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COMMENTARY

A simplified formula for rapid dilution of catecholamines in initial emergency and critical care resuscitation

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Abstract

Inotropes and vasopressors may require to be rapidly administered in emergency situations in any setting (pre-hospital resuscitation, hospital wards, intensive care units, emergency departments, operating theatres). Simple formulas to dilute drugs and set infusion rates may be of great help in emergency situations to improve efficiency, speed of administration, and limit mistakes. We propose a simple formula used for decades in our institution that rapidly allow to dilute and set infusion rates of commonly administered inotropes and vasopressors (epinephrine, norepinephrine, dopamine and dobutamine) by simply multiplying patient's weight by 6. We believe that our formula will be of great help to any healthcare professionals in these fields of expertise.

Keywords

Inotropes; Vasopressors; Catecholamines; Shock; Hemodynamic management; Medical emergency

Vasoactive drugs are increasingly administered in emergency situations outside the intensive care unit (ICU), including in pre-hospital settings, the emergency department, and the operating room [1–9]. In particular, vasopressors are frequently required to provide initial stabilization before reaching an ICU, and several studies suggest potential improvement in survival with early vasopressors administration [2, 5, 7]. For example, early initiation of norepinephrine infusion during prehospital care of septic shock patients was independently associated with a greater than 50% reduction in 30-day mortality [2].

Unfortunately, in these contexts, dilution errors are common but largely preventable [10, 11]. The use of simple formulas for drug dilution and infusion rate calculation is crucial in emergency situations to simplify tasks, improve efficiency, and reduce the possibility of mistakes [12–14]. We read with great interest the article by Alpar *et al.* [15] that introduces the "fast inotropic bag" (FiB) formula, providing a quick method to calculate doses for positive inotropic drug infusions. However, it has limitations and might not be applicable in all clinical contexts.

A simple unit conversion error led to the administration of an incorrect norepinephrine dose, ultimately resulting in the patient's death—a stark reminder of the potentially fatal consequences of dosing errors with vasoactive agents [16, 17].

The FiB formula [15] is likely to help healthcare professionals in many emergency situations. However, we believe that the formula still has some limitations. Different drug formulations (such as bitartrate, tartrate, and hemitartrate [18–21]) may be available in different institutions, limiting generalizability of the formula. These salt formulations have extra counterions that increase their molecular weight, so the actual amount of active norepinephrine base in a vial is less than the total weight listed [19, 21]. For example, our institution uses norepinephrine vials that contain 2 mg of norepinephrine tartrate in 1 mL, which corresponds to only 1 mg of norepinephrine base. This means that if a clinician calculates the dose assuming base but uses the salt formulation, a prescribed dose of 1 μg/kg/min would effectively deliver only about 0.5 μg/kg/min of active base [21]. To further complicate the picture, different salt formulations of norepinephrine are available [18–21], containing different amounts of the pharmacologically active norepinephrine base molecule. Unfortunately, many clinicians are not yet aware of this issue and variably administer norepinephrine referring to the base or salt dose [22–26]. The lack of awareness regarding the specific norepinephrine formulation used concerned 50% of participants in a recent study assessing compliance with the 2016 Surviving Sepsis Campaign Guidelines [26]. There is a growing consensus regarding the need for the prospective

implementation of a standardized reporting system based on norepinephrine base [27]. Therefore, considering a standard 4 mg/4 mL vial of norepinephrine in the FiB formula may lead to different dosing among different clinicians or institutions.

In addition, multiplying by 0.15 may not be immediate in many situations, decimal-based and multi-step calculations have been shown to substantially increase the risk of dosing errors, occurring in approximately 11% of preparations [28].

We therefore would like to propose an updated formula for rapid dilution of inotropes, based on practice that has been used in our institution for decades.

We use the following formula for epinephrine and norepinephrine (base): first multiply patient's weight × 6 and then divide by 100. The resulting number is the amount of mg of epinephrine or norepinephrine base to be diluted in 100 mL of normal saline or 5% glucose. With this dilution, an infusion rate of 1 mL/h corresponds to a dose of 0.01 μg/kg/min, and an infusion rate of 10 mL/h corresponds to a dose of 0.1 μg/kg/min, regardless of patient's weight. For dopamine and dobutamine, we apply the following formula: multiply patient's weight × 6. The resulting number is the amount of mg of epinephrine or norepinephrine to be diluted in 100 mL of normal saline or 5% glucose. With this dilution, an infusion rate of 1 mL/h corresponds to a dose of 1 μg/kg/min, and an infusion rate of 10 mL/h corresponds to a dose of 10 μg/kg/min, regardless of patient's weight (Table 1).

