SUPPLEMENTATION OF METHIMAZOLE TREATMENT WITH MODERATE DOSES OF IODIDE (38 MG/DAY) QUICKLY IMPROVES HYPERTHYROIDISM

Takata K, Amino N, Kubota S, Sasaki I, Nishihara E, Kudo T, Ito M, Fukata S, Miyauchi A. **Benefit of short-term iodide supplementation to antithyroid drug treatment of thyrotoxicosis due to Graves' disease.** Clin Endocrinol (Oxf) 2010;72:845-50.

SUMMARY

BACKGROUND

Combining an antithyroid drug with high doses of potassium iodide (KI) is a well-established procedure to rapidly alleviate thyrotoxic symptoms in severely ill patients with Graves' disease who are scheduled for thyroid surgery. This method takes advantage of the inhibitory action of iodine not only on the synthesis of thyroid hormones, but also on their secretion. However, long-term treatment of Graves' disease with KI is not advisable because of the possible escape, the so-called Wolff–Chaikoff effect. It is only in patients who have undergone treatment with partly ablative doses of radioactive iodine (^{131}I) and in patients with hyperthyroidism who have been treated with ipodate that this rule does not apply. Yet, so far—with few exceptions—only the effect of very large doses of KI have been studied and most patients included in these studies were living in areas with low or moderate iodine intake. In the article under discussion, the effect of treatment of ordinary patients with Graves' disease with the combination of methimazole (MMI) and a relatively small dose of KI was studied in a Japanese population who did not have iodine deficiency.

METHODS

In this study, 162 patients with Graves' disease were initially selected; 134 successfully fulfilled the requirements of the protocol, which was designed to study the response of serum free thyroxine (T_4) and free triiodothyronine (T_3) to an MMI treatment with and without the addition of 38 mg iodide (50 mg of KI per tablet). Four similarly sized groups of patients matched for sex and age were prospectively studied. Group 1 received 30 mg of MMI; group 2 received in addition one tablet of KI; group 3 received only 15 mg of MMI, and group 4 received 15 mg of MMI plus one tablet of KI. This treatment schedule was maintained until the free T_4 decreased into the normal range. At this time (i.e., 2 to 8 weeks after the beginning of treatment), KI was stopped. Therefore, KI was given for only a rather short period. MMI treatment was maintained, adjusted, and then stopped when serum free T_4 and serum thyrotropin (TSH) were in the normal range for more than 6 months. Patients were considered to be in remission if, after this date, they remained euthyroid (normal free T_4 and normal serum TSH values) for 1 year.

RESULTS

Independent of the dose of MMI, the addition of KI resulted in a more rapid normalization of serum free T_4. With 30 mg of MMI plus KI, free T_4 normalized in 58% of the patients within 2 weeks, while with 15 mg of MMI, this result was achieved in 53% of the patients. At 4 weeks of treatment, the response was still in favor of those receiving KI, but the difference was no longer significant. After ending the KI treatment, there was transient, clinically irrelevant rebound of free T_4 and free T_3.

The percentage of remissions, defined as 1 year of treatment-free euthyroidism, was not different among the groups. There was a nonsignificant tendency for a higher remission rate in patients who had received the combined treatment.

CONCLUSION

Combined treatment with methimazole and potassium iodide improved the short-term control of hyperthyroidism and did not cause worsening hyperthyroidism when KI was stopped.

COMMENTARY

It is to be expected, as again confirmed here, that adding a supraphysiological dose of iodine to an antithyroid drug in order to achieve remission in patients with Graves' disease will result in a more efficient blockade of hormone secretion from the thyroid gland. The work of Takata et al. adds some valuable information about the dose–response relationship, the kinetics, and the late outcome of the combined treatment. While most (though not all) related studies used much higher iodine doses (mostly 250 to 500 mg iodine as Lugol's or supersaturated potassium iodide [SSKI] solution), only one tablet of 50 mg of KI containing 38 mg of iodine was used in this study (1,2). Nevertheless, most clinicians would probably have expected a more dramatic effect of the combined treatment than that observed in the study. Indeed, in the group receiving 30 mg of MMI, it was only at 2 weeks that free T_4 and free T_3 were significantly lower with added iodine than without it. In the group receiving 15 mg of MMI, a significant difference was also observed in the 4th week of treatment, suggesting that this dose of MMI does not achieve the same degree of thyroid blockade as does 30 mg of MMI. A very few patients were apparently more or less resistant to both forms of treatment, particularly when treated with 15 mg of MMI. Taken together with the all-important observation that the incidence, the quality, and the duration of long-term remission did not differ among patients given 30 mg of MMI alone or in combination with iodine, I conclude that the present work does not provide convincing evidence to suggest a compelling need to add iodine to MMI in ordinary patients with Graves' disease. It is, however, remarkable that stopping KI treatment did not result in relapses. The occasional use of KI may therefore be worthwhile in patients with adverse cutaneous reactions to high doses of MMI.

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REFERENCES

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