Analysis of radioactive iodine treatment in patients with hyperthyroidism: A narrative review

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ABSTRACT
Hyperthyroidism is defined as a thyroid dysfunction, with Graves' disease as the most common representative. Its prevalence is 5 to 10 times higher in women. The pathology is characterized by a manifestation called thyrotoxocytosis, a clinical condition associated with the excessive production of thyroid hormones, which cause several systemic changes when in excess in the circulation. Therapeutic options consist of thionamides (Methimazole and Propylthiuracil), thyroidectomy and radioactive iodine. The present study aims to analyze, through a narrative literature review, the advantages and disadvantages of radioiodine therapy as a definitive treatment for hyperthyroidism, taking into account its indications and contraindications. Results obtained from the following databases were interpreted: LILACS-BIREME and SciELO.

Keywords: Hyperthyroidism, Iodine, Indications, Contraindications, Complications, Disadvantages.

1 INTRODUCTION

Hyperthyroidism is the leading cause of thyrotoxicosis, defined by the systemic response to excess thyroid hormones. Among the main causes of hyperthyroidism, the most common is Graves' disease, usually found in young women, followed by toxic multinodular goiter, more apparent in the elderly population. Toxic adenoma and thyroiditis are less frequent causes. In addition, medications such as amiodarone, levothyroxine, interferon, and lithium can lead to thyrotoxicosis, and therefore require periodic monitoring of thyroid function (SCHUCH et al., 2021).

The general symptoms of hyperthyroidism may consist of: insomnia, agitation, increased sweating, heat intolerance, weight loss, acceleration of intestinal transit, alteration of the menstrual cycle, weakness, hair loss and palpitation. Such phenomena occur due to adrenergic discharges,

resulting from the increased expression of receptors of this neurotransmitter system due to the high serum level of circulating thyroid hormones (KRONENBERG et al., 2010).

In addition, in Graves' disease, diffuse goiter is present, and some other more specific symptoms may arise, such as: pretibial myxedema (receptors similar to TSH receptors present at the site, when activated, generate an inflammatory response with deposition of glycosaminoglycans), acrypathy (digital beating) and Graves' ophthalmopathy (exophthalmos or ocular proptosis, which consists of the same pathophysiological mechanism as pretibial myxedema) (VILAR et al., 2013).

In view of the above, it is essential to analyze the importance of treating hyperthyroidism, as it is a disease that has such symptomatic repercussions and an exuberant clinical picture for its patients. The three main aspects of treatment, in the case of the main causes described above, include: the use of antirheoidal drugs (Methimazole and Propylthiouracil), thyroidectomy and radioactive iodine. The last two consist of definitive therapies. (WAJCHENBERG et al., 2014).

Hertz and Roberts pioneered iodine therapy in patients with hyperthyroidism at Massachusetts General Hospital in 1941. Since then, it has been widely used, as it is considered easy to administer, fast and inexpensive. Radioactive iodine, after being taken up by the thyroid gland, generates marked thyroiditis, interstitial fibrosis and, consequently, glandular atrophy (ANDRADE et al., 2004). Next, we will take a deeper look at the clinical aspects of this therapy.

2 METHOD OF ADMINISTRATION OF RADIOACTIVE IODINE

Souza and Mendes (2013) show that radioactive iodine is used both for the differential diagnosis of the causes of hyperthyroidism by scintigraphy with radioactive iodine uptake by the thyroid, and for definitive treatment, administered orally in the form of a solution or capsules. In addition, the calculation of the therapeutic dose of the substance depends on this uptake in 24 hours, the weight of the gland, the patient's age, and the dose intended to be contained in the thyroid cells.

Physiologically, the thyroid gland is able to store iodine to produce thyroid hormones (triiodothyronine (T3) and tetraiodothyronine (T4)). In hyperthyroidism, the thyroid cells are greedy for iodine, that is, there is a high selectivity for the substance. Therefore, when radioiodine iodine (iodine-131) is administered, these cells cannot distinguish whether the iodine being ingested is radioactive or not, capturing it in the same way. Consequently, iodine-131 accumulates inside the gland, emitting radiation and reducing the production of thyroid hormones.

The ideal dose to be administered is not yet a consensus in the literature, however, the main objective is the resolution of thyrotoxicosis, considering cured not only those patients who maintained euthyroidism, but also those who inevitably evolved to hypothyroidism after therapy, with adequate replacement of Levothyroxine.

One caution that should be taken is not to administer thionamides immediately before or after radiotherapy with iodine-131, because especially Propylthiouracil had a radioprotective effect of up to 55 days. Therefore, if necessary, it is preferable to use Methimazole so as not to interfere with therapeutic efficacy (WAJCHENBERG et al., 2014).

According to the study by Mendes and Souza (2013), there are two protocols (fixed dose and calculated dose) for the administration of radioactive iodine in therapeutic dosages, which reveal:

> The fixed dose ranges from 10 mCi to 15 mCi. The calculated dose can be estimated by two methods, both taking into account the 24-hour uptake. In the first method, the thyroid weight in grams is estimated, multiplied by 80–120 μCi of 131I, and then divided by the 24-hour uptake. The second, on the other hand, does not use the weight in grams of the thyroid, being calculated with the objective of leaving 8 mCi in the thyroid. Using one of these two calculation methods, typical doses range from 5 to 15 mCi (MENDES; SOUZA, 2013, p. 14).

Therefore, it is important to emphasize that the choice of dose should be evaluated individually according to the clinical condition of each patient, considering the scintigraphy, thyroid volume, and degree of hyperthyroidism. In addition, the therapeutic result is also dependent on the radiosensitivity of the exposed thyroid tissue of each individual, and is not exclusively related to the dose administered (MENDES; SOUZA, 2013).

