Topic: AMIODARONE-INDUCED THYROTOXICOSIS

Title: Amiodarone-induced thyrotoxicosis is a predictor of adverse cardiovascular outcome.

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SUMMARY

Background: Amiodarone-induced thyrotoxicosis (AIT) is a clinical condition that is notoriously difficult to manage. The relative risk of adverse cardiovascular events in such patients is largely unknown.

Objective: The authors compared the clinical characteristics and major adverse cardiovascular events (MACE) in AIT & euthyroid patients.

Method: Patients at a tertiary referral centre who had been prescribed amiodarone for at least 3 months were analyzed retrospectively. Baseline clinical characteristics, laboratory parameters & outcome events were evaluated. MACE was defined as cardiovascular mortality, myocardial infarction, stroke & heart failure or ventricular arrhythmias that required hospitalization.

Results: A total of 354 patients (mean age of 62 years, with 65% male) with a mean follow up of 49 months were studied. AIT, euthyroid status, and amiodarone-induced hypothyroidism was identified in 57 (16.1%), 224 (63.3%), and 73 (20.6%) patients, respectively. No differences in baseline clinical characteristics were observed between AIT & euthyroid patients. Nonetheless, AIT patients demonstrated a higher MACE rate (31.6 vs. 10.7%; p <0.01), mostly driven by a higher rate of ventricular arrhythmias that required admission (7.0 vs. 1.3%; p = 0.03). Cox-regression multivariate analysis revealed that AIT (Hazard Ratio [HR]: 2.68; P <0.01) and left ventricular ejection fraction <45% (HR: 2.52; p <0.01) were independent predictors of MACE.

Conclusion: In patients prescribed long term amiodarone therapy, the occurrence of AIT is associated with a 2.7 fold increased risk of MACE. Regular and close biochemical surveillance is advisable to identify and treat this high-risk group of patients.

COMMENT

The aim of the present retrospective study (analysis of medical charts between 2000 & 2005) was to identify the frequency and clinical characteristics of patients receiving amiodarone, who developed thyroid dysfunction and determine whether the development of amiodarone-induced thyrotoxicosis (AIT) affects the clinical course. During follow-up, thyroid function tests were systematically performed 3-4 months after onset of amiodarone administration and, thereafter, every 4-6 months. As a consequence of amiodarone treatment, both hypo- (AIH) & hyperthyroidism (AIT) were observed, with a prevalence that was almost similar for both dysfunctions, as well as with a similar follow-up duration before the dysfunction occurred: 16 % of cases presented AIT (after 28 months) and 21 % AIH (after 27 months). Among 73 patients with hypothyroidism, amiodarone treatment was interrupted in 27 patients (18 required L-T4 administration). Among 57 patients
with hyperthyroidism, 5 presented AIT type 1 and 13 AIT type 2. The AIT type remained uncertain in the remaining cases (the majority). Concerning management of hyperthyroidism, amiodarone was stopped in 89% of patients. Furthermore, 47/57 patients received antithyroid drugs, 5 radioiodine, and 3 required prednisolone. Restoration of a euthyroid status took five months, on average.

MACE (defined as cardiovascular mortality, myocardial infarction, stroke & heart failure or ventricular arrhythmias with hospitalization) occurred in 32% of patients with hyperthyroidism and cardiovascular mortality reached 12.6%.

This study confirms the high incidence of AIT occurring during amiodarone administration and the expected worse cardiovascular outcome in such patients.

This commentator insists on the following notions:
1) There was a similar prevalence of both hypo- and hyperthyroidism associated with amiodarone therapy (similar to our experience).
2) The period of time after which thyroid dysfunction occurs in amiodarone-treated patients can be extremely long (up to more than 2½ years in this study).
3) This study also demonstrates that amiodarone administration was probably not necessary in some of these patients, since it could be stopped in almost all of them.
4) Finally, the study confirms the common observation that many patients who develop AIT do not necessarily correspond etiologically to type 1 or type 2 AIT.

(Daniel Glinoer, M.D.; Ph.D.)

See Figure below

![Graph showing proportion without MACE vs months](image-url)