

# The usefulness of amiodarone in management of refractory supraventricular tachyarrhythmias

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■ The efficacy of amiodarone was evaluated in 85 patients with supraventricular tachycardia (SVT) refractory to several antiarrhythmic agents (mean  $3.8 \pm 1.0$ ). All but six patients had organic heart disease. Patients were followed for 19 months (range 2–60 months). Response to amiodarone treatment was considered excellent (no recurrence of SVT) in 22 of 52 patients with paroxysmal atrial fibrillation (PAF), in four of 13 patients with chronic atrial fibrillation (CAF), and in three of 15 patients with Wolff-Parkinson-White syndrome-related circus movement tachycardia (WPW-CMT). Response was improved (marked improvement in symptoms with partial suppression of SVT) in 22 patients with PAF, in seven patients with CAF, in 10 patients with WPW-CMT, and in four patients with atrioventricular nodal re-entry tachycardia. Response was considered poor (insignificant or no suppression of SVT) in three patients with PAF, in one patient with CAF, and in one patient with WPW-CMT. Seven patients required discontinuation of amiodarone due to adverse effects. We conclude that amiodarone is efficacious and relatively safe for control of SVT refractory to conventional antiarrhythmic agents irrespective of the underlying electrophysiologic mechanism.

□ INDEX TERMS: AMIODARONE; ARRHYTHMIA □ CLEVE CLIN J MED 1989; 56:238–242

**D**URING the last decade there have been important therapeutic advances in the management of supraventricular tachyarrhythmia (SVT).<sup>1</sup> Despite these recent developments, there remains a small group of patients in whom SVT cannot be controlled by conventional antiarrhythmic drug therapy. Amiodarone was first reported to be efficacious for SVT more than a decade ago.<sup>2</sup> Management of potentially lethal ventricular arrhythmias has been the main indication for amiodarone treatment.<sup>3</sup> We report our experience with amiodarone in patients with SVT

that was either refractory to or intolerant of several conventional antiarrhythmic agents administered alone or in combination. The efficacy and safety of amiodarone were evaluated in four different groups: 1) paroxysmal atrial fibrillation (PAF), 2) chronic atrial fibrillation (CAF), 3) circus-movement tachycardia associated with Wolff-Parkinson-White syndrome (WPW-CMT), and 4) atrioventricular nodal re-entry tachycardia (AVNRT).

## PATIENTS AND METHODS

Eighty-five patients (46 men and 39 women) received amiodarone for refractory SVT between January 1981 and May 1986. Types of SVT are shown in *Figure 1*. Patients who underwent surgical therapy, catheter ab-

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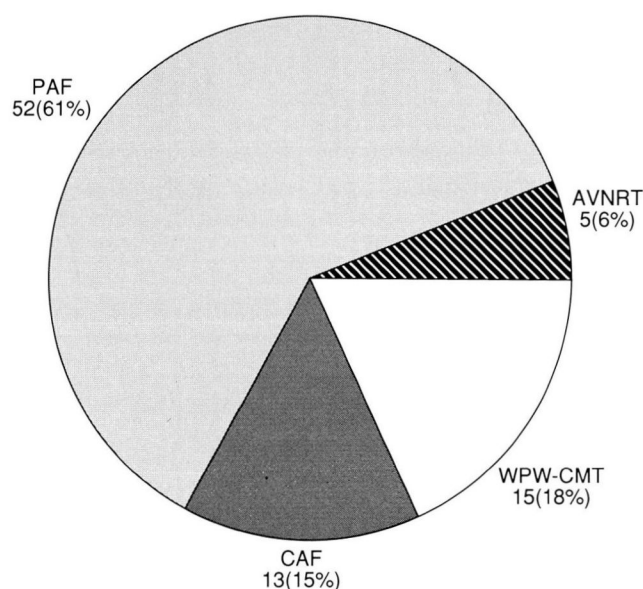
TYPES OF SUPRAVENTRICULAR  
TACHYARRHYTHMIAS IN 85 PATIENTS

FIGURE 1. Types of supraventricular tachyarrhythmias. PAF = paroxysmal atrial fibrillation; CAF = chronic atrial fibrillation; WPW-CMT = Wolff-Parkinson-White syndrome-related circus-movement tachycardia; AVNRT = atrioventricular nodal reentry tachycardia.

lation, or pacemaker treatment and patients with coexistent sustained ventricular tachycardia were excluded. Mean age was 57 years (range 25–82 years). The average duration of tachycardia prior to commencement of amiodarone therapy was 75 months (range 2–396 months).

