

Monitoring thyroid function status in elderly patients on amiodarone

Anthony Fiorini

Abstract

Objectives: To evaluate whether elderly patients on amiodarone were having their thyroid function status monitored as recommended in the literature and to identify the frequency and type of thyroid function test abnormalities noted.

Methods: Patients on amiodarone were identified by examining the prescription charts and medical files of consecutive admissions into Zammit Clapp Hospital (ZCH) and residents at St Vincent de Paul Residence (SVPR). Data was obtained on whether thyroid function tests had been checked at the start of the medication and every six months; the results of such tests carried out over the previous year; the clinical indication to prescribe the medication; and the course of action followed when results were abnormal.

Results: 1334 prescription charts were examined. 69 patients (5.2%) were on amiodarone. The most common clinical indication for the medication was atrial fibrillation (68.1%). As regards thyroid status, 39.1% of subjects had blood tests checked at the start of the medication but only 2.9% every 6 months. Although 75.4% had had their thyroid status checked over the previous year, 8.7% never had any thyroid function tests carried out whilst they were on the medication. In all 27.5% of subjects had thyroid gland dysfunction of which 13% had subclinical hypothyroidism, 11.6% clinical hypothyroidism and 2.9% clinical hyperthyroidism. All patients with abnormal results had been kept on amiodarone even when the arrhythmia had abated.

Conclusions: Thyroid dysfunction is a common side effect of amiodarone medication. The regular measurement of thyroid function tests, as recommended, should be adhered to in a stricter manner.

Keywords

Amiodarone, geriatric, monitoring, thyroid function

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Introduction

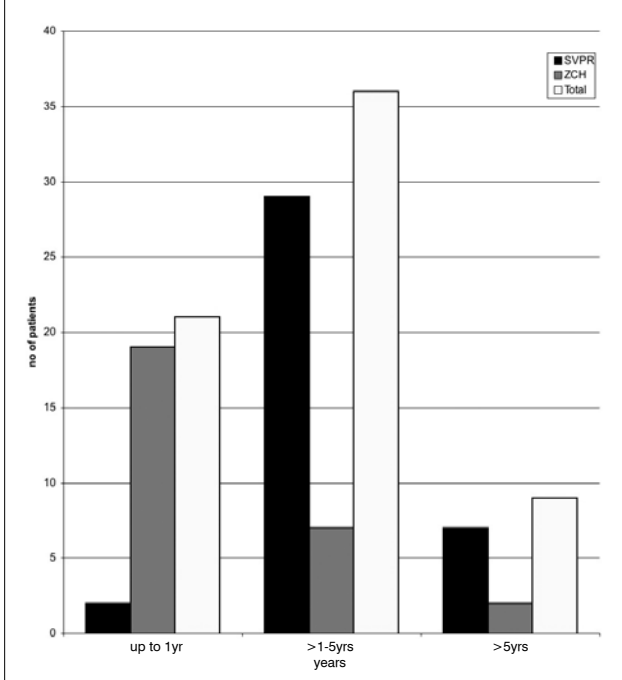
Amiodarone is classified as a Class III anti-arrhythmic drug which can be effective in the management of both supraventricular and ventricular tachyarrhythmias, including atrial fibrillation and flutter.¹ Each molecule of amiodarone contains two atoms of iodine and a normal maintenance dose of this medication will lead to a significant increase in a patient's daily iodine intake.² The list of potential side effects with amiodarone therefore includes thyroid gland dysfunction¹ which may require specific treatment.

Both hypothyroidism and hyperthyroidism have been described as complications of amiodarone medication.³ The overall incidence of amiodarone-induced thyroid dysfunction has been reported to range from 2 to 24%.⁴ Such a wide incidence range has mainly been attributed to different diagnostic criteria being used by various authors⁵ as some studies only included patients with clinical or overt thyroid dysfunction [defined as abnormal levels of both Thyroid Stimulating Hormone (TSH) and Thyroxine/Tri-iodothyronine (T₄/T₃) with clinical features] whilst other studies also included subjects with subclinical findings [defined as abnormal TSH levels only with normal T₄/T₃ levels and no clinical features].^{3,6} For example, Fuks *et al*⁵, who found a particular high incidence of abnormalities of thyroid function tests (33.9%) in their sample of 56 patients on amiodarone (mean age 58.0 years), diagnosed subclinical thyroid dysfunction in 21.4% and clinical thyroid dysfunction in 12.5%.

