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Research Article

Effect of Radioiodine (I^{-131}) to TSH, T₃ and FT₄ Hormone Levels in Hyperthyroidism High Uptake Patients

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Abstract

Background: Thyroid hormones have an important role for the body metabolism. Hyperthyroidism is a condition when thyroid hormone increases due to abnormalities in thyroid gland. Hyperthyroidism is a second largest endocrine disease in Indonesia, some risk factors that aggravate age, gender and smoking. Radioiodine (I^{-131}) is one of the effective therapies for high uptake hyperthyroidism. **Objective:** The purpose of this study is to determine characteristics and therapeutic effect of radioiodine (I^{-131}) to TSH, T₃ and FT₄ hormone levels hyperthyroidism high uptake patients in Nuclear Medicine Department, Dr. Hasan Sadikin Hospital Bandung, Indonesia 2014-2015 periods. **Materials and Methods:** This study was analytic with cross sectional design. Data obtained from 234 hyperthyroid patient's medical records. The data was statistically analyzed with Wilcoxon test. **Results:** The results showed that hyperthyroidism high uptake occurred at young adult and in women patients, hyperthyroid patients had a history of taking antithyroid drugs before radioiodine therapy and radioiodine (I^{-131}) therapeutic dose was mostly given 8 mCi. Hormone level of TSH had increased but T₃, FT₄ had decreased and FT₄ hormone levels before and after therapy has significant difference ($p < 0.005$). **Conclusion:** Radioiodine (I^{-131}) was one of the effective therapies for high uptake hyperthyroidism patients.

Key words: Radioiodine (I^{-131}), therapy, hormone, TSH, T₃, FT₄, hyperthyroid

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Hyperthyroidism is a condition when thyroid hormone production increases as a result of thyroid gland excessive activity. The thyroid glands are the largest endocrine glands in the body and have an important role in metabolism and physiological activity in almost all organ systems of human body. Excess thyroid gland function will increase thyroid hormones production which can affect the body metabolism causing symptoms of hyperthyroidism, such as: Palpitations, sweating, weight loss, anxiety, intolerance to heat and others¹. Hyperthyroidism is a second largest endocrine disease in Indonesia². Some risk factors that aggravate hyperthyroidism are age, gender and smoking. These factors favor of hyperthyroidism by affecting the immune system that causes a Grave's disease³. Grave's disease is an autoimmune disease that is found incidence between the ages of 40 and 60 years old. In addition to age, risk factors that can lead to Grave's disease is gender that more common in women when compared with men. Other risk factors that may affect to thyroid hormone is a history of smoking⁴.

The National Health and Nutrition Examination Survey (NHANES III) to retrieve data from the United States and epidemiological survey in England showed that Grave's disease predominantly in female patients and the prevalence of hyperthyroidism was lower when compared with hypothyroidism. The results showed a prevalence of approximately 1-2% in women. Overall incidence in women was estimated at 1 case per 1000 per year during 20 years of follow-up. The annual incidence of Grave's disease in the world was estimated at about 5 per 10,000 people^{3,4}. In Indonesia, according to health research database (RIKESDAS) in 2013 recorded the prevalence of hyperthyroidism in Indonesia based on interviews diagnosed by a doctor of 0.4%. In West Java for the prevalence of 0.5% was ranked fourth after DI Yogyakarta, Jakarta and East Java². The amounts of patients undergoing radiotherapy were 48 people in January-June, 2014 in Cipto Mangunkusumo National General Hospital Jakarta⁵.

