Mini Review

Thyrotoxicosis and radioiodine therapy: Does the dose matter?

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ABSTRACT

There are 3 treatment options for thyrotoxicosis: Antithyroid drugs, Surgery and radioiodine. The choice of treatment varies geographically. Radioiodine therapy is preferred in the United States. The aim of radioiodine is to destroy sufficient thyroid tissue to cure the hyperthyroidism. There is a lack of consensus towards what dose of radioiodine should be used. Several methods are used to determine the dose. In our practice we administer 400 MBq to patients with Graves and in patients with large multinodular goiter, we would administer 800 MBq.

Key words: Thyrotoxicosis, radiodine therapy, Dose

Thyrotoxicosis is a disorder of excess thyroid hormone. The tissue effects of high concentration of thyroid hormones have many clinical manifestations. Two main hormones are synthesized and released by the thyroid gland. Thyroxine (T4) and triiodothyronine (T3). T4 is a prohormone, whereas T3 is biologically active through interaction with specific nuclear receptors that are present in nearly all tissues. Hyperthyroidism, which specifically describes increased thyroid hormone synthesis and secretion, is common in the UK with prevalence of 2% in women and 0.2% in men. Incidence increases with age, is highest in Caucasian populations and in iodine-deficient areas. The most common cause of thyrotoxicosis is Graves' disease, in which auto-antibodies bind to stimulate the thyrotropin receptors found on the surface on the thyroid follicular cells. The next most common cause is autonomous overproduction of thyroid hormones by one or more nodules within the thyroid. The frequency of these forms of thyrotoxicosis varies with iodine intake. Hyperthyroidism has well-known unacceptable consequences including cardiovascular disease, such as atrial fibrillation and heart failure, osteoporosis and reproductive problems. Left untreated, thyrotoxicosis can progress to a thyroid storm.[1,2]

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After biochemical confirmation of thyrotoxicosis, a choice between the 3 treatment types is required: anti thyroid drugs, surgery and radioiodine therapy. The choice of treatment varies significantly geographically. Radio-iodine therapy is preferred in the USA whereas anti-thyroid drugs are favoured in continental Europe and Japan. Radio-iodine can be used as a first line treatment of hyperthyroidism, is the most common form of treatment for Graves' disease in the UK and is the treatment of choice in relapsed cases of thyrotoxicosis. Contraindications include pregnancy or lactation, desire of pregnancy within the next months, suspicion or diagnosis of co-existing thyroid cancer and inability to comply with radiation protection regulations. Radio-iodine is safe, effective, inexpensive and has been used for more than 60 years.[1]

The aim of radioiodine therapy in Graves' disease and in any form of thyrotoxicosis is to destroy sufficient tissue to cure the hyperthyroidism. This process renders the patient either euthyroid or hypothyroid. Radioiodine therapy induces an intense radiation thyroiditis and subsequent fibrosis, thereby destroying the synthetic capacity of the

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thyroid. There is a lack of consensus towards what dose of radioiodine should be used and whether the aim of treatment is to render the patient euthyroid for a period of time or hypothyroid.[3-5] Some endocrinologists believe that sustained euthyroidism would clearly be the most desirable outcome but this would appear to be futile. A review from the 1980s stated unequivocally that the goal of radioactive iodine treatment in patients' with Graves' disease should be complete ablation of the gland.[6] This is because eventual hypothyroidism is virtually inevitable. Numerous studies investigating different doses of radioactive iodine activity administered have demonstrated an instance of hypothyroidism of approximately 2-3% many years after therapy.[7,8]

It is suggested that the radionuclide scan has three main uses in imaging hyperthyroidism: establishing the cause, selection of appropriate radioiodine 131 regimens and follow-up of patients after radioiodine therapy. Several different methods have been used to determine the radioiodine activity that should be administered to thyrotoxic patients.[9] In addition, several factors have been considered as influencing the outcome of radioiodine treatment required. Studies have suggested that patients with larger volume thyroid glands and severe hyperthyroidism are more likely to fail to respond to a single administration of radioiodine.[1] Techniques have been undertaken to assess gland size, either estimated clinically or with imaging and doses have been calculated on the basis of gland size, iodine uptake and sometimes iodine turnover.[10] Many hospitals do not have the resources or facilities to undertake routine radioiodine uptake scans at 4 and 24 h along with detailed radioiodine kinetics calculations.[11] The uses of these methodologies add to the complexity of the procedure and significantly increase the cost related to the therapy. As radioactive iodine therapy is relatively inexpensive, incurring further costs determining the dose of radioiodine that should be administered needs to be justified.[5]

