Point of view

Is an individualized treatment possible in patients with paroxysmal supraventricular reentrant tachycardia?

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Paroxysmal supraventricular tachycardia (SVT) is commonly caused by atrioventricular (AV) nodal reentry or reentry involving a retrograde AV accessory pathway. If, during sinus rhythm, conduction through the accessory pathway is also anterograde, the electrocardiogram will include evidence of ventricular preexcitation. In this paper we deal with paroxysmal SVT without ventricular preexcitation. In the general population, the prevalence of reentrant SVT is about 2 per 1000 persons[1]. In the majority of patients it is not associated with signs of underlying heart disease. The most frequent symptoms are: palpitations (> 90%), dizziness (about 80%), dyspnea (about 40%), chest discomfort (about 40%) and diaphoresis (about 20%)[2]. In some patients dyspnea may be secondary to anxiety whereas in others it may be related to the marked increase in left atrial pressure, and consequently in pulmonary circulation pressures, induced by SVT[3,4]. Disabling symptoms such as syncope or severe hypotension are reported in about 20% of patients with SVT[2]; they appear related to both a decrease in cardiac output and to a vasovagal reflex[3,5]. In spite of the unavailability of large prospective studies, paroxysmal SVT is considered benign. We will now evaluate the available therapeutic options for SVT.

Antiarrhythmic prophylaxis

Until the early 1990s, long-term antiarrhythmic prophylaxis was the only therapeutic option and several drugs have been utilized; the results reported in the literature are summarized in table I. Verapamil and diltiazem have been evaluated in some randomized trials, and appear to significantly reduce both the total number of SVT attacks as well as the duration of tachycardia when it occurs[6,7]. A randomized, double-blind comparison of verapamil with digoxin and propranolol failed to demonstrate the superiority of one drug over the others[8]. Side-effects often limit the long-term use of calcium-channel blockers, whereas digoxin is often well tolerated. The class 1A drugs procainamide[9], quinidine[10] and disopyramide[11] offer a similar efficacy but are often associated with adverse effects that lead to poor tolerance and/or compliance by the patient.

The agents most extensively studied are the class 1C agents flecainide and propafenone. In some studies flecainide has been shown to be effective for the prophylaxis of reentrant SVT[12,13]. In a multicenter study, Henthorn et al.[12] revealed freedom from arrhythmia recurrence in nearly 80% of patients receiving flecainide

Table I. Efficacy of prophylactic antiarrhythmic treatment in patients with paroxysmal supraventricular reentrant tachycardia.

	Efficacy (%)	Follow-up (months)
Verapamil	68 (13-88)	12
Flecainide	73 (30-99)	8
Propafenone	65 (54-90)	18
Amiodarone	75 (70-93)	14
Sotalol	55 (25-87)	16

compared to 15% in those taking placebo over an 8-week period. Anderson et al.[14] reviewed several studies involving flecainide and their analysis revealed an overall efficacy for the long-term control of SVT in about 70% of patients. In an editorial comment, Benditt et al.[15] compared their own literature review to that of Anderson et al.[14] and found that flecainide was effective in the same percentage of patients. Both analyses reported a similar percentage of adverse cardiac effects (7.5%) and of proarrhythmia (5%), usually non fatal and almost always in patients with underlying heart disease. Reports of adverse cardiac reactions in patients receiving flecainide have ranged from 1 to 17%[16]. Non cardiac adverse effects are more commonly visual and do not necessitate discontinuation; they have been reported in up to 20 to 30% of patients[16,17].

Propafenone also proved to be efficacious in the long-term suppression of SVT[18-20]. Pritchett et al.[18] demonstrated that over a 6-month period, propafenone treatment resulted in a rate of recurrence, which was equal to one fifth that of placebo. Of particular note in this study is the significant number of patients (11 out of 33) requiring discontinuation of the medication as a result of adverse effects.

Data regarding the use of sotalol, a class 3 agent, in patients with SVT are limited. In a variety of open studies, sotalol prevented clinical recurrences of paroxysmal SVT in about 50% of patients[21,22]. Amiodarone therapy has not been extensively investigated in patients with SVT but, at dosages ranging from 100 to 300 mg daily, it seems to be effective in about 75% of cases. This, even in refractory cases, that is in patients showing relapses during previous antiarrhythmic treatments[23].

