Breaktrough drug combination for Congenital Junctional Ectopic Tachycardia: a pediatric case report.

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Abstract

Introduction: Congenital Junctional Ectopic Tachycardia (JET) is a rare tachyarrhythmia that remains difficult to manage with suboptimal control in the majority of cases.

Methods: Here, we report the successful use of Ivabradine in combination with Flecainide for the therapy of congenital JET resistant to multiple antiarrhythmic agents.

Results: This new drug combination was effective in completely suppressing JET .

Conclusion: Ivabradine in combination with Flecainide may be considered a new therapeutic strategy of congenital JET with satisfactory efficacy/tolerability ratio in patients resistant to conventional drug combinations.

Key words: junctional, ectopic, tachycardia, pediatric, therapy.

Case report

One-year old female patient. On day two of life, Junctional Ectopic Tachycardia (JET) was diagnosed **(Figure 1)** in absence of structural cardiopathies or previous surgery. Amiodaron (300 mg/m2/day) was started as first-line therapy with a satisfactory result in terms of heart-rate control. Later onset of severe hypothyroidism induced withdrawal of Amiodaron and introduction of Flecainide (5 mg/kg/day) and Propranolol (4 mg/kg/day). This second-line therapy did not show acceptable arrhythmia control. For this reason, a third-line therapy was started with Propranolol (4 mg/kg/day) - Ivabradine (0,25 mg/kg/day) in combination. This association was able to ensure satisfactory heart-rate control, however without restoring sinus rhythm. Despite this, the patient was discharged with this therapeutic regimen and underwent follow-up.

After four months, the recurrent elevated heart rate associated with echocardiographic evidence of biatrial and left ventricle dilation led the patient to re-hospitalization. In agreement with fellow endocrinologists, it was decided to reintroduce Amiodaron as the best therapeutic option although the risk of hypothyroidism. High doses of Amiodaron (350 mg/m2/day) alone were not able to prevent high heart rate phases. Therefore, Ivabradine (0.25 mg/kg/day) was added with a better heart rate control but not as expected. Consequently, it was decided to try a new therapeutic strategy, never tried before in the management of JET. It was introduced Ivabradine (dose 0.3 mg/kg/day) – Flecainide (5 mg/kg/day) association with complete conversion to normal sinus rhythm within few hours **(Figure 2)**.

During sleep, the patient showed too low heart rate. For this reason, the doses of both drugs were reduced as following: Ivabradine (0.25 mg/kg/day) and Flecainide (4 mg/kg/day). This therapeutic choice led to satisfactory results: excellent heart rate values, most of the time in sinus rhythm with only few hours/day in Junctional rhythm at heart rate values not so higher than those in sinus rhythm. At discharge echocardiography showed normal sized cardiac chambers and normal biventricular function. After 4 months follow-up to date, this therapy continues to show satisfactory results in terms of clinical conditions and control of JET.

Discussion

Congenital Junctional Ectopic Tachycardia is a rare arrhythmia that can occurs in infants with a structurally normal heart and without previous cardiac surgery. This is often refractory to medical therapy and persistent JET in children often results in ventricular dysfunction, heart failure and high mortality.[1-2]

Amiodarone usually represents the first choice in JET treatment and it has been used either alone or in combination with Propranolol or Flecainide in infants.[3]

Radiofrequency ablation is effective but is a difficult procedure in small children and is not as widely available.

Ivabradine, which works by selective inhibition of hyperpolarization−activated cyclic nucleotide−gated channels, has shown to be an effective drug for the treatment of JET in children with rapid rate control and establishment of sinus rhythm.[4-5]

Ivabradine in combination with Flecainide, as reported here, is indeed new and may be considered a valid therapeutic strategy for congenital JET with a satisfactory efficacy/tolerability ratio in patients resistant to conventional drug combinations.

References

1. Ranjit I. Kylat and Ricardo A. Samson, Junctional ectopic tachycardia in infants and children. J Arrhythm. 2020 Feb; 36(1): 59–66.
2. Collins KK, Van Hare GF, Kertesz NJ, Law IH, Bar-Cohen Y, Dubin AM, *et al.* Pediatric nonpost-operative junctional ectopic tachycardia medical management and interventional therapies. J Am Coll Cardiol 2009;53:690-7**.**

3. Saul JP, Scott WA, Brown S, Marantz P, Acevedo V, Etheridge SP, et al. Intravenous amiodarone for incessant tachyarrhythmias in children: a randomized, double‐blind, antiarrhythmic drug trial. Circulation. 2005;112(22):3470–7.
4. SALEH AL-GHAMDI, MAJID I. AL-FAYYADH and ROBERT M. HAMILTON. Potential New Indication for Ivabradine: Treatment of a Patient with Congenital Junctional Ectopic Tachycardia. Journal of Cardiovascular Electrophysiology Vol. 24, No. 7, July 2013.
5. Kothari SS, Kidambi BR, Juneja R. Ivabradine for congenital junctional ectopic tachycardia in siblings. Ann Pediatr Card 2018;11:226-8.

