**The Effective Treatment of Multifocal Atrial Tachycardia with Amiodarone**

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**SUMMARY**

Multifocal atrial tachycardia (MAT) was observed in 9 patients aged 60–85 (mean 72.1±8.6) years during exacerbation of their chronic lung and/or cardiac disease. Four, in whom the rapid heart rate caused symptoms of pulmonary congestion, were treated with intravenous amiodarone (450–900 mg over 2 hours) with restoration of sinus rhythm soon after the termination of the drug infusion. In 1, with recurrence of MAT, the same intravenous dosage was repeated for 2 consecutive days, with final achievement of stable sinus rhythm. Five patients, apart from the conventional management of their underlying disease (digitalis, diuretics, aminophylline) were treated with oral amiodarone (600 mg/day). Sinus rhythm was restored in all and remained stable during their hospitalization, under a maintenance dosage of 200–400 mg daily. Amiodarone may be the drug of choice for the treatment of MAT, for which up to now no effective therapy has been established.

**Additional Indexing Words:**
Multifocal atrial tachycardia Amiodarone Atrial arrhythmias Antiarrhythmic treatment

MULTIFOCAL atrial tachycardia (MAT) is recognized as a distinct atrial arrhythmia.1)–3) It is almost always found in seriously ill, elderly individuals suffering mainly from chronic obstructive airway disease and/or atherosclerotic heart disease.4)–6) Although management of the underlying disease may sometimes result in disappearance of this arrhythmia,3),7) most patients are refractory to the usual treatment. As with most atrial tachyarrhythmias with a fast ventricular response, it may ultimately lead to or facilitate cardiac decompensation or myocardial ischemia. Thus, specific antiarrhythmic treatment may be needed for this category of pa-

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### Table I. Clinical Details

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Underlying disease</th>
<th>Concurrent medications</th>
<th>K⁺ mEq/l</th>
<th>Blood urea mg%</th>
<th>BP mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1M</td>
<td>65</td>
<td>Chronic obstructive lung disease</td>
<td>Aminophylline Furosemide Amiloride</td>
<td>4.2</td>
<td>45</td>
<td>130/80</td>
</tr>
<tr>
<td>2 F</td>
<td>76</td>
<td>Severe aortic stenosis, Cardiac failure, Diabetes mellitus</td>
<td>Digitalis Furosemide Amiloride Glybenclamide</td>
<td>3.1</td>
<td>63</td>
<td>140/85</td>
</tr>
<tr>
<td>3 F</td>
<td>62</td>
<td>Chronic obstructive lung disease, Hypertension, Atherosclerotic heart disease</td>
<td>Aminophylline Nifedipine Furosemide Amiloride</td>
<td>2.8</td>
<td>40</td>
<td>170/100</td>
</tr>
<tr>
<td>4 M</td>
<td>85</td>
<td>Atherosclerotic heart disease, Diabetes mellitus, Bronchitis cardia failure</td>
<td>Digitalis Furosemide Amiloride Ampicillin</td>
<td>4.5</td>
<td>70</td>
<td>160/90</td>
</tr>
<tr>
<td>5 F</td>
<td>60</td>
<td>Obstructive lung disease, Right heart failure</td>
<td>Aminophylline Thiazides Amiloride</td>
<td>3.9</td>
<td>50</td>
<td>150/80</td>
</tr>
<tr>
<td>6 M</td>
<td>68</td>
<td>Atherosclerotic heart disease</td>
<td>Nitrates Nifedipine Thiazides Amiloride</td>
<td>4.6</td>
<td>40</td>
<td>130/80</td>
</tr>
<tr>
<td>7 M</td>
<td>75</td>
<td>Atherosclerotic heart disease, Cardiac failure, Bronchitis, Uremia</td>
<td>Digitalis Furosemide Amiloride Nitrates Aminophylline</td>
<td>3.8</td>
<td>95</td>
<td>150/90</td>
</tr>
<tr>
<td>8 M</td>
<td>80</td>
<td>Chronic obstructive lung disease</td>
<td>Digitalis Furosemide Amiloride Nitrates Aminophylline</td>
<td>4.0</td>
<td>80</td>
<td>130/80</td>
</tr>
<tr>
<td>9 M</td>
<td>77</td>
<td>Chronic obstructive lung disease</td>
<td>Digitalis Furosemide Aminophylline</td>
<td>3.9</td>
<td>60</td>
<td>140/75</td>
</tr>
</tbody>
</table>

M = male; F = female; SR = sinus rhythm.