Data reported in table I show a rather good efficacy of prophylactic treatment, but a wide range, that is a marked variability, from one study to another. On the whole, the higher the number of tachycardic attacks, the more frequent the relapses during antiarrhythmic treatment; that means that antiarrhythmic drugs are less effective in case of a very severe clinical picture. Other disadvantages of prophylactic antiarrhythmic treatment include the daily intake of these agents, sometimes in multiple doses, and the frequent occurrence of adverse effects.

Radiofrequency catheter ablation

In the last decade radiofrequency ablation has been utilized in clinical practice and has proven to be a highly effective curative therapy for reentrant SVT. In patients with SVT caused by AV nodal reentry or reentry involving an AV accessory pathway, catheter ablation can be accomplished successfully in ≥ 95% of patients[24,25]. In 5-8% of patients, tachycardia recurs after an apparently successful procedure and necessitates a second ablation procedure[24,25]. Radiofrequency ablation markedly improves the quality of life[26]. However, major complications have been reported in up to 3% of patients submitted to this technique[25,27]. Death constitutes a very rare event (0.1%) and it is observed almost exclusively in patients with severe heart disease[25,28]. The most common complication, especially in patients with AV nodal SVT, is II or III degree AV block which requires pacemaker implantation in about 1% of the patients and, in some high volume centers, even less (0.3%)[29]. Cryothermal ablation could further reduce the risk of this complication[30]. Very rare complications include stroke, myocardial infarction, valve damage, tamponade, pneumothorax and embolic events. These data suggest that catheter ablation should be recommended in patients whose quality of life is adversely affected by paroxysmal SVT. In the American College of Cardiology/American Heart Association guidelines regarding the indications for catheter ablation procedures[31], class I recommendation was the following: "Patients with symptomatic and sustained SVT that is drug-resistant or patients who are drug-intolerant or do not desire long-term therapy". This recommendation has been accepted all over the world. In the recent Italian guidelines, this recommendation has been changed for the first time[32]. Catheter ablation remains indicated in patients whose quality of life is adversely affected by paroxysmal SVT, but the terms "drug-resistant or drug-intolerant" have been omitted. The difference is only apparently substantial; actually, as previously reported, patients with frequent SVT episodes sooner or later present with recurrences during prophylactic antiarrhythmic treatment.

Episodic treatment

Some patients with SVT have rare and well tolerated episodes but, because of the long duration of these episodes, require admission to the emergency room. In these patients, neither long-term antiarrhythmic prophylaxis nor catheter ablation seem to be the most appropriate first-line treatment. An appropriate approach appears to be the episodic treatment with a single dose of an oral antiarrhythmic drug at the time of the onset of arrhythmia. To date, the episodic treatment of paroxysmal SVT has been investigated in small groups of patients[33,34]. We sought to verify the efficacy of a single oral dose of antiarrhythmic drugs in terminating paroxysmal SVT in patients with infrequent (< 5 per year) and well tolerated episodes, requiring treatment in an emergency room at least once yearly[35]. Patients for whom episodic treatment is indicated account for 13% of all patients with reentrant SVT and thus constitute a small group[35]. In view of the fact that previously reported results have been encouraging[33,34], we used oral flecainide and oral diltiazem plus propranolol in a controlled design. Thirty-seven patients were enrolled and 33 had an inducible SVT during

