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The Effect of 131-I Treatment of Graves' Disease May Be Potentiated by the Coadministration of Lithium

Martin NM, Patel M, Nijher GM, Misra S, Murphy E, Meeran K. Adjuvant lithium improves the efficacy of radioactive iodine treatment in Graves' and toxic nodular disease. Clin Endocrinol 2012;77:621-7.

SUMMARY

BACKGROUND

Lithium shares with iodide a strong inhibiting effect on thyroid hormone secretion. It differs from iodide by not interfering with the transport of iodide by the sodium/iodide symporter (NIS) into the follicles. As a consequence, it increases the time that single doses of iodide and its isotopes are retained within the thyroid. This is the basis for postulating an increased efficiency of ^{131}I treatment (RAI) if given together with lithium as compared with ^{131}I alone. Lithium does not affect the peripheral metabolism of thyroid hormones. Indeed, the majority of studies performed so far indicate a higher efficiency of RAI plus lithium than of RAI alone. The present study confirms these findings in by far the largest group of patients hitherto reported.

METHODS AND RESULTS

A total of 204 patients were studied: 103 received RAI alone and 101 received lithium in addition to RAI. Approximately 80% of these patients were suffering from Graves' disease, and the remainder presented with multinodular toxic goiter. An average dose of 500 MBq (13.5 mCi) was given. A standard dose of 800 mg of lithium per day was started 3 days before RAI and given for a total of 10 days. Antithyroid drug treatment was not resumed after treatment with RAI. Thyroxine treatment (100 μg of T_4 per day) was started whenever serum FT_4 fell below 14.5 pmol/L. Serum thyroid hormone concentrations were monitored frequently while serum lithium concentrations were not evaluated.

During the 12-month follow-up, serum FT_4 and FT_3 were clearly lower at all times in the lithium-treated group. FT_4 and FT_3 were decreased by approximately 12% to 17% with respect to the RAI-alone group. With lithium added to RAI, the proportion of patients cured after 1 year of treatment was slightly higher (93% vs. 84%). The time to remission was also shortened by lithium treatment, which seemed to be as effective in patients with multinodular goiter as in those with Graves' disease, but the group of multinodular goiters

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was too small for any definite statement. The group of patients with endocrine ophthalmopathy was also small and, moreover, these patients were often receiving steroid treatment, making any conclusions in this respect impossible.

CONCLUSIONS

This article confirms that combined treatment with RAI and lithium induces euthyroidism or hypothyroidism more rapidly and in a greater percentage of patients than in those receiving a standard dose of ^{131}I (approximately 500 MBq) only. An additional advantage results from the inhibiting effect of lithium on thyroid hormone secretion, since this strategy obliterates the well-known transient increase of FT_4 and FT_3 following the administration of radioactive iodine. The treatment was as effective in multinodular goiter as in Graves' disease.

ANALYSIS AND COMMENTARY

One question not addressed in this study is that of the potential adverse effects of lithium. Indeed, in patients with cardiac and renal disorders, lithium needs to be given with great caution, and its blood level should be monitored during the treatment. This was not done in the present article, but the dose of 800 mg per day is in the low range. Even this dose had a clear-cut inhibitory effect on thyroid hormone secretion. Indeed, the peaking of circulating hormones after ^{131}I irradiation may have been avoided. Throughout the study, serum thyroid hormone levels were slightly lower in the lithium-treated patients, despite the fact that lithium was given over only 10 days. There is little doubt that the addition of lithium increases the efficiency of ^{131}I treatment.

This is certainly a great advantage in areas where legal limitations do not allow giving high doses of ^{131}I. For instance, in Switzerland and Germany, the maximum outpatient dose allowed is 200 MBq (5.4 mCi). In these areas, the combined treatment is most advantageous. However, in countries such as Britain and the United States, where legislation is more liberal, one has to leave it to individual doctors and their patients to decide whether it is preferable to simply increase the dose of ^{131}I without adding lithium.

It is astonishing that in this study the success rate of treatment of multinodular goiters with the same dose of ^{131}I and lithium was similar to that in Graves' disease. In a country like Switzerland, where large goiters were formerly a frequent clinical finding, the dose of irradiation per gram of goiter tissue varies greatly, with higher doses being recommended for larger goiters. Today, the observation of multinodular goiters of large size has become exceptional.

— Albert G. Burger, MD