As regards conventional antiarrhythmic agents used up to now, beta blockers are unsatisfactory and frequently contraindicated because of underlying lung disease or severe heart failure, digoxin and quinidine have proved...
of 9 Patients with MAT

<table>
<thead>
<tr>
<th>Total dose of amiodarone administered till conversion to SR</th>
<th>Day of conversion to SR</th>
<th>Daily maintenance dose mg</th>
<th>Days of Hospital observation after conversion</th>
<th>Heart rate (HR) (beats/min)</th>
<th>QTc</th>
<th>Follow up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1800 mg orally</td>
<td>3</td>
<td>200</td>
<td>4</td>
<td>MAT: 130 SR: 100</td>
<td>MAT: 0.42 SR: 0.50</td>
<td>lost</td>
</tr>
<tr>
<td>450 mg intravenously</td>
<td>1</td>
<td>400</td>
<td>3</td>
<td>MAT: 140 SR: 95</td>
<td>MAT: 0.440 SR: 0.530</td>
<td>4</td>
</tr>
<tr>
<td>3000 mg orally</td>
<td>5</td>
<td>200</td>
<td>4</td>
<td>MAT: 100 SR: 60</td>
<td>MAT: 0.380 SR: 0.440</td>
<td>6</td>
</tr>
<tr>
<td>3000 mg orally</td>
<td>5</td>
<td>200</td>
<td>3</td>
<td>MAT: 135 SR: 120</td>
<td>MAT: 0.460 SR: 0.460</td>
<td>died after 2 months, excluded</td>
</tr>
<tr>
<td>2400 mg orally</td>
<td>4</td>
<td>200</td>
<td>4</td>
<td>MAT: 120 SR: 90</td>
<td>MAT: 0.420 SR: 0.470</td>
<td>6</td>
</tr>
<tr>
<td>1800 mg orally</td>
<td>3</td>
<td>400</td>
<td>5</td>
<td>MAT: 130 SR: 65</td>
<td>MAT: 0.420 SR: 0.460</td>
<td>8</td>
</tr>
<tr>
<td>1350 mg intravenously</td>
<td>3</td>
<td>400</td>
<td>9</td>
<td>MAT: 160 SR: 100</td>
<td>MAT: 0.380 SR: 0.450</td>
<td>died after 3 months, excluded</td>
</tr>
<tr>
<td>1500 mg intravenously</td>
<td>1</td>
<td>300</td>
<td>4</td>
<td>MAT: 115 SR: 73</td>
<td>MAT: 0.423 SR: 0.483</td>
<td>just discharged (not included)</td>
</tr>
<tr>
<td>900 mg intravenously</td>
<td>1</td>
<td>200</td>
<td>4</td>
<td>MAT: 120 SR: 77</td>
<td>MAT: 0.452 SR: 0.464</td>
<td>just discharged (not included)</td>
</tr>
</tbody>
</table>

ineffective,8,9) and verapamil has proven to be only partially successful.10–12

We present the successful treatment of 9 consecutive patients with MAT using oral amiodarone in 5 and intravenous in 4.
METHODS

MAT was diagnosed in 9 consecutive patients, 6 men and 3 women, aged 60 to 85 (mean 72.1±8.6) years according to the following criteria, which were present in all:
1. Presence of at least three different P-wave forms in the same lead of the ECG.
2. Variation of P-P, P-R and R-R intervals.
3. A mean atrial rate of more than 100 beats per minute.

The clinical details of the patients are shown in Table I. All were symptomatic because of exacerbation of their underlying disease. Five had significant chronic obstructive lung disease and 1 suffered from severe aortic stenosis together with cardiac failure and diabetes mellitus. The other 3 had severe ischemic heart disease with cardiac failure; diabetes mellitus was present in 1. MAT was an incidental finding on the ECG; however, although dyspnea in 5 patients was due mainly to severe cardiac and/or pulmonary disease, we felt that a slower heart rate would be clinically beneficial. Four patients presented with severe congestive heart failure and impending pulmonary edema. In these 4 the fast rates (>115/min) clearly contributed to a great extent to the deterioration of their condition.

Amiodarone was administered orally acutely to 5 patients and only intravenously to the 4 mentioned. The oral administration was 600 mg/day divided in 3 equal doses and the intravenous dose was 450 mg in 100 dl of 5% dextrose infused over 2 hours in patient 2, 1350 mg (450 mg daily) in patient 7, 1500 mg during the first 24 hours in patient 8 and 900 mg intravenously in 2 hours in patient 9. After the restoration of sinus rhythm the patients continued receiving the drug at a maintenance dose of 200–400 mg/day. Serial ECGs were obtained twice or 3 times a day in each patient until the conversion to sinus rhythm and thereafter one ECG a day was recorded. Serum electrolytes and blood urea were measured in all patients at the time of admission. QTc was calculated before the initiation of therapy with amiodarone and after the conversion to sinus rhythm according to Bazett’s formula. In 6 of our patients digitalis was being given at the time that MAT developed. The drug was not stopped. No other antiarrhythmic drug was tried before amiodarone.