Previous therapy with one or more conventional antiarrhythmic medications (mean  $3.8 \pm 1.0$ ) either alone or in combination was unsatisfactory in all patients. Arrhythmias had been refractory or patients were intolerant to the therapy. Antiarrhythmic drugs utilized before amiodarone therapy included beta blockers in 73 patients, digoxin in 69 patients, quinidine in 57 patients, verapamil in 55 patients, procainamide in 49 patients, and disopyramide in 23 patients. Primary underlying cardiac diagnoses are shown in Figure 2.

All 85 patients were symptomatic during arrhythmia episodes. Seventy-nine percent had palpitations, 50%

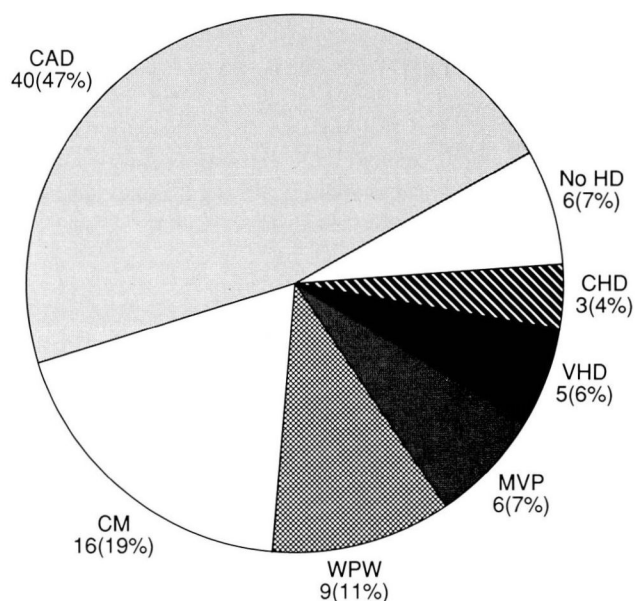
UNDERLYING PRIMARY CARDIAC  
DIAGNOSIS IN 85 PATIENTS

FIGURE 2. Underlying primary cardiac diagnosis. CAD = coronary artery disease; CM = cardiomyopathy; WPW = Wolff-Parkinson-White syndrome; MVP = mitral valve prolapse; VHD = valvular heart disease; CHD = congenital heart disease; No HD = no underlying heart disease.

experienced dizziness, light-headedness, and/or syncope, and 42% had dyspnea associated with tachyarrhythmia. Arrhythmia precipitated congestive heart failure in 9%. Systemic embolization was observed in 4% of patients, all of whom had atrial fibrillation.

Prior to initiation of amiodarone therapy, signed informed consent was obtained from all patients. Patients received 600–1200 mg per day of amiodarone for 5–7 days as a loading dose. Thereafter, the mean daily dose was  $245 \pm 120$  mg. Prior to therapy and at three-month intervals, patients were interviewed and examined, and 12-lead ECG, chest radiography, standard blood chemistry studies, and 24-hour ambulatory ECG monitoring were performed. Thyroid function tests, pulmonary function tests and ophthalmologic examinations were performed prior to treatment, at the 6- or 12-month visit, and at other times if indicated. Mean duration of therapy was 19.4 months. All patients with WPW-CMT

and AVNRT and 54% of patients with AF had electrophysiologic studies before commencement of amiodarone therapy.

Efficacy of amiodarone therapy was graded as follows:

**Excellent:** The patient had no symptomatic arrhythmia. In patients with chronic AF, sinus rhythm was maintained for the period following DC cardioversion.

**Improved:** SVT recurred but was self-terminating, less frequent, more abbreviated, and minimally symptomatic compared with the pre-amiodarone period. In CAF, ventricular response was controlled and symptoms were ameliorated.