electrophysiological study. In the latter, three treatments – placebo, flecainide (200 mg) and diltiazem (120 mg) plus propranolol (80 mg) – were administered in a random order 5 min after the induction of the SVT on 3 different days. Conversion to sinus rhythm occurred within 2 hours in 52, 61 and 94% of patients on placebo, flecainide and diltiazem plus propranolol respectively ($p < 0.001$). The conversion time was shorter after diltiazem plus propranolol (32 ± 22 min) than after placebo (77 ± 42 min) or flecainide (74 ± 37 min) ($p < 0.001$). Four patients developed hypotension and 4 a sinus rate < 50 b/min following the interruption of SVT (1 patient after placebo, 3 after flecainide and 4 after diltiazem plus propranolol). Therefore, the results obtained during the acute testing show that compared to placebo, in general diltiazem plus propranolol, but not flecainide, proved to be effective in shortening the conversion time. The selection of drug therapy on the basis of the results of acute testing was associated with a satisfactory clinical outcome during the follow-up. In fact, oral diltiazem plus propranolol interrupted within 2 hours all out-of-hospital arrhythmic episodes in 81% of the patients; in the remaining patients, this therapeutic regimen was not completely successful and one or more episodes occurred as a result of drug ineffectiveness or drug unavailability. During follow-up, 1 patient, discharged on diltiazem plus propranolol, had an episode of syncope 15 min after drug ingestion. Although paroxysmal SVT may cause syncope[5], this symptom was probably a drug-related adverse effect. Although it is rare, the possibility of syncope should prompt physicians to recommend that the patient be seated while taking a self-administered oral agent. An important result of this treatment strategy was the dramatic reduction in the number of patients calling for emergency room assistance as compared to the year before enrollment (9 vs 100%, $p < 0.0001$). These data are clinically relevant because emergency room admissions are often undesirable for SVT patients and constitute the most important concern. The results of our study show that out-of-hospital episodic treatment with diltiazem 120 mg, and propranolol 80 mg, is seemingly effective in patients with paroxysmal SVT, and that the incidence of severe adverse events seems low. Since it avoids the disadvantages of long-term antiarrhythmic prophylaxis and the potential complications that are associated with catheter ablation, episodic treatment is appealing for patients who are rarely symptomatic. However, before the physician prescribes diltiazem plus propranolol, this combination must be tested for its efficacy and safety inside the hospital, possibly during a spontaneous SVT episode. The treatment of non responders remains to be investigated and may include testing of alternative drugs. Because episodic treatment with diltiazem plus propranolol was not tested in patients with ventricular preexcitation, sinus bradycardia or left ventricular dysfunction, this combination cannot be proposed for these patients.

Conclusions

The available therapies for patients with paroxysmal SVT include antiarrhythmic prophylaxis, catheter ablation, episodic treatment and no treatment. On the basis of the clinical features of SVT attacks, an individualized treatment, within certain limits, appears possible.

Patients with infrequent, short-lasting (minutes or a couple of hours) and well tolerated SVT episodes or episodes promptly terminated by autonomous vasovagal maneuvers, do not necessitate any treatment.

In patients with infrequent and well tolerated SVT episodes which, however, last long enough to necessitate emergency room admission, the most appropriate treatment appears the episodic one. In fact, in these patients oral prophylaxis with daily intake of antiarrhythmic drugs does not appear feasible for the prevention of just a few and well tolerated episodes yearly. Moreover, the risks of catheter ablation appear excessive for such a mild clinical problem. These patients represent a small group and account for about 10% of all subjects with reentrant SVT.

In patients whose quality of life is adversely affected by paroxysmal SVT because of frequent and/or ill tolerated tachycardic episodes causing hemodynamic (syncope, severe hypotension, heart failure) or psychological distress, the first-line treatment appears catheter ablation. In fact, this procedure definitively resolves the

Table II. Indications to the various available therapeutic options for paroxysmal supraventricular tachycardia (SVT).

SVT characteristics	Treatment
Patients with infrequent, short-lasting and well tolerated SVT episodes or episodes promptly terminated by vagal maneuvers performed autonomously	No treatment
Patients with infrequent, well tolerated but long-lasting SVT episodes	Out-of-hospital episodic treatment
Patients whose quality of life is adversely affected by paroxysmal SVT (frequent and/or ill tolerated tachycardic episodes causing hemodynamic or psychological distress)	Catheter ablation
Patients who refuse catheter ablation or in whom the procedure fails	Prophylactic antiarrhythmic treatment

SVT in ≥ 95% of patients and markedly improves the quality of life. In these patients an attempt with prophylactic antiarrhythmic treatment can be made but, almost unavoidably, SVT recurs and the real therapeutic decision is only delayed.

