The DOREMI Trial: *Milrinone – Dobutamine Match in Cardiogenic Shock!*

Michelle Cancel M.D.[a], Bassam Omar, M.D., Ph.D.[a, b]

Abstract

Cardiogenic shock is defined by end organ hypoperfusion from low cardiac output [1]. Vasopressors and inotropes are the standard of care [2]. Two inotropes commonly used are milrinone and dobutamine. Milrinone is a phosphodiesterase 3 inhibitor [3]. It will increase cardiac inotropy, lusitropy and cause peripheral vasodilatation. Milrinone can also reduce pulmonary artery pressure and improve right ventricular function. Dobutamine is a synthetic catecholamine [4]. It is a beta-1 and beta-2 receptor agonist and can improve blood pressure by increasing cardiac output. However, dobutamine can increase propensity for cardiac arrhythmias. The hemodynamic efficacy and clinical outcomes of dobutamine and milrinone in advanced decompensated heart failure appear to be equivalent [5]. The DOREMI trial's [6] primary aim was to compare the efficacy and safety of milrinone and dobutamine in patients with cardiogenic shock.

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a Division of Pulmonary Medicine. University of South Alabama, Mobile, AL 36617

b Corresponding Author: Bassam Omar, Division of Cardiology, University of South Alabama, 2451 USA Medical Center Dr., Mobile, AL 36617, USA.

Email: bomar@health.southalabama.edu

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Study Details

- Design: Randomized, controlled.
- Setting: Quaternary cardiac ICU.
- Site: Single, in Ottawa, Canada.
- Subjects: 192 participants (96 per group).
- Started 09/2017; completed 05/2020

Inclusion criteria:

1. Adults acutely admitted to cardiac ICU.
2. Cardiogenic shock per SCAI definition [7].

Exclusion criteria:

1. Pregnancy.
2. Inability/unwillingness to provide consent.
3. Indication for a particular inotrope.
4. Out-of-hospital cardiac arrest.

Treatment Strategies

1. Intervention:

   Milrinone titrated gradually in 5 stages from 0.125 mcg/kg/min to > 0.500 mcg/kg/min.

2. Control:

   Dobutamine titrated gradually in 5 stages from 2.5 mcg/kg/min to > 10 mcg/kg/min.

Results

Primary outcomes:

Composite of in-hospital death from any cause, resuscitated cardiac arrest, receipt of a cardiac transplant or mechanical circulatory support, nonfatal myocardial infarction, transient ischemic attack or stroke diagnosed by a neurologist or initiation of renal replacement therapy:

- 47 patients in milrinone and 52 patients in dobutamine group (relative risk 0.90, 95% confidence interval 0.69 - 1.19, P = 0.47).
- Time to event analysis: no significant difference between milrinone & dobutamine groups with respect to the primary outcome.

Secondary outcomes:

- In-hospital death from any cause: 35 in milrinone & 41 in dobutamine group (37% vs 43%; RR 0.85, 95% CI 0.6-1.21)
- Arrhythmia requiring intervention: 48% in milrinone vs 44% in dobutamine group (RR 1.19, CI 0.85-1.57).
- No significant differences with respect to: resuscitated cardiac arrest, receipt of mechanical circulatory support, occurrence of transient ischemic attack or stroke diagnosed by a neurologist, initiation of renal replacement therapy, total inotropic treatment duration, total hospital length of stay or ICU length of stay, noninvasive or invasive mechanical ventilation after inotrope initiation, total duration of ventilation.
- No significant differences with respect to: secondary safety outcomes, including atrial or ventricular arrhythmias, sustained hypotension or increase in dose or addition of a new vasopressor.

Discussion

The goal of the DOREMI study was to compare milrinone and dobutamine in the management of patients with cardiogenic shock. There was no significant advantage to either inotrope over the other with respect to the primary and secondary outcomes. The authors discuss some limitations:

1. In-hospital outcomes were assessed only, for data completeness. Differences beyond hospitalization may have been missed.
2. Medication titration was at the physician discretion, potentially introducing variability between the treatment groups.
3. Patients were randomized from one single center, limiting applicability of findings to other settings.
4. Power calculation presumed a large treatment effect; thus underpowered the study to detect smaller effects.

Clinical Implications

Studies of cardiogenic shock have differed in their design, and there remains uncertainty about the optimal first-line vasoactive medication [8]. Despite different characteristics of dobutamine and milrinone, the overall clinical outcomes may after all be partly related to the rapid achievement and maintenance of adequate hemodynamic stability [9]. Practice patterns remain variable among providers [10] with little guideline guidance, likely due to the heterogeneity of patient presentations. Further research aiming at elucidating such heterogeneity may help guide targeted inotropic therapy in the future [11].

References

1. Vahdatpour C, Collins D, Goldberg S. Cardiogenic Shock. J Am Heart Assoc. 2019 Apr 16;8(8):e011991.
2. Bistola V, Arfaras-Melainis A, Polyzogopoulou E, et al. Inotropes in Acute Heart Failure: From Guidelines to Practical Use: Therapeutic Options and Clinical Practice. Card Fail Rev. 2019 Nov 4;5(3):133-139.
3. Ayres JK, Maani CV. Milrinone. 2021 Aug 6. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan–.
4. Ashkar H, Adnan G, Makaryus AN. Dobutamine. 2021 Jul 26. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan–.
5. Yamani MH, Haji SA, Starling RC, et al.. Comparison of dobutamine-based and milrinone-based therapy for advanced decompensated congestive heart failure: Hemodynamic efficacy, clinical outcome, and economic impact. Am Heart J. 2001 Dec;142(6):998-1002.
6. Mathew R, Di Santo P, Jung RG, et al. Milrinone as Compared with Dobutamine in the Treatment of Cardiogenic Shock. N Engl J Med. 2021 Aug 5;385(6):516-525.
7. Baran DA, Grines CL, Bailey S, et al. SCAI clinical expert consensus statement on the classification of cardiogenic shock: This document was endorsed by the American College of Cardiology (ACC), the American Heart Association (AHA), the Society of Critical Care Medicine (SCCM), and the Society of Thoracic Surgeons (STS) in April 2019. Catheter Cardiovasc Interv. 2019 Jul 1;94(1):29-37.
8. van Diepen S, Katz JN, Albert NM, et al; American Heart Association Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; Council on Quality of Care and Outcomes Research; and Mission: Lifeline. Contemporary Management of Cardiogenic Shock: A Scientific Statement From the American Heart Association. Circulation. 2017 Oct 17;136(16):e232-e268.
9. Torgersen C, Schmittinger CA, Wagner S, et al. Hemodynamic variables and mortality in cardiogenic shock: a retrospective cohort study. Crit Care. 2009;13(5):R157.
10. Scheeren TWL, Bakker J, Kaufmann T, et al. Current use of inotropes in circulatory shock. Ann Intensive Care. 2021 Jan 29;11(1):21.
11. Zweck E, Thayer KL, Helgestad OKL, et al. Phenotyping Cardiogenic Shock. J Am Heart Assoc. 2021 Jul 20;10(14):e020085.

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