Radioiodine (I^{131}) is one treatment option for hyperthyroidism. Radioiodine (I^{131}) produces thyroid ablation without complications due to surgery and can be performed by several unsuccessful antithyroid drug therapies. Treatment of radioiodine (I^{131}) is effective depends on proper radiation. The method for determining radioiodine (I^{131}) therapeutic dose in patients with hyperthyroidism consists of two methods. The first method is a therapeutic dose can be determined by the thyroid gland weight estimation data obtained from the ultrasound of the thyroid gland, the

second method is a therapeutic dose can be given 10-15 mCi doses⁶. Almost all types hyperthyroid therapy radioiodine (I^{131}) showed high uptake of iodine. The therapy side effects in the form of radiation-induced thyroiditis and worsening of radiation symptoms-induced thyroiditis exophthalmos happen through destroying the thyroid follicular cells structure after patients received radioiodine (I^{131}). Thyroid follicular cells secreted protein globular (thyroglobulin) in the thyroid follicle to form thyroid hormone in human bodies⁷. Exophthalmos symptoms caused by presence of antigen in orbital fibroblasts, eye muscles similar to TSH receptor in thyroid gland tissues⁸. Therefore the result of radioiodine (I^{131}) therapy only in thyroid gland, free thyroid hormones in blood leading to same antigen in eye area which caused exophthalmos⁹. Radioiodine (I^{131}) generated changes thyroid cells molecular by the ray's ionization effect to destroyed hyper functioning thyroid tissue. Therefore, this study aimed to analyze effect of radioiodine (I^{131}) therapy in patients with hyperthyroidism high uptake to thyroid hormones levels.

MATERIALS AND METHODS

This study was conducted at the Department of Nuclear Medicine Dr. Hasan Sadikin Hospital Bandung Indonesia. Research carried out an analytical study with cross-sectional design of hyperthyroid patients medical records undergoing radioiodine (I^{131}) therapy in the Department of Nuclear Medicine Dr. Hasan Sadikin Hospital 2014-2015 periods. Sampling methods was consecutive sampling and obtained 14 samples from 234 samples that meet the criteria. In undertaking this study, performed data collection for age, gender, smoking history, history of antithyroid drugs use and hormone levels of TSH, T3, FT4 in the hyperthyroid high uptake patients who have radioiodine therapy (I^{131}) from the medical record. Data were analyzed by univariate and bivariate analysis. Univariate analysis aimed to describe the characteristics of the study subjects include age, gender, smoking history, history of antithyroid drugs use and therapeutic doses of radioiodine (I^{131}) in hyperthyroidism high uptake patients with shown in the diagrams. The bivariate analysis aimed to compare the levels of hormone TSH, T3 and FT4 before and after radioiodine (I^{131}) therapy. Normality data using the Shapiro-Wilk test and result was not normal to have the Wilcoxon test.

Research ethics aspects: Ethical approval was obtained from the Research Ethics Committee Dr. Hasan Sadikin Hospital (RSHS) Bandung with No. LB.04.01/A05/EC/471/XI/2015.

RESULTS

Hyperthyroidism high uptake patient characteristics in Dr. Hasan Sadikin Hospital 2014-2015 periods: The result showed hyperthyroid patients found mostly early adulthood aged 26-35 years (42.86%). The age distribution of hyperthyroid patients can be seen in Fig. 1.

Hyperthyroid patients found the majorities were women with a number of 10 patients (71.43%) and men with a number of 4 patients (28.57%). Characteristics of hyperthyroid patients by gender in Nuclear Medicine Department Dr. Hasan Sadikin Hospital can be seen in Fig. 2.

Results of study on the characteristics hyperthyroidism patients with smoking history can be seen in Fig. 3. Hyperthyroid high uptake patients in Nuclear Medicine Department Dr. Hasan Sadikin Hospital found had no history of smoking.

Results of study on the characteristics hyperthyroidism patients in antithyroid drug consumption history can be seen in Fig. 4. There were 92.9% hyperthyroid patients who have a history of taking antithyroid drugs.

Radioiodine (I^{131}) therapy dose characteristics of hyperthyroid high uptake patients can be seen in Fig. 5. Based on data obtained therapeutic dose of radioiodine (I^{131}) was a range of 8-10 mCi.