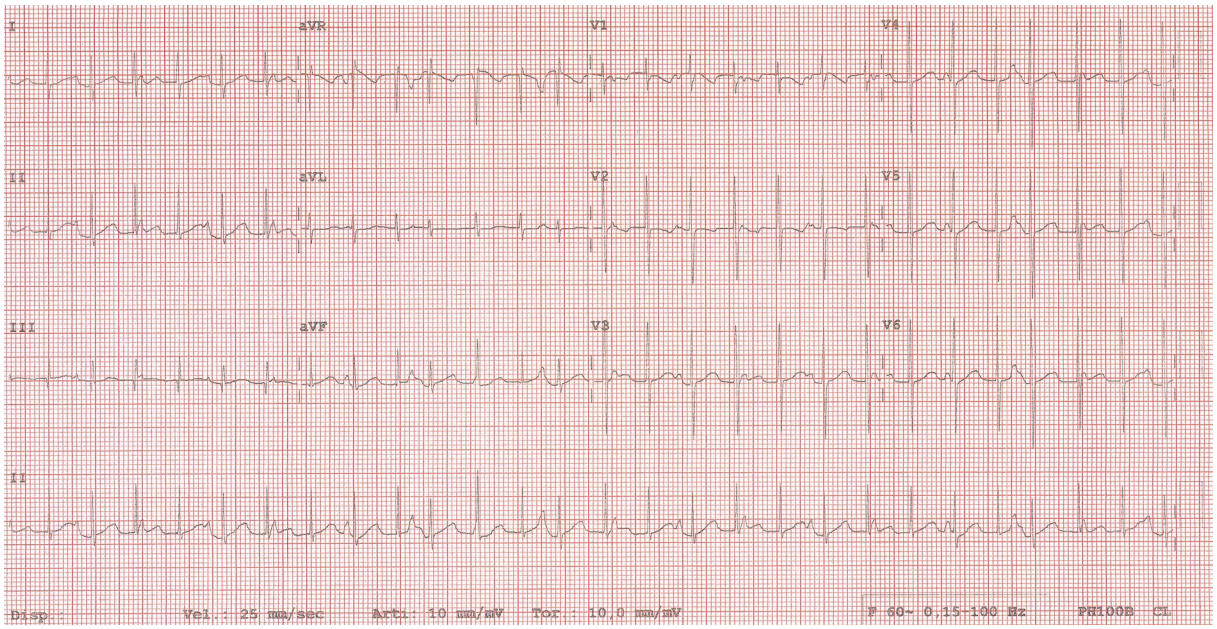

Figure 1

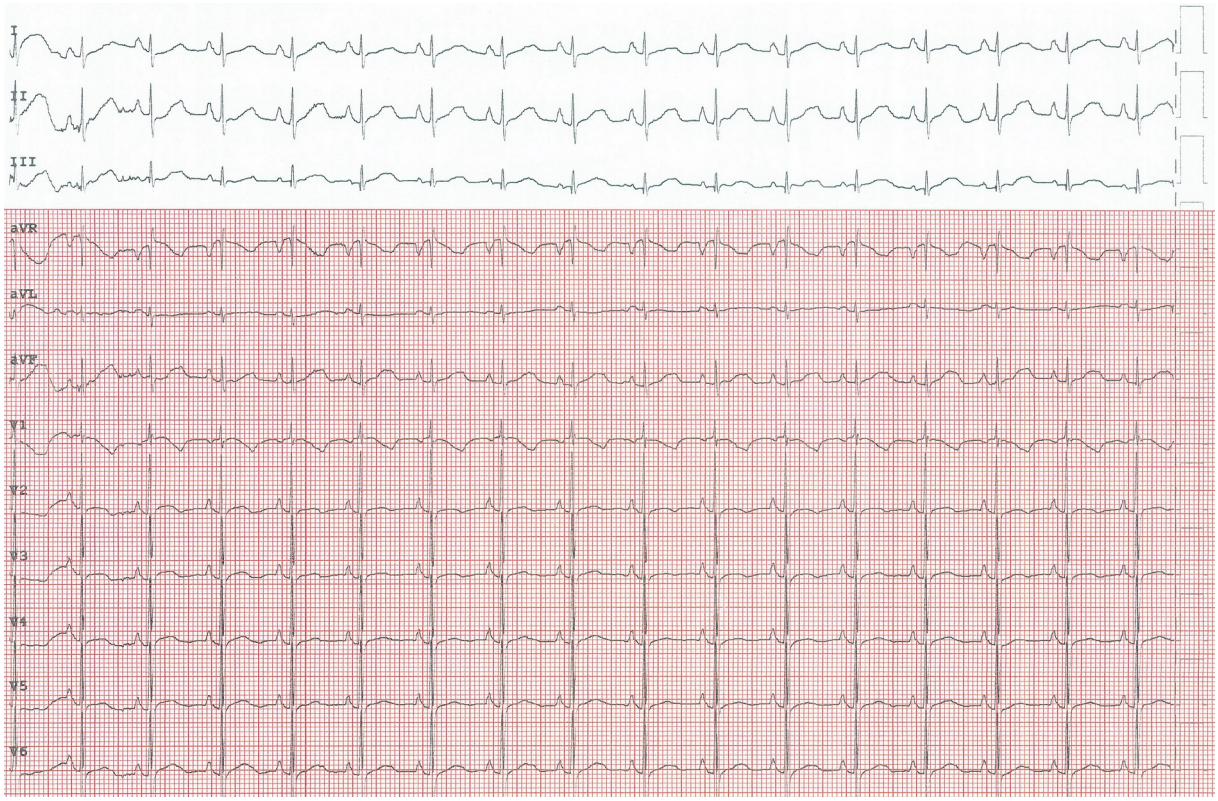

Figure 2

Figure Legend

Figure 1: Junctional Ectopic Tachycardia (JET) at diagnosis.

Figure 2: Restoration of sinus rhythm in patient with JET treated by Ivabradine in combination with Flecainide.