KORONER ANJİOGRAFİDEN SONRA İYOD'A BAĞLI TİROTOKSİKOZİS: 2 YILLIK TAKİP SONUÇLARI

IODINE INDUCED THYROTOXICOSIS AFTER CORONARY ANGIOGRAPHY: TWO YEARS FOLLOW-UP

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Özet

Bu çalışmada, iyod eksikliği olan bölgelerde koroner anjiografi yapılan hastalarda İyod'a bağlı gelişen tirotoksikozis sıklığını araştırdık. Çalışmaya alınan hasta ve kontrol grubunda troid bezinin hacmi, bazal tirotropin (TSH), serbest troxin (T_4) ve antiperoksidaz ölçümleri farklı zamanlarda yapıldı. Çalışma süresince 44 hastanın birinde aşikar hipertroidizm gelişirken, on beş hastada subklinik hipertroidizm gelişti. Buna karşın kontrol grubundaki 40 hastanın 7 tanesinde subklinik hipertroidizm tespit edildi. İyoda bağlı hipertroidizm gelişen hasta ile subklinik hipertroidizm gelişen 15 hastanın 9 tanesi risk grubuna dahildiler. Subklinik hipertroidizm gelişen 15 hastanın 6 tanesi ise iyoda bağlı tirotoksikosis açısından risk grubunda değildi. Bu çalışmada koroner anjiografide kullanılan kontrast maddenin riskli ve risksiz grupta iyoda bağlı tirotoksikosise yol açabileceği gösterildi. Özellikle iyoddan fakir bölgelerde kontrast madde alan hastaların koroner anjiografiden sonra TSH ve troid hormon seviyeleri takip edilmelidir.

Anahtar kelimeler: *İyoda bağlı tirotoksikosis, Koroner Anjiografi*

Summary

In this study, we investigated the frequency of iodine-induced thyrotoxicosis in patients performed coronary angiography (CA) in the iodine deficiency regions. In the study and control group patients the thyroid volume, basal thyrotropin (TSH), free thyroxine (T_4) and thyroid antibodies against thyroid peroxidase (TPO) were measured at different times. While one of 44 patients developed clinical hyperthyroidism, fifteen patients developed subclinical hyperthyroidism during the study period in study group. Subclinical hyperthyroidism was diagnosed in seven of 40 in control group. The subject showing iodine induced hyperthyroidism, and nine of fifteen patients having subclinical hyperthyroidism in the study belonged to the so-called risk group. Six of 15 patients with subclinical hyperthyroidism did not belong to risk group for iodine-induced thyrotoxicosis. This study showed that contrast media used during the coronary angiography could lead to iodine-induced thyrotoxicosis in patients with and without risk group. Therefore in patients receiving contrast media, especially in areas iodine-deficiency, TSH and thyroid hormone levels should be followed-up after coronary angiography.

Key words: *Iodine-induced thyrotoxicosis, Coronary angiography*

Introduction

Iodine-induced thyrotoxicosis (IIT) is a common disease, and the recognition and treatment of iodine-induced thyrotoxicosis, particularly in elderly patients and patients with goiter, are of clinical importance. Iodine-induced thyrotoxicosis or "jodbasedow phenomenon" has been reported throughout the world since iodine has been administered to treat endemic goiter (1). IIT is most commonly encountered in older persons with long standing nodular goiter and in regions of chronic iodine deficiency (2,3). The presence of functionally autonomous portions of the thyroid is a precondition for the occurrence of iodine-induced hyperthyroidism after the administration of intravenous contrast media, in the form either latent immunogenic hyperthyroidism (Graves's disease) or in localized or diffuse autonomy. The healthy thyroid can adapt to an iodine excess in many different ways. The autoregulation mechanisms may, however, fail in a diseased thyroid and severe hyperthyroidism may result (4). Review of available literature and experience supports a recommended daily iodine intake of 150 µg for adults. In iodine deficiency area, following salt iodinization, the number of thyrotoxic patients have increased sharply by 2 to 6 folds (5). Contrast media are most commonly used in many radiological examinations such as coronary angiography, computed tomography and hysterosalpingography. During the coronary invasive procedures, patients receive amount of supraphysiologic of iodine. Coronary angiography is followed by an iodine load of 15 to 20 mg for the thyroid and may be the cause of iodine-induced hyperthyroidism (6). The aim of the study was to identify the number of cases of iodine-induced thyrotoxicosis following coronary angiography (CA).

Materials and Methods

Subjects

Forty four patients who performed elective coronary angiography as study group and 40 patients not performed coronary angiography as control group in cardiology department were admitted for the study. Control group patients were selected among those without coronary artery disease (CAD). The mean age of the patients in study group (12 male, 32 female) was 55.7 ±10.3) years. The mean age of the patients in control group (28 male, 12 female) was 56.3±11.4 years. The patients taking glucocorticoids, propranolol, iodine-containing drugs such as amiodarone, antitussive agents and known thyrotoxicosis, diabetes mellitus, malign disease were excluded from the study.

