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ORIGINAL ARTICLE

An Audit of Amiodarone-induced Thyrotoxicosis - do Anti-thyroid Drugs alone Provide Adequate Treatment?

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Introduction Amiodarone is a widely used anti-arrhythmic drug. A common long-term complication is amiodarone-induced thyrotoxicosis (AIT). We examined retrospectively the efficacy of anti-thyroid drugs with or without prednisolone and the role of surgical thyroidectomy in the treatment of AIT in a single centre, in an iodine-replete region of Australia.

Methods A retrospective audit of patients with AIT was performed between 2002-2012 at this centre. Twenty-seven patients, mean age 60.9 ± 2.3 years were identified. Medical therapy (anti-thyroid drugs, prednisolone) was commenced according to the treating endocrinologist. The main outcomes were time to euthyroidism and number proceeding to thyroidectomy.

Results Of 11 patients commenced on anti-thyroid drugs alone, seven (64%) required the addition of prednisolone. Baseline free T4 was significantly higher in those ultimately treated with prednisolone (58.4 ± 6.3 pmol/L) versus those not (31.7 ± 3.4 pmol/L, P<0.05). Although similar results were seen with free T3, the difference was not significant (P=0.06). In patients with baseline free T4 <30 pmol/L, 75% (3/4) achieved euthyroidism without prednisolone. Neither the use of prednisolone nor continuation of amiodarone significantly influenced time to euthyroidism. Eleven patients (41%) proceeded to surgical thyroidectomy, which was undertaken by an experienced surgical team without significant complications and no mortality.

Conclusion Patients with AIT generally required glucocorticoids. Mild disease (free T4 <30 pmol/L) may be successfully treated with anti-thyroid drugs alone. Surgical thyroidectomy is a safe and effective treatment for those refractive to medical therapy.

Keywords Amiodarone • Arrhythmias • Ventricular tachycardia • Thyrotoxicosis • Prednisolone • Thyroidectomy

Introduction

Amiodarone is a widely used antiarrhythmic drug. It is often reserved for patients with serious cardiac disease and is sometimes the only effective agent in patients with significant structural heart disease, particularly impaired left ventricular systolic dysfunction. Thyroid dysfunction occurs in up to 20% of patients [1–3]. While hypothyroidism is treated simply with thyroxine supplementation, amiodarone induced thyrotoxicosis (AIT) can be complex and challenging to manage. Amiodarone is iodine rich and has a structure similar to thyroxine [4]. A typical daily dose of 200 mg contains 75 mg of iodine and results in 7 mg of available iodine per day, significantly more than the recommended optimal daily iodine intake of 150-200 µg [5]. The effects of amiodarone on the thyroid are due to both its iodine content and intrinsic drug effects [3]. AIT has been classified as Type 1 or Type 2. Type 1 AIT is typically seen in patients with

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underlying thyroid disease and is due to the iodine load from amiodarone exacerbating autonomous thyroid function by providing more substrate. In contrast, Type 2 AIT is a drug-induced destructive thyroiditis affecting a previously normal thyroid gland [1,2,4]. Type 2 AIT is more prevalent, particularly in iodine-replete areas [1,4,6]. Methods of distinguishing Type 1 and Type 2 AIT include the use of radioactive iodine uptake (RAIU) scanning and colour flow Doppler sonography (CFDS) [3,4,7,8], and recommended management involves the use of anti-thyroid drugs (ATD) for Type 1 AIT and glucocorticoids for Type 2 [1,9]. However, accurately determining the type of AIT is not always possible as the relevant investigations may be unavailable and mixed disease forms also exist, hence clinical practice worldwide remains variable [10–12].

We have reviewed retrospectively the outcome of AIT at an Australian tertiary cardiology referral centre with an interest in electrophysiology in an iodine-replete region where diagnostic RAIU scanning and CFDS were not routinely performed. We aimed to identify a sub-group of patients who might be managed with anti-thyroid drugs alone, to review the outcome of patients managed medically and with surgical thyroidectomy and determine if continuation of amiodarone delayed time to achieve euthyroidism.

