Background Amiodarone causes thyrotoxicosis in two ways. First,

Amiodarone May Be Continued in Patients

it provides a large iodide load that can induce hyperthyroidism in susceptible individuals with underlying Graves' disease or multinodular goiter—called type 1 amiodarone-induced thyrotoxicosis (AIT). Second, it can cause thyrotoxicosis through a destructive effect on thyrocytes, a form of thyroiditis called AIT type 2. The treatments for AIT usually require discontinuation of amiodarone, in addition to other measures. The aims of the present study were to demonstrate the feasibility of continuing to administer amiodarone in AIT type 2, and to determine whether perchlorate was useful for its treatment.

Methods

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SUMMARY • • • • • • • •

Patients with AIT type 2 were recruited from 10 centers in The Netherlands. The criteria for the diagnosis were TSH <0.4 mU/L, FT_4 >25 pmol/L (1.94 ng/dl), negative anti-TPO and anti-TSH-receptor antibodies, no visualization of the thyroid on 99mTc-pertechnetate scintigraphy, absence of nodular goiter on ultrasonography, and patient consent to continue amiodarone. Patients were randomly assigned to one of three treatment groups, but physicians and patients were not blinded with regard to study medication: group A, prednisone 30 mg/day plus methimazole 30 mg/day; group B, sodium perchlorate 500 mg twice daily plus methimazole 30 mg/day. Follow-up

evaluation occurred at 4-week intervals to 28 weeks, then at 8-week intervals up to 2 years. Medication was adjusted based on thyroid-function tests.

Clinical

THYROIDOLOGY

Results

with Amiodarone-Induced Thyroiditis Treated with Prednisone

Eskes SA, Endert E, Fliers E, Geskus RB, Dullaart RP, Links TP, Wiersinga WM. Treatment of amiodarone-induced thyrotoxicosis type 2: a randomized clinical trial. J Clin Endocrinol Metab

The number of patients randomly assigned to groups A, B, and C were 12, 14, and 10, respectively (6 of the 42 patients initially randomized were excluded because they either had stopped taking amiodarone, had moved out of the country, or had positive tests for anti-TSH receptor). The median time for FT₄ levels to reach <25 pmol/L was 4 weeks in group A and 12 weeks in the other groups, but there were no significant differences in the time to normalization of FT₄ and TSH between groups. The serum TSH normalized with the therapy in all the patients initially receiving prednisone (groups A and C), however prednisone needed to be added to 4 of the 14 patients in group B. Recurrent thyrotoxicosis occurred in 1 patient in group A at 24 weeks when he was not on therapy with prednisone and methimazole, and in 2 patients in group C at 12 and 76 weeks when they were off the triple therapy. Subclinical hypothyroidism developed in about 40% of patients.

Conclusions

Euthyroidism was reached in all patients despite the continuation of amiodarone. Prednisone remains the preferred treatment for AIT type 2 because perchlorate given alone or in combination with prednisone did not produce better outcomes.

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ANALYSIS AND COMMENTARY • • • • • •

In European regions with relatively low iodine intake, there is a nearly 10% incidence of AIT in patients on amiodarone. Bartalena, Martino, and associates in Italy were the first to show that prednisone was effective in the treatment of type 2 AIT (1). The main goal of the current study was to show that amiodarone could be continued while patients were undergoing therapy for type 2 AIT, and that the condition would resolve. This contradicts the usual approach of stopping amiodarone when either form of AIT occurs, as has been recently recommended (2). Bogazzi et al. reported that 5 of 7 patients who continued amiodarone during prednisone therapy for type 2 AIT relapsed after prednisone was withdrawn (3).

The decision to use methimazole for all three groups is surprising. It is the mainstay of treatment in addition to withdrawal of amiodarone in type 1 AIT, in which there is overproduction of thyroid hormone, but it is not recommended when the diagnosis of type 2 AIT is made with confidence. The Italian group has shown that methimazole is ineffective in type 2 AIT in comparison with prednisone (4).

The second aim of the current study is curious. Perchlorate was given with methimazole in group B, and with methimazole and prednisone in group C. The usual reason to administer perchlorate is to deplete the thyroid of iodide that comes from amiodarone; perchlorate is used in type 1 AIT, but not in type 2 AIT. The study showed that 71% of group B who only received perchlorate and methimazole had improvement, an unexpected finding. Nevertheless, prednisone was the more effective therapy. There are patients who are thought to have a combination of types 1 and 2 AIT. "Shotgun" therapy with prednisone and methimazole is effective in these patients, and I use it initially in patients who have severe AIT and in whom the diagnosis of type 1 versus type 2 is unclear. Interestingly, sestamibi scans may be helpful in this differential diagnosis (5). Type 1 patients take up the sestamibi tracer and type 2 patients do not.

— Jerome M. Hershman, MD

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