We believe that this simpler formula allows to rapidly calculate (even without a calculator) dilution and infusion dose of commonly administered inotropes and vasopressors in any emergency situations (for example, the pre-hospital setting [29] or emergencies in general wards) and may potentially reduce dilution mistakes. Furthermore, the resulting catecholamine concentrations in the diluted solution correspond to values that remain within the upper reported concentration range reported for short-term peripheral norepinephrine administration under monitored conditions [1, 30, 31]. For example, applying our formula yields concentrations of 42 μg/mL in a 70-kg patient and 60 μg/mL in a 100-kg patient, which has been reported to be administered also in peripheral venous lines.

Notably, the formula was never tested in prospective benchmarking against established preparation workflows; therefore, potential reductions in preparation time or calculation errors have not been formally demonstrated. The arithmetic simplicity of the formula might not necessarily translate into improved clinical performance, particularly under stressful conditions, where cognitive load, vial interpretation (base versus salt), and practical preparation steps may affect usability. Future prospective simulation-based studies are needed to determine the practical implications of this method in emergency settings.

We do not expect the described formula to replace standardized infusion protocols, smart infusion systems, or prediluted drugs. Rather, it is conceived as a pragmatic alternative for emergency situations or care environments in which prestandardized concentrations, smart pump libraries, or ready-to-administer preparations are not readily available, including low-resource settings.

Another possible limitation of the formula we suggest is

TABLE 1. Examples of practical use of the proposed formula.

Drug	Formula for dilution (mg in 100 mL)	Final concentration (µg/mL)	Infusion rate equivalence	Examples
Epinephrine	(Patient's weight × 6)/100	42 µg/mL (for 70 kg) 60 µg/mL (for 100 kg)	1 mL/h = 0.01 µg/kg/min 10 mL/h = 0.1 µg/kg/min	70 kg patient: 4.2 mg in 100 mL → 42 µg/mL 10 mL/h = 0.1 µg/kg/min 100 kg patient: 6 mg in 100 mL → 60 µg/mL 10 mL/h = 0.1 µg/kg/min
Norepinephrine	(Patient's weight × 6)/100	42 µg/mL (for 70 kg) 60 µg/mL (for 100 kg)	1 mL/h = 0.01 µg/kg/min 10 mL/h = 0.1 µg/kg/min	70 kg patient: 4.2 mg in 100 mL → 42 µg/mL 10 mL/h = 0.1 µg/kg/min 100 kg patient: 6 mg in 100 mL → 60 µg/mL 10 mL/h = 0.1 µg/kg/min
Dopamine	(Patient's weight × 6)	4200 µg/mL (for 70 kg) 6000 µg/mL (100 kg)	1 mL/h = 1 µg/kg/min 10 mL/h = 10 µg/kg/min	70 kg patient: 420 mg in 100 mL → 4200 µg/mL 10 mL/h = 10 µg/kg/min 100 kg patient: 600 mg in 100 mL → 6000 µg/mL 10 mL/h = 10 µg/kg/min
Dobutamine	(Patient's weight × 6)	4200 µg/mL (for 70 kg) 6000 µg/mL (for100 kg)	1 mL/h = 1 µg/kg/min 10 mL/h = 10 µg/kg/min	70 kg patient: 420 mg in 100 mL → 4200 µg/mL 10 mL/h = 10 µg/kg/min 100 kg patient: 600 mg in 100 mL → 6000 µg/mL 10 mL/h = 10 µg/kg/min

the need for elevated infusions rate in patients requiring high dose vasopressors. However, patients will likely receive catecholamines in these settings (pre-hospital, emergency departments, or general wards) for a relatively short period of time before either recovery or transfer to the ICU, where different protocols and dilutions could be used in a safer environment. In addition, we do believe that current practice of administration of combined, low-dose multiple vasopressors will make this situation unlikely [32–34].

AVAILABILITY OF DATA AND MATERIALS

Not applicable. No individual patient data reported.

AUTHOR CONTRIBUTIONS

AB, CM—performed the research. YK, AN, AKK—formal analysis. AB, AKK—investigation. CM, YK, AN—data curation. AB, CM, AKK—wrote the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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CONFLICT OF INTEREST

YK: Consulting Feed from Viatris.

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