

# Ivabradine monotherapy in congenital junctional ectopic tachycardia

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## ABSTRACT

**Congenital JET (junctional ectopic tachycardia) is a rare and often difficult to treat tachyarrhythmia in young infants. The addition of Ivabradine to standard Congenital JET therapy has been shown to improve arrhythmia control. However, Ivabradine has not been reported as a single drug in the control of congenital JET. We report a pre-term neonate in whom Ivabradine monotherapy was successful in treating congenital JET.**

**Keywords:** Automatic tachycardia, funny sodium current, nonpostoperative junctional ectopic tachycardia

Congenital junctional ectopic tachycardia (JET) is an uncommon and often incessant tachyarrhythmia, which presents in early infancy.<sup>[1]</sup> It is characterized by a lack of response to adenosine unlike the more common re-entrant tachyarrhythmias and poor response to conventional antiarrhythmic therapy.<sup>[2]</sup> In recent times, ivabradine has been used as an adjunctive therapy in JET with promising results.<sup>[3]</sup> However, ivabradine is seldom used as the first-line agent.<sup>[4]</sup> We report a neonate with congenital JET who reverted to sinus rhythm with ivabradine monotherapy.

A neonate was delivered prematurely at 34 weeks gestational age after persistent tachycardia was noted during a routine prenatal ultrasound. The girl weighed 2.1 kg at birth. After initial stabilization, the heart rate was persistently above 200 beats/min varying between 190 and 215 beats/min. The blood pressure records were normal for gestation, peripheral pulses were easily palpable, and peripheral perfusion was preserved with warm peripheries. A 12-lead electrocardiogram showed a regular narrow complex tachycardia with a heart rate of 188/min and 1:1 ventriculoatrial (V-A) conduction [Figure 1]. Bedside echocardiogram performed confirmed a structurally normal heart

with depressed ventricular contractility on subjective assessment. The ejection fraction estimated by M mode in the parasternal long axis was 40%.

An umbilical venous access was obtained, and intravenous adenosine was administered at a dose of 0.2 mg/kg. A single lead electrocardiogram was recorded during adenosine administration. There was



**Figure 1: A standardized 12 lead electrocardiogram of the neonate obtained shortly after birth. This demonstrates a regular narrow complex tachycardia with 1:1 ventriculoatrial conduction**

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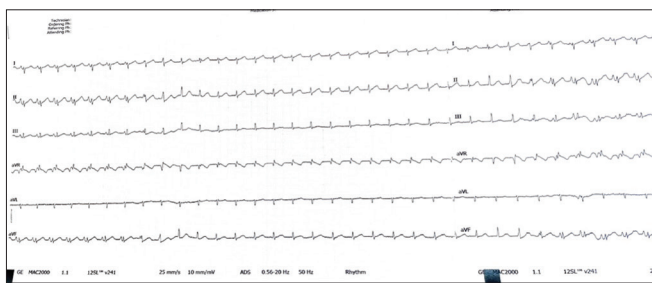
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no change in the ventricular rate. However, transient atrioventricular (A-V) dissociation was evident. This confirmed a diagnosis of congenital JET. Ivabradine was started at a dose of 0.1 mg/kg per dose twice daily given through orogastric tube mixed with breast milk. There was return to sinus rhythm with a heart rate of 100–120/min 2 h after the administration, and the baby remained in sinus rhythm for the next 3 days. A repeat echocardiogram 48 h later showed normal cardiac contractility with an ejection fraction of 60%. Attempts to stop ivabradine therapy were unsuccessful on day 7 of life, with a return of JET at a heart rate of 180 min. Ivabradine was hence reinitiated with a rate control at 120/min. The baby was discharged after 15 days of hospitalization.

At review in the cardiac clinic, 2 weeks after discharge, the baby was thriving well. The heart rate was 120/min, and the ventricular function was normal. There was predominantly sinus rhythm with intermittent junctional rhythm on electrocardiogram, but the ventricular rate remained well controlled [Figure 2].

JET is an often incessant narrow complex tachyarrhythmia with A-V disassociation or, less commonly, 1:1 V-A conduction. The largest multicenter retrospective study on nonpostoperative JET of all age groups reported only 94 cases including 47 infants younger than 6 months of age.<sup>[5]</sup> It has been reported to run in families,<sup>[4]</sup> and a possible monogenic etiology has been purported.<sup>[6]</sup> The mechanism of tachyarrhythmia in congenital JET is believed to be due to an enhanced automaticity of the A-V nodal region.<sup>[2]</sup> The molecular mechanism of enhanced automaticity has been shown to be due to the slow, inward sodium current (the funny sodium current or  $I_f$ ) which causes depolarization of the sinus node.<sup>[7]</sup> This funny sodium current enters the cell through specific hyperpolarization-activated cyclic nucleotide-gated (HCN4) sodium channels. Overactivity of the HCN4 channels is purported to be the molecular mechanism of the tachyarrhythmia, and ivabradine, as a selective inhibitor of the HCN4 channels, could potentially block this molecular mechanism. It has also been shown to decrease A-V conduction in animal models.<sup>[8]</sup>



**Figure 2: A standardized 6 lead electrocardiogram of the infant obtained during follow-up. There is sinus rhythm interspersed with a junctional rhythm. However, the ventricular rate remained below 120/min**

JET is a challenging arrhythmia to treat with most infants requiring a combination of anti-arrhythmic medications.<sup>[5]</sup> The combination of amiodarone with a beta-blocker is preferred by most pediatric electrophysiologists.<sup>[5]</sup> Dieks *et al.* added ivabradine as an adjunctive treatment in five children with poor control on amiodarone and beta-blocker. It resulted in conversion to sinus rhythm in four and good rate control in the other. There were no significant adverse effects attributable to ivabradine therapy during a follow-up period of 7 months.<sup>[3]</sup> Other groups have also utilized ivabradine in JET, which is refractory to other medications.<sup>[4,9]</sup> However, despite the poor response to other medications, ivabradine has not been utilized as the first-line therapy in neonates and young infants with congenital JET.

Our report suggests that ivabradine can be effective as the only drug in the management of neonates with congenital JET. JET is a difficult to control arrhythmia often necessitating treatment for a prolonged period. Although the safety of ivabradine in children has been demonstrated in small studies with a short follow-up period, the safety and continued efficacy need to be established over longer periods.

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**Conflicts of interest**

There are no conflicts of interest.

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