

5. Yang Y, Muzny DM, Xia F, Niu Z, Person R, Ding Y, et al. Molecular findings among patients referred for clinical whole-exome sequencing. *JAMA*. 2014;312:1870–89.

José D. Santotoribio<sup>a,\*</sup>, Esperanza Lepe-Balsalobre<sup>a</sup>, Irene Alonso-Pérez<sup>b</sup>, Andrea Campo-Barasoain<sup>b</sup>, Hada C. Macher<sup>a</sup>

<sup>a</sup> *Servicio de Bioquímica Clínica, Laboratorio de Diagnóstico Molecular, Hospital Universitario Virgen del Rocío, Sevilla, Spain*

<sup>b</sup> *Servicio de Pediatría, Hospital Universitario Virgen Macarena, Sevilla, Spain*

\* Corresponding author.

E-mail address: [jdsantotoribioc@gmail.com](mailto:jdsantotoribioc@gmail.com) (J.D. Santotoribio).

<https://doi.org/10.1016/j.anpede.2020.05.017>

2341-2879/ © 2021 Asociación Española de Pediatría. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-SA license (<http://creativecommons.org/licenses/by-nc-sa/3.0/>).

## Use of ivabradine in pediatric post-operative junctional ectopic tachycardia<sup>☆</sup>



## Uso de ivabradina en el tratamiento de la taquicardia ectópica de la unión tras cirugía cardiaca

To the Editor:

Junctional ectopic tachycardia (JET) is one of the most frequent arrhythmias that develop after surgical intervention of congenital heart disease. It is characterised by abnormal automaticity within the auriculoventricular (AV) node manifesting as narrow QRS tachycardia, usually associated with AV dissociation and haemodynamic instability. Conventional management consists of the rational use of inotropes, moderate hypothermia, correction of electrolyte abnormalities, optimization of sedation/analgesia, restoration of atrioventricular synchrony with a pacemaker and antiarrhythmic drugs. In general, treatment protocols include amiodarone as the first-line drug.<sup>1</sup> In refractory cases, a second drug may need to be added and, in some cases, low cardiac output may require support with extracorporeal membrane oxygenation (ECMO).

Ivabradine is a drug that acts on the I(f) (“funny”) current by blocking hyperpolarization-activated cyclic nucleotide-gated (HCN) channels at the sinus and AV nodes,<sup>2</sup> reducing their intrinsic automaticity and without a negative inotropic effect. It has been used successfully for treatment of inappropriate sinus tachycardia and of patients with dilated cardiomyopathy and chronic heart failure resistant to beta-blockers. It has also proven effective for treatment

of congenital JET,<sup>3,4</sup> although the evidence on its use for refractory postoperative JET is scarce.<sup>5,6</sup>

We present 3 cases that illustrate the efficacy ivabradine for treatment of postoperative JET refractory to conventional treatment. **Table 1** presents the characteristics of these cases. Implementation of conventional treatment measures, including antiarrhythmic therapy (amiodarone in all cases, combined with esmolol in one), failed to bring the heart rate (HR) below 170 bpm, which prevented restoration of atrioventricular synchrony with a pacemaker. Ivabradine, delivered through a nasogastric tube, was added at a dose of 0.1 mg/kg/12 h in the context of sustained haemodynamic instability. We defined haemodynamic instability as tissue hypoperfusion despite an increase in the vasoactive-inotropic score and/or volume expansion. It was considered “sustained” when it lasted more than 4 h past the onset of JET (during which the loading dose of amiodarone was administered to prevent adverse events). In a mean time of 180 min following the loading dose, the HR had decreased to a mean of 145 bpm, which allowed restoring atrioventricular synchrony through AV pacing. After implementation these measures, there was a clear improvement in cardiac output. Treatment with ivabradine continued for a mean of 3.3 days, with a mean time elapsed to conversion to sinus rhythm of 64 h. We did not observe any significant adverse effects in any of the patients.

