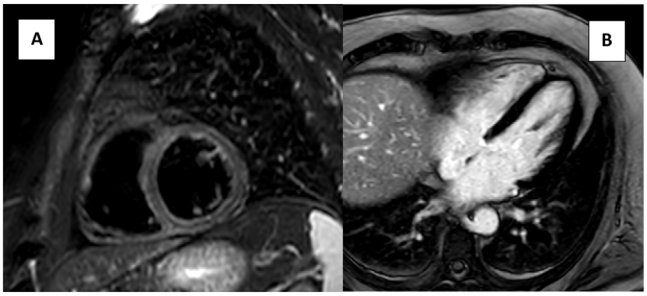

Figure 2. Cardiac magnetic resonance shows absence of edema or fibrosis. 2A: STIR sequence; 2B: late gadolinium enhancement sequence.

Although we could not demonstrate inflammation, we speculated that localized inflammation of the conduction system associated with an inflammatory response to vaccination caused CHB and started empiric corticotherapy (1 mg/kg/d), with rapid improvement of cardiac conduction. There was no fibrosis on CMR, which could explain the recovery. Standard prednisone tapering was done (reduction of 10 mg every 5 days).

Hitherto, only isolated clinical cases have reported an association between HB and SARS-CoV-2 vaccination, mostly in elderly patients with underlying conduction disorders. Nasab et al.[6] published a case report of a 65-year-old patient without previous cardiac disease who developed 2:1 AV block a few days after COVID-19 vaccination and required permanent pacemaker implantation.

Our case is the first to show a CHB in a young patient without pre-existing conduction disease and evidence of resolution of the conduction disorder with corticotherapy. Whether HB was related to an excessive inflammatory response to the vaccine remains unknown and the use of alternative anti-inflammatory therapies needs further investigation.

In this case, we report a patient with CHB with a consistent temporal association with COVID-19 vaccine administration, who recovered normal AV conduction after 4 weeks of corticotherapy. Although the etiology of the HB is unknown, the clinical course and effect of the corticosteroid suggests inflammation of the conduction system due to an inflammatory response to vaccination. CHB as a possible vaccine-related adverse event is a finding that requires further study.

FUNDING

The authors received no financial support for the research, authorship and/or publication of this article.

AUTHORS' CONTRIBUTIONS

Conceptualization: P. Mañas; writing - original draft: A. Pons-Riverola; writing - review and editing: A. Pons-Riverola, P. Mañas, E. Claver, O. Meroño, J. Comín-Colet, I. Anguera; supervision: P. Mañas, J. Comín-Colet, and I. Anguera.

CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest.

Alexandra Pons-Riverola,* Pilar Mañas, Eduard Claver, Oona Meroño, Josep Comín-Colet, and Ignasi Anguera

Servicio de Cardiología, Hospital Universitario de Bellvitge, L'Hospitalet de Llobregat, Barcelona, Spain

* Corresponding author.
E-mail address: aponsr@bellvitgehospital.cat (A. Pons-Riverola).
@alexandrapons4

Available online 24 October 2022

REFERENCES

1. Our World in Data. Coronavirus (COVID – 19) Vaccinations. Available at: https://ourworldindata.org/covid-vaccinations?country=ESP. Accessed: 11 Aug 2021.
2. Pfizer-biontech covid-19 vaccine (bnt162, pf-07302048) vaccines and related biological products advisory committee briefing document. Meeting date: 10 December 2020. Available at: https://www.fda.gov/media/144246/download. Accessed 11 Aug 2021.
3. Patone M, Mei Xue. Handunnetthi L, et al. Risks of myocarditis, pericarditis, and cardiac arrhythmias associated with COVID-19 vaccination or SARS-CoV-2 infection. *Nat Med.* 2022;28:410–422.
4. World Health Organization. COVID-19 subcommittee of the WHO Global Advisory Committee on Vaccine Safety (GACVS): updated guidance regarding myocarditis and pericarditis reported with COVID-19 mRNA vaccines. 2021. Available at: https://www.who.int/news/item/09-07-2021-gacvs-guidance-myocarditis-pericarditis-covid-19-mrna-vaccines. Accessed 11 Aug 2021.
5. Chen W, Jeudy J. Assessment of Myocarditis: Cardiac MR, PET/CT, or PET/MR? *Curr Cardiol Rep.* 2019;21:76.
6. Nasab EM, Athari SS. The first report of 2:1 atrioventricular block following COVID-19 vaccination. *Clin Case Rep.* 2022;10:e05797.