In the elderly, reaching a diagnosis of thyroid dysfunction can be rendered more difficult by a lack of classical clinical features even when patients have both TSH and T₄/T₃ abnormalities. Over thirty years ago, Bahemuka and Hodkinson⁷ had noted that a non-specific clinical picture was particularly common in the elderly with laboratory confirmed hypothyroidism since less than a third of cases showed typical symptoms and signs. More recently, Findlay and Seymour⁸ described a case of amiodarone-induced thyrotoxicoses in an elderly patient without any classical presenting features but which was identified with 'routine' blood tests. Rae *et al*⁹ have stated that the diagnosis of thyroid disease in the elderly is even more dependent on laboratory results when compared to younger age groups.

In the elderly, hypothyroidism is a more common reported complication of amiodarone medication than hyperthyroidism.² In a UK study carried out on 134 elderly patients taking long-term amiodarone (80% aged > 70 years) it was found that

Figure 1: Time period on amiodarone



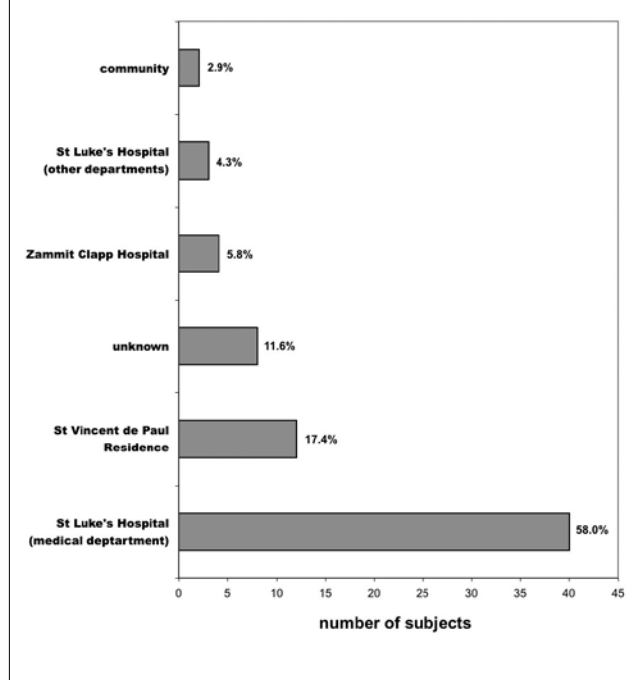
14% had developed hypothyroidism whilst 6% had features of thyrotoxicoses.¹⁰ Another UK study identified 15% of their sample with hypothyroidism (mean age 74 years) but hyperthyroidism was not noted.¹¹ A local study on thyroid dysfunction in the elderly¹² had noted that out of 20 patients on amiodarone medication, 40% had shown abnormalities in their thyroid function test results, of whom 2 patients (10%) had overt hypothyroidism, 5 (25%) had subclinical hypothyroidism and 1 patient (5%) had subclinical hyperthyroidism.

In view of the documented common complication of clinical and subclinical thyroid dysfunction coupled with a lack of classical symptoms and signs in the elderly, various authors have advised measuring thyroid function status on a regular basis on all patients on amiodarone. For example, the British National Formulary¹ recommends that appropriate thyroid status blood tests are carried out, both at the start of the medication and at six month intervals thereafter, for as long as each patient remains on amiodarone.

When overt thyroid dysfunction does occur in patients on amiodarone, various treatment options have been described including stopping the medication if the arrhythmia has subsided or switching to another anti-arrhythmic if the arrhythmia is still present or adding appropriate thyroid medication if amiodarone cannot be discontinued.² On the other hand, no specific intervention is required for sub-clinical abnormalities but patients should be kept under review for as long as they remain on amiodarone in case overt thyroid dysfunction does occur.²

This study was mainly carried out to evaluate whether elderly patients taking amiodarone were having their thyroid function monitored as recommended in the literature and to identify which thyroid function test abnormalities were being noted and what course of action was being followed.

