

Sapula Klaudia, Golacki Jakub, Hordejuk Michalina, Marczak Aleksandra, Iwaszko-Sochal Klaudyna. Graves-Basedow disease treated by complementary medicine leading to severe thyrotoxicosis – a case report. *Journal of Education, Health and Sport*. 2022;12(7):340-346. eISSN 2391-8306. DOI <http://dx.doi.org/10.12775/JEHS.2022.12.07.032>  
<https://apcz.umk.pl/JEHS/article/view/JEHS.2022.12.07.032>  
<https://zenodo.org/record/6795122>

The journal has had 40 points in Ministry of Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of December 21, 2021. No. 32343. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical Culture Sciences (Field of Medical sciences and health sciences); Health Sciences (Field of Medical Sciences and Health Sciences).

Punkty Ministerialne z 2019 - aktualny rok 40 punktów. Załącznik do komunikatu Ministra Edukacji i Nauki z dnia 21 grudnia 2021 r. Lp. 32343. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przepisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).

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The authors declare that there is no conflict of interests regarding the publication of this paper.

Received: 20.06.2022. Revised: 20.06.2022. Accepted: 04.07.2022.

## **Graves-Basedow disease treated by complementary medicine leading to severe thyrotoxicosis – a case report**

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## **ABSTRACT:**

Graves' disease is a common cause of hyperthyroidism. Inadequate treatment or non-compliance can lead to serious complications, including thyroid storm.

We present the case of a 22-year-old woman who had been treated with antithyroid drugs (ATD) for almost 7 years, however decided to suspend conventional treatment and turned towards complementary and alternative medicine methods. Following the bioenergotherapist's advice, she began taking Lugol's solution (LS) at a dose of 30 drops per day. After about one month of such therapy, the patient was urgently admitted to the Emergency Department with thyrotoxicosis with a high risk of thyroid storm development. With the implementation of intensive thyrostatic treatment and steroid therapy, euthyroidism was successfully restored.

**Keywords:** thyrotoxicosis, Lugol's solution, non-compliance, complementary and alternative medicine

## **INTRODUCTION:**

Thyrotoxicosis is the clinical manifestation of the impact of excessively high concentrations of thyroid hormones on the organism. Graves-Basedow disease (GD) is the most common cause of thyrotoxicosis in iodine-sufficient areas. [1]

The diagnosis of GD includes characteristic clinical presentation, biochemically confirmed suppression of thyrotropic hormone (TSH) accompanied by elevated levels of triiodothyronine (T3) and thyroxine (T4), typical ultrasound image of the thyroid gland, and the presence of autoantibodies directed against the thyrotropin receptor (TRAb). [2] Common manifestations include anxiety, irritability, heat intolerance, increased sweating, tachycardia, distal tremor, goiter, and thyroid nodules. In extreme cases, thyrotoxicosis can progress to a life-threatening thyroid storm. [3]

There are three effective and relatively safe treatment options for GB: antithyroid drugs (ATD), radioactive iodine ablation (RAIU) and surgical treatment. Long-term thioamide-based pharmacotherapy is the most common and widely used treatment worldwide, while surgical treatment is considered the most effective. [3] Thyroidectomy can only be performed in full euthyroidism, so it must be preceded either by months of ATD or short-term administration of saturated potassium iodide solution. Typically, Lugol's solution (LS) is used for this purpose at a dose of 15-20 drops per day for 10 days. [3]. Intake of high doses of exogenous iodine causes a transient inhibition of iodine uptake by the thyroid gland in the Wolff-Chaikoff effect. In rare cases, usually as a result of excessive or intensive iodine use, an iodine-induced thyrotoxicosis called the Iodine-Basedow phenomenon may occur. [4]

We report the case of a 22-year-old woman who was urgently admitted to the Emergency Department due to severe thyrotoxicosis caused by GB. The patient had been treated with ATD for almost 7 years, but about a month earlier she had suspended this therapy and, on the advice of a bioenergotherapist, began taking LS at a dose of 30 drops daily.

## CASE REPORT

The clinical history of the patient's disease and treatment is well known. According to the information given by the patient, hyperthyroidism was diagnosed in December 2015. During the thyrostatic treatment, fluctuating hormone levels were observed, including periods of hypothyreosis. In August 2017, she was hospitalized because of severe hyperthyreosis. Based on clinical presentation, complete TSH suppression, positive TRAb (31.9 IU/l), ultrasound findings of heterogeneous echostructure and increased vascular flow, a diagnosis of Graves-Basedow disease was made at that time. In order to exclude thyroid orbitopathy MRI was performed, where no pathological enhancement was found. Due to significant immunological activity the patient wasn't qualified for radioiodine treatment and the decision of surgical treatment was postponed until euthyroidism was achieved. Despite the subsequent hormonal normalization, the patient refused to be surgically treated.