https://doi.org/10.1016/j.recesp.2022.08.013
1885-5857/

Usefulness of ambulatory milrinone perfusion in a cohort of advanced heart failure patients

Utilidad de la perfusión ambulatoria de milrinona en una cohorte de pacientes con insuficiencia cardiaca avanzada

To the Editor,

Recent years have seen an increase in the number of patients with advanced heart failure (HF).[1] Accordingly, the following types of patients are increasingly being encountered: *a)* with advanced inotrope-dependent HF who not candidates for durable ventricular assist devices (dVADs) and who require inotropic support until they can undergo heart transplantation (HT); *b)* with group 2 pulmonary hypertension (PH) who are contraindicated for HT and are not candidates for dVAD therapy; and *c)* with the need for palliative care. For these situations, physicians in the United States use ambulatory intravenous milrinone perfusion, a modality practically unknown in Spain.

We analyzed all patients administered ambulatory milrinone perfusion between October 2015 and June 2022 in a transplant center. The study was approved by the ethics committee of the center. Informed consent was not considered necessary due to the retrospective observational nature of the study. In all patients, perfusion was initiated during hospital admission in conjunction with electrocardiographic monitoring to confirm the absence of

severe adverse effects. All patients had to have been implanted with an implantable cardioverter-defibrillator (ICD), except those in palliative care. The continuous ambulatory perfusion was performed via a peripherally inserted central venous catheter using a portable CADD Legacy pump (ICU Medical, United States). Infusion speed was calculated for an approximate duration of 24 hours and a dose of 0.3 to 0.4 μg/kg/min. Patients and their family members were instructed on how to refill the pump and to dress the catheter at home. The patients attended the day hospital every 3 weeks for a clinical check-up and nursing care.

To analyze the usefulness of the treatment, we distinguished 3 groups with the following distinct objectives: *a)* as bridge to HT in inotrope-dependent patients (with success in this case considered HT without need to transition to urgent status); *b)* as bridge to candidacy in patients with PH who were contraindicated for HT (with success in this group considered achievement of a PH improvement permitting inclusion of the patient in the HT list); and *c)* as palliative care (in this case, the objective was to allow patients to remain at home with adequate symptom control until death). Overall, 19 patients were analyzed; their median age was 58 [53-67] years and 4 were women (21%).

Treatment objective was bridge to HT in 9 patients (47%), bridge to candidacy in 3 (16%), and palliative care in 7 (37%). The median treatment duration was 83 [35-229] days.

In the bridge to HT group, 7 patients (78%) achieved this objective as an elective procedure. Only 1 patient experienced primary graft failure, dying 7 days after the transplantation. The remaining patients survived more than 1 year after the HT. Two patients required implantation of a short-term ventricular assist device before the HT.

The 3 patients in the bridge to candidacy group due to PH were not candidates for dVAD due to biventricular HF. During the milrinone therapy, the median values of the mean pulmonary pressures fell from 46 [40-58] to 35 [33-37] mmHg while those of the median pulmonary vascular resistance fell from 5.8 [4.0-8.9] to 3.4 [2.5-4.5] WU. All patients used other oral pulmonary vasodilators, such as tadalafil and macitentan, and all patients achieved transplantation criteria (2 of them have since undergone transplantation, without primary graft failure and with successful outcomes).

Of the 7 patients treated with palliative intent, 4 (57%) remained at home with adequate symptom control until death. The other 3 experienced complications requiring treatment withdrawal (table 1).

Overall, ambulatory milrinone therapy achieved the desired objective in 74% of patients. The most frequent complication was local infection of the venous access, affecting 5 patients (26%). All patients responded satisfactorily to targeted antibiotic therapy. No case of endocarditis was recorded. Four patients (19%) developed sustained ventricular tachycardia (SVT) during the treatment; it was successfully treated with an ICD discharge but required milrinone withdrawal in all cases. SVT was most frequent in the palliative group (3 of the 4 cases) and in patients not treated with beta-blockers (8% vs 60%; $P = .053$). No other adverse effects requiring treatment cessation were recorded. There were no deaths directly attributable to milrinone.

Ambulatory milrinone therapy is barely used in Spain. The present series is the first to report the experience in Spain with this therapy. Although no large randomized studies have been conducted with ambulatory milrinone, some series have been published showing that milrinone can be useful in the above-mentioned contexts:

- As palliative treatment: the available registries show improved quality of life[2-4]; this is in line with our experience, with hospitalizations and emergency department visits avoided in 57% of patients.
- As bridge to HT: the published registries report success rates for this strategy of 65% to 92%,[3,4] similar to that of our series (78%).