Methods

Thyroid ultrasound was performed for the patients before the study and after 12^{th}–24^{th} months of the study. Basal thyrotrophin (TSH), free thyroxine (FT_4) and thyroid antibodies against thyroid peroxidase (TPO) were measured at five different times; before coronary angiography, and 4 and 12 weeks**,** 12 and 24 months after coronary angiography. The samples taken from patients were frozen at minus 80ºC and they were analyzed at the end of the study.

Conventional thyroid ultrasound was carried out using short focused, small a perts 7.5-mHz transducer (Toshiba, Tokyo, Japan). The volume of thyroid gland exceeding 18 mL in female and 25 mL in male was defined as an enlarged thyroid gland. Both clinical and subclinical hypo-hyperthyroidism were diagnosed on the basis of the FT_4 and TSH levels in combination with clinical signs. Serum TSH and FT_4 were measured with the automated ACS: 180 system (Bayer, USA) using chemulisence immunoassay. Normal ranges were 0.35-5.5 µU/l and 1.8-4.4 pg/l, respectively.

During the coronary angiography, out with different amounts of Hegzabrix® ionic and Omnipaque® nonionic contrast media were given.

Statistical analysis

Statistical comparisons were made by the paired t test. TSH, FT_4 levels were given as median values. $P< 0.05$ was considered statistically significant.

Results

During the study, the mean TSH, FT_4 and thyroid volume of both groups have been shown in table 1. Study and control group characteristics were similar to each other. In 14 (31.8 %) of the study group and in 13 (32.5 %) of the control group, nodules were detected at the start of the study.

At the beginning, in the study group, TSH and FT_4 levels were normal. Four weeks later, patients had not developed thyroid disorder. Twelve weeks after coronary angiography, 5 of 44 patients showed subclinical hyperthyroidism. Of the patients showing subclinical hyperthyroidism, 4 thyroid volume were at normal range and 1 thyroid volume had increased. Patients with subclinical hyperthyroidism were recommended salt without iodination and all of these patients became euthyroid in twelve months. Clinical hyperthyroidism occurred in one subject (a 51-year-old male). TSH and FT_4 levels were 0.06 µU/ml and 2.15

Table 1. *During the Study Thyroid Volume, the TSH and FT_4 Levels of all Patients*

	TSH (µU/ml)		FT_4 (ng/dl)		Thyroid volum(mL)	
	patient	control group	patient	control group	patient	control group
before study	1.48±1.13	1.42±0.9	1.21±0.19	1.28 ±0.16	19.8±4.2	20.1±3.6
1 th month	1.26±1.01*	1.28±1.1*	1.29± 0.33	1.24 ±0.25		
3 th month	0.92±0.85*	1.23±0.8*ϕ	1.31±0.34	1.37±0.14		
12th month	0.80±0.91*	1.14±1.0*ϕ	1.46±0.22	1.41± 0.42	20. 3±3.7	21.2±4.0
24 th month	0.85±0.5 *	0.80±0.6*	1.40±0.28	1.39 ± 0.27	20.9±3. 6	21.6±3.8

**p< 0.01 Significant changes from baseline in TSH in study group and control group*
ϕp< 0.01 Changes in TSH levels in3rd and 12th months between study and control group

ng/dl, respectively. A nodule of 10x8 mm diameter was determined in the thyroid ultrasonography. The volume of the thyroid was 18.3 mL. Thyrotoxicosis history was negative. He had never received contrast media. Antithyroid therapy was given for this patient.

Subclinical hyperthyroidism was observed 12 months later in 4 of the patients who were diagnosed to have euthyroid at the end of 12th week in the study group. Thyroid volumes of 4 patients were over normal levels. While thyroid nodule was found in 3 of these patients, diffuse goiter was determined in one patient. Anti-thyroid treatment was given to one patient with CAD. The other patients were recommended salt without iodination. In the control 3 months later, 4 patients with subclinical hyperthyroidism were observed to became euthyroid.

Subclinical hyperthyroidism was determined in 6 patients at the end of the second year. 4 of the patient were male and 2 were female. While thyroid volumes of 2 patients were normal and they had no nodule in their thyroid, 4 had nodular goiter. Of the 6 patients with subclinical hyperthyroidism, 2 with CAD were recommended antithyroid treatment, and only salt without iodination was recommended to 4 patients without CAD. Thyroid function disorder (subclinical and clinical hyperthyroidism) occurred in 16 (36%) patients in study group and 7 (17.5%) in control group during the study. In both groups the patients developing subclinical hyperthyroidism and clinical hyperthyroidism had normal anti-TPO antibodies.