RESULTS

In all patients conversion to sinus rhythm was obtained (Figs. 1–5). In 2 of them who received oral amiodarone sinus rhythm was noted on the
3rd day, in 1 on the 4th day and in 2 on the 5th day. In 3 patients (2, 8 and 9) who received the drug intravenously, conversion to sinus rhythm was seen soon (30 min) after completion of the infusion. The rhythm remained stable on a maintenance oral dose of 400 mg daily of the drug in patient 2, and on oral maintenance doses of 300 mg and 200 mg daily in patients 8 and 9 correspondingly. Patient 7 who was also treated with intravenous amiodarone infusion converted to sinus rhythm 45 min after the end of the administration of the drug but returned to MAT after approximately 8 hours. The same intravenous dose (450 mg) was repeated the next day. Sinus rhythm was restored (Fig. 3) and remained for 12 hours, but degenerated to MAT once again. Stable sinus rhythm was finally obtained on the 3rd day, the patient having received a total dose of 1350 mg amiodarone intravenously. He also was kept on a maintenance dose of 400 mg daily. Although all our patients
Fig. 3. 12 lead ECG of patient 7 with MAT on the day of admission. Lead I at the bottom showing sinus rhythm on the day of discharge.

Fig. 4. 12 lead ECG of patient 4. a: on admission, b: at discharge.
had been receiving oral preparations of digitalis, no signs of toxic digitalization and no relation of digitalis to MAT could be established. Patient 4 was severely hypokalemic (K = 2.8 mEq/l) because of intensive diuretic treatment, but the arrhythmia proved resistant to the administration of adequate doses of KCl preparations which corrected the electrolyte disturbance. Six patients were receiving aminophylline preparations, which were continued in the same dosage throughout the study. Serum levels were not measured. In no patient (apart from patient 7 already mentioned) did MAT recur during subsequent hospitalization (3–9, mean 5.7±2 days) and no temporary transition to another rhythm such as atrial fibrillation or flutter prior to conversion to sinus rhythm was observed. All patients were kept on the same amiodarone maintenance dose at discharge. Follow up was available in 6 patients; 4 are alive 6 to 8 (mean 6.0±1.6) months after hospitalization; all are in sinus rhythm. Two (Nos. 4 and 7) died of congestive heart
failure, 2 and 3 months after discharge, in sinus rhythm.

Serum amiodarone concentrations were not measured in any patient during the initial administration of the drug, or during maintenance therapy. The only side effect seen in 1 patient in follow up was sinus bradycardia, which necessitated reduction of the digoxin and amiodarone dosages to half. Specifically, no abnormalities of thyroid function were seen in any patient during the follow up interval. The degree of corneal deposition was judged to be light in all.
DISCUSSION

MAT has also been called chaotic atrial mechanism,\(^4\),\(^8\) chaotic atrial tachycardia\(^9\) multifocal atrial rhythm\(^6\) and wandering pacemaker in the atria\(^14\) by different authors. However, the electrocardiographic pictures under these various names are either identical or very similar.\(^3\) Its incidence compared to other supraventricular arrhythmias is low. Phillips et al\(^4\) detected 31 instances of MAT among approximately 24000 interpreted ECGs (0.13\%) during a 2 year period. Kones et al\(^8\) found an incidence of 0.32\% of the total number of interpreted ECGs and Lipson et al\(^15\) identified 31 cases while examining the records of supraventricular arrhythmias of adult patients (60000 ECGs) over a 6 year period. The arrhythmia may be more frequent than reported because it is sometimes overlooked and its frequency may now be increasing. Its occurrence in adults, in contrast to its benign character in childhood,\(^8\),\(^16\) usually portends a grave prognosis because they tend to be elderly, severely ill and incapacitated by chronic obstructive lung disease and/or atherosclerotic cardiovascular disease.\(^3\)–\(^6\) Diabetes mellitus, general anesthesia, pulmonary embolism with or without infarction (16\%),\(^3\),\(^8\) hypokalemia, valvular heart disease and hypertensive heart disease have also been associated with MAT in adults.\(^1\),\(^3\)–\(^6\) The use of aminophylline in patients with pulmonary disease in association with the onset of MAT has been noted.\(^1\),\(^17\),\(^18\)

The mechanism responsible for MAT remains unclear. Multiple ectopic foci,\(^8\) reentrant circuits\(^19\) or triggered activity\(^10\),\(^18\),\(^20\) have been incriminated, but invasive electrophysiological studies have not been undertaken to date. Its duration is variable. It may last for as short a period as a few seconds, or up to months or even years.\(^4\) Phillips et al\(^4\) found that 1 week is the usual duration. Lipson et al\(^15\) reported that it disappeared within 1 day in 10 of 31 (32\%) cases and that no episode exceeded 1 week. It may be persistent or intermittent and many recurrences of a short duration may be missed due to the difficulty in obtaining serial or continuous ECGs in the majority of patients. Although it may frequently be a stable autonomous arrhythmia\(^4\) it degenerates to atrial fibrillation or atrial flutter\(^9\),\(^15\) in as many as 46\% of cases.\(^16\)

