The Use of Atropine for Facilitation of Direct Current Cardioversion from Atrial Fibrillation—Results of a Pilot Study

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Summary

Background: The importance of the role of the autonomic nervous system (ANS) in the initiation and propagation of atrial fibrillation has been demonstrated in the condition of paroxysmal atrial fibrillation. However, the role of the ANS in patients with chronic atrial fibrillation is less clear. Some patients with chronic atrial fibrillation are resistant to the standard techniques of direct current (DC) cardioversion.

Hypothesis: We sought to investigate whether excessive vagal tone might prevent the restoration of sinus rhythm and to establish that the abolition of vagal tone using intravenous atropine will facilitate DC cardioversion in patients with atrial fibrillation who are resistant to the standard cardioversion techniques.

Methods: Beginning in August 1994, a change in the protocol for elective DC cardioversion of atrial fibrillation was made to include the use of intravenous atropine for patients resistant to the standard techniques of DC cardioversion.

Results: Over a 2-year period, 140 elective cardioversions were performed for atrial fibrillation. Sinus rhythm could not be restored on 31 occasions. Intravenous atropine prior to a further 360 J shock with paddles in the anteroposterior position allowed sinus rhythm to be restored on nine occasions. Patients with successful cardioversion after atropine had significantly better left ventricular function than those who remained in atrial fibrillation ($p = 0.001$) as well as a tendency toward a smaller left atrium.

Conclusion: This study suggests that high vagal tone, which is dominant in patients with structurally normal hearts, may prevent the termination of atrial fibrillation by standard techniques of DC cardioversion, and that the abolition of high vagal tone by atropine facilitates the restoration of sinus rhythm.

Key words: atrial fibrillation, cardioversion, atropine, parasympathetic nervous system

Introduction

Several authors and investigators have highlighted the importance of the autonomic nervous system in the initiation and propagation of atrial fibrillation.^{1–4} The role of the autonomic nervous system in atrial fibrillation seems particularly important in the condition of paroxysmal atrial fibrillation.⁵ Sufferers of this condition may fall into two clearly distinct categories: vagal fibrillators who fibrillate at times of high vagal tone, for example after a large meal or in the early hours of the morning; and sympathetic, or adrenergic, fibrillators who fibrillate at times of exercise or emotion. Vagal fibrillators are predominantly young men who have structurally normal hearts and who rarely progress to chronic atrial fibrillation. Adrenergic fibrillators are much more likely to have structural heart disease and are more likely to progress to chronic atrial fibrillation.

For patients in whom atrial fibrillation has become chronic, DC cardioversion can restore sinus rhythm with improved control of symptoms, exercise capacity, and ventricular function.^{6,7} The success rate of DC cardioversion is up to 90%,⁸ although increasing duration of arrhythmia and increasing age reduce the likelihood of its success.⁹ In some patients, DC cardioversion is unsuccessful despite the absence of these factors. Vagal tone is predominant in the structurally normal heart, whereas vagal withdrawal and sympathetic predominance is one of the first responses to structural heart disease.¹⁰ It is possible that high vagal tone prevents the restoration of sinus rhythm in some patients undergoing cardioversion. We postulated that the withdrawal of vagal tone, using intravenous atropine, might facilitate cardioversion in patients resistant to the standard DC cardioversion techniques.

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Methods

Beginning in August 1994, a change in the protocol for elective DC cardioversion of atrial fibrillation was made.

Stage 1: Using paddles in the apicosternal position, a single 200 J shock was administered followed by assessment of the cardiac rhythm. If atrial fibrillation persisted, a 360 J shock was administered and, if this did not restore sinus rhythm, a further 360 J was administered.

Stage 2: For persistent atrial fibrillation, we changed the paddles to the anteroposterior position. A 360 J shock was administered with the new paddle position.

Stage 3: If sinus rhythm was not restored, 600 mcg of intravenous atropine was given. After a few minutes, a fifth and final 360 J shock was administered with the paddles in the anteroposterior position.

Over the subsequent 2-year period, we analyzed the results of cardioversion and correlated them with the clinical and echocardiographic features of the patients.