Since ivabradine acts on the pathogenic mechanism of postoperative JET, it may be an effective therapeutic option for management of JET refractory to conventional antiarrhythmic drugs. There is ample experience on its use in adults and the evidence of its use in children is growing. Despite the potential limitation in critical patients of the exclusive enteral route of administration, our experience shows that it can achieve an effective reduction in HR in a mean time of less than 180 min (range described in the literature: 50–300 min).<sup>5</sup> Although the initial dose of ivabradine is not well established for the paediatric population, the current literature suggests starting with a dose of 0.05 mg/kg/12 h,<sup>3,5</sup> and the maximum reported dose of 0.14 mg/kg/12 h. Sinus bradycardia is the most widely documented adverse event associated with ivabradine, a

<sup>☆</sup> Please cite this article as: López Fernández E, Montañes Delmas E, Granados Ruiz MÁ, Oviedo Melgares L, Ramos Casado V. Uso de ivabradina en el tratamiento de la taquicardia ectópica de la unión tras cirugía cardiaca. *An Pediatr (Barc)*. 2021;95:118–120.

**Table 1** Characteristics of the patients that received ivabradine for management of JET.

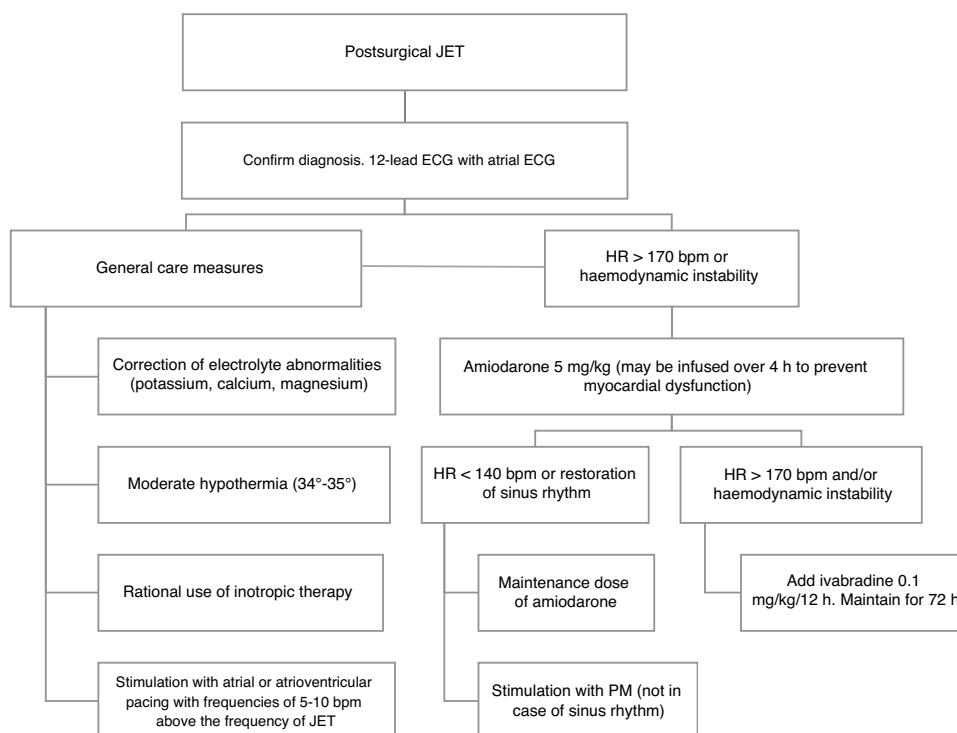
	Patient 1	Patient 2	Patient 3
Age at onset of JET (m)	2.5	5	5.6
Reason for admission	Cardiac surgery with ECC	Cardiac surgery with ECC	Cardiac surgery with ECC
Cardiological diagnosis	Heterotaxia, right isomerism. Complete unbalanced AV septal defect with mitral atresia, hypoplastic left heart, double outlet right ventricle, pulmonary atresia, non-confluent pulmonary arteries with origin at BCT and aortic arch	Complete AV septal defect	ASD, VSD, pulmonary valve stenosis
Surgery	Aortic valve valvuloplasty, unifocalization of pulmonary arteries. EXIT to ECMO due to severe ventricular failure	Complete repair	Complete AV septal defect
Onset of JET	Immediate	Immediate	Complete repair
Maximum HR (bpm)	210	220	200
HR after initiation of ivabradine (bpm)	120	160	160
Time to significant decrease of HR (min)	240	60	180
Time to conversion to sinus rhythm (h)	48	48	96
Inotropic support at initiation of JET ( $\mu\text{g}/\text{kg}/\text{min}$ )	Epinephrine 0.05 Milrinone 0.6 Norepinephrine 0.1	Epinephrine 0.05 Milrinone 0.6	Epinephrine 0.05 Dopamine 6 Milrinone 0,6
Antiarrhythmic treatment and general supportive measures prior to ivabradine	Amiodarone 5 mg/kg Esmolol 250 $\mu\text{g}/\text{kg}/\text{min}$  Reduction in vasoactive drugs Cooling (34°) Deep sedation	Amiodarone 5 mg/kg Reduction in vasoactive drugs Cooling (34.5°)  Deep sedation Neuromuscular blockade	Amiodarone 5 mg/kg Reduction in vasoactive drugs Cooling (34°)  Deep sedation Neuromuscular blockade
Duration of ivabradine (d)	3	4	3
Initial dose of ivabradine (mg/kg/12 h)	0.1	0.1	0.1
Adverse effects	None	None	None

