Clinical Critical Care

E-ISSN 2774-0048

VOLUME 33 NUMBER 1

JANUARY-DECEMBER 2025

Clinical Critical Care

Clinical Critical Care
Volume 33, Article ID e250024, 3 pages
https://doi.org/10.54205/ccc.v33.276808

LETTER TO THE EDITOR

eISSN 2774-0048

Metaraminol in critical care and anesthesia: A safe alternative for hypotension management?

Camila Gomes Dall'Aqua, Bruno Vinícius Castello Branco, André Luis Vieira Drumond, Marina Ayres Delgado

Division of Anesthesiology, Department of Surgery, Hospital das clínicas de Belo Horizonte, Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais, Brazil

OPEN ACCESS

Citation:
Dall'Aqua CG, Branco BVC, Drumond ALV, Marina Ayres Delgado MA. Metaraminol in critical care and anesthesia: A safe alternative for hypotension management? Clin Crit Care 2025; 33: e250024.

Received: July 29, 2025
Revised: October 1, 2025
Accepted: October 29, 2025

Corresponding author:
Marina Ayres Delgado
Division of Anesthesiology, Department of Surgery, Hospital das clínicas de Belo Horizonte, Universidade Federal de Minas Gerais, Brasil Cep:30130-100
E-mail: marina.ayres.delgado@gmail.com

ABSTRACT:

Metaraminol, a synthetic sympathomimetic amine with predominant alpha-1 adrenergic agonist activity, is increasingly used to manage arterial hypotension in critical care and anesthesia. Its pharmacological effects include peripheral vasoconstriction and indirect stimulation of norepinephrine release, producing effective hemodynamic support through intravenous bolus or infusion. Compared with norepinephrine, metaraminol may offer advantages such as reduced arrhythmogenic potential, improved coronary and renal perfusion, and suitability for peripheral administration, minimizing risks associated with central venous access. However, evidence supporting its broader use outside obstetric anesthesia remains limited, largely derived from small observational studies. Uncertainties persist regarding optimal dosing, pharmacokinetic variability, and dose equivalence with norepinephrine. Reported adverse effects include prolonged hypertension, tissue ischemia, and reflex bradycardia. Despite these gaps, surveys indicate widespread clinical use, reflecting its practicality for rapid hemodynamic stabilization. Current data suggest non-inferiority to norepinephrine in obstetric anesthesia, but robust randomized trials are needed to define efficacy, safety, and pharmacodynamic profiles across patient populations. Standardization of dosing strategies and further evaluation in critical care settings are essential to clarify metaraminol's role as a safe and effective vasopressor alternative.

Keywords: Metaraminol; Sepsis; Hypotension

To editor,

Metaraminol, a synthetic sympathomimetic amine, has been employed for managing arterial hypotension in ICU (intensive care units) patients and in obstetric anesthesia, but its use in other anesthetic scenarios has been a field of study. Its pharmacological action encompasses both direct and indirect mechanisms: firstly, the agonism of alpha-1 adrenergic receptors results in peripheral vasoconstriction; secondly, the drug stimulates norepinephrine release from sympathetic nerve terminals, which enhances the vasopressor effect. Metaraminol is administered via intravenous bolus or continuous infusion. A bolus dose of 0.5–1 mg rapidly increases blood pressure within 1–2 minutes, with effects lasting 20–60 minutes For continuous infusion, the recommended rate is typically 15–100μg/min, titrated according to blood pressure response. [1].

Differing from norepinephrine, which exerts a dual alpha-1 and beta-1 adrenergic agonist effect, metaraminol primarily exhibits selective alpha-1 adrenergic activity at typical doses. This selectivity may confer several advantages, including a lower risk of cardiac arrhythmias, enhanced coronary perfusion, decreased myocardial oxygen consumption, improved hemodynamic stability in neurogenic shock, reduced myocardial ischemia during infarction and improved uterine and fetal perfusion during cesarean delivery [2, 3].

With regard to the infusion route, metaraminol is classified as a peripheral vasopressor, which means that it eliminates the need for central venous access -and its associated risks-, allowing time-sensitive hemodynamic benefits [1]. However, its increasing use outside obstetric settings has outpaced the pace of evidence-generation.

