

## Use of ivabradine in supraventricular tachycardia caused by refractory focal atrial tachycardia in neonates to avoid radiofrequency ablation

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### ABSTRACT

Supraventricular tachycardia (SVT) is a clinical condition caused by many arrhythmias and from different etiologies. Any arrhythmogenic focus above the ventricles due to reentrant or isolated ectopic focus can cause SVT. Neonates usually tolerate tachy- and bradyarrhythmias better than any other age groups. In SVT, the signs of cardiac failure appear after at least 36–48 hrs. We are here presenting a case report of SVT caused by unifocal atrial ectopic focus and treated by ivabradine as it was not responding to usual antiarrhythmic drugs. Literature showing the usage of ivabradine in SVT in pediatric age group is scarce; therefore, we are reporting this case.

**Key words:** Arrhythmias, Focal atrial tachycardia, Ivabradine, Neonate, Supraventricular tachycardia

Supraventricular tachycardia (SVT) is the most common arrhythmia in a neonate with an incidence of 1 in 200–250 [1]. In SVT, heart rate is usually >220 beats/min. Mechanisms causing SVT could be enhanced automaticity with triggered foci above the ventricles or enhanced conduction with the presence of reentrant circuits [2]. SVT caused by a reentrant mechanism is the most common form. The diagnosis of focal atrial tachycardia (FAT) was based on electrocardiogram (ECG). Ectopic atrial tachycardias are manifested as narrow complex tachycardias with an abnormal P wave preceding the QRS complex.

The following criteria have been used for diagnosing the FAT, (1) narrow complex tachycardia with visible P waves at a rate inappropriate for age and activity, (2) identical abnormal P wave morphology in the first and all subsequent tachycardia beats, (3) routine ECG atrial rate >150% of the predicted mean, (4) inverted and notched P wave in V1, (5) P wave axis in the horizontal plane <0°, and (6) P wave duration >90 ms in V1. In unifocal type of FAT, P wave morphology is similar in all leads (Fig. 1) and in multifocal type of FAT, P wave morphologies were different (Fig. 2). Spontaneous resolution is usually anticipated in FAT; therefore, it is better to consider medical therapy than ablation as it is associated with a number of side effects, particularly in children [3].

### CASE REPORT

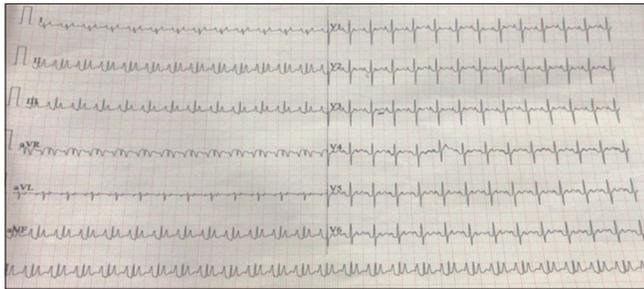
A 15-day-old male, term baby was admitted with complaints of excessive cry, lethargy, and decreased acceptance of feeds. He was born to a Primi mother by spontaneous vaginal delivery with

birth weight of 2800 g and having no significant antenatal history reported. The baby mother noticed that the baby had sudden onset of restlessness since night and she also observed sweating over the forehead and palpitations when she was trying to breastfeed the baby. The baby cried immediately after birth and was given breastfeeds within ½ h after birth. The baby was on exclusive breastfeeds until now and received Bacille Calmette–Guerin, oral polio vaccine immediately after birth.

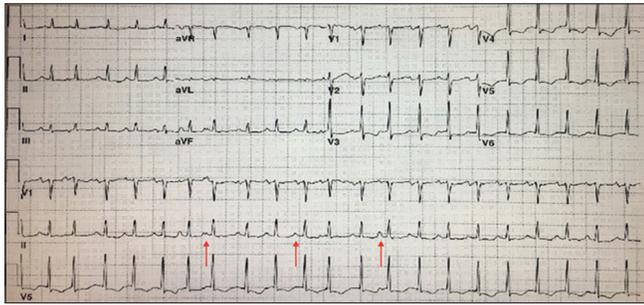
On thorough clinical examination, the baby looked ill and lethargic with no pallor, cyanosis, and jaundice. His heart rate was varying between 240/min and 320/min, respiratory rate was 58/min, and capillary filling time was <3 s. His heart sounds were difficult to differentiate due to tachycardia. He had no significant audible murmur and lung base was clear. The baby had no signs of congestive cardiac failure; no hepatosplenomegaly and urine output was adequate.

Electrocardiography revealed narrow complex QRS waves with 2:1 AV block with abnormal P wave morphology suggestive of FAT (Fig. 1). Serum electrolytes were normal having sodium 142 meq/L, potassium 5.2 meq/L, chloride 132 meq/L, and ionized calcium of 8 mg/dl. Blood urea was 13 mg/dl and serum creatine was 0.3 mg/dl. Septic screen was negative with C-reactive protein 3 mg/dl, complete blood picture was normal with hemoglobin 13 mg/dl, packed cell volume 45%, total leukocyte count 8500 cells/mm<sup>3</sup>, and platelets 200,000/mm<sup>3</sup>. Chest X-ray was normal without any cardiomegaly. Echocardiography revealed features of the left ventricular dysfunction.

Initially, adenosine was administered followed by digoxin (10 mcg/kg/day) and beta-blocker (propranolol – 1 mg/kg/day); however, it failed to control heart rate. Then, amiodarone followed



**Figure 1: Abnormal P waves with similar morphology (indicates unifocal origin)**



**Figure 2: P wave with different morphologies multifocal atrial tachycardia**

by flecainide was given but we found no effect. Electric cardioversion was also tried without any response. As a last resort, the baby was started on ivabradine (0.05 mg/kg/day) before considering surgical ablation of focus and it ameliorated the atrial tachycardia and the heart rate was normalized. Ivabradine and propranolol were continued throughout his hospital stay and his heart rate was normalized which was evident in serial electrocardiograph. The baby was discharged after 2 days and was advised to continue ivabradine for 1 month. On follow-up, the baby was stable. A written consent was taken from the parents for administrating the drug and for publication.