Figure 2: Site where medication commenced



Methodology

This study was carried out at two local institutions providing medical services for the elderly in Malta i.e. St Vincent de Paule Residence (SVPR), a long-stay chronic care facility and Zammit Clapp Hospital (ZCH), a short-stay assessment and rehabilitation unit.

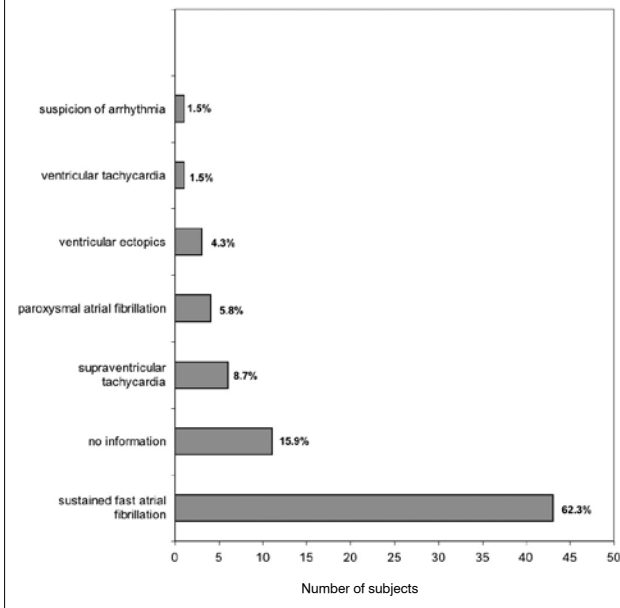
Subjects included (a) patients who were residents at SVPR during the time of the study and (b) consecutive admissions into ZCH. Data was collected over a 5 month period. Patients on amiodarone were identified from their prescription charts and their medical files examined to obtain the following information:

1. The duration of treatment
2. The reason why the medication was started
3. Where the decision was made to start the medication
4. Whether thyroid function tests had been checked at:
 - a. the start of the medication,
 - b. every 6 months
 - c. or over the previous 12 months.
5. The results of the last documented thyroid function tests.
6. Whether any patient was already taking, or was started on, thyroid medication for identified hypothyroidism or hyperthyroidism.
7. The report of the last documented ECG.

Results and data analysis

During the period of this study, 985 prescription charts were examined at SVPR and 349 at ZCH. 38 residents at SVPR were identified as taking amiodarone on a regular basis (3.9% of residents) and 31 patients at ZCH (8.9% of admitted patients) giving a total sample of 69 (5.2%) out of 1334 prescription charts examined.

Figure 3: Reason to commence amiodarone



69.6% of the total sample were females and 30.4% males. Their mean age was 82.3 years (range 68 – 94).

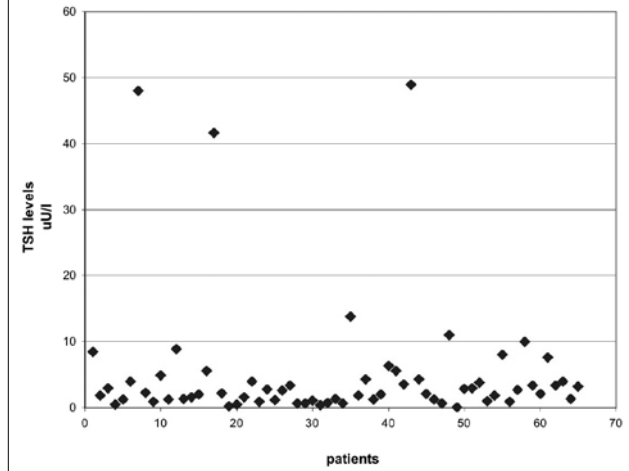
The majority of patients in this sample (52.2%) had been taking amiodarone for between 1 to 5 years (Figure 1). The overall range varied from 7 days to 16 years. Out of the total sample, 30.4% had been taking the medication for up to a year whilst 65.2% had been taking the medication for more than a year (Figure 1). However, there were differences between the SVPR and ZCH samples as nearly two thirds of the ZCH sample had been on the medication for less than a year whilst nearly all the SVPR sample had been taking the medication for greater than one year (Table 1).

