



Beneficial Effects of Lithium and Radioiodine Therapy in the Treatment of Hyperthyroidism

Lityum ve Radyokatif İyot Tedavisinin Hipertiroidi Tedavisindeki Etkinliği

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Abstract

Intravenous contrast media used for coronary angiography are iodine-based and could induce thyroid gland dysfunction. We present the case of a 58-year-old woman with coronary artery disease who developed hyperthyroidism after percutaneous coronary intervention. Treatment with thiamazole induced agranulocytosis, complicated with severe tonsillitis. During recurrence of hyperthyroidism, after careful assessment of available methods of treatment, she was recommended to undergo radioiodine therapy (^{131}I). The patient received lithium carbonate as pre-treatment. After 13 days of pre-treatment, patient received the therapeutic dose of ^{131}I . Neither thyrotoxicosis progression nor acute coronary syndrome occurred. After 3 weeks, her thyroid hormones were found to be within normal ranges. Lithium therapy could be used as an effective treatment in patients who developed serious side-effects due to previous treatment with thionamides. *Turk Jem 2014; 18: 92-94*

Key words: Hyperthyroidism, coronary artery disease, lithium, agranulocytosis

Özet

Koroner anjiyografi sırasında kullanılan kontrast madde iyot içeriği nedeni ile tiroid disfonksiyonuna neden olabilir. Burada koroner arter hastalığı olan ve koroner anjiyografi sonrasında hipertiroidi gelişen bir hastayı sunuyoruz. Thiamazol ile tedavi ağır tonsillit ile komplike olan agranülositoza neden oldu. Hipertiroidinin nüks ettiği görüldükten sonra hastaya radyoiyot (^{131}I) tedavisi önerildi. Hasta öncül tedavi olarak lityum karbonat da kullandı. On üç günlük öncül tedavi sonrasında hasta terapötik dozda ^{131}I aldı. Ne tirotoksikoz ne de Akut koroner sendromda kötüleşme izlenmedi. Üç hafta sonra tiroid hormonlarının normal sınırlar arasında olduğu görüldü. Lityum tedavisi, thionamidler ile ciddi yan etki gözlenen hastalarda etkin bir tedavi olabilir. *Turk Jem 2014; 18: 92-94*

Anahtar kelimeler: Hipertiroidi, koroner arter hastalığı, lityum, agranulositoz

Introduction

Coronary angiography is commonly used to determine the presence and extent of obstructive coronary artery disease (CAD) and to assess the effects of various forms of therapy, such as revascularization by percutaneous coronary intervention (PCI) or surgical interventions. Renal insufficiency and anaphylactic reaction to contrast medium used for angiography require special attention (1). Moreover, iodine contrast media could impair thyroid function inducing subsequent hyperthyroidism (2). Patients with CAD often experience a marked worsening in symptoms with hyperthyroidism (3). When the treatment of hyperthyroidism with antithyroid drugs cause life-threatening agranulocytosis (absolute neutrophil count $< 500/\mu\text{L}$), choice of the available method of treatment is significantly limited (4).

It persuades us to search for new potential therapeutic agents in patients where a prompt decrease in thyroid hormones is

required. One of these therapeutic agents could be lithium. The effects of lithium on thyroid enlargement was first observed in 1968 (5). Its use in treatment for mood disorders increase the prevalence of thyroid dysfunction (6). Goiters and hypothyroidism are well-known patient complications, however, lithium-induced hyperthyroidism is a more rare event (7). The mechanism by which lithium predisposes to thyroid dysfunction remains unknown. It is well known that lithium accumulates in the thyroid tissue and increases iodine retention, inhibits the coupling of iodotyrosine residues of thyroglobulin, inhibits the release of thyroxine and triiodothyronine from the thyroid gland and the conversion of thyroxine to triiodothyronine. Therefore, therapy with lithium carbonate could be a useful tool in the treatment of hyperthyroidism (8). Since lithium does not affect thyroidal radioiodine (^{131}I) uptake, it is used in the pretreatment ^{131}I therapy (9).

