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Etripamil: Self-management of supraventricular tachycardia is not far away?

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Supraventricular tachycardia (SVT) includes a variety of reentrant fast heart rhythms originating in any part of the heart's conduction system above the ventricles [1]. SVTs have an estimated incidence of 35 per 100,000 person-years, with a prevalence of 2.29 per 1000 persons affecting 1.7 million people and over 600,000 healthcare admissions in the US alone per year [2]. SVTs are classified based on the origin and regularity. Atrioventricular nodal tachycardia is the most common type of SVT, representing 50% to 90% of all SVT cases. Episodes typically present with constellations of symptoms such as palpitations, dizziness, presyncope, nausea, anxiety, atypical chest pain, diaphoresis, and frank syncope [3]. While it is not as life-threatening as sudden cardiac death or other ventricular arrhythmias, many features of SVT make it particularly difficult and frustrating for patients to deal with. The unpredictability of the episodes and inability to control the disabling symptoms can render the patient incapacitated. Patients with SVT have averaged four hospital admissions or emergency department visits per year in the preceding two years before radiofrequency ablation treatment [4].

Once an SVT is identified, the next objective is to assess for hemodynamic instability. If a patient is unstable, immediate synchronized cardioversion is considered [5]. In a stable patient, vagal maneuvers (including Valsalva and carotid sinus massage) are the first-line intervention for acute conversion of SVT, although their success rate remains limited (<30%). When vagal maneuvers fail, we could use a single oral dose to terminate an episode of SVT in outpatient acutely. This so-called "pill in the pocket" approach necessitates the use of a drug that has a rapid onset of action (i.e., immediate-release preparations), and currently, no such drugs are available for non-parenteral self-administration. Although oral verapamil, diltiazem, beta blockers, and flecainide have been utilized in these situations, their onset of action is relatively slow, and their efficacy is modest. Therefore, in many patients with sustained SVT, acute termination of the arrhythmia often requires intravenous drug therapy in a controlled medical environment. Catheter ablation remains the mainstay of treatment for patients with supraventricular tachycardia (SVT) especially for those who are unresponsive or intolerant to drug therapy. For patients requiring therapy who are reluctant to undergo catheter ablation, drug therapy remains a viable alternative, although with significantly lower efficacy rates [6].

Etripamil is being studied to address this critical issue in patients who need a safe, convenient and rapidly efficacious self-administered medication for the treatment of SVT episodes and is currently under evaluation in Phase 2 clinical trial (NODE-1). Etripamil has been developed as a self-administered intranasal nasal spray to terminate paroxysmal supraventricular tachycardia (PSVT) at the onset of episodes. Etripamil is a potent and novel short-acting calcium channel antagonist intended for the treatment of patients with SVT. Results of phase 1 showed that etripamil had a rapid onset and had reached a therapeutic level within 5 min of administration. Etripamil is short-acting and metabolized rapidly which helps to avoid the potential complications of current long-term therapies. The study of BS Stambler et al. included 104 patients that were randomized and received this drug in an electrophysiology (EP) lab setting [7]. Following 5-min of induced PSVT (mainly atrioventricular reentry tachycardia or atrioventricular nodal reentrant tachycardia), patients received Etripamil at doses of 70 mg, 105 mg, and 140 mg. It demonstrated conversion rates of 87%, 75%, and 95% respectively and the primary endpoint was the termination rate of PSVT within 15 min of study drug administration, that was significantly better than the 35% conversion rate in the placebo group. The mean conversion time ranged from 2.60 min to 3.37 min in the Etripamil groups. Times were faster with patients given higher doses. The most common adverse event that occurred to patients who used

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the Etripamil therapy was transient nasal congestion or irritation and a temporary reduction in blood pressure was observed at the two highest doses, and one case of hypotension was reported as an adverse event.

Although a self-administered etripamil nasal spray can potentially become an important approach for the acute management of SVT, its safety and efficacy still need to be verified in phase III controlled studies conducted outside of the electrophysiology laboratory in non-sedated patients. Additionally, whether study findings can be extended to patients with longer durations of sustained SVT and those with other SVT mechanisms is yet to be evaluated.

It is anticipated that the results of the NODE-1 trial are promising and has the potential to be implemented for self-administration in the setting of acute termination of SVT. We hope that this drug would change the treatment paradigm of the acute management of SVT.

Conflict of interest

There is no conflict of interest.

References

[1] C.M. Janson, M.J. Shah, Supraventricular tachycardia in adult congenital heart disease: mechanisms, diagnosis, and clinical aspects, Card Electrophysiol. Clin. 9 (2) (Jun 2017) 189–211.
[2] L.A. Orejarena, H. Vidaillet Jr., Paroxysmal supraventricular tachycardia in the general population, J. Am. Coll. Cardiol. 31 (1) (Jan 1998) 150–157.
[3] K. Wood, Mechanisms and clinical manifestations of supraventricular tachycardias, Prog. Cardiovasc. Nurs. 10 (2) (1995) 3–14.
[4] L.M. Epstein, N. Chiesa, M.N. Wong, R.J. Lee, J.C. Griffin, M.M. Scheinman, et al., Radiofrequency catheter ablation in the treatment of supraventricular tachycardia in the elderly, J. Am. Coll. Cardiol. 23 (1994) 1356–1362.
[5] N.A. Shilkofski, K.L. Nelson, Recognition and treatment of unstable supraventricular tachycardia by pediatric residents in a simulation scenario, Simul. Healthc. 3 (1) (Spring 2008) 4–9.
[6] R.L. Page, J.A. Joglar, M.A. Caldwell, H. Calkins, 2015 ACC/AHA/HRS guideline for the management of adult patients with supraventricular tachycardia: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society, Circulation 133 (14) (Apr 5 2016) e506–e574.
[7] B.S. Stambler, P. Dorian, P.T. Sager, Etripamil nasal spray for rapid conversion of supraventricular tachycardia to sinus rhythm, J. Am. Coll. Cardiol. 72 (5) (Jul 31 2018) 489–497.