**Poor:** Patients continued to have symptomatic arrhythmia after a total of 6 weeks of amiodarone therapy.

**Intolerant:** Drug was discontinued because of side effects.

## RESULTS

Response to amiodarone therapy in the different groups is shown in Table 1. For 44 of the 52 patients with PAF, response was considered excellent or improved. Of 13 patients with CAF, 11 had an excellent or improved response (two patients converted spontaneously to sinus rhythm during amiodarone therapy and two remained in sinus rhythm during maintenance amiodarone therapy following cardioversion). Of 15 patients with WPW-CMT, 13 had an excellent or improved response. Four of the five patients with AVNRT had an improved response.

For the entire study group of 85 patients, response during the follow-up period (mean 19.4 months) was

**TABLE 1**  
RESPONSE TO AMIODARONE IN DIFFERENT TACHYARRHYTHMIAS

Arrhythmia	Response				Total n
	Excellent n (%)	Improved n (%)	Poor n (%)	Intolerant n (%)	
PAF	22 (42)	22 (42)	3 (5)	5 (11)	52
CAF	4 (30)	7 (54)	1 (8)	1 (8)	13
WPW-CMT	3 (20)	10 (68)	1 (6)	1 (6)	15
AVNRT	—	4 (80)	1 (20)	—	5
Total	29 (34)	43 (51)	6 (7)	7 (8)	85

PAF = paroxysmal atrial fibrillation; CAF = chronic atrial fibrillation; WPW-CMT = Wolff-Parkinson-White syndrome-related circus-movement tachycardia; AVNRT = atrioventricular nodal reentry tachycardia.

**TABLE 2**  
RESPONSE TO AMIODARONE IN PAROXYSMAL ATRIAL FIBRILLATION AND FLUTTER

Study	Pts (n)	Excellent (%)	Improved (%)	Total (%)
Rosenbaum et al <sup>2</sup>	30	97	—	97
Wheeler et al <sup>4</sup>	7	57	43	100
Ward et al <sup>5</sup>	15	53	27	80
Graboyes et al <sup>7</sup>	95	78	6	84
Heger et al <sup>8</sup>	56	78	—	73
Horowitz et al <sup>9</sup>	27	55	26	81
Gold et al <sup>10</sup>	68	79	—	79
Haffajee et al <sup>11</sup>	48	85	—	85
Blomström et al <sup>12</sup>	8	50	50	100
Leak and Eyd <sup>13</sup>	18	83	—	83
Blevins et al <sup>14</sup>	13	54	23	77
TOTAL	385	76	16	83
Tuzcu et al	52	42	42	84

**TABLE 3**  
RESPONSE TO AMIODARONE IN CHRONIC ATRIAL FIBRILLATION

Study	Pts (n)	Excellent (%)	Improved (%)	Total (%)
Wheeler <sup>4</sup>	8	50	50	100
Horowitz et al <sup>9</sup>	11	45	—	45
Blomström et al <sup>12</sup>	22	50	36	86
Leak and Eyd <sup>13</sup>	5	100	—	100
Blevins et al <sup>14</sup>	25	40	40	80
TOTAL	71	50	40	80
Tuzcu et al	13	30	54	85

judged to be excellent in 29 patients, improved in 43 patients, and poor in six patients (Table 1).

Forty-three of 85 patients experienced some form of side effect. These included gastrointestinal adverse effects in 16 patients, subjective visual disturbances in 15 patients, dermatologic problems in 14 patients, abnormal thyroid function tests in nine patients, insomnia and nightmares in six patients, peripheral neuropathy in five patients, impotence in three patients, pulmonary toxicity in two patients, and elevation of liver enzyme

levels in one patient. Most of the side effects were mild and amiodarone was discontinued in only seven patients as follows: gastrointestinal side effects in three, hepatitis in one, hypothyroidism and impotence in one, and pulmonary toxicity in two. In five other patients, dosages of amiodarone had to be reduced because of serious side effects. In all patients side effects disappeared after the dose of amiodarone was reduced or the drug discontinued.