From January 2018 until February 2022, the patient had been periodically without specialist supervision. Results of irregular follow-up tests presented by the patient showed evidence of unstable thyroid function, with an initial trend toward hypothyreosis and, since August 2019, persistent TSH suppression despite treatment with methimazole at therapeutic doses. High TRAb levels, reaching over 40 IU/l, reflect the lack of immune remission throughout the entire treatment period.

The most recent ambulatory test results, two months prior to hospitalization, suggested complete suppression of TSH and hyperthyroidism. According to the patient's report, she began taking Lugol's solution at a dose of 30 drops per day in mid-January 2022, as recommended by the "bioenergotherapist" (no details or documentation of recommendations available). After about a month of such therapy, the patient was admitted to the Hospital Emergency Department and then to the Department of Endocrinology, Diabetology and Metabolic Diseases. The patient presented symptoms of severe thyrotoxicosis: tachycardia up to 160/min, blood pressure around 140/90 mmHg, muscle tremor, intolerance of heat and anxiety. Enlarged thyroid gland and mild exophthalmos were observed during physical examination. The risk of developing thyroid storm was estimated at 45 points on the Burch-Wartofsky scale. Severe hyperthyreosis (FT3 >20.00 pg/ml, FT4 5.77 ng/dl) with complete suppression of TSH (<0.008 mIU/L), and high levels of antithyroid antibodies TRAb 29 IU/L and ATPO 2114.0 U/ml were detected. Furthermore, impaired fasting glycaemia (IFG) was observed. Ultrasound examination of the thyroid gland was performed, which showed significant enlargement of the gland compared to previous examinations, heterogeneous echogenicity and increased vascular flow.

Intensive thyreostatic treatment was administered during hospitalization. Nevertheless, the full therapeutic effect has not been achieved. The symptoms of thyrotoxicosis were only partially reduced: muscle tremor and anxiety decreased, but tachycardia above 100/min persisted. Moreover, a normalization of hormone levels wasn't achieved as well. After several days, despite persistent hyperthyroidism and other indications for hospital treatment, the patient refused further hospitalization. Numerous discussions with the patient did not change her decision, so she was provided with detailed recommendations for future management and discharged from the hospital on her own request.

## **TREATMENT**

During hospitalization typical thyrostatic treatment was administered, i.e. methimazole, propranolol, sodium perchlorate, vitamin supplementation. The treatment was gradually intensified with the implementation of steroid therapy using methylprednisolone. Since the patient left the hospital prematurely, a detailed plan of ambulatory control of biochemical parameters and treatment was prescribed. The patient was advised to perform an urgent thyroidectomy once euthyroidism is achieved. To evaluate possible cardiac complications, the patient was referred to the Cardiology Outpatient Clinic. In addition, an inpatient follow-up visit was scheduled in two weeks.

## **FOLLOW UP**

The patient attended a follow-up visit two weeks later. No significant improvement was observed, so the treatment was modified: the dosage of steroid was increased, lithium supplementation was added, sodium perchlorate therapy was continued, antiarrhythmic treatment was intensified, and the dose of methimazole was reduced. After two more weeks, another follow-up visit took place. The symptoms of hyperthyroidism were reduced, euthyroidism was obtained, and the TRAb level decreased to 13.6 IU/l. Treatment was well tolerated, however minor side effects were observed: acne, dry skin, itchy rash and nightmares. It was decided to gradually reduce the doses of thyrostatic, beta-blocker and steroid. Treatment with sodium perchlorate was discontinued, while the current dosage of lithium was maintained. The patient was reminded about recommended thyroidectomy soon after hormonal balance is achieved.

## **DISCUSSION**

The medical case described above leads us to consider how the therapeutic process of a patient with GD should be conducted in order to achieve the best and long-lasting effects. Regardless of the chosen method, in most cases the treatment lasts many years, often the whole patient's life, therefore the trust and cooperation between the physician and the patient is crucial.

In our patient's case the choice of therapeutic method was dictated by the current European Thyroid Association (ETA) guidelines, which indicate ATD as the first-line treatment in GD. According to the recommendations, treatment should begin with a dose of 10-40 mg methimazole per day, progressively reducing the dose until euthyroidism is achieved, which is usually possible after about 6 weeks of therapy. [5] Maintenance treatment should be continued for 12-18 months. [5] Regular monitoring of thyroid hormones and TSH levels initially every 3-4 months and then every 6 months, as well as periodic thyroid ultrasound examinations are a guarantee of good control of the patient's treatment. [6]

Despite the prescribed treatment, euthyroidism and sustained remission has not been achieved. Follow-up examinations were performed irregularly and the results indicated hormonal imbalance, which could have been the result of the patient's noncompliance. The lack of satisfying results was probably the reason for searching alternative methods of treatment, in this case iodine supplementation in the form of Lugol's solution.