After the introduction of new therapeutic strategies, the role of prophylactic therapy appears very restricted. At present, it seems to be indicated in patients with frequent SVT episodes who refuse catheter ablation or in whom the procedure fails. The indications to the various therapeutic options are summarized in table II.

References

1. Orejarena LA, Vidaillet H, De Stefano F, et al. Paroxysmal supraventricular tachycardia in the general population. J Am Coll Cardiol 1998; 31: 150-7.
2. Wood KA, Drew BJ, Sheinman MM. Frequency of disabling symptoms in supraventricular tachycardia. Am J Cardiol 1997; 79: 145-9.
3. Alboni P, Fucà G, Paparella N, Scarfò S, Mele D, Pedini I. Hemodynamics of supraventricular reentrant tachycardia. European Journal of Clinical Pacing and Electrophysiology 1997; 7: 115-9.
4. Mele D, Alboni P, Fucà G, Scarfò S, Paparella N, Levine RA. Atrioventricular nodal versus atrioventricular supraventricular reentrant tachycardias: characterization by an integrated Doppler electrophysiological hemodynamic study. Pacing Clin Electrophysiol 2000; 23: 2078-85.
5. Leitch JW, Klein GJ, Yee R, Leather RA, Kin YH. Syncope associated with supraventricular tachycardia. An expression of tachycardia rate or vasomotor response? Circulation 1992; 85: 1064-71.
6. Mauritson DR, Winniford MD, Walker WS, Rude RE, Cary JR, Hills LD. Oral verapamil for paroxysmal supraventricular tachycardia: a long-term, double-blind randomized trial. Ann Intern Med 1982; 96: 409-12.
7. Mannino MM, Mehta D, Gomes A. Current treatment options for paroxysmal supraventricular tachycardia. Am Heart J 1994; 127: 475-80.
8. Winniford MD, Fulton KL, Hillis LD. Long-term therapy of paroxysmal supraventricular tachycardia: a randomized, double-blind comparison of digoxin, propranolol and verapamil. Am J Cardiol 1984; 54: 1138-9.
9. Bauernfeind RA, Wyndham CR, Dhingra RC, et al. Serial electrophysiologic testing of multiple drugs in patients with atrioventricular nodal reentrant paroxysmal tachycardia. Circulation 1980; 62: 1341-9.
10. Wu D, Hung JS, Kuo CT, Hsu KS, Shieh WB. Effects of quinidine on atrioventricular nodal reentrant paroxysmal tachycardia. Circulation 1981; 64: 823-31.
11. Brugada P, Wellens HJJ. Effects of intravenous and oral disopyramide on paroxysmal atrioventricular nodal tachycardia. Am J Cardiol 1984; 53: 88-92.
12. Henthorn RW, Waldo AL, Anderson JL, et al. Flecainide acetate prevents recurrence of symptomatic paroxysmal supraventricular tachycardia. Flecainide Supraventricular Tachycardia Study Group. Circulation 1991; 83: 119-25.
13. Neuss H, Schlepper M. Long-term efficacy and safety of flecainide for supraventricular tachycardia. Am J Cardiol 1988; 62: 56D-61D.
14. Anderson JL, Jolivette DM, Fredell PA. Summary of efficacy and safety of flecainide for supraventricular arrhythmias. Am J Cardiol 1988; 62: 62D-66D.
15. Benditt DG, Dunningan A, Buetikofer J, Milstein S. Flecainide acetate for long-term prevention of paroxysmal supraventricular tachycardia. Circulation 1991; 83: 345-7.
16. Cockrell JL, Scheinman MM, Titus C, et al. Safety and efficacy of oral flecainide therapy in patients with atrioventricular reentrant tachycardia. Ann Intern Med 1991; 114: 189-94.
17. Pritchett EL, Wilkinson WE. Mortality in patients treated with encainide and flecainide for supraventricular tachycardia. Am J Cardiol 1991; 67: 976-80.
18. Pritchett EL, McCarthy EA, Wilkinson WE. Propafenone treatment of symptomatic paroxysmal supraventricular tachycardia: a randomized, placebo-controlled crossover trial in patients tolerating oral therapy. Ann Intern Med 1991; 114: 539-44.
