

## ORIGINAL ARTICLE

# The effect of radioactive iodine therapy on urine sterilization in patients with differentiated thyroid cancer

Atena Aghaee<sup>1</sup>, Pooya Darmani<sup>2</sup>, Ghasemali Divband<sup>1</sup>, Seyed Rasool Zakavi<sup>1</sup>, Susan Shafeie<sup>1</sup>, Abbasali Zeraati<sup>2</sup>, Narjess Ayati<sup>1\*</sup>

\*Nuclear Medicine Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

## ABSTRACT

**Background:** Urinary tract infection is the most common infection which necessitates antibiotics prescription. On the other hand, the appearance of antimicrobial resistance is one of the major health problems due to irrational antibiotic administration. Radio iodine therapy, using I-131 following thyroidectomy, is the standard treatment for the patients with differentiated thyroid cancer (DTC). After the consumption of radioactive iodine, it mainly excretes through the urinary system. This study is aimed to assess the effect of radioactive iodine (I-131) in the eradication of asymptomatic bacteriuria (ABU).

**Methods:** Between September 2015 and May 2017, all the patients with DTC who were hospitalized to Nuclear Medicine Department for radio iodine ablation therapy were enrolled in the study. Urine analysis and culture were done for all the patients before iodine administration. If the result of the urine assessment was positive for the infection, urine culture repeated 1 week later and compare with pre-treatment results.

**Results:** Of 182 patients, 10 cases had abnormal urine culture results. Five patients had CFU under 100,000, therefore was not considered as ABU; however, two of these patients had sterile urine after the treatment. Our only positive case had post treatment sterile urine.

**Conclusion:** Considering radioactive iodine urine excretion, high radiation induced by radioactive iodine that passes through urinary tract may eradicate infection of genitourinary system.

**Keywords:** Radioiodine therapy, Iodine-131, asymptomatic bacteriuria, urinary tract infection, differentiated thyroid cancer.

## INTRODUCTION

Urinary tract infection (UTI) is a common urologic disease, which had been caused more morbidities before discovery and widespread using of antibiotics. Currently, UTI, which includes a wide range of clinical manifestations from asymptomatic bacteriuria (ABU) to pyelonephritis, is one of the most common pathology for which antibiotics are prescribed [1].

The major health problems facing communities now is the emergence of antimicrobial resistance. The World Health Organization's report in 2014 states that there is widespread resistance to various types of infectious diseases [2]. Accordingly, warning the patients and physicians about the side effects and disadvantages of consumption and prescribing unneeded antibiotics, or prescribing herbal medicine [1] in parallel with studying the effect of new materials, such as radioactive iodine on bacteria and the discovery of new methods for treating infectious diseases, are mandatory.

ABU by definition is the presence of at least 100,000 colony formation units per milliliter (CFU/ml) in two different urine specimens that are collected in sterile condition from a patient without

symptoms of UTI [2,3]. The prevalence of ABU is related to factors, such as age, gender, sexual activity, and anatomical abnormalities of the urinary tract. The prevalence of ABU in premenopausal women is reported to be between 1% and 5%, which may reach up to 40% in elder women [3,4].

ABU not only increases the risk of clinical UTI [5], but also makes pregnant women more susceptible to premature delivery and having low birth weight infants [5–9].

Differentiated thyroid cancer (DTC) is the most common endocrine malignancy [10] and its prevalence is approximately 7 per 100,000 individuals per year [11,12]. The incidence of this disease in women is twice than that of men. Radio-iodine therapy 4–6 weeks after the complete removal of the thyroid gland is the main treatment method in DTC patients. Post-thyroidectomy radio-iodine treatment is performed with three goals: thyroid remnant ablation, and thus increasing the sensitivity and specificity of serum thyroglobulin measurements in patient's follow up, destruction of macroscopic and microscopic cancer cells, and the possibility of complete functional imaging of the body following radio-iodine therapy by iodine 131

### Address for correspondence

Narjess Ayati

\*Nuclear Medicine Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.

Email: [ayatin@mums.ac.ir](mailto:ayatin@mums.ac.ir)

Full list of author information is available at the end of the article.