Subclinical hyperthyroidism was observed in 7 subjects in the control group. 5 of these patients had nodular goiter and 2 had diffuse goiter. Since 2 patients in control group, who were found to have subclinical hyperthyroidism, had cardiac failure, they were given antithyroid treatment, and the other patients were given treatment with salt without iodination. Of the patients in the study, 12 were given ionic contrast media, and 32 non-ionic contrast media. The amount of contrast media performed to the patients was 174.84±105.83 ml for ionic contrast media and 194.17 ± 89.46 mL for non-ionic contrast media. There was no difference between media amounts, age and sex ($p<0.05$). There was no difference between the sort of media and alterations of the thyroid hormone levels.

Discussion

Coronary angiography is generally used in elderly patients. It is known that iodine-contained drugs can develop hyperthyroidism (7). This development depends on two factors: the volume of autonomous tissue and the quantity of iodine exposure (8). The recognition and treatment of iodine-induced thyrotoxicosis, particularly in elderly patients and patients with goiter, are of clinical importance, because symptoms and signs of hyperthyroidism are absent (9,10). The aim of the study was to find out the risk of iodine-induced hyperthyroidism in our region having 65 % iodine deficiency and 27 % goiter (11).

Throughout our study hyperthyroidism was determined in only one of 44 patients. This case can be connected to the iodine exposure through coronary angiography. A subject showing iodine induced hyperthyroidism in the study belongs to the so-called risk group(i.e. in older persons having long standing nodular goiter and living in the chronic iodine deficiency region). Thyroid volume of that patient was 18.3 mL and there was a nodule in the gland.

Subclinical hyperthyroidism occurred in 15 of 44 subjects (5 in 3 months, 4 in 12 months, and 6 in 24 months). Sixty percent of subclinical hyperthyroidism cases our study were observed to occur at the end of the 1 th year. Azizi et al (12) reported that thyroid dysfunction was 0.6% and most of it occurred in the first five months following iodine oil injection. While thyroid volume was within the normal range in 6 subjects showing thyroid disorder, it exceeded to in others. In our cases, while thyroid gland was normal in 6 subjects, thyrotoxicosis was observed to develop. Also, Hintze et al (13) determined that there was iodine induced hyperthyroidism in those subjects having no thyroid nodules, and within normal range of thyroid

volume. At the end of study, thyroid function disorder was seen in 36.6% of all subjects due to received supraphysiologic iodine. The potential risks of iodine supplementation is of iodine-induced thyrotoxicosis. Galofre et al (14) have shown that the increase of the incidence of thyrotoxicosis comprised of both nodular and diffuse goiters, and dietary iodine supplementation may induce an increase of the incidence thyrotoxiccosis. Turkey is a risk country as regards iodine deficiency. Our region is also at a high risk in this respect. For this reason iodine salt prophylaxis has been applied for almost 2 years. That 17.5% subclinical hyperthyroidism was observed in subjects in the control group in the study indicates that iodine prophylaxis increases the number of patients with subclinical hyperthyroidism. We found that in cases having similar age and ways of living but who had not been applied coronary angiography, thyrotoxicosis range was lower than those who had been applied CA. This shows that in regions where iodine prophylaxis is performed, these patients face a higher thyrotoxicosis risk following examinations with radiocontrast media.

Antithyroid treatment is suggested for subjects having autonomous nodule over age 40 before application of iodine-containing contrast media. As a result of this application, it is shown that thyrotoxicosis cannot be prevented in a few patients (15). On the other hand, the studies done by Hintze et al (13) have shown that the mean of iodine-induced thyroid disorder is not high. Therefore, treatment is not suggested for those patients due to the side effects of antithyroid drugs. Potential risks of subclinical hyperthyroidism are progression to overt hyperthyroidism, cardiovascular effects, and osteoporosis (16). Subclinical hyperthyroidism has a prevalence 1%. The incidence of progression to overt thyrotoxicosis is approximately 5 % per years. Without treatment, nearly 30 % of these patients will develop atrial fibrillation within 10 years (9). We gave antithyroid treatment to cases co-occurring with subclinical hyperthyroidism and CAD and only salt without iodination to those with no CAD. 6 patients with thyroid function disorder became euthyroid at the end of 12th week, and 4 at the end of 12th month. Treatment of 6 patients who had subclinical hyperthyroidism at the end of 24th month is still kept on. Of all the patients who were applied coronary angiography, 5 were diagnosed to have subclinical hyperthyroidism and 1 clinical hyperthyroidism in the 12th week, 6 subclinical hyperthyroidism in the 24th month of the study, and the number of subclinical hyperthyroidism in control group in the same period was 3, 2, and 2, respectively. In conclusion, those patients who have goiter or who live in regions where iodine intake is low, for instance in iodine-deficient areas like Erzurum, are especially at risk (11). Therefore clinicians should be aware that IIT often develops several weeks after the administration of the contrast media. Follow-up of such patients after radiocontrast agent performs is therefore advisable. Considering the wide use of radiocontrast media, the probability of inducing thyrotoxicosis by these substances must be low. Therefore, we think that any prophylactic antithyroid drugs for the patients intaking iodine at supraphysiological doses is not necessary, but follow-up at particular period is.

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