Treatment with antiarrhythmic drugs has been considered unsatisfactory\(^1\),\(^4\),\(^5\),\(^15\) and more emphasis has been placed on the general management of the underlying disease than on the use of antiarrhythmic agents. Some cases of MAT have been ascribed to digitalis toxicity.\(^1\),\(^15\) Digitalis has usually proven to be ineffective in slowing the ventricular response.\(^14\),\(^19\) However, it is believed that, although MAT may coexist with digitalis ad-
ministration, this drug usually is not its cause.\textsuperscript{3,4,8} Quinidine used alone has failed to abolish MAT and propranolol usually is contraindicated in patients with bronchospasm and/or congestive heart failure.\textsuperscript{8} Kones et al\textsuperscript{8} maintain that the combination of quinidine and propranolol was efficacious in 10 of 20 patients with MAT although it is not clearly reported or illustrated in ECG records if conversion to sinus rhythm was attained. Recently the use of intravenous and oral verapamil was reported to be successful in controlling atrial and ventricular rates in 6 patients with MAT, converting 3 to sinus rhythm.\textsuperscript{10} Aronow et al\textsuperscript{11} and Hazard and Burnett\textsuperscript{12} reported conversion to sinus rhythm in about a quarter of their patients. The latter authors noted a decrease in pO\textsubscript{2} from 150 to 78 mmHg, which could be deleterious to individuals with chronic lung disease. Zeevi et al\textsuperscript{21} very recently reported the first successful treatment of a child with MAT and congestive heart failure due to congenital heart disease (corrected transposition of the great arteries) using amiodarone, whereas verapamil previously administered intravenously was ineffective.

Recently oral metoprolol has proved effective in 11 patients,\textsuperscript{22} and magnesium therapy in 3/6 patients.\textsuperscript{23}

Our communication describes for the first time the successful treatment of 9 consecutive adult patients with MAT with amiodarone. Amiodarone is a class III antiarrhythmic agent which prolongs the refractory period of contractile fibers of the atrial and ventricular myocardium.\textsuperscript{24} As a result of its action, excitability is reduced but conduction in myocardial cells is not modified. It has been widely used with great success over almost the whole spectrum of cardiac arrhythmias.

It has proven especially efficacious in preventing recurrences of paroxysmal atrial fibrillation with a success rate of 80\textsuperscript{25} to 96\%.\textsuperscript{26} However, it is not devoid of side effects during long-term use. Apart from the well described corneal deposits, among those potentially more dangerous are pulmonary fibrosis, to which patients with pre-existing respiratory abnormalities may be more susceptible,\textsuperscript{27} thyroid\textsuperscript{28} and hepatic\textsuperscript{29} abnormalities. Thus, the rationale for employing it to prevent recurrence of MAT in patients, who in a large percentage of cases have pre-existing pulmonary parenchymal disease, is not clear at the present. It would be justified in those individuals who have a high cardiac rate during MAT, which produces or exacerbates heart failure.

Of course, the incidental conversion to sinus rhythm cannot be absolutely excluded. However, it must be taken into consideration that the highest reported success rate is only 50\% in various series,\textsuperscript{8,12,13} while it was 100\% in ours. Moreover, in 3 of our patients, intravenous administra-
It is possible that all our patients were converted to sinus rhythm as soon as substantial myocardial levels of amiodarone had been achieved, as was indicated by flattening and lengthening of the T wave, as well as by prolongation of the QTc. Repeated ECGs showed that sinus rhythm remained stable during their hospitalization while the patients were on maintenance therapy with amiodarone. We did not use high oral loading doses as advocated by other authors. However, at the time of their conversion to sinus rhythm, 5 patients had received at least 1800 mg of the drug orally, one 450 mg, one 900 mg, one 1350 mg and one 1500 mg i.v., and the QT had started to become prolonged. Zeevi et al used 5 mg/kg i.v., a dosage similar to the one used by us. Changes in various electrophysiologic parameters and effective serum levels are already evident by 1 week with amiodarone therapy. Moreover, in the dog the atrial refractory period has been found to become more readily prolonged than the ventricular refractory period with amiodarone.

We conclude that amiodarone appears to be an effective and safe antiarrhythmic drug for the short-term treatment of MAT. We believe that it should be an adjunct to the standard treatment of underlying disease. Its intravenous administration may prove life-saving in marked tachycardia. More widespread use of this drug in MAT is indicated with the aim of gathering further information.

REFERENCES

versus placebo on PAT and MAT (paroxysmal atrial tachycardia and multifocal atrial tachycardia). Cur Ther Res 27: 823, 1980