Case Report

A 58-year-old female patient presented to the hospital with unstable angina in May 2012. She underwent coronary angiography and PCI with a drug-eluting stent (DES) placed in the left anterior descending coronary artery. According to the European Society of Cardiology guidelines, she was managed with conventional dual antiplatelet therapy: (clopidogrel and acetylsalicylic acid) (10). She had no previous history of thyroid disease or glucose intolerance. Six weeks after coronary angiography and stent placement, thyroid function tests indicated hyperthyroidism with free thyroxine (FT4) level of 52.62 pmol/L (normal 9.0-20.0 pmol/L), free triiodothyronine (FT3) of 17.07 pmol/L (4.0-8.3 pmol/L) and thyroid stimulating hormone (TSH) of 0.008 mIU/L. She was treated with thiamazole 60 mg daily, which resulted in improvement of her symptoms. The dose of thiamazole was gradually reduced to 5 mg daily. Moreover, diabetes was diagnosed, and accordingly, she was treated with metformin and glimepiride. Five weeks later, the patient was referred again to the hospital because of fever and sore throat as a result of acute purulent infection of the upper respiratory tract. She was euthyroid (TSH was 1.5 mIU/L), but routine examination of blood cell count revealed that her white cell count was decreased to 1300/ μ L and neutrophil count was 90/ μ L (neutrophils 0.7%). Consequently, thiamazole was immediately discontinued. Aside from broad spectrum antibiotic with antipseudomonal activity, granulocyte colony-stimulating factor was given subcutaneously once a day. The patient made a progressive and marked clinical improvement. Her white cell count returned to normal. She was discharged in a good clinical condition with a white cell count of 18.000/ μ L.

Three months later, the patient was admitted to our clinic, in a bad general condition. She presented with shortness of breath on exertion, malaise, heat intolerance, increased sweating, tremors, palpitations and recent worsening muscle fatigue. She had a low-grade fever, tachycardia with a heart rate of 120 bpm and quiet heart sounds. Blood pressure was within normal range (130/60 mmHg). The patient was noted to have significant edema in bilateral lower extremities. The thyroid gland was slightly enlarged, with the presence of a bruit over the right lobe. Mild proptosis was observed bilaterally. Serial 12-lead electrocardiograms showed sinus tachycardia with the evidence of subtle ST segment ischemic changes. Cardiac troponin I levels were within normal ranges. High serum levels of thyroid hormones and low level of TSH indicated recurrence of hyperthyroidism (TSH=0.009 mIU/L, FT4=40.66 pmol/L and FT3=21.81 pmol/L). The high level of anti-TSH receptor antibody (8.6 U/L; normal <1.5 U/L) confirmed the diagnosis of Graves' disease. Anti-thyroid peroxidase antibodies were elevated (560.8 IU/ml; normal <35 IU/ml) and anti-thyroglobulin antibodies were in the upper limit of the reference range (34.8 IU/ml; normal <20 IU/ml). Ultrasonography of the thyroid gland suggested autoimmune thyroid disease, the thyroid gland was slightly enlarged and diffusely hypoechoic.

A radioactive iodine uptake test was performed twenty-four (T24=51.1%) and forty-eight hours (T48=51.5%) after 131 I

administration. Thyroid scintigraphy was performed as well. The thyroid gland in 131 I scintigraphy was slightly increased, especially in the right lobe, in which the content of radioiodine was higher than that on the opposite lobe.

A complete blood count on admission showed a normal total leukocyte count (5,920/ μ L) with 3.980 neutrophils/ μ L. Blood glucose level exceeded 300 mg/dL.

Due to severe hyperthyroidism, uncontrolled diabetes and CAD, owing to the risk of acute coronary syndrome, she was admitted to the emergency room. The patient was started on intravenous glucocorticoids and oral beta-blockers. Additionally, she received insulin. Approximately 24 hours following the administration of beta-blocker agents, she developed first- and second-degree intermittent atrioventricular block. Due to contraindications to antithyroid drugs (thiamazole-induced agranulocytosis) and to thyroidectomy (risk of bleeding complication in patient with dual antiplatelet therapy after PCI with DES implantation), she was referred for radioiodine therapy. As the pre-treatment, she was given lithium carbonate 250 mg TID for 13 days. Serum lithium level was maintained within the therapeutic range of 0.6-1.2 mmol/L. In view of the considerable improvement in symptoms and since the FT3 level was down to 7.99 pmol/L (FT4 level was 55.78 pmol/L), she could have received 767.7 MBq (20.75 mCi) of radioactive iodine. Oral prednisone 30 mg daily was continued and, after 10 days, was gradually withdrawn. There were no symptoms or signs of overt thyrotoxicosis or acute coronary syndrome. She was discharged.

