

Letter to the Editor

Quinidine therapy in children affected by Brugada syndrome: are we far from a safe alternative?

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Dear Sir,

Brugada syndrome is an inherited arrhythmogenic disease characterized by a typical electrocardiographic pattern consisting of ST-segment elevation in the right precordial leads, and is known to carry a predisposition to sudden cardiac death.^{1–3} Its prevalence is 1–5 per 10,000 inhabitants worldwide. It is responsible for one-fifth of sudden deaths in patients with structurally normal hearts, with a mean age at death of 40 years.¹ Prevalence of the syndrome in children is much lower than in adults,^{4,5} but Brugada syndrome is known to cause sudden infant death syndrome, and also to be responsible for sudden cardiac death during childhood.^{6–9}

To date, implantation of an automatic cardioverter-defibrillator is the only recommended treatment for patients with the syndrome who are considered to be at high risk.¹⁰ Implantation of such devices in young children is challenging, and implies replacements of the devices over a lifetime, together with the likelihood of numerous complications.¹¹ How to manage children with Brugada syndrome, therefore, remains a matter of debate,¹² with no safe alternatives between the options of administering no medication, courting the risk of sudden cardiac death occurring mostly in adulthood,¹ or implanting a cardioverter-defibrillator.

Lifestyle measures are part of the programme to prevent sudden cardiac death, and include such features as prompt treatment of febrile illnesses with antipyretics, since fever represents the most important precipitating factor for arrhythmic events in children with Brugada syndrome.⁹ A pharmacological alternative is desirable, but class IA and IC antiarrhythmic drugs are contra-indicated, while

amiodarone and beta-blockers are ineffective.¹ One current theory to explain arrhythmogenesis in Brugada syndrome is based on an imbalance between depolarizing and repolarizing currents during the early repolarization phase of the action potential, mainly in epicardial cells of the right ventricle, which express a strong potassium transient outward current I_{to} supporting phase 2 reentrant activity.^{13,14} Quinidine, a specific class IA anti-arrhythmic agent with I_{to} blocking properties,¹⁵ has therefore been suggested as being useful in Brugada syndrome.

The clinical relevance of this suggestion has been proved by reports of quinidine-induced electrocardiographic normalization in patients with the syndrome.¹⁶ Some clinical trials have shown quinidine to be safe in preventing both inducible and spontaneous ventricular fibrillation in adults with the syndrome known to be at high risk, when given at both high and low doses.^{17–19} In these trials, quinidine prevented ventricular fibrillation induction in up to nine-tenths of asymptomatic patients with an inducible arrhythmia, as well as reducing the recurrence of ventricular arrhythmias in symptomatic patients.^{17,18} Oral quinidine is also used to treat electrical storms in adults with Brugada syndrome.²⁰

The dosage of quinidine for children is 30–60 mg/kg/day, given in 4 divided doses.²¹ Children with Brugada have been successfully treated in this fashion.^{8,9,22} Suzuki et al, for example, reported an event-free period of 5 months following treatment of a symptomatic infant by combined oral therapy including quinidine and prophylactic implantation of a cardioverter-defibrillator placement after an electrical storm.⁸ We reported a period of follow-up of 16 months after treating a 3-year-old child exclusively with oral hydroquinidine after a first episode of ventricular tachycardia.²² In the largest affected population of

Correspondence to: Dr Alban-Elouen Baruteau, Département de Cardiologie et Maladies Vasculaires, Hôpital Pontchaillou, CHU de Rennes, 2 rue Henri Le Guilloux, 35033 Rennes cedex, France. Tel: (00 33) 299282525; Fax: (00 33) 299282510; E-mail: alban.baruteau@wanadoo.fr

children published to date, 4 of the 30 children, aged 4 months to 10 years, including our 3-year-old boy, safely received oral quinidine, with a mean follow-up of 28 months.⁹

Challenging high-risk affected children with the syndrome remains a key issue. No clinical trial has assessed the safety of quinidine when used in children. It may be interesting to test this pharmacological treatment in the following situations. First, in symptomatic children with multiple appropriate shocks delivered from implantable cardioverter-defibrillators. Second, in high-risk asymptomatic children with inducible ventricular arrhythmias. Treatment should be guided by electrophysiological studies in such patients. Should the arrhythmias still be inducible despite treatment with quinidine, implantation of a cardioverter defibrillator must be recommended.

Further studies are needed to determine the right place of treatment with quinidine. At this stage, nonetheless, it appears to be a promising alternative to implantation of cardioverter-defibrillators in young children with the syndrome who are known to be at high risk, not only because of its safety, but also because of its excellent long-term tolerability at low doses.¹⁹ As previously proposed, it could constitute a bridge to implantation of cardioverter-defibrillators in children known to be at high risk.²³

Alban-Elouen Baruteau^{1,2,3,4}, Philippe Mabo^{1,2,5,6},
Vincent Probst^{3,4,7}

¹Centre Hospitalier Universitaire de Rennes, Service de Cardiologie et Maladies Vasculaires, Rennes, France

²Institut National de la Santé et de la Recherche Médicale, Unité 642, Rennes, France

³Institut National de la Santé et de la Recherche Médicale, Unité 915, Nantes, France

⁴Université de Nantes, Faculté de Médecine, l'institut du thorax, Nantes, France

⁵Institut National de la Santé et de la Recherche Médicale, Centre d'Investigation Clinique et de l'Innovation Technologique 804, Rennes, France

⁶Université de Rennes 1, Laboratoire de Traitement du Signal et de l'Image, Rennes, France

⁷Centre Hospitalier Universitaire de Nantes, l'institut du thorax, Service de Cardiologie, Nantes, France

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