Effect of radioiodine (I^{131}) to hormone levels of TSH, T3 and FT4 hyperthyroidism high uptake patients in Dr. Hasan Sadikin Hospital 2014-2015 periods: This study begins by doing the test data normality using the Shapiro Wilks test for the amount of 50 samples or less on all the variables studied and the results showed that all variables have no

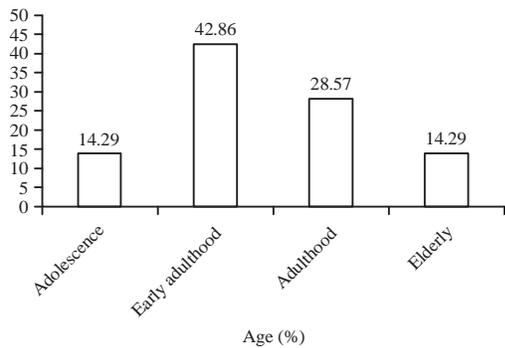


Fig. 1: Age characteristics of hyperthyroidism high uptake patients at Dr. Hasan Sadikin Hospital Bandung Indonesia in 2014-2015 periods

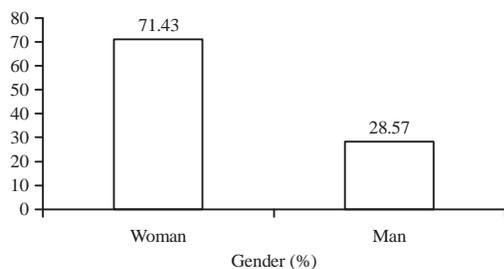


Fig. 2: Gender characteristics of hyperthyroid high uptake patients at Dr. Hasan Sadikin Hospital Bandung Indonesia in 2014-2015 periods

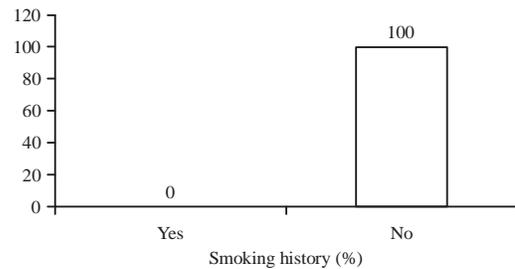


Fig. 3: Smoking history characteristics of hyperthyroid high uptake patients at Dr. Hasan Sadikin Hospital Bandung Indonesia in 2014-2015 periods

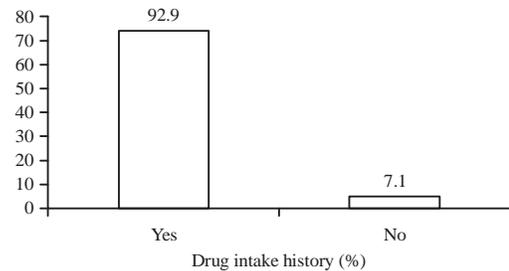


Fig. 4: Antithyroid drug use history characteristics of hyperthyroid high uptake patients at Dr. Hasan Sadikin Hospital Bandung Indonesia in 2014-2015 periods

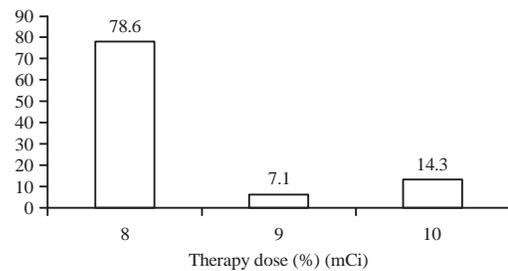


Fig. 5: Radioiodine (I^{131}) therapy dose characteristics of hyperthyroid high uptake patients at Dr. Hasan Sadikin Hospital Bandung Indonesia in 2014-2015 periods

Table 1: Normality test data of TSH, T3 and FT4 hormone levels

Variables	Median	Range	p-value
TSH			
Before	0.003	0.0025-0.332	0.000
After	0.004	0.001-75.68	0.000
T3			
Before	5.32	1.03-9	0.047*
After	1.625	0.25-15.7	0.000
FT4			
Before	3.3	1.01-24.86	0.000
After	1.495	0.4-6	0.016*

Shapiro-wilk test, *p>0.05 significantly

Table 2: Effect of radiiodine (¹³¹I) therapy on TSH, T3 and FT4 hormone levels

Variables	Measurement		p-value
	Before	After	
TSH			
Median	0.114	0.005	0.185
Range	0.0025-0.332	0.001-75.68	
T3			
Median	5.36	1.625	0.084
Range	1.03-9	0.25-15.7	
FT4			
Median	3.3	1.495	0.026*
Range	1.01-24.86	0.4-6	