Three weeks after the radioactive iodine treatment, her FT4 level was 18.40 pmol/L and FT3 was 2.51 pmol/L. During the next 2 months, the patient's TSH level rose to 17.57 mIU/L, (FT4 and FT3 were in the normal range, 12.6 pmol/L and 4.0 pmol/L, respectively) and then, she was given thyroxine. She is now being treated with thyroxine 75 mcg/day and is well, her TSH level is maintained at 1.4 mIU/L. The attempts to discontinue the thyroxine have resulted in clinical and biochemical hypothyroidism with a rise in TSH. Simultaneously, she is receiving metformin 500 mg TID for diabetes and her blood glucose is within normal range.

Discussion

Antithyroid drugs, surgical thyroidectomy and 131 I administration are all treatment options for hyperthyroidism. In the case of our patient, a previously administered high-dose thiamazole induced the development of agranulocytosis which was then further complicated with purulent infection of the upper respiratory tract. Therefore, the second course of therapy with thiamazole could induce life-threatening complications and was a greatest risk in this patient. Moreover, after PCI with DES implantation, she was advised to continue dual antiplatelet therapy for a duration of at least one year (10). This ongoing therapy further complicated the case due to the increased chance of surgical bleeding. Therefore, surgery was contraindicated in the patient even after pretreatment with glucocorticoids and beta-adrenergic blocking agents. Consequently, beta-blockers also had adverse effects in our patient and were subsequently discontinued due to the development of atrioventricular block. Thus, after the

determination of radioiodine uptake was completed, it was decided that this patient was eligible for radioiodine therapy. Usually a single iodine load (e.g. radiocontrast for a CT scan) may transiently reduce the radioiodine uptake in patients with Graves' disease or toxic nodular goiter to less than 10 percent for up to two to four weeks, but in the case of our patient ^{131}I uptake was studied 12 weeks after coronary angiography. Since accentuation of hyperthyroidism may occur following administration of ^{131}I , pre-treatment with an anti-thyroid drug was necessary to avoid the potentially lethal complication. After consideration the risk of unstable angina associated with thyroid surgery and agranulocytosis after thiamazole, it was decided that the most appropriate method was treatment with lithium carbonate. Lithium has been used in the treatment of hyperthyroidism for forty years, however, it is not the established drug of choice because of its side effects and toxicity (11). It is only indicated in patients who develop serious side-effects due to thionamides or in patients who do not respond well to these drugs.

The recommended dose of lithium is 500 to 1500 mg/day, so that serum lithium levels are maintained between the ranges of 0.6-1.2 mmol/L (12,13). Lithium increases thyroid gland retention of iodine and allows the use of lower doses of ^{131}I , therefore, increases the efficacy of radioactive iodine therapy (14). The recommendations are to start lithium therapy 5 days before and to continue for 7 days after radioiodine therapy (15). Lithium therapy given concomitantly with ^{131}I is associated with a quicker control of hyperthyroidism and prevents the serum thyroid hormone increase usually observed two weeks after radioiodine therapy. This is particularly important in patients with underlying cardiovascular disorders (unstable angina) for whom even a transient exacerbation of thyrotoxicosis may be disastrous.

Although previous authors did not confirm the beneficial effects of lithium in patients treated with radioiodine therapy (16), the recent studies indicated that adjuvant lithium increases the efficacy of radioactive iodine (9).

In the case of our patient, lithium normalized FT3 and decreased FT4, reducing the risk of acute coronary syndrome after radioiodine treatment.

Glucocorticoids are not routinely used in the pretreatment to radioiodine therapy. However, we know that they inhibit peripheral T4 to T3 conversion, reduce thyroid secretion in patients with Graves' disease, treat potentially associated limited adrenal reserve (17). Therefore, for us, the use of glucocorticoids is indicated in patients with severe, life-threatening hyperthyroidism. The modern clinical diagnostic and interventional procedures frequently use contrast media to improve visualization. The intravenous contrast media are typically based on iodine. Sudden exposure to high iodide levels may cause thyroid dysfunction (18). To reduce the incidence of iodine-induced hyperthyroidism, it has been suggested that prophylactic drugs should be administered starting before examination. In patients with acute coronary syndrome referred to emergency PCI, it could be difficult. We suggest that in these patients, TSH should be measured before and three or four weeks after administration of the iodine containing contrast media to evaluate thyroid function and minimize the risk of development of thyroidal complications. Another solution in patients with underlying thyroid disease is the use of alternative contrast agent (19).

Conclusions

Lithium therapy could be used as an effective treatment in patients who develop serious side-effects due to previous treatment with thionamides.

Conflicts of Interest

There are no conflicts of interest.

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