Non-compliance is a very frequent problem. According to WHO, this issue affects more than 50% of chronically ill patients. [7] The most common example of non-adherence to medication is taking less than 80% of the prescribed doses or not taking medication at all. [8] Sometimes non-adherence manifests itself in substituting conventional medicine with complementary and alternative medicine methods without consulting a physician. This exposes the patient to an increased risk of acute exacerbations and chronic complications due to inadequate disease control, side effects and interactions. [9] VM Jose et al. attempted to determine the frequency of emergency hospital admissions in India due to non-adherence to conventional medicine after conversion to alternative therapies. Out of 506 patients studied, 168 (33%) were non-compliant, out of which 69 patients (41%) were admitted to hospital directly due to complementary and alternative methods. They found that the most common predictors of nonadherence were complexity of the treatment regimen, lack of understanding of the disease and drug effects, economical and social considerations, adverse drug reactions, overdose, suicidal intent, poor patient-physician relationships, and use of alternative methods alone. [9]

We were unable to determine the reasons why our patient turned to alternative treatments. We have not found recommendations in the literature similar to those recommended to our patient by the bioenergotherapist. Indeed, Lugol's solution, containing 100 mg/ml potassium iodide and 50 mg/ml iodine [10], has the potential for use in the treatment of GD, especially in the period preceding thyroidectomy, but it is never as prolonged and intensive therapy as the one recommended here. According to American Thyroid Association (ATA) guidelines, Lugol's solution can be administered at 5-7 drops three times a day for 10 days prior to surgery. [3] Our patient took 30 drops daily for nearly a month, far exceeding the recommended dosage. High concentrations of exogenous iodide induce the Wolff-Chaikoff effect, which involves an acute, transient inhibition of thyroid hormone synthesis [11] and indirectly results in reduced intraoperative bleeding. [3] In the majority of patients, return to euthyroidism occurs within 24 to 48 hours. In some patients, the opposite reaction may occur. They develop hyperthyroidism that escapes the physiological mechanisms of autoregulation. This phenomenon is known as Iodine-Basedow syndrome. [4] Patients who develop iodine-induced hyperthyroidism are recommended to be treated with corticosteroids to accelerate the return of thyroid hormones to normal levels. In addition, symptoms can be managed with a beta-blocker and antithyroid drugs, and lithium may also be considered. [4] This was also the procedure implemented in the case described.

We have searched the available literature for similar cases of off-label use of iodine preparations.

Ji Wei Yang and Jacques How described a case of painless thyroiditis induced by Lugol's solution. A 59-year-old Canadian woman took 4 drops of Lugol's solution daily to relieve menopausal symptoms. After 6 months, she was diagnosed with hyperthyroidism. Short-term treatment with methimazole was introduced leading to hypothyroidism. Over the next few months, the patient spontaneously achieved clinical and biochemical euthyroidism. What is interesting, the patient reported that her brother and sister-in-law, independently also received Lugol's solution from their family physician for an extended period of time to treat non-thyroid disorders. [10]

Linda Daffini et al. described the case of a 55-year-old Italian woman who was admitted to the Intensive Care Unit for congestive heart failure and thyrotoxicosis. She had been suffering from GB for two years. Instead of conventional treatment, she chose alternative methods with phytotherapeutic and homeopathic drugs containing potassium iodide and dried sheep thyroid. This resulted in severe iodine poisoning with concentrations almost a thousand times above the reference range. Unfortunately, the poisoning was fatal. [12]

Finally, Leuştean L. described a case of a 50-year-old woman with GB treated with ATD for many years, in whom surgical treatment was planned. Preoperative preparation with Lugol's solution was decided. Due to a misunderstanding, the administration of iodine solution was prolonged for about 30 days, resulting in iodine-Basedow syndrome. The patient was treated with high doses of ATD, glucocorticoids and beta-blockers with gradual reduction of symptoms. One month later, the patient underwent thyroidectomy without preoperative preparation. The surgical and postoperative course went without complications. [13]

This case report should not only educate clinicians about the management of patients with Iodine-Basedow syndrome, but also alert them about the dangers of non-compliance and insufficient physician-patient cooperation. Patients' use of alternative, non-evidence-based treatment methods is a serious concern and may lead to severe health consequences, even life-threatening.

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