Wilcoxon test, *p<0.05 significantly

Table 3: TSH and thyroid hormone levels before and after radioiodine therapy (¹³¹I)

Variables	Amount	Percentage
TSH		
TSH after therapy<TSH before therapy	4	28.57
TSH after therapy>TSH before therapy	6	42.86
TSH after therapy = TSH before therapy	4	28.57
Total	14	100.00
T3		
T3 after therapy<T3 before therapy	11	78.57
T3 after therapy>T3 before therapy	3	21.43
T3 after therapy = T3 before therapy	0	0.00
Total	14	100.00
FT4		
FT4 after therapy<T4 before therapy	11	8.57
FT4 after therapy>T4 before therapy	3	21.43
FT4 after therapy = T4 before therapy	0	0.00
Total	14	100.00

normal distribution (p<0.005). Normality test data on the variables studied were presented in Table 1.

Based on the results of the test data normality was found not normal distribution we used nonparametric tests to determine ratio between the levels of hormone TSH and thyroid hormone levels before and after radioiodine therapy (¹³¹I) in patients with hyperthyroidism high uptake by using the Wilcoxon test. Effect of radiiodine (¹³¹I) therapy on TSH, T3 and FT4 hormone levels can be seen in Table 2. The comparison between TSH hormone levels and thyroid hormone levels before and after radioiodine therapy (¹³¹I) were presented in Table 3.

Based on the results of the Wilcoxon test, FT4 hormone levels obtained significance value p = 0.026 (p<0.05), it can be concluded that there were significant differences between FT4 hormone levels before and after radioiodine therapy (¹³¹I), whereas the levels of hormones TSH and T3 significant value p>0.005 there were no significant differences. The results shown in Table 3 that there was an increase in TSH hormone levels after radioiodine therapy (¹³¹I) at 6 hyperthyroid patients, while for T3 and FT4 hormones levels were decreased by 11 patients (78.57%).

DISCUSSION

The prevalence and incidence of thyroid disorders was influenced primarily by sex and age. Thyroid disorders were more common in women than men and in older adults compared with younger age groups¹⁰. The prevalence of unsuspected overt hyperthyroidism and hypothyroidism were both estimated to be 0.6% or less in women, based on several epidemiologic studies. Age was also a factor; for overt hyperthyroidism, the prevalence rate was 1.4% for women aged 60 or older and 0.45% for women aged 40-60 by DeRuiter¹¹.

Hyperthyroid disease in Indonesia mostly occurs in over 45 years with a percentage up to 2%. This can occur due to Thyroid Binding Globulin (TBG) is a molecule that binds T3 and T4 hormone levels decline with age, so it affects thyroid hormone levels circulating in the blood increase. When T4 hormone circulates in bloodstream and amount of hormone is excessive, it will cause hyperthyroidism symptoms such as weight loss, excessive sweating, fatigue, defecation frequency increased, tremor and others, whereas in early adulthood can also affect the thyroid gland due to early adulthood are of reproductive age so that levels of the hormone estrogen is high. Estrogen is thought to be one factor in the onset of an autoimmune reaction that causes Grave's disease^{4,12}.

Women have a higher risk of hyperthyroid disease compared to men due to their gender steroids, namely estrogen dominant in women. Estrogen is thought to be one factor in the onset of an autoimmune reaction that causes an increase in thyroid hormone levels TSI. The TSI is an IgG that bind to TSH hormone. Increased TSI hormone levels causes increased release of thyroid hormones that were affected by TSH hormone. The condition is called Grave's disease which one cause of hyperthyroidism high uptake most circumstances⁴.

The result of this study showed that all hyperthyroid patients had no history of smoking. Smoking is one risk factor for disorders of the thyroid substances contained in cigarettes one of which can cause increased thyroglobulin and

slightly decreasing levels of TSH¹³. Thiocyanate in cigarettes can lead to increased levels of thyroid hormone, causing hyperthyroidism circumstances. In addition, smoking can cause inflammation that increases the risk of thyroid disorders¹⁴.

