactive Iodine; Alkaline Phosphatase; Serum Calcium; Parathyroid Hormone

### Introduction

One of the most important effects of radiation on various organs is their late effects, which occur at different and long intervals after irradiation from low

doses. In such effects, there is a noticeable time interval between exposure and the time of symptoms onset. These effects include an imperceptible reduction in the life span, the emergence of genetic impacts on future generations, and the occurrence of various can-

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cers [1-3]. Cancer affects more than one-third of the population, accounting for more than 20% of all deaths, and it is responsible for more than 10% of total health care costs in developed countries [4]. In 2000, there were 10 million new cases of cancer and 6 million cases of cancer-related deaths worldwide [5]. Each year, approximately 1.5 million people in the United States are diagnosed with some cancers for the first time [6]. According to reports, in 2003, about 556,000 people died related to malignancies, which is equivalent to 1,500 daily deaths, and only deaths caused by cardiovascular diseases are more prevalent than this amount [7]. The most common cancers are prostate, lung, and colon cancers in men, and breast, lung, and colon cancers in women. Lung, breast, prostate, and colon cancers caused more than 50% of cancers diagnosed, as well as cancer deaths in the United States [8-9].

Regarding applications of ionizing radiation, including radiology, nuclear medicine, and computed tomography scans, in addition to the benefits of diagnosing and treating diseases, the risk of radiation should also be considered [10]. Iodine 131 is a radioactive substance widely used to diagnose and treat diseases. The dose of iodine 131 used for the diagnostic cases is 5 millicurie (mCi), but the doses used for therapeutic purposes are much higher (about 20 to 250 mCi) and even more in some cases [11]. One of the major differences between radioactive iodine (RAI) 131 and other radiopharmaceuticals used in nuclear medicine is the confirmed type of radiation, which is a beta type that has a greater practical biological effect than gamma rays [12]. Recently, many studies have been conducted on the extent of biological damage following treatment with RAI. This substance is used to treat thyroid cancers with doses above 100 mCi and in the treatment of hyperthyroidism with lower doses [13-14]. One of the biological effects of beta radiation is chromosomal abnormalities that can be measured in different ways in individuals who have undergone diagnostic or therapeutic studies with RAI [15-16]. One of the indicators of the harmful effects of the medical application of ionizing radiation, including

radioactive substances, is the changes in the levels of enzymes and hormones among patients. The aim of this study was to evaluate the changes in serum alkaline phosphatase (ALP), Calcium (Ca), and parathyroid hormone (PTH) at different doses of RAI therapy in patients with papillary thyroid cancer.

## Materials and Methods

### *Patients*

This cross-sectional study was performed on 60 patients with papillary thyroid cancer who were referred to the RAI therapy division of the nuclear medicine department of Namazi Hospital, Shiraz, Iran, during 2013-2019.

### *Inclusion and Exclusion Criteria*

A definitive diagnosis of papillary thyroid cancer was confirmed by nuclear medicine professors and pathology reports (in cases in which the diagnosis was based on biopsy). Patients with other thyroid pathologies, previous history of radiation, pregnancy, and breastfeeding were excluded from the study.

### *Data Collection*

Baseline characteristics of patients, such as age, sex, weight, height, and body mass index were recorded. The serum levels of Ca, ALP, and PTH before and 60 days after RAI therapy were obtained. Also, the patients were divided into three groups based on received doses of iodine as 100, 150, and 200 mCi. The subjects' demographics and clinical characteristics are reported in Table-1.

### *Ethical Approval*

This study was approved by the Shiraz University of Medical Sciences Institutional Review Board (IR.SUMS.MED.REC.1400.234). The declaration of Helsinki was considered during the study, and written informed consents were obtained from the patients.

### *Data Analysis*

Data analysis was performed using SPSS software (The IBM® SPSS® software), and t-test and chi-squared test were applied. A

P-value of <0.05 was considered statistically significant.

## Results

The mean age of patients was 38 (63.3%) were female.

According to Table-1, the changes in serum ALP level at a dose of 100 mCi were statistically significant (P=0.002) and increased from 287.3±73.09 to 330.1±30.3 U/L. However, there were no significant changes in Ca and PTH levels among patients

who received a dose of 100 mCi (P=0.65 and P=0.88, respectively).

As shown in Table-1, among patients who received doses of 150 and 200 mCi, serum ALP levels were significantly increased after RAI therapy compared to the baseline levels (P=0.001 and P=0.004, respectively). The Ca and PTH levels of patients in groups 150 and 200 mCi were decreased after RAI therapy. However, findings showed Ca and PTH levels were not significantly changed after RAI therapy with doses of 150 and 200 mCi (Table-2).

**Table 1.** Changes in Serum Alkaline Phosphatase (ALP), Parathyroid Hormone (PTH), and Calcium (Ca) Levels before and after Radioactive Iodine (RAI) with Different Doses

Variables	RAI Therapy		P-Value
	Before (mean±SD)	After (mean±SD)	
<b>ALP (U/L)</b>			
100 mCi	287.3±73.09	330.1± 61.3	0.002
150 mCi	247.9±72.79	281.5±68.4	0.001
200 mCi	243.9±57.7	289.1±74.38	0.004
<b>PTH (pg/ml)</b>			
100 mCi	37±13.65	37.2±14.69	0.88
150 mCi	44.7±15.19	41.8±12.39	0.24
200 mCi	39.4±11.16	42.4±13.37	0.2
<b>Ca (mmol/l)</b>			
100 mCi	7.33±0.71	7.29±0.55	0.65
150 mCi	7.68±1.06	7.55±0.86	0.35
200 mCi	7.8±0.92	7.58±0.85	0.31