Patients and Methods

This was a retrospective audit of patients diagnosed with AIT between 2002 and 2012 at a tertiary level hospital in Brisbane, Australia. The state of Queensland is considered iodine replete [13]. The patient records from the Endocrinology Outpatient Clinic were searched for a diagnosis of amiodarone-induced thyrotoxicosis. This was defined on clinical grounds as a free thyroxine (fT4) level above the upper limit of the assay reference range plus a fully suppressed thyroid stimulating hormone (TSH) level below the assay detection limit, associated with the current or recent (within 12 months) therapeutic use of amiodarone. Patients on amiodarone and their general practitioners were instructed to monitor thyroid function tests three times per year. The reason for amiodarone prescription was determined in each case. All patients had undergone transthoracic echocardiography prior to the development of AIT and the result was accessed retrospectively from the charts. Left ventricular systolic ejection fraction (LVEF) was measured using a standard Simpson biplane method [14].

The initial search disclosed 32 patients. On review, five of these patients did not have a fully suppressed TSH and were excluded from subsequent analysis, leaving a total of 27 patients. Baseline demographic data are outlined in Table 1. Amiodarone was prescribed for 19 cases of atrial fibrillation, one case of atrial flutter and seven cases of ventricular tachycardia. Overall, the LVEF ranged from 25 to 70%, but was significantly lower in the ventricular arrhythmia group (32 ± 3% versus 50 ± 3%, P<0.01). Eight patients had an ejection fraction of ≤35% of whom five had ventricular arrhythmias as their primary arrhythmia.

Table 1 Baseline Characteristics of 27 subjects with amiodarone-induced thyrotoxicosis.

	Patients (n=27)
Male	19 (70%)
Age (mean ± SEM)	60.9 ± 2.3 years
Atrial arrhythmia	15 (55.6%)
Atrial arrhythmia + cardiomyopathy	5 (18.5%)
Ventricular arrhythmia	7 (25.9%)
Symptomatic thyrotoxicosis	20 (74%)
Amiodarone Continued	5 (18.5%)
Free T4 (mean ± SEM)	51.5 ± 5.3 pmol/L
Free T3 (mean ± SEM)	10.6 ± 1.2 pmol/L
Ejection fraction (mean and range)	45% (25 – 70%)

Over one quarter of the cohort (7/27) did not report symptoms of thyrotoxicosis. The treating endocrinologist determined the initial medical management. Outcomes examined included the proportion of patients initially managed with anti-thyroid drugs (ATD) alone versus ATD + prednisolone, the proportion of patients ultimately managed with ATD + prednisolone, the starting dose of ATD, the proportion of patients referred for thyroidectomy and time to euthyroidism in the medically treated group. Time to achieve euthyroidism was recorded as time to fT4 normalisation and time to TSH normalisation.

Statistical analysis

Data are expressed as mean ± standard error of the mean (SEM). Treatment groups were compared using the unpaired t-test. Spearman correlation was used to examine the relationship between initial dose of ATD and baseline fT4 level since the data regarding ATD dose did not satisfy parametric assumptions. Fisher's exact test was used to examine if the proportion of patients proceeding to thyroidectomy differed between those continuing versus ceasing the amiodarone. A P value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS Statistics Version 21.

Results

Initial medical management

Initially, 11/27 patients (41%) were prescribed ATD alone and 13/27 (48%) patients were commenced on a combination of ATD and prednisolone therapy. The remaining three (11%) patients were not prescribed any medication at the time of diagnosis. There was no significant difference between the baseline fT4 or fT3 in those treated initially with prednisolone versus those not (Fig. 1, a and b). Subsequently, 7/11 (64%) patients originally treated with ATDs alone were started on prednisolone, most within two months of diagnosis. In six patients this was due to a poor response to ATDs and in one case it was due to abnormal liver function tests. Those patients who ultimately required