Based on Fig. 4 there were 13 hyperthyroid patients who have a history of taking antithyroid drugs with a percentage of 92.9% and as much as 1 hyperthyroid patient that there was no history of use of antithyroid drugs with a percentage of 7.1%. Hyperthyroid patients at Dr. Hasan Sadikin Hospital mostly been taking antithyroid drugs before radioiodine therapy (I^{131}) due largely refer patients. Antithyroid drugs were drugs known as thionamide (methimazole, propylthiouracil and Carbimazole). Antithyroid drugs given to inhibit thyroid hormone synthesis and inhibit conversion of T4 hormone to T3 hormone become more active^{6,8}. Antithyroid drug delivery was needed to reduce the risk of thyroid crisis and in patients who will perform thyroidectomy and radioiodine because prior to these therapies thyroid must be in a euthyroid state, but methimazole was recommended because propylthiouracil has an effect on radioactivity which can reduce the effectiveness of the therapeutic radioiodine (I^{131})¹.

Therapeutic dose of the most widely used was 8 mCi with (78.6%). There were two methods for calculating the dosage of radioiodine therapy (I^{131}). The first method required the thyroid gland weight estimation data obtained from the ultrasound of the thyroid gland. As for the fractional radioiodine uptake was 10-30% in 24 h^{9,15}. Second method was usually a therapeutic dose of radioiodine (I^{131}) given between 10-15 mCi. It was estimated that with a therapeutic dose of 10 mCi thyroid state will be hypothyroid within one year and a dose of 15 mCi will cause hypothyroid state within 6 months. Therapeutic radioiodine (I^{131}) was usually given as a single dose, but in certain cases, therapeutic radioiodine (I^{131}) was given several times to reach a state of hypothyroidism or euthyroid¹².

Treatment option for hyperthyroid disease includes antithyroid medication, surgery or radioactive iodine radioiodine (I^{131}). Radioiodine (I^{131}) has been commonly used for the treatment of both benign and malignant thyroid conditions since the 1940s by Ross¹⁶. Radioiodine (I^{131}) is a β -emitting radionuclide with maximum energy of 0.61 MeV and it remains the radionuclide with long half-life of just over 8 days so it can treat hyperthyroidism by destroying sufficient thyroid tissue. Iodine in radioiodine (I^{131}) is the precursor of thyroxine. The radioactive form of iodine is taken up by iodide transporter of the thyroid. The β particle destroys the follicular cell gradually leading to volume reduction⁸.

Based on analysis of therapeutic radioiodine (I^{131}) in patients with hyperthyroidism high uptake can be declared a success because there were no significant differences in FT4 hormone levels before and after therapy. There were 6 patients with elevated levels of the hormone TSH, 11 patients with decreased levels of hormones T3 and 11 patients with decreased hormone levels FT4. Therapeutic radioiodine (I^{131}) will cause damage to the thyroid follicular cells followed by loss of colloids. Damage to the thyroid follicles will affect the synthesis of the thyroid hormones T3 and T4 so that thyroid hormone levels will decrease, the symptoms of hyperthyroidism will be reduced and the expected size of the thyroid gland will shrink. The FT4 decrease in causing the symptoms of hyperthyroidism diminished since FT4 is a hormone that will circulate to the peripheral tissues and affect the body's metabolism¹⁷⁻¹⁹.

CONCLUSION

Characteristics of patients with hyperthyroidism high uptake by age most occur in early adult patients and women. Based on the patient's smoking history obtained all nobody has a previous history of smoking. Hyperthyroid high uptake patients with radioiodine therapy (I^{131}) had a history of previous antithyroid drug consumption. Therapeutic radioiodine (I^{131}) dose at most was 8 mCi. There was significant effect of radioiodine (I^{131}) in patients with hyperthyroidism high uptake to TSH hormone and thyroid hormone levels. Further research in cohort study is needed regarding the treatment of hyperthyroidism particularly high uptake of radioiodine therapy (I^{131}) so that patients can return to optimal health.

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