

openheart The challenges of performing ajmaline challenge in children with suspected Brugada syndrome

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Brugada syndrome (BS) is an inheritable syndrome characterised by coved-type ST segment elevation in the right precordial leads (V1–V3) and increased risk of sudden death in the absence of structural heart disease.¹ Intravenous administration of class IC antiarrhythmic drugs is an established tool to unmask the diagnostic Brugada ECG pattern in patients with suspected BS and non-diagnostic ECG.² Current data indicate that ajmaline is the most effective drug for the diagnosis of BS, mainly because of its kinetics and strength of rate-dependent sodium channel blocking effects.³

McMillan *et al* report on feasibility and outcomes of ajmaline challenge in children. Ninety-five participants aged 18 years or less (mean age: 12.5±3.3 years) underwent ajmaline challenge for suspected BS⁴. Forty-eight per cent of them were BS family members. Ajmaline unmasked diagnostic Brugada type I ECG in 20% of individuals. Drug infusion was discontinued in all patients before reaching the target dose in case of appearance of diagnostic Brugada ECG or if QRS duration increased by 150% or more. No ajmaline-induced sustained ventricular arrhythmia (sVA) was observed. After a mean follow-up time of 3.66 years, no patient with drug-induced BS died or experienced any arrhythmic event. Of note, three patients (3%) with an initial negative ajmaline challenge repeated drug test after a mean time of 5 years. Among them, a 15-year-old girl developed a positive response at the repeat ajmaline challenge.

Prevalence of BS in the paediatric population is extremely low (0.009%) as compared with the adult population (0.14–0.7%).^{5, 6} Moreover, the mean age of patients presenting with either symptomatic or asymptomatic BS has been reported to be in the fourth or fifth decade.⁷ Although rarely diagnosed in children, BS can manifest at every age and may cause sudden death in childhood even

in the first month of life.⁸ Therefore, patients with suspected BS and non-diagnostic baseline ECG should undergo ajmaline test at all ages from birth, taking into consideration the clinical circumstances and wishes of family. Performing ajmaline challenge for suspected BS has been considered to be a safe procedure if drug discontinuation criteria are followed.⁹ However, specific data on the effects and safety of ajmaline test in individuals younger than 12 years are lacking. Recently, our group reported an incidence of ajmaline-induced sVA in 4.4% of patients younger than 18 years with ajmaline-induced BS.¹⁰ Experiencing an arrhythmic event during a diagnostic drug challenge could have tragic consequences, particularly if the patient is a child with BS. Although the occurrence of episodes of sVA might be significantly lower in a subject without a sodium channelopathy, ajmaline challenge should always be performed under close supervision in an appropriate environment with all advanced life support facilities available, ideally including the possibility of performing a venoarterial extracorporeal membrane oxygenation placement in case of an intractable episode of ventricular fibrillation. Further studies conducted in more selected patients' populations (<12 years) could be helpful to clarify these important aspects, concerning the safety of ajmaline challenge in children with suspected BS.

Clinical aspects and prognosis of either spontaneous or drug-induced BS have been previously described in individuals younger than 16 years, and, as in adults, a higher risk of arrhythmic events has been found in symptomatic patients and in those displaying a spontaneous type I ECG.¹¹ No systematic studies have yet been carried out to assess the clinical characteristics and the long-term follow-up of drug-induced BS in patients younger than 12 years. Screening of the



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family of a proband with BS is always recommended. However, the ideal age for screening of BS family members is unknown and different centres use different protocols for the screening of the paediatric first-degree relatives. Moreover, the clinical significance of repeating ajmaline challenge after puberty in paediatric family members of BS patients with an initial negative drug test is unknown. Hormonal changes can play an important role in the clinical presentation of BS. In particular, testosterone has been suggested as a potential hormone responsible for the age-dependent manifestation of BS phenotype, as suggested by the disappearance of Brugada type I ECG after surgical castration for prostate cancer.¹² The existence of an age-dependent response to ajmaline challenge is intriguing and might have relevant clinical implications. However, repeating ajmaline challenge after puberty in patients with an initial negative drug test remains controversial and should be further investigated.

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