19. UK Propafenone Paroxysmal Supraventricular Tachycardia Study Group. A randomized, placebo-controlled trial of propafenone in the prophylaxis of paroxysmal supraventricular tachycardia and paroxysmal atrial fibrillation. Circulation 1995; 92: 2550-7.
20. Tendera M, Wnuk-Wojnar AM, Kulakowski P, et al. Efficacy and safety of dofetilide in the prevention of symptomatic episodes of paroxysmal supraventricular tachycardia: a 6-month double-blind comparison with propafenone and placebo. Am Heart J 2001; 142: 93-8.
21. Camm AJ, Paul V. Sotalol for paroxysmal supraventricular tachycardia. Am J Cardiol 1990; 65: 67A-73A.
22. Wanless RS, Anderson K, Joy M, et al. Multicenter comparative study on the efficacy and safety of sotalol in the prophylactic treatment of patients with paroxysmal supraventricular tachyarrhythmias. Am Heart J 1997; 133: 441-6.
23. Kopelman HA, Horowitz LN. Efficacy and toxicity of amiodarone for the treatment of supraventricular tachycardia. Prog Cardiovasc Dis 1989; 31: 355-66.
24. Kay GN, Epstein AE, Dailey SM, Plumb VJ. Role of radiofrequency ablation in the management of supraventricular arrhythmias: experience in 760 consecutive patients. J Cardiovasc Electrophysiol 1993; 4: 371-89.
25. Calkins H, Yong P, Miller JM, et al. Catheter ablation of accessory pathways, atrioventricular nodal reentrant tachycardia, and the atrioventricular junction. Final results of a prospective, multicenter clinical trial. Circulation 1999; 99: 262-70.
26. Lau CP, Tai YT, Lee PWH. The effects of radiofrequency ablation versus medical therapy on the quality-of-life and exercise capacity in patients with accessory pathway-mediated supraventricular tachycardia: a treatment comparison study. Pacing Clin Electrophysiol 1995; 18: 424-32.
27. Chen SA, Chiang CE, Tai CT, et al. Complications of diagnostic electrophysiologic studies and radiofrequency catheter ablation in patients with tachyarrhythmias: an eight-year survey of 3966 consecutive procedures in a tertiary referral center. Am J Cardiol 1996; 74: 41-6.
28. Schaffer MS, Gow RM, Moak JP, Saul JP. Mortality following radiofrequency catheter ablation (from the pediatric radiofrequency ablation registry). Am J Cardiol 2000; 86: 639-43.
29. Gaita F, Rinardi R, Scaglione M, Caponi D. Catheter ablation of typical atrioventricular nodal reentrant tachycardia. In: Zipes DP, Haissaguerre M, eds. Catheter ablation of arrhythmias. Armonk, NY: Futura Publishing, 2002: 230-50.
30. Skanes AC, Dubuc M, Klein GJ, et al. Cryothermal ablation of the slow pathway for the elimination of atrioventricular nodal reentrant tachycardia. Circulation 2000; 102: 2856-60.
31. ACC/AHA Task Force Report. Guidelines for clinical intracardiac electrophysiological and catheter ablation procedures. Circulation 1995; 92: 673-91.

32. Linee guida ANMCO-SIC-AIAC sull'uso appropriato delle metodiche di elettrostimolazione cardiaca. Ital Heart J Suppl 2000; 1: 551-68.
33. Musto B, Cavallaro C, Musto A, D'Onofrio A, Belli A, De Vincentis LD. Flecainide single oral dose for management of paroxysmal supraventricular tachycardia in children and young adults. Am Heart J 1992; 124: 110-5.
34. Yeh SJ, Lin FC, Chou YY, Hung JS, Wu D. Termination of paroxysmal supraventricular tachycardia with a single oral dose of diltiazem and propranolol. Circulation 1985; 71: 104-9.
35. Alboni P, Tomasi C, Menozzi C, et al. Efficacy and safety of out-of-hospital self-administered single-dose oral drug treatment in the management of infrequent, well-tolerated paroxysmal supraventricular tachycardia. J Am Coll Cardiol 2001; 37: 548-53.