ASD, atrial septal defect; AV, atrioventricular; BCT, brachiocephalic trunk; bpm, beats per minute; d, days; ECC, extracorporeal circulation; ECMO, extracorporeal membrane oxygenation; h, hours; HR, heart rate; JET, junctional ectopic tachycardia; min, minutes; PM, pacemaker; VSD, ventricular septal defect.

condition that can be easily treated in the immediate post-operative period with temporary epicardial pacing. Due to its potential to prolong the QT interval, especially in association with other drugs, it is important to perform ECGs at regular intervals.

Although our experience in the use of ivabradine in this context is limited, we believe that it may

be a safe and effective treatment option due to its rapid action and few adverse effects. For this reason, we recommend its early administration for treatment of refractory postoperative JET (Fig. 1), titrating the dose based on the clinical response, tolerability and QTc.



**Figure 1** Algorithm for the management of postoperative JET. bpm, beats per minute; HR, heart rate; JET, junctional ectopic tachycardia; PM, pacemaker.

## References

1. Cools E, Missant C. Junctional ectopic tachycardia after congenital heart surgery. *Acta Anaesthesiol Belg.* 2014;65:1–8.
2. Marger L, Mesirca P, Alig J, Torrente A, Dübel S, Engeland B, et al. Functional roles of Ca v 1.3, Ca v 3.1 and HCN channels in automaticity of mouse atrioventricular cells: Insights into the atrioventricular pacemaker mechanism. *Channels.* 2011;5:251–61, <http://dx.doi.org/10.4161/chan.5.3.15266>.
3. Dieks J-K, Klehs S, Müller MJ, Paul T, Krause U. Adjunctive ivabradine in combination with amiodarone: a novel therapy for pediatric congenital junctional ectopic tachycardia. *Heart Rhythm.* 2016;13:1297–302, <http://dx.doi.org/10.1016/j.hrthm.2016.03.015>.
4. Ergul Y, Ozturk E, Ozgur S, Ozyurt A, Cilsal E, Guzeltas A. Ivabradine is an effective antiarrhythmic therapy for congenital junctional ectopic tachycardia-induced cardiomyopathy during infancy: case studies. *Pacing Clin Electrophysiol.* 2018;41:1372–7, <http://dx.doi.org/10.1111/pace.13402>.
5. Krishna MR, Kunde MF, Kumar RK, Balaji S. Ivabradine in post-operative junctional ectopic tachycardia (JET): breaking new ground. *Pediatr Cardiol.* 2019;40:1284–8, <http://dx.doi.org/10.1007/s00246-019-02149-5>.
6. Kumar V, Kumar G, Joshi S, Sharma V. Ivabradine for junctional ectopic tachycardia in post congenital heart surgery. *Indian Heart J.* 2017;69:666–7, <http://dx.doi.org/10.1016/j.ihj.2017.09.007>.

Eduardo López Fernández\*

*Unidad de Cuidados Intensivos Pediátricos, Hospital 12 de Octubre, Madrid, Spain*

Elena Montañes Delmas, Miguel Ángel Granados Ruiz

*Instituto Pediátrico del Corazón, Hospital 12 de Octubre, Madrid, Spain*

Lidia Oviedo Melgares, Victoria Ramos Casado

*Unidad de Cuidados Intensivos Pediátricos, Hospital 12 de Octubre, Madrid, Spain*

\* Corresponding author.

E-mail address: [eduardopado@hotmail.com](mailto:eduardopado@hotmail.com)

(E. López Fernández).

27 July 2020 3 September 2020

<https://doi.org/10.1016/j.anpede.2020.09.008>

2341-2879/ © 2021 Asociación Española de Pediatría. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).