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Therapeutic aspects of multinodular non-toxic goitre

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Surgery is, of course, a very effective treatment for patients with multinodular goitre. However, surgery of large goitres is not without risk, especially in patients with cardiovascular or pulmonary problems. Therapy with iodine or L-thyroxine, although effective in the treatment of goitres in hypothyroid patients with severe iodine deficiency, is largely ineffective in patients with a non-toxic, multinodulair goitre.

Radioiodine (^{131}I), usually given in single doses of 100-150 µCi per gram of thyroid tissue corrected for the 24-hour uptake (RAIU), is effective in reducing thyroid volume in over 90% of patients with nodular goiter. The average reduction in thyroid volume is approximately 40% after one year and 50% to 60% after two to five years. In most patients compressive symptoms improve as well. The decrease in compressive symptoms is accompanied by significant tracheal widening and improvement of respiratory function. Also venous obstruction can improve after radioiodine therapy. Early adverse effects of radioiodine therapy are usually mild and transient, and include radiation-induced thyroiditis and esophagitis. The main late adverse effect is the development of Graves' hyperthyroidism in approximately 5% of patients, especially those with anti-TPO antibodies. Hypothyroidism develops in 22% to 58% of patients within 5 to 8 years, especially in patients with small goitres and / or anti-TPO antibodies.

^{131}I treatment is especially attractive in elderly patients who have a high operative risk and in those who refuse surgery. However, in patients with non-toxic, nodular goitre thyroid radioactive iodide uptake (RAIU) is usually rather low, especially in areas with a high iodine intake. As a result, high doses of ^{131}I are often needed for thyroid volume reduction, causing a relatively high radiation burden to extrathyroidal organs.

In recent years, the use of recombinant human thyrotropin (rhTSH) to stimulate RAIU in patients with non-toxic goiter has been studied. It was shown that a single, low dose of 0.01 or 0.03 mg rhTSH doubled 24-h RAIU in these patients and caused a more homogeneous distribution of radioiodine. Pretreatment with 0.01 or 0.03 mg rhTSH allowed approximately 50-60% reduction of the therapeutic dose of radioiodine without compromising the efficacy of thyroid volume reduction.

Furthermore, the possibility of improving the efficacy of thyroid volume reduction by pretreatment with rhTSH has been studied. For this purpose, the dose of radioiodine is not adapted (reduced) to the increase in RAIU after administration of rhTSH. A prospective, randomized double-blind trial has been published, comparing size reduction of relatively small benign non-toxic nodular goitres by radioiodine therapy with and without pretreatment with 0.3 mg recombinant human TSH. At 12 months, the average thyroid volume reduction was 46% in the placebo group and 62% in the rhTSH group. Adverse effects related to hyperthyroid symptoms and thyroid growth occurred significantly more frequent in the rhTSH group.

However, before rhTSH can be advised as an adjunct to improve the efficacy of radioiodine therapy in nodular goitre, further studies are needed, looking carefully at dose-response relationships with respect to efficacy and adverse effects. This year, an international multicenter trial covering these aspects will be started.

References

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