Despite the advantages associated with its potent vasopressor response, the role of metaraminol in managing hypotension in critically ill patients deserves reflection. Firstly, it must be emphasized that the established use in ICUs comes from evidence, most of them, derived from small or retrospective studies. This gap is striking given the frequent off-label use in peripheral settings where rapid hemodynamic intervention is crucial. Then, its pharmacological characteristics, such as a prolonged half-life and unique hepatic metabolism, which may result in less predictable effects compared to norepinephrine, present a challenge in dose titration for unstable patients. Risks associated with its use are also poorly understood. Although it has a lower arrhythmogenic potential than adrenaline and dopamine, it may cause prolonged hypertension, tissue ischemia, and reflex bradycardia, particularly with continuous infusions [1]. Regardless of some evidence, a UK survey found that 88% of emergency physicians and 67% of critical care specialists use metaraminol in clinical practice [1]. Early vasopressor initiation, usually administered via peripheral access, has been linked to reduced fluid accumulation, lower incidence of acute kidney injury and improved mortality outcomes [1]. Another study has demonstrated that metaraminol achieved target blood pressure 73.4% of the time during peripheral infusion, with only 12.8% requiring central venous catheter insertion due to persistent hemodynamic instability. The authors concluded that peripheral metaraminol infusion can provide effective hemodynamic support while avoiding complications associated with central venous catheter use. Notably, Han and Zhou did not specify the dosing strategy for peripheral metaraminol infusion, which further underscores the uncertainty surrounding its use [4]. In our view, this omission reflects a wider issue: most physicians remain unfamiliar with metaraminol infusion, irrespective of whether it is administered via peripheral or central routes.

Comparative studies between metaraminol and norepinephrine are limited. A 2021 systematic review aimed to analyze the efficacy and safety of metaraminol continuous infusion compared to other vasopressors in critically ill patients. Only three observational studies and one case-control study were included in this review. They found no difference in hospital mortality or in the effect on mean arterial pressure, heart rate or stroke volume between metaraminol and norepinephrine, although none reported the duration of infusion [5]. Even the dose equivalence between metaraminol and norepinephrine remains unclear. Sardaneh et al suggest a conversion ratio of 10:1 (metaraminol μg/kg/min : norepinephrine μg/kg/min) in critically ill patients with shock [5]. This uncertainty in dose conversion highlights an important barrier to wider clinical implementation and calls for standardized pharmokinetic-pharmacodynamic studies.

It is likely—though not exclusively—that metaraminol's adoption in critically ill patients originated from its established use in anaesthesia, where it serves as a short-acting vasopressor ideal for peripheral administration during brief episodes of hypotension induced by anaesthetic agents [1].

Specifically, regarding the drug infusion regimen, the bolus administration of metaraminol is particularly effective for managing transient hypotension, such as during anesthesia induction in scenarios other than spinal anesthesia in cesarean deliveries. While this is a common clinical practice, few studies validate the drug's safety in this context, as highlighted by Ngan Kee et al [3]. A continuous infusion offers sustained hemodynamic support by maintaining stable plasma concentrations, enabling real-time titration based on blood pressure response. Infusions, commonly initiated at 0.5–2 mg/h (25–100 μg/min) are adjusted as needed to avoid excessive vasoconstriction and can be safely intravenous administered via peripheral or central venous routes, a feature that represents a practical advantage of metaraminol over other vasopressors [1].

On obstetric anesthesia, studies have demonstrated that metaraminol is non-inferior to norepinephrine and is associated with a lower incidence of maternal and fetal complications compared to other sympathomimetic agents [3]. However, the pharmacological response to metaraminol varies among individuals due to differences in adrenergic receptor profiles—factors that remain underexplored in the literature

The main limitation of this letter is the lack of robust clinical evidence supporting metaraminol's use, both in critically ill patients and more notably in anesthesia (where the little evidence of its use is concentrated in obstetric anesthesia). Most available data come from small, observational studies with high risk of bias, limiting generalizability and applicability in clinical practice. The pharmacological profile of metaraminol seems to be more complex, which confuses its dosing and titration. Moreover, there are few studies comparing it with other vasopressors, particularly norepinephrine.

Yet this very lack of evidence—contrasted with frequent use—should spur clinical inquiry. Despite these challenges, metaraminol offers potential benefits as a vasopressor, such as effective hemodynamic support with a lower risk of arrhythmias and improved coronary and renal perfusion. However, further high-quality randomized controlled trials are needed to assess its efficacy, safety, and pharmacological properties. Investigating dose equivalency, its role in specific shock types, and the potential for peripheral infusion would help clarify its use in critical care and anesthesia.

AUTHORS' CONTRIBUTIONS

(I) Conceptualization: Bruno Vinícius Castello Branco; (II) Data curation: Bruno Vinícius Castello Branco; (III) Software: Vieira Drumond; (IV) Recourses: Vieira Drumond; (V) Investigation methodology: Camila Gomes Dall'Aqua; (VI) Visualization: Vieira Drumond; (VII) Project administration: Vieira Drumond; (VIII) Validation: Marina Ayres Delgado; (IX) Formal analysis: Marina Ayres Delgado; (X) Writing-original draft: Camila Gomes Dall'Aqua; (XI) Writing- review and editing: Marina Ayres Delgado; (XII) Supervision: Marina Ayres Delgado.

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