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whole body scan in the selected cases [13]. Evaluating the cumulative amount of radioiodine in urine has shown that 70% of administered radio-iodine is excreted from the urinary system in a period of 48 hours [14] depending upon the administered dose metabolic activity, disease extension, the renal system of the patient, residual tissues of thyroid, thyroid uptake fraction and also liquid intake of patient within first 24 hours. Consequently, the major route of radioactive iodine excretion is urinary system. By accumulation of radioiodine in the bladder, it is exposed to the highest radiation dose among extra-thyroid organs [14]. Therefore, it can be hypothesized that the microorganisms within the bladder could be irradiated at the time of radioiodine therapy as well.

Despite the increasing use of nuclear medicine modalities in both diagnosis and therapeutic fields, no clinical study on the effect of radiopharmaceuticals in elimination of UTI has been done by now. If the effect of radioactive iodine on urine sterilization can be proven, the hypothesis of using radioactive materials in eradication of resistant microorganisms could be proposed.

## MATERIALS AND METHODS

All the female patients with DTC who were referred to Nuclear Medicine Department for radio iodine therapy between September 2015 and May 2017 were enrolled in the study. Urine analysis and culture were done for all the patients before radio-iodine administration. The urine was collected in sterile and specially prepared containers. These specimens were collected from the middle portion of the urine flow and immediately sent to the laboratory for analysis. Samples were cultivated in standard conditions and quantitative analysis was reported, using CFU. Quantitative criteria for definition of ABU was as follows: (1) at least 100,000 bacterial colonies (CFU) per ml of urine in a sample that is not contaminated by the environment and is collected as midstream urinary flow [15] and (2) the minimum of 100 CFU/ml urine, in the urine sample collected using a urinary catheter.

To avoid false negative results, patients were questioned about the consumption of antibiotics in the last 2 weeks. Women were questioned about history of previous UTIs and menstrual status.

The presence or absence of bacteriuria, type of microorganism, and colony count in milliliters of urine were investigated.

Regardless of the result of urinary culture, radio-iodine therapy was performed according to the usual nuclear medicine protocol. In the cases of the positive initial culture, the test was repeated and if the result was positive for UTI again, urine culture was repeated after 1 week of radio-iodine administration and was compared with the pre-iodine samples.

## RESULTS

One hundred and eighty-two women with DTC, who were candidates for radio-iodine therapy from September 2015 to May 2017, underwent complete urine analysis and urine culture before radio-iodine treatment. The mean age of patients was 36.9 years (ranging from 18 to 80 years). Table 1 shows the basic characteristics of the patients.

Urinalysis was reported normal in 172 (94.5%) cases. Ten patients (5.5%) had abnormal urine tests. All these 10 patients had papillary thyroid cancer and their age ranged from 21 to 73 years with an average age of 40.5. Two patients had clinical symptoms of UTI, and thus were treated before performing the second test. One of them, who had been diagnosed with urosepsis, immediately transferred to the Urology Department after radio-iodine therapy. Another

patient who had symptoms, including dysuria and fecal complaints, underwent antibiotic therapy before radio-iodine administration. Radio-iodine therapy was canceled in one patient with positive bacteriuria, according to the physician's decision and because she was categorized as low risk (T1bN0M0) DTC. Another patient with positive bacteriuria did not respond to our calls, so was excluded from the study, as well.

Five patients had bacteriuria with less than 100,000 colony counts, so did not fulfilled the criteria. However, in two of these patients, the urine test was sterilized after radio-iodine therapy. A patient with ABU (positive culture and colony count over a hundred thousand) was re-evaluated after receiving 5,550 MBq radio-iodine ( $I-131$ ), which had a complete normal urine analysis and negative urine culture, thereafter.

Accordingly, definite ABU was completely resolved after radio-iodine therapy in our patient. Table 2 lists the patients who had abnormal urine test prior to radio-iodine therapy, the presence or absence of clinical symptoms and the count of colonization in urine culture.

## DISCUSSION

This study was aimed to evaluate the effect of radio-iodine therapy on ABU in patients who were diagnosed with DTC and underwent radio-iodine therapy.

