**Topic:** THE CHANGING EPIDEMIOLOGY OF AMIODARONE-INDUCED THYROTOXICOSIS

**Title:** Proportion of type 1 and type 2 amiodarone-induced thyrotoxicosis has changed over a 27-year period in Italy.

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**SUMMARY**

**Context:** Two main forms of amiodarone-induced thyrotoxicosis (AIT) exist. Type 1 AIT is a form of iodine-induced hyperthyroidism. Its management is complex and includes thionamides, potassium perchlorate and, occasionally, thyroidectomy. Type 2 AIT is a destructive thyroiditis, responds to glucocorticoids, and usually does not require further thyroid treatment once euthyroidism has been restored.

**Objective:** To assess retrospectively the prevalence and relative proportion of type 1 and type 2 AIT over a 27-year period at a tertiary referral centre in Italy.

**Patients:** Consecutive patients with AIT (N = 215) seen at the department of endocrinology of the University of Pisa between 1980 and 2006.

**Results:** Type 1 AIT constituted the most frequent AIT form (60%) during the first years covered by this study. The annual mean number of type 1 AIT patients was 3.6 at the beginning of the study period, and 2.5 during later years. In contrast, the mean annual number of new cases of type 2 AIT progressively increased from 2.4 to 12.5. Likewise, the proportion of type 2 AIT increased in a significant linear manner (P<0.0001), currently accounting for 89% of AIT cases. Type 2 AIT patients showed a male preponderance, higher serum FT4/FT3 ratio (P<0.002), lower 3-hr & 24-hr thyroidal radioactive iodine uptake values (P<0.0001), and received a higher cumulative dose of amiodarone (P<0.0001) than type 1 AIT patients.

**Conclusions:** Over a 27-year period, the epidemiology of AIT changed, as the prevalence of type 2 AIT progressively increased and that of type 1 remained constant. Thus, under most circumstances, endocrinologists nowadays deal with type 2 AIT, which is a destructive thyroiditis, generally treated successfully with glucocorticoids. Although no additional treatment is usually required after the destructive process subsides, periodic assessment of thyroid function is warranted, because of the occurrence of hypothyroidism (up to 17%) during long-term follow-up of these patients.

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**COMMENT**

Amiodarone, a very effective anti-arrhythmic drug, causes thyroid dysfunction in 15-25% of long term-treated patients. It has been claimed that amiodarone-induced hypothyroidism was more prevalent in iodine-sufficient areas (such as the USA), while amiodarone-induced thyrotoxicosis (AIT) develops more frequently in iodine-deficient regions. Such differences in prevalence may, however, be only relative, since (for instance) in a retrospective review of consecutive patients with amiodarone-induced dysfunction seen in the department of cardiology in our institution (HStP; Brussels), such a difference in prevalence was not confirmed.
Our Italian colleagues (Enio Martino et al.) have described two types of AIT in 1984. The type 1 represents true “poisoning” of the thyroid gland by excess iodine. It is a form of iodine-induced hyperthyroidism, and occurs more often in glands with pre-existing abnormalities. The type 2 represents an inflammatory, “destructive” thyroiditis, with the release of preformed hormone stores, and it occurs more often in normal thyroid glands. It should however be remembered that this classification is somewhat arbitrary, since cases have been described of patients who ‘shuttle’ between the types 1 & 2. Furthermore, many mixed cases coexist, with both pathogenic mechanisms eventually contributing to the development of thyrotoxicosis.

In present study, the authors showed a significant trend, in the more recent years, for a change in the epidemiology of AIT, with type 2 patients representing nowadays more than 80% of all cases. These changes are attributed to the fact that most patients who are eligible for amiodarone therapy are first being screened for thyroid function.

The authors concluded that since the majority of patients with AIT present the destructive thyroiditis, the addition of glucocorticoids should be considered a mainstay in the management of these patients. Also, because the type 2 disease may be followed in the long term by permanent hypothyroidism, they propose lifelong assessment of thyroid function after the restoration of euthyroidism.

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See Figure below

![Figure 1: Prevalence of type 1 and type 2 AIT over a 27-year period](image)

(b) Proportion of type 1 (or mixed) or type 2 AIT during the study period. Overall, 215 AIT patients were included in the present study: 70 type 1 and 145 type 2 AIT.