

## Loss of sodium channel function-like phenotypes: Diagnostic and therapeutic aspects in children

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### Introduction

Loss of sodium channel function-like phenotypes are a spectrum of diseases including Brugada Syndrome (BrS) and cardiac conduction disease, ranging in presentation from asymptomatic to sudden cardiac death (SCD) in young individuals. This study aimed to analyze the diagnostic and therapeutic aspects of these disorders in children.

### Methods

Patients (n=37) were included if they presented below 18 years of age with (a) pertinent cardiac symptoms plus abnormal ECG (BrS ECG and/or prolonged conduction intervals), (b) abnormal ECG during family-screening for confirmed sodium channelopathy or (c) incidental observation of abnormal ECG with family history of sudden unexplained death. Conduction intervals were considered prolonged if longer than 2 standard deviations for age.

### Results

Age at presentation was  $6\pm 5$  years and 13 (35%) were female. Of the symptomatic patients (n=18, 49%), 4 presented in the first year of life. Syncope (n=9) was the most common symptom followed by arrhythmias (n=8). Symptoms were associated with fever in 6 (33%) of the symptomatic patients, 2 of which occurred during vaccination-related fever episodes. SCD occurred in a 3 month old male following vaccination. Heart-rate on the earliest available ECG was  $90\pm 25$  bpm, PR interval  $163\pm 37$  ms, QRS duration  $110\pm 17$  ms and QTc  $411\pm 27$  ms. BrS ECG was present in 11 (30%) patients, prolonged PR in 21 (57%) and prolonged QRS in 28 (76%) patients. Of the genetically tested patients (n=35), loss-of-function SCN5A mutations were present in 30, results were pending in 2 and 3 patients were genotype-negative. Genetic testing was not performed in 2 patients due to parental unwillingness. Treatment was instituted in 11 (61%) of the symptomatic patients and included beta-blocker alone (n=3), ICD alone (n=3), beta-blocker and ICD (n=4) or beta-blocker and pacemaker (n=1). During follow-up ( $4\pm 4$  years), 2 patients had recurrence of ventricular tachycardia, there were no deaths.

### Conclusions

Loss of sodium channel function-like phenotypes present with varying severity in infants and children. Fever and vaccination are the commonest arrhythmia triggers. Prolonged conduction intervals are seen more often than BrS ECG. Management includes careful monitoring during fever and vaccination, beta-blockers in patients with tachycardia-related arrhythmias and ICD for the resistant cases.