Table 1: Time period on amiodarone

	SVPR Sample n = 38	ZCH Sample n = 31	Total Sample n = 69
Up to 1 month	0	11	11
2 to 6 months	2	6	8
7 to 12 months	0	2	2
Number of subjects taking medication for up to a year	2 (5.3%)	19 (61.3%)	21 (30.4%)
> 1 year to 5 years	29	7	36
6 years to 10 years	5	0	5
11 years and over	2	2	4
Number of subjects taking medication for more than a year	36 (94.7%)	9 (29.0%)	45 (65.2%)
Unknown	0	3	3

SVPR – St Vincent de Paule Residence
ZCH – Zammit Clapp Hospital

Figure 4: TSH levels



The majority of patients were started on amiodarone whilst under the care of physicians at St Luke’s Hospital, the local acute/general hospital (Figure 2), whilst the most common clinical indication to commence this medication (Figure 3) was sustained or paroxysmal atrial fibrillation (68.1%).

Table 2 indicates whether thyroid function tests were checked at the start of the medication and every 6 months as recommended in the literature. For the majority the answer was no, as less than a third of subjects had their thyroid gland status checked at the start, whilst only 2 subjects had their thyroid function tests checked every 6 months.

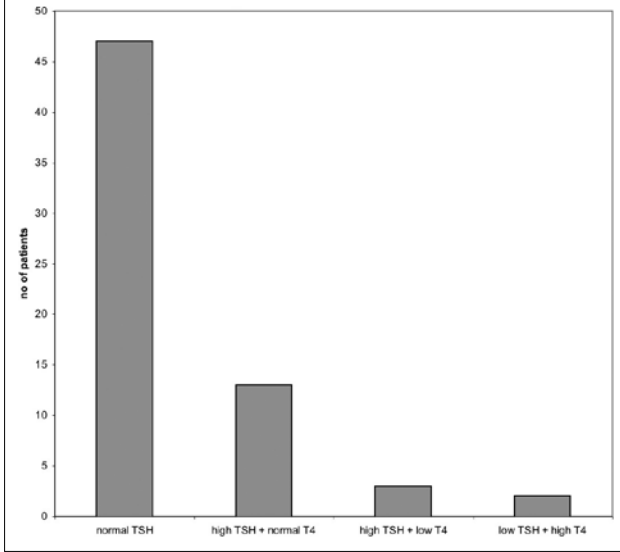
As can also be noted in Table 2, the study identified 47 patients who had been on amiodarone for more than 6 months but who did not have their thyroid function status checked regularly. Data on this sample showed (Table 3) that 4 patients had never had any thyroid function tests carried out, 6 had only one result documented whilst 37 patients who had 2 or more thyroid function test results filed in their medical notes had a mean period of 26.2 months between their last two tests.

Although the majority of subjects did not have their thyroid function status regularly measured within the recommended time frame, thyroid function tests had actually been carried out over the previous year for 52 subjects (75.4% of the total sample) an indication that doctors were aware that such monitoring should take place. On the other hand, 6 patients (8.7%) had

Table 2: Thyroid function tests checked at start and every 6 months

Thyroid function checked	At start of medication	Every 6 months
Yes	27 (39.1%)	2 (2.9%)
No	33 (47.8%)	47 (68.1%)
Too early (on medication for less than 6 months)	Not relevant	18 (26.1%)
Unknown	9 (13.1%)	2 (2.9%)
Total	69 (100%)	69 (100%)