The most frequent complications are catheter infections; however, these are usually local and have little impact on patients' quality of life. The most severe complication is SVT, which is more common in palliative care and in patients not receiving beta-blocker therapy; however, ICD therapy correctly treated all cases of SVT in our series.

In conclusion, we present the first experience in Spain with ambulatory milrinone therapy, which could be an alternative treatment option in patients with advanced HF as bridge to HT, bridge to candidacy, or palliative care. In our series, the success rate of this therapy was 74% and its safety profile was acceptable for the patients' characteristics.

Table 1
Characteristics of the patients who received ambulatory milrinone perfusion

	Bridge to transplant (n = 9)	Bridge to candidacy (n = 3)	Palliative care (n = 7)	Total (n = 19)
Age, y	58 [55-62]	54 [52.5-56.7]	63 [53-67]	58 [53-57]
Female sex	2 (22.2)	1 (33.3)	1 (14.3)	4 (21)
Ischemic dilated cardiomyopathy	4 (44)	1 (33)	4 (57)	9 (47)
Nonischemic dilated cardiomyopathy	3 (33)	2 (66)	1 (14)	6 (31)
Hypertrophic cardiomyopathy	1 (11)	0	1 (14)	2 (10)
Congenital heart disease	0	0	1 (14)	1 (6)
Infiltrative cardiomyopathy	1 (11)	0	0	1 (6)
Milrinone dose, μg/kg/min	0.40 [0.34-0.45]	0.38 [0.37-0.5]	0.41 [0.38-0.48]	0.40 [0.37-0.48]
Ventricular arrhythmias	1 (11)	0	3 (43)	4 (21)
Previous AF/flutter	5 (56)	2 (66)	6 (86)	13 (68)
New-onset supraventricular arrhythmias	0	0	0	0
Local infection of the venous access	2 (22)	2 (66.7)	1 (14.3)	5 (26.3)
Bacteremia	1 (11)	2 (66.7)	1 (14.3)	4 (21)
Endocarditis	0	0	0	0
Duration of ambulatory milrinone perfusion, d	77.9 [35-101]	513.5 [249-778]	96 [41-211]	83 [35-229]
Treatment success, %	7 (77.8)	3 (100)	4 (57.1)	14 (73.6)

AF, atrial fibrillation.
Results are presented as number of patients (%) or median [interquartile range].

AUTHORS' CONTRIBUTIONS

J.M. Viéitez Flórez and F.J. Hernández Pérez contributed to patient care, data collection, and manuscript drafting. C. Mitroi, S. Jiménez Lozano, M. Gómez Bueno, and J. Segovia Cubero contributed to patient care, data collection, and manuscript revision.

FUNDING

None.

CONFLICTS OF INTEREST

None.

Acknowledgments

We thank Dr Mercedes Rivas Lasarte for correcting the article and helping with the statistical analysis and for her connection to this project.

José María Viéitez Flórez,* Francisco José Hernández Pérez, Cristina Mitroi, Sara Lozano Jiménez, Manuel Gómez Bueno, and Javier Segovia Cubero

Unidad de Insuficiencia Cardiaca Avanzada y Trasplante Cardiaco, Hospital Universitario Puerta de Hierro-Majadahonda, Majadahonda, Madrid, Spain

* Corresponding author.
E-mail address: chemavieitez@gmail.com (J.M. Viéitez Flórez).

Available online 28 January 2023

REFERENCES

1. Crespo-Leiro MG, Metra M, Lund LH, et al. Advanced heart failure: a position statement of the Heart Failure Association of the European Society of Cardiology: Advanced heart failure: HFA position statement. *Eur J Heart Fail.* 2018;20:1505–1535.
2. Nanayakkara S, Mak V, Crannitch K, Byrne M, Kaye DM. Extended Release Oral Milrinone, CRD-102, for Advanced Heart Failure. *Am J Cardiol.* 2018;122:1017–1020.
3. Rao A, Anderson KM, Mohammed S, et al. Chronic Intravenous Inotropic Support as Palliative Therapy and Bridge Therapy for Patients With Advanced Heart Failure: A Single-Center Experience. *J Card Fail.* 2021;27:974–980.
4. Hashim T, Sanam K, Revilla-Martinez M, et al. Clinical Characteristics and Outcomes of Intravenous Inotropic Therapy in Advanced Heart Failure. *Circ Heart Fail.* 2015;8:880–886.

https://doi.org/10.1016/j.rec.2022.10.020
1885-5857/