To the extent of our knowledge, no study has been done in this area, so far. Only the effect of radio-iodine on eradication of *Helicobacter pylori* in the stomach has been studied [16]. In that

**Table 1.** Basic characteristics of the patients.

	Total number	Percent
Total number of patients	182	
Age	36.5 ± 7.5	Na-11
Sex-females	182	100
Type of DTC: papillary thyroid cancer(PTC):	178	97.8
Follicular thyroid cancer (FTC)	2	1.1
Hertle cell carcinoma	1	0.5
Unknown type of cancer	1	0.5

**Table 2.** Grouping patients with abnormal urine test before radio-iodine therapy.

Total number of patients and the percent	Presence of symptoms	Presence of bacteria in urine analysis	Presence of bacteria in urine culture (colony count less than 100,000)
2 (20%)	Yes	Yes	No
3 (30%)	No	Yes	No
2 (20%)	No	Yes	No
3 (30%)	No	Yes	Yes

study, GholamrezaNejad et al. assessed the possible effect of radio-iodine therapy on *H. pylori* in patients with DTC. Among 71 patients, positive for *H. pylori* before starting treatment, 23 had negative UBT after treatment. In other words, 32.4% of the UBT positive subjects, turned to be UBT negative after radio-iodine treatment ( $p < 0.001$ ). However; a significant relationship was not found between the amount of iodine 131 and degree of decrease in UBT values ( $p = 0.2$ ).

In the present study, due to the low prevalence of ABU, a relatively high volume of patients (182 patients) were included. The prevalence of ABU has been reported to be 1%–20% based on previous studies, while in our study, only 3 of 182 patients (1.64%) had positive urine cultures. One of these three patients completed our follow-up process, who did not receive any antibiotics between the two tests, which may suggest the effect of radio-iodine therapy on the eradication of bacteriuria. So far, no study has been done in this area and although the results of this study are not significantly conclusive due to the very low volume of patients detected with ABU, it can serve as a way forward for future studies.

The entrance of radioactive materials into the urinary bladder through a urinary

catheter is commonly performed in patients who referred for vesicoureteral reflux assessment by direct radionuclide cystography. Dosimetric studies show that the radiation burden to the patient is completely negligible, due to the lack of systemic absorption of radioactive material. Of course, this radiation level needs to be further investigated for higher levels of radioactive materials.

Considering the resistance of some species of bacteria to different types of antibiotics and the possibility of serious complications of UTI in high-risk patients, including diabetic ones, and also difficulties in the treatment of antibiotic resistant UTI cases, the results of this study could propose the effect of radio-isotopes on the elimination of infections of the Urinary tract.

The main limitation of our study is the low volume of UTI positive patients, which is due to the low prevalence of ABU in the study population.

As radio-iodine administration was performed in all the cases as a definite therapeutic modality, there was no ethical prohibition of radiation exposure; however, exposing the patient to radioactive materials, solely in order to treat UTI, requires more extensive investigations, and it may be more reasonable and cost-effective to carry out *in vitro* studies first.

## CONCLUSION

Radioactive iodine, with the main excretion from urinary system, may have bacteriocidal effect on the urinary tract microorganisms.

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## List of Abbreviations

CFU	Colony formation unit
DTC	Differentiated thyroid cancer
UTI	Urinary tract infection

## Funding

None.

## Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

## Consent for publication

Written informed consent was taken from the participants.

## Ethical approval

The study was approved by the Ethics Committee, Mashhad University of Medical Sciences via approval code: 940471.

## Author details

Atena Aghaee<sup>1</sup>, Pooya Darmani<sup>2</sup>, Ghasemali Divband<sup>1</sup>, Seyed Rasool Zakavi<sup>1</sup>, Susan Shafeie<sup>1</sup>, Abbasali Zeraati<sup>2</sup>, Narjess Ayati<sup>1</sup>

1. Nuclear Medicine Research Center, Mashhad University of Medical Sciences, Mashhad, Iran
2. Mashhad University of Medical Sciences, Mashhad, Iran

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