## DISCUSSION

The most common cause of SVT in neonates is usually reentrant mechanism. IV adenosine (0.1–0.3 mg/kg/dose) and rapid IV push are extremely effective in cardioversion of hemodynamically stable babies. Electrical cardioversion is useful in hemodynamically unstable babies. Holding a child upside down (with proper support) and placing a small bag or glove filled with ice over the entire face for 10–15 s is an effective maneuver (because it is a dive reflex, the majority of the face must be covered by ice). Calcium channel blockers should not be used for treating any type of SVT in neonate because neonatal myocardium is 20 times more sensitive than adults and might result in sudden death. In neonatal population for treating SVT, gagging, ocular pressure, and anal stimulation should be avoided.

In FAT, nodal blockade is not useful as pathology does not present in AV node. Adenosine administration usually blocks only AV nodal conduction that is why atrial arrhythmia will not be decreased by adenosine. Digoxin is also not generally effective

as it also acts at AV node but may temporarily abate the rate. Sometimes, digoxin can cause AV dissociation by blocking AV node, further contributing to hemodynamic instability in addition to the rapid atrial rate. Direct current cardioversion may interrupt the arrhythmia but is most likely to reinitiate spontaneously after sometime.

FAT is usually diagnosed by ECG criteria as mentioned above; intermittent AV block (such as 2:1 conduction or Wenckebach pattern) could be seen sometimes. Due to aberrant ventricular conduction, sometimes, wide QRS may be seen similar to ventricular tachycardia (Ashman phenomenon). Focus is usually present at crista terminalis or ostia of the pulmonary veins [3]. Atrial ectopic tachycardia may be attempted with medications such as beta-blockers (propranolol), sodium channel blockers (flecainide), or Class III antiarrhythmic medications (sotalol and amiodarone). Catheter ablation of FAT in children aged <1.5 years and particularly in neonatal period is usually associated with more complications [4].

FAT occurs as a result of irritation of tissues during cardiac surgery, with the placement of intracardiac lines, application of sutures, or cutting cardiac tissue during surgery. In our case, there was no structural heart disease as evident in 2D echo, so the cause for the focus could be due to increased automaticity by a focus of cells through funny current channels. Funny current is a mixed sodium/potassium inward current activated on hyperpolarization in the diastolic range of voltages. Funny current channels are responsible for automaticity of myocytes in SA node.

Ivabradine selectively inhibits the funny current limited to the sinoatrial node in a dose-dependent manner without affecting any other cardiac ionic channels. Ivabradine blocks the intracellular aspect of the hyperpolarization-activated cyclic nucleotide-gated transmembrane channel, which is responsible for the transport of sodium (Na<sup>+</sup>) and potassium (K<sup>+</sup>) ions across the cell membrane, in the open state. It decreases the heart rate through deceleration of conduction through funny current channels. Ivabradine can be safe and potentially effective therapy for arrhythmias with enhanced automaticity. It is more effective in high heart rate conditions as it works on opened funny current channels.

The use of ivabradine in sinus tachycardia was noted in some case reports and small randomized trials. In a case series, Dieks *et al.* used ivabradine in five consecutive patients aged 10 days–3.5 years with a mean age of 8 weeks in junctional ectopic tachycardia (JET). The authors observed that four patients had satisfactory control of JET, whereas one patient had effective heart rate control with persistent slow JET with mean heart rate reduced by 31% compared to pre-ivabradine ( $p=0.03$ ) [5]. Al-Ghamdi *et al.* treated resistant JET with oral ivabradine in a 3-year-old girl [6]. Bohora *et al.* reported a case of reversal of tachycardiomyopathy due to the left atrial tachycardia in a child by ivabradine [7]. Janson *et al.* reported diverse arrhythmia substrates, two cases of focal FAT of focal EAT in a structurally normal heart; one case of JET in a patient with a history of a neonatal mass involving the AV junction, associated with residual AV conduction disease; and one case of atrial tachycardia in a teenager following heart transplant. Ivabradine was safe in all patients, with no adverse events or side effects [8].

The safety of oral ivabradine therapy in infants and children has been established in a cohort of children with dilated cardiomyopathy and stable heart failure [9]. In a randomized, double-blind, placebo-controlled trial, 116 children with dilated cardiomyopathy received either ivabradine (n=74) or placebo (n=42); the majority of patients in both the study groups were on beta-blocker, and many were also on digoxin. Adverse event rates were low overall and similar in both arms, there were no instances of AV block, atrial fibrillation, or other arrhythmias. Importantly, this trial also established that oral ivabradine has a similar pharmacokinetic and pharmacodynamic profile in children aged 6 months–18 years to that seen in adults [10,11]. Ptaszynski *et al.* and Cappato *et al.* also used ivabradine successfully in pediatric age group to treat sinus tachycardia and JET [12,13].

FAT originating in the atrial appendages is more likely to respond to ivabradine than those arising from other atrial sites. Around 60%–80% of SVTs that present in the neonatal period resolve spontaneously within the 1<sup>st</sup> year of life. FAT in neonates resolve spontaneously in early months of life, long-term therapy is rarely necessary [14].

## CONCLUSION

Ivabradine can be considered as a treatment option for FAT which is refractory to the other antiarrhythmic drugs. Ivabradine can be considered before resorting to invasive surgical ablation of the focus as ablation is associated with more complications.

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