Amiodarone and the Thyroid

To the Editor: Mazason and associates (1) report that myxedema is not an uncommon occurrence during amiodarone therapy. However, the exact metabolic effect of amiodarone on the thyroid function remains unclear. Singh and Nademanee (2) originally monitored reverse triiodothyronine as a guide to therapeutic effectiveness of amiodarone, but this is probably an early indication of amiodarone's overall effect on thyroid function. Martinez and colleagues (3) have shown that hyperthyroidism is commoner in patients with low iodine intake, and hypothyroidism is commoner in patients with a normal iodine intake. In all three groups (13.6 IU/mL in euthyroid patients, 26.4 IU/mL in patients receiving methimazole), in all three groups. However, the reverse triiodothyronine (normal, 20 to 32% and that of hyperthyroidism, approximately 23%). The thyrotrophin level (normal. 0 to 4 IU/mL) was elevated in 72 of 104 patients (69%). The incidence of hypothyroidism was approximately 32% and that of hyperthyroidism, approximately 23%. The mean dose of amiodarone was 311 mg/d, and the mean length of follow-up was 28 months.

Comparisons were made of 11 patients receiving levothyroxine (mean follow-up, 22 months), 1 patient receiving methimazole (follow-up, 28 months), and 8 patients (mean follow-up, 18 months) who remained euthyroid. The hypothyralmic pituitary axis was elevated. The triiodothyronine resin uptake, thyrotropin, free thyroxine index, triiodothyronine shown by radioimmunoassay, and thyrotropin-releasing factor shown by radioimmunoassay were within normal ranges in all three groups. However, the reverse triiodothyronine (normal, 20 to 53 mg/dL) was elevated in the euthyroid patients (mean, 64 mg/dL) and in the patient receiving methimazole (56 mg/dL). The thyrotropin level (normal, 0 to 4 IU/mL) was elevated in all three groups (13.6 µU/mL in euthyroid patients, 26.4 µU/mL in patients on levothyroxine, and 4.3 µU/mL in the patient on methimazole). In all groups the thyrotropin level rose greater than two times the baseline 30 minutes after receiving thyrotropin-releasing factor (4). We have recently tested for radioactive iodine-131 uptake in four additional patients who have developed hyperthyroidism while receiving amiodarone therapy. However, the radioactive iodine uptake was less than 5% in these patients. Thyroid-binding globulins were normal, and there was no clinical evidence of active thyroiditis. On the basis of these data and those previously published, it is clear that amiodarone's effects on thyroid metabolism remain unexplained. The data suggest an intracellular effect on thyroid hormone metabolism independent of the thyroid-pituitary axis or an effect on peripheral degradation of thyroid hormone.

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