Results

Over a 2-year period, 140 elective cardioversions were performed for atrial fibrillation in 105 patients (76 men, 29 women, age range 30–84 years, mean age 62.2 years). Successful cardioversion to sinus rhythm, defined by the presence of sinus rhythm at the time of discharge, was achieved on 109 occasions (78%) in 88 patients before Stage 3 was reached. Unsuccessful cardioversions using the standard techniques occurred on 31 occasions in 28 patients; 43.1% of the successful cardioversions and 41.9% of the unsuccessful cardioversions were preceded by antiarrhythmic therapy. In Stage 3, atropine at a dose of 600 mcg was administered on 23 occasions. The main reason for not administering atropine was an inadequately controlled ventricular rate. In this group of 22 patients, sinus rhythm was obtained in 9 patients with atrial fibrillation resistant to the standard DC cardioversion techniques.

Thus, 28 of 105 patients had atrial fibrillation resistant to DC cardioversion using the standard techniques. With the selective use of atropine on 23 occasions, we were able to achieve cardioversion to sinus rhythm in nine patients.

Patients with successful cardioversion after atropine had significantly better left ventricular function than the patients who remained in atrial fibrillation ($p = 0.001$, Student's *t*-test). Although the patients were also slightly younger and had a smaller left atrium, these differences were not statistically significant (Table I).

Discussion

The multiple wavelet theory of atrial fibrillation, first proposed in the 1960s by Moe and subsequently confirmed in 1985 by Allessie *et al.*, suggests a mechanism by which high vagal tone perpetuates atrial fibrillation.^{11, 12} One action of the vagus nerve is to shorten the refractory tail (or wavelength) of

TABLE I Patients receiving intravenous atropine in Stage 3 of cardioversion protocol

	Successful DC cardioversion with atropine (n = 9)	Unsuccessful DC cardioversion with atropine (n = 14)	p Value
Mean age	59.7	61.7	NS
Hypertension	5	10	NS
Mean LA size ± SD (cm)	4.17 ± 0.59	4.38 ± 0.74	NS
Mean EF ± SD	67.1 ± 10.1	51.1 ± 8.2	0.001

Abbreviations: DC = direct current, LA = left atrium, SD = standard deviation, EF = ejection fraction, NS = not significant.

the depolarizing wavefront. This results in the depolarizing wavefront constantly encountering excitable myocardium, thus perpetuating the reentry phenomenon. Slowed conduction due to vagal stimulation also has the effect of shortening the refractory tail (Fig. 1).

In patients with chronic atrial fibrillation, it is possible that vagal influences play a role in the potential for successful cardioversion. One possible mechanism for resistance to the standard techniques of DC cardioversion is the presence of high vagal tone which may be abolished by the use of intravenous atropine. Our change of protocol, administering intravenous atropine before a final DC shock, resulted in successful cardioversion for a number of patients who would otherwise have had an unsuccessful procedure. Our data suggest that this strategy is more likely to be beneficial in patients without evidence of significant structural heart disease, in keeping with our theory that atropine acts to inhibit the vagal tone that is predominant in these patients.

Our findings should be interpreted with the following limitations: First, our theory assumes that the factors responsible for the initiation of atrial fibrillation in paroxysmal atrial fibrillation are likely to be as important in the maintenance of atrial fibrillation in patients with chronic atrial fibrillation.

FIG. 1 Factors promoting atrial fibrillation. The use of atropine may prevent increased vagal tone, which itself causes slowed conduction and a shorter refractory period. These factors combine to reduce wavelength, thus promoting multiple wavelet formation.

Second, our data are from a nonrandomized pilot study with no control group. Although the administration of atropine prior to a final DC shock resulted in the restoration of sinus rhythm in approximately one-third of our resistant patients, we cannot discount the possibility that it is the administration of the fifth and final DC shock with paddles in the anteroposterior position and not the administration of atropine which produced conversion to sinus rhythm in at least some of these patients. Third, it is unclear whether the longer-term success of cardioversion is related to the ease with which cardioversion is initially achieved. Although these data are yet to be collected, it seems reasonable to suppose that patients in whom sinus rhythm is more difficult to achieve are more likely to revert to atrial fibrillation soon after cardioversion. Finally, we made no formal assessment of vagal tone in our patients prior to DC cardioversion. Support for our theory would be provided by, for example, lower average heart rates during electrocardiographic monitoring in those patients in whom atropine facilitated DC cardioversion.

A more rigorous assessment of our theory would require a large-scale, randomized, placebo-controlled trial with the administration of placebo agent or atropine before a final shock and with clinical estimation of predominantly vagal or sympathetic tone prior to cardioversion. This would require a multicenter study because the majority of patients admitted electively for DC cardioversion will achieve sinus rhythm before the final stages of this protocol are reached. Our pilot study suggests that such large-scale studies are now warranted.

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