3 INDICATIONS AND CONTRAINDICATIONS OF RADIOACTIVE IODINE

3.1 INDICATIONS

The use of iodine-131 as radioactive therapy for hyperthyroidism is the definitive treatment choice for patients who relapse on thionamide therapy. In addition, it is an alternative for individuals who have allergic reactions, hepatotoxicity, and agranulocytosis to these antithyroid drugs (ATDs) (PEREIRA et al., 2021). It should also be indicated in patients with heart disease and the elderly as an initial therapy, since they need a definitive and rapid control of hyperthyroidism (MAIA et al., 2013).

In addition to being one of the main therapeutic resources in Graves' Disease, the use of radioiodine is also beneficial in toxic adenoma and toxic multinodular goiter. In the latter, radioiodine therapy can be administered alone or with previous recombinant TSH stimulation. In addition, radioactive iodine may be indicated, after total thyroidectomy, in patients with confirmed diagnosis of well-differentiated thyroid cancer (papillary or follicular) (PEREIRA et al., 2021).

3.2 CONTRAINDICATIONS

According to Pereira et al. (2021), the absolute contraindications for the administration of radioactive iodine are: pregnancy, lactation, and pregnancy planning in the next 6 months. Nevertheless, Wajchenberg et al. (2014) argue in their studies that there is no defined teratogenic risk for iodine-131, but that its reckless use after the 10th/12th weeks of gestation, a period in which the

thyroid has already developed, can cause congenital hypothyroidism. Thus, radioiodine therapy should be avoided in cases of evidence of pregnancy or its planning.

In addition, very large goiters, uncontrolled hyperthyroidism or high free T3 values, diagnostic purpose in children under 10 years of age, patients with dysphagia, sphophage stenosis, active gastritis, gastric erosions, gastroduodenal ulcer, suspected decreased gastrointestinal motility, lung metastases, restriction of salivary gland function, bone marrow depression, and severe infiltrative ophthalmopathy are relative contraindications (LOUREIRO, 2014). In cases of eye disease where vision is threatened, antithyroid drug therapy (ATDs) should be the option of choice (VILAR et al., 2013). On the other hand, this therapeutic strategy has a higher rate of hyperthyroidism recurrences and, therefore, can negatively impact the evolution of ophthalmopathy (MAIA et al., 2013).

Despite controversial studies, fine-needle aspiration (FNA) is recommended before iodine-131 administration in patients with Graves' disease with non-functioning nodules larger than 1 to 1.5 cm, due to a higher risk of malignancy (VILAR et al., 2013).

4 ADVANTAGES AND DISADVANTAGES OF RADIOIODINE THERAPY

4.1 ADVANTAGES

As already mentioned, radioiodine therapy is widely used in the definitive treatment of hyperthyroidism, has a low cost, is easily administered, minimally invasive and painless. Therefore, it is a method well accepted by patients and significantly reduces the need for surgical intervention. In addition, even though it is a radioactive approach, studies have shown that it does not have significant oncogenetic risks (PEREIRA et al., 2021).

The thyroid gland exposed to iodine-131 undergoes a reduction in size about 6 to 8 weeks after contact with the substance, a process that can last up to 18 months. Therefore, the superiority of this therapy over thyroidectomy can be perceived, as only the postoperative recovery time can persist for approximately 24 weeks. In relation to ATDs, the advantage is related to the duration of treatment, since the use of the drug is estimated at 2 years, which causes difficulty in adhering to the proposed treatment (MENDES; SOUZA, 2013).

4.2 DISADVANTAGES

The main complication of radioactive iodine therapy is transient or permanent thyroid hypofunction after exposure of the gland (VILAR et al., 2013). In addition, around 1% of patients who were exposed to iodine-131 radiation may develop thyroiditis 5 to 10 days after treatment, manifesting pain in the glandular region and temporary worsening of hyperthyroidism (WAJCHENBERG et al., 2014).

In addition to the thyroid, other tissues can be affected by radioiodoterpy, causing: lacrimal gland dysfunction, gastritis, transient inflammatory tracheitis, sialadenitis (inflammation of the salivary glands) and hypospermia, bone marrow depression (leukopenia and thrombocytopenia) (LOUREIRO, 2014).

In addition, Pereira et al. (2021) found that in men between 18 and 55 years of age, there were transient changes in testicular function after iodine administration131, more specifically changes in the production of hormones due to a dysfunction of Sertoli and Leydig cells, sperm structure, and chromosomal transformations. On the other hand, another study evaluated the effect of the therapy in women submitted to the use of radioiodine, by measuring the production of Anti-Mullerian hormone (AMH) in these patients, which demonstrated a low risk for infertility.

Finally, radioactive iodine may anticipate or intensify infiltrative ophthalmopathy in some individuals. However, corticosteroid therapy can avoid this complication and should be considered in smokers, active ocular disease, and severe hyperthyroidism (VILAR et al., 2013).

5 FINAL THOUGHTS

At the end of the research, it was possible to conclude that radioactive iodine therapy is a safe and highly effective option, with a high cost-benefit ratio. There are complications that may arise after the administration of the substance in question, which deserve attention from the medical professional who is indicating such therapy for his patient, since it is a radioactive substance.

However, the advantages for the sick individual outweigh the possible adverse effects. In addition, during the study, it was not possible to find relevant data on the disadvantages that would support the idea that radioiodine therapy cannot be considered first-line in the treatment of hyperthyroidism, when well indicated.

Regarding contraindications, it is necessary to be very careful when subjecting a patient to exposure to iodine-131. Therefore, the choice of treatment should be made individually, always evaluating the risk-benefit.

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