Figure 5: Thyroid function tests results

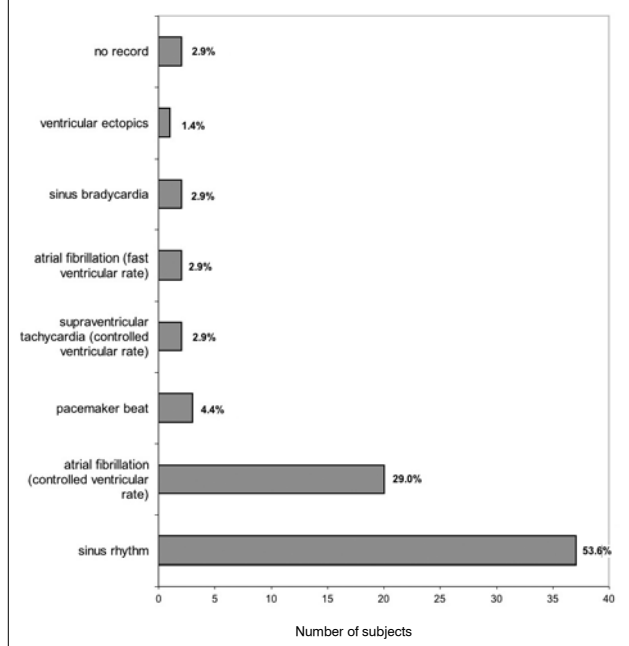


never had their thyroid function tests checked at any stage, of which 2 had been on the medication for less than 6 months.

Table 4 lists the results of the last recorded thyroid function tests per subject. These results are based either on tests carried out as part of the routine clinical work-up on patients or on blood tests that were requested for the purpose of this study when it was noted that no results for the previous year were available. Data on thyroid stimulation hormone (TSH) levels is mainly presented (Figure 4) as in the majority of cases this was the only test performed by the laboratory. Serum thyroxine levels (T4) were usually only measured automatically by the laboratory if TSH levels were above or below normal whilst none of the subjects had T3 levels measured even when the TSH level was noted to be low.

In all, 18 patients (26.1%) had abnormal thyroid function tests, with the most common abnormality being a raised TSH level with a normal T4 level (Figure 5). However, an interpretation of these results has to keep in mind that a number of patients were already taking thyroxine at the time when the blood samples were taken. For example, one patient on thyroxine had normal thyroid function tests, indicating adequate treatment, whilst 4 of the patients with high TSH levels and normal T4 levels were also taking thyroxine medication,

Figure 6: Report of last recorded ECG



indicating the optimal dose had not as yet been achieved. Therefore, an examination of the whole picture, i.e. patients on thyroid medication and the results of thyroid function tests, can conclude that, in all, 19 patients (27.5% of the total sample) on amiodarone had thyroid gland dysfunction, of whom 8 (11.6%) were being treated for hypothyroidism, 9 (13.0%) had subclinical features of hypothyroidism and were not on treatment and 2 (2.9%) had hyperthyroidism but were not receiving specific treatment.

There was no evidence in any of the files that a patient had been taking thyroxine prior to being prescribed amiodarone nor were there any abnormal thyroid function tests documented in patients who had such measurements carried out prior to commencing amiodarone. The abnormal thyroid function tests detected in this study can therefore be attributed to an adverse effect of amiodarone.

Discussion

Although this study only identified a small percentage of patients on amiodarone, both at St Vincent de Paule Residence and at Zammit Clapp Hospital, it has shown that in a majority of

Table 3: Analysis of data on patients who had been on amiodarone for more than 6 months but who did not have their thyroid function status checked every 6 months

Thyroid function checked	Number of patients	
Never	4	Mean period on amiodarone 40.5 months (range 36 – 44 months)
Once	6	Mean period on amiodarone 37.0 months (range 16 – 69 months)
Twice or more	37	Mean period between last 2 Thyroid Function Tests 26.2 months (range 7 to 108 months)
Total	47	

Table 4: Results of thyroid function tests

Thyroid function results	Number of patients and % of sample	Mean and range of TSH levels ($\mu\text{U/L}$)	Mean and range of T4 levels (pmol/L)	Number of patients on thyroid medication
high TSH low T4	3 (4.4%)	46.2 (41.7 -49.0)	4.5 (2.9-5.4)	3
high TSH normal T4	13 (18.8%)	7.6 (4.3-13.8)	17 (12.0-24.0)	4
low TSH high T4	2 (2.9%)	0.16 (0.1+0.23)	25.8 (25.0+26.5)	0
low TSH normal T4	0			0
normal TSH	47 (68.1%)	1.9 (0.4-4.0)		1
unknown	4 (5.8%)			0
Total	69 (100%)			8

Normal range: TSH=0.4 – 4.0 $\mu\text{U/l}$ T4=10.3 – 24.45 pmol/l

cases, follow up procedures, as recommended in the literature, were not strictly adhered to. Thyroid function tests were not performed routinely, in a high percentage of cases, both at the start of the medication and on a regular six month basis. Similar findings have been reported in the literature. For example, McCulloch et al¹⁰ found that thyroid function tests were performed in 67% of their sample at the start of the medication and in only 30% of patients at the 6 and 12 month intervals.