## DISCUSSION

Previous investigators have reported favorable results with amiodarone therapy in patients with paroxysmal atrial flutter and AF.<sup>2,4-11</sup> Excellent or improved responses were reported in 77% to 100% of patients (Table 2). In our study, complete suppression of PAF with amiodarone therapy did not occur as frequently as in most of these previous studies; however 84% of our patients had either total (excellent) or partial (improved) suppression of their arrhythmias. The variance in success rates could be due to differences in the type and severity underlying heart disease, dosage regimens, duration of treatment, methods and duration of follow-up, or definition of response.

In CAF, previous investigators have reported marked decrements in ventricular rate, improvement in symptoms, and successful maintenance of sinus rhythm following electrical cardioversion in 45% to 100% of patients<sup>9-14</sup> (Table 3). In our study, ventricular rate decreased and symptoms improved in 54% of patients. In two patients, sinus rhythm was maintained with amiodarone therapy following electrical cardioversion. The role of amiodarone in spontaneous conversion of AF to sinus rhythm is not clear. Four reports give the rate of chemical cardioversion as 0% to 32%.<sup>9,12-14</sup> Only two of our patients showed spontaneous conversion to sinus rhythm during amiodarone therapy. However, Santos et al<sup>15</sup> reported conversion to sinus rhythm with amiodarone in 86% of 88 episodes in 80 patients. The reason for the disparity between their study and others, including ours, is uncertain but may be related to the difference in patient characteristics and duration of CAF before amiodarone therapy. Present evidence suggests that amiodarone's predominant effect on persistent AF is control of ventricular response rather than conversion to sinus rhythm.

Amiodarone has been reported to be efficacious in patients with paroxysmal atrial tachycardia, particularly those with WPW syndrome.<sup>2,5,7,13</sup> Rosenbaum et al<sup>2</sup> and Leak and Eyd<sup>13</sup> reported total suppression of WPW-re-

lated tachycardia by amiodarone. Ward et al<sup>5</sup> reported 59% total and 23% partial suppression of CMT with amiodarone therapy. Wellens et al<sup>16</sup> noted no spontaneous episodes of tachycardia in 27 of 30 patients (97%) with WPW-CMT even though CMT could still be initiated by programmed stimulation in 23 of these 30 patients. Only 20% of our 15 WPW-CMT patients had an excellent response to amiodarone therapy; however, 68% were improved with the treatment, suggesting that amiodarone significantly ameliorates the WPW-CMT in the majority of patients. Three of our patients with WPW had both CMT and AF and amiodarone was effective in the management of both types of arrhythmia.

Several investigators have reported quite favorable results with amiodarone therapy in patients with recurrent paroxysmal supraventricular tachycardia resistant to other antiarrhythmic agents.<sup>2,5,13</sup> However, Rowland and Krikler<sup>17</sup> found amiodarone successful in only four of nine patients (44%) with re-entry atrioventricular tachycardia. Although our patient population was small, our study suggests that amiodarone is not very efficacious in suppressing AVNRT.

Adverse effects other than corneal deposits of amiodarone during treatment of SVT have been reported in 30%<sup>11</sup> to 75%<sup>7</sup> of patients. Various investigators report 6%<sup>7</sup> to 18%<sup>13</sup> amiodarone discontinuation rates due to severe side effects. Minor adverse effects of amiodarone were more common in our patient population than in other reported studies, but severe side effects required discontinuation of the drug in only seven patients (8%).

Our results support previous reports that suggest amiodarone is an important and potent agent in the management of various SVTs resistant to other antiarrhythmic drugs. Although prevalence of side effects is quite high, our study demonstrates that amiodarone is relatively well tolerated in patients with SVT at doses that are moderate compared with those used in the treatment of ventricular tachycardia.<sup>18</sup> Nevertheless, it is our current practice not to consider amiodarone as a first-line agent in the management of supraventricular tachyarrhythmias. We recommend conventional antiarrhythmic agents before proceeding with amiodarone therapy. The relative risk/benefit must always be considered, particularly in view of serious drug-related complications such as pulmonary toxicity and liver dysfunction.<sup>19</sup>

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