**ALP:** Alkaline phosphatase; **Ca:** Calcium; **PTH:** Parathyroid hormone; **RAI:** Radioactive iodine

**Table 2.** Changes in Variables before and after RAI with Dose of 100, 150 and 200 mCi for Three Groups of Patients

Variable	Before RAI (mean±SD)	After RAI (mean±SD)	RAI dose (mCi)	<sup>a</sup> P-value
<b>ALP (U/L)</b>	287.3±73.09	330.1±61.3	100	0.002
	247.9±72.79	281.5±68.4	150	0.001
	243.9±57.7	289.1 ±74.38	200	0.004
<b>Ca (mmol/l)</b>	7.33±0.71	7.29±0.55	100	0.65
	7.68±1.06	7.55±0.86	150	0.35
	7.8±0.92	7.58±0.85	200	0.31
<b>PTH (pg/ml)</b>	0.37±13.65	37.2±14.69	100	0.88
	44.7±15.19	41.8±12.39	150	0.24
	11.16±39.4	42.4±13.37	200	0.2

**ALP:** Alkaline phosphatase; **Ca:** Calcium; **PTH:** Parathyroid hormone; **RAI:** Radioactive iodine

<sup>a</sup>Comparison of changes between baseline and follow-up

## Discussion

The results of the present study were in line with the results obtained by Wang *et al.* that evaluated changes in liver enzymes following RAI therapy [17]. Changes in PTH and ALP were mentioned as consequences of RAI therapy [18], while in our study, only changes in ALP level were significant. Guven *et al.* [19] evaluated the effect of a high dose of RAI therapy on the parathyroid function of patients with various types of thyroid cancer. They studied biochemical parameters, such as serum Ca, phosphate, creatinine, ALP, intact PTH (iPTH), and urinary Ca levels [19]. The results indicated no significant changes in serum Ca levels, while the changes in iPTH and ALP levels were significant [19].

Some research indicated that the therapeutic effect of RAI on toxic and non-toxic goiter is based on the fact that it emits strong beta-ionizing radiation, which causes damage to thyrocytes [20]. The maximum range of beta radiation from iodine 131 decay is about 2.4 mm [21]. Hence, the RAI radiation not only affects the tissue of the thyroid gland but also reaches more than 2 mm of its surroundings, and by increasing the radiation dose, its effect also increases [22-24]. Anatomically, it has been shown that the parathyroid glands are located in the vicinity of the posterior thyroid gland in the vicinity of thyrocytes and can therefore penetrate the thyroid gland by beta radiation from iodine 131 [25]. It should be considered whether this type of radiation may lead to parathyroid defects or not. Although various researchers have studied this issue, the available results—mainly based on a limited number of patients—are often contradictory [26-28]. Some authors believe that radiation from the thyroid uptake of iodine 131 causes temporary damage to the parathyroid glands, leading to temporary dysfunction [29]. However, other researchers believe that the same radiation causes parathyroid dysfunction [30, 31]. Also, there are studies that indicated radiation from iodine 131 thyroid uptake might lead to parathyroid

adenoma, as well as cases indicating no evidence regarding the risk of such phenomenon [32]. The results of our study represented a slightly decreased trend in the serum PTH and Ca levels.

In addition, the cause of parathyroid dysfunction in patients with differentiated thyroid cancer (DTC) after RAI therapy is still unknown. It has been reported that a non-targeted effect of ionizing radiation may reduce parathyroid function after RAI therapy, which is called the "bystander effect" in adjacent cells [27]. Guven *et al.* reported that PTH decreased temporarily but generally did not lead to hypocalcemia [13]. However, some studies have shown that RAI therapy does not affect parathyroid function in patients with DTC [28]. Szumowski *et al.* [31] stated that RAI therapy for hyperthyroidism induces transient hyperparathyroidism. They believe that inflammation of the parathyroid glands after radiation may cause excessive release of PTH in parathyroid cells [31]. Also, they found that the higher the dose of thyroid absorption have the greater effect on the parathyroid function [31]. Evidence showed that the dose of RAI therapy was higher for patients with hyperthyroidism than for patients with thyroid cancer [28]. High doses of thyroid absorption in patients with hyperthyroidism may cause transient hyperparathyroidism after RAI treatment [28].

Regarding the stability of serum Ca values, it is worthwhile to mention that the thyroid hormones could increase the absorption and release the Ca from bones; hence, they contribute to a higher concentration of serum Ca [32]. Exogenous thyroxine normalizes levels of the thyroid-stimulating hormone leading to increased Ca and decreased PTH. Thus, the previous authors emphasize the effect of thyroid hormones and PTH on bone metabolism and Ca levels in the body [33]. Meanwhile, our study has indicated that the increase in PTH was not the consequence of the hormonal dysfunction of the thyroid gland. It is noteworthy that serum Ca concentrations were stable, probably related

to high PTH level for a short time and other mechanisms that regulate Ca homeostasis.

### Conclusion

The changes in serum ALP level were significant in all three different doses, and despite the changes in serum Ca and PTH levels, the results were not significant. The changes in PTH and ALP levels may be due to changes in hepatocytes and parathyroid cells due to gamma iodine and radioactive

beta energy. So, antioxidant therapy is recommended before and after RAI therapy.

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### Conflict of Interest

The authors declare that they have no conflict of interest.

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