The possibility could be raised that patients might have had their thyroid function status checked elsewhere, such as in the community, by health centre doctors or specialists or even private family practitioners and therefore results would not be documented in the patient's hospital file which formed the basis of this study. It was not possible to ascertain if the main hospital laboratory or private laboratories had any records of such monitoring in the community. However, most of the patients in the study sample (59 out of 69) were commenced on amiodarone by hospital based departments and the onus should be on doctors working in such departments to continue monitoring patients. This study has shown that such monitoring was not carried out on a recommended regular basis.

Although this study was carried out on patients under the care of doctors working in the Department of Geriatric Medicine, most patients on this medication were 'inherited', as the decision to start amiodarone was mainly made whilst they were being managed by specialists working in the Department of Medicine at St Luke's Hospital. Also, a number of patients had been on the medication for a considerable time before they required clinical input from the Department of Geriatric Medicine. No attempt was made in this study either to compare the two departments or to compare SVPR with ZCH as regards the recommended monitoring of patients. Suffice to say that both departments and both institutions need to ensure that thyroid function status is measured on a more regular basis. For example, 2 cases of clinical hypothyroidism and 1 of clinical hyperthyroidism were only identified because laboratory tests were requested for the purpose of this study. Doctors looking after such patients were

informed about such abnormal findings and advised on what appropriate action to take.

This study has also confirmed that locally, thyroid function is commonly impaired in elderly patients on amiodarone, thereby emphasizing even further the need for regular monitoring. Hypothyroidism, both clinical and subclinical, was a more common abnormality affecting 24.6% of patients in this sample. On the other hand, only 2.9% showed features of hyperthyroidism. In all, 27.5% of patients had thyroid function abnormalities. Although this percentage is not as high as previously quoted, when 40% of patients were found to have abnormalities of thyroid function tests¹², it is still more than the incidence rate of 2% to 24% as reported in the literature.⁴ As already stated, none of the patients in this study had documented thyroid dysfunction before starting amiodarone. Therefore, the abnormalities noted can be attributed to the medication.

It was also interesting to note from this study that over half of the subjects had documented evidence that the electrocardiogram abnormality which had precipitated the start of the medication had resolved (Figure 6). In other words, these patients were still kept on amiodarone even though the original clinical indication had abated. For example, 4 patients had been on amiodarone for more than 10 years, of whom 3 showed persistently normal electrocardiogram recordings. Throughout the course of this study, amiodarone was discontinued in only one patient because a marked bradycardia was noted. Even those patients who required thyroxine were kept on amiodarone. As already discussed in the introduction, an accepted alternative treatment could have been to stop amiodarone and see if the thyroid function corrects itself. For example in a study by Hyatt et al¹¹, which documented clinical hypothyroidism in 9 patients, the thyroid dysfunction reverted to normal in 5 patients by simply withdrawing the medication, 2 patients needed to remain on amiodarone and were commenced on thyroxine, whilst the other 2 patients still required thyroxine even though amiodarone was discontinued.

Conclusion and recommendations

Thyroid dysfunction is a common side-effect of amiodarone medication. This study has shown that patients on amiodarone need to be followed up more carefully whilst the regular measurement of thyroid function tests, needs to be adhered to in a stricter manner. Furthermore, in a number of cases, amiodarone may no longer be required and any regular follow-up should pose the question whether the medication can and should be discontinued. Certainly, stopping the medication is one management alternative which should be considered when thyroid dysfunction is noted.

The findings of this study have been formally presented to doctors working in the Department of Geriatric Medicine in an attempt to optimize patient monitoring. However, omissions by other clinical departments prescribing this medication were also identified by this study. It is hoped that this publication will serve to remind all doctors about the recommended clinical guidelines for patients prescribed amiodarone. These include the measurement of thyroid function status at the start of the medication and at regular 6 monthly intervals even if previous results are normal, with the added recommendation that if thyroid dysfunction is noted, amiodarone is either stopped (especially if the arrhythmia has subsided) or appropriate thyroid medication added to the patient's regime.

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