In Ayrshire and Arran, Scotland we have had two District General Hospitals that have historically delivered two different fixed doses of radioiodine to treat thyrotoxic patients. We compared the efficacy of 370 MBq (10 millicuries) with 555 MBq (15 millicuries) radioiodine activities for therapy in patients with Graves' disease over a period of 10 years. We excluded patients with moderate to severe dysthyroid eye disease. We also documented whether these patients had previous treatment with Carbimazole, propylthiouracil and previous radioiodine therapy. Overall, 90% of the patients had a successful outcome from treatment with no significant difference between the higher and lower activities and no difference between the genders.[5] We now administer 400 MBq capsules to all patients with Graves' disease who require radioiodine therapy and continue to have a 90% success rate.

There is no doubt that larger doses of radioiodine (>600 MBq) will lead to a larger percentage of patients becoming euthyroid or hypothyroid more quickly than smaller doses (<400 MBq).[12,13] Recently, the American Thyroid Association and American Association of Clinical Endocrinologists Taskforce on Hyperthyroidism and Other Causes of Thyrotoxicosis proposed that radiation should be administered in a single dose, typically 370 to 555 MBq, to render the patient with Graves' disease euthyroid. It also recommended that no patient should be treated with a dose less than 370 MBq.[14] There are a number of factors that predict the need for either a second dose (typically given 2-6 months after the initial dose) or a higher initial dose. These include male sex, high free T_4 at diagnosis and a palpable goitre.[8] Larger doses of radioiodine are also required for patients in areas where the iodine content of their diet is high or they are on iodine-containing drugs e.g. amiodarone. Because of the risk of hypothyroidism, thyroid function should be checked every 4-6 weeks. Once euthyroidism has been established annual thyroid function checks are required.[1]

However, larger doses of radioiodine are not without possible complications. The Royal College of Physicians clinical guidelines indicate that although they found no evidence of increased instance of leukaemia, there was a possible increase in small bowel cancer and gastric cancer.[15] The potential benefits using a small radioiodine activity are in line with the international commission on radiological protection recommendations regarding the "linear no threshold" model for radiation risk.[16,17] Restrictions on behavior of out-patients post-treatment can also be reduced with the administration of a lower activity. When 555 MBq is administered the guidance notes suggest a restriction period of 25 days to ensure that the radiation dose to members of the public is kept below 1 mSv. For activity of 370 MBq, this period can be reduced to 21 days, with obvious benefits to patient, families and carers.[15] Another, potential environmental benefit for administering low activity is the reduction in the release of iodine 131 via sewage system.

There are two further possible theoretical considerations. It is recognized that patients on a low iodine diet are more sensitive to radioiodine therapy. However, compliance with dietary advice is recognized to be poor.[13] In addition, rTSH is known to increase radioiodine uptake and has been used to facilitate radioiodine uptake in thyroid cancers and large thyroid goitres. However, rTSH needs to be administered

some hours before the radioiodine and does make a simple treatment regimen much more complex.[18-20]

It is our practice to administer 400 MBq to patients with Graves' disease. In patients with large goitres, particularly multinodular goitres, we would administer 800 MBq. We would not routinely use carbimazole or propylthiouracil pre-radioiodine to render the patient euthyroid. However, carbimazole or propylthiouracil pre-radioiodine would be considered in a frail elderly patient where there may be a concern regarding a thyroid storm. In patients with thyroid eye disease, we would be resistant to the administration of radioiodine to a smoker. We would prescribe steroid therapy for patients with thyroid eye disease undergoing radioiodine therapy and ensure that they were closely followed-up post treatment in order to deter the progression of the eye disease.

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