Journal of Critical Care 35 (2016) 155–160

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.jccjournal.org

Effects of propofol on vasopressor use in patients with sepsis and severe sepsis: A pilot study☆

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ARTICLE INFO

Keywords:
Propofol
Sepsis
Vasopressor
Hypotension
Continuous sedation

ABSTRACT

Purpose: Propofol is one of the most commonly used sedatives in the intensive care unit (ICU) despite its undesirable hypotensive effects. The purpose of this study was to determine the effects of continuous intravenous (CIV) propofol on vasopressor requirements in mechanically ventilated patients with sepsis.
Materials and methods: A multicenter, retrospective, propensity-matched pilot study was conducted comparing patients with sepsis or severe sepsis who received CIV propofol for sedation to those who did not. The primary outcome was incidence of vasopressor support. Secondary outcomes included change in mean arterial pressure, mortality, and length of stay.
Results: A total of 279 patients (149 CIV propofol, 130 non-CIV propofol) were evaluated, with 174 patients matched 1:1 based on propensity score. There was no difference in vasopressor support requirements (49.4% vs 54%; $P = .65$) or in those experiencing a greater than 20% decrease in mean arterial pressure from baseline (58.6% vs 63.2%; $P = .53$) in the CIV propofol and non-CIV propofol groups. Furthermore, there were no differences in any secondary outcomes including hospital mortality (32.2% vs 33.3%; $P = .87$).
Conclusions: Continuous intravenous propofol for sedation did not increase vasopressor requirements in this septic population. Furthermore, CIV propofol was not associated with significant differences in the use of multiple vasopressors, change in mean arterial pressure, length of stay, or mortality.

1. Introduction

Propofol is an intravenous γ-amino butyric acid agonist used for continuous sedation in intensive care unit (ICU) patients [1,2]. Advantages of propofol include ease of titration, fast onset and offset of action, and favorable pharmacokinetic properties [2]. The pharmacokinetic properties of propofol are beneficial as they allow for rapid awakenings and a reduced risk of drug accumulation, especially in patients with hepatic and renal dysfunction. Furthermore, recent literature has demonstrated that propofol is associated with a decreased length of mechanical ventilation compared to benzodiazepines, making it a preferred agent for patients requiring continuous sedation [3].

Although commonly used in ICU patients, propofol does have several significant disadvantages, including the development of hypotension secondary to a reduction in vascular sympathetic tone [2,3]. Based on previous studies, the development of hypotension during propofol administration occurs in approximately 25% to 30% of ICU patients receiving the drug [1,4]. As a result of this potential risk, clinicians may prefer alternative sedatives over propofol in patients at risk for developing hypotension [5,6]. It is well known that critically ill patients with sepsis have an increased risk of hypotension and require early resuscitation to maintain hemodynamic stability and perfusion of critical vascular beds [7,8]. Failure to maintain hemodynamic stability can result in

☆ All authors of this study have no direct or indirect conflicts of interest to disclose. No funding was obtained for the conduction of this study. The results of this study have not been presented previously.
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http://dx.doi.org/10.1016/j.jcrc.2016.05.015
0883-9441/

progression to shock, resulting in potential increases in mortality as high as 46% [9–13]. Therefore, avoiding factors that may amplify hypotension and the progression to septic shock is critical to patient care.

Risk factors for progression to septic shock have been previously identified and include increased age, hyperthermia, increased shock index, pulmonary disease, and site of infection [9,11]. Although some medications have been postulated to increase the risk of death in septic patients, definitive literature confirming this risk is lacking [14,15]. Etomidate has been hypothesized to influence the progression to septic shock by causing adrenal suppression, although data from multiple studies have failed to demonstrate an effect on hemodynamics or other clinical outcomes [16–18]. Although hypotension has been widely reported with propofol administration, it has not been described in the setting of sepsis as a risk factor for progression to shock. As propofol remains the most commonly used sedative in the ICU and has the potential to cause clinically relevant hypotension in septic patients, the purpose of this investigation was to determine the effects of continuous intravenous (CIV) propofol administration on the need for vasopressor support in patients with sepsis and severe sepsis.

2. Materials and methods

This was a multicenter, retrospective, pilot study of patients with sepsis or severe sepsis who required mechanical ventilation. Patients were enrolled from 2 separate urban teaching hospitals. Patients discharged between the years 2011 and 2014 were identified through corporate patient financial services using the *International Classification of Diseases, Ninth Revision, Clinical Modification*, codes for sepsis and mechanical ventilation. Patients were included if they were at least 18 years of age, intubated within 24 hours of hospital admission, and met sepsis or severe sepsis criteria within 2 hours before intubation [7]. We excluded those who were not septic within 2 hours of intubation, immunosuppressed, intubated before arrival, or received vasopressor support within 24 hours before study inclusion or within 15 minutes of a propofol bolus for intubation. The institutional review boards at both institutions approved the project design.

The experimental group consisted of patients who received CIV propofol for at least 30 minutes within 48 hours after intubation, whereas the control group consisted of patients who did not receive CIV propofol during the 48-hour period after intubation. A minimum enrollment of 200 patients was planned with an approximate equal distribution between the CIV propofol and non-CIV propofol groups. A power analysis was not performed to determine an adequate sample size due to a lack of data describing the rate of hypotension with propofol in this population. Therefore, this investigation served as a pilot study in this area. We followed patients for a period of 48 hours after the initial intubation to measure primary and secondary outcomes. We selected the 48-hour evaluation period based upon the hypothesis that any changes in mean arterial pressure (MAP) would occur earlier in treatment instead of after prolonged administration. We abstracted all data included in the study directly from the electronic medical record at both institutions.

The 2012 Surviving Sepsis Guidelines were used to categorize sepsis and severe sepsis, whereas hospital-associated infections were defined using guidelines from the Infectious Disease Society of America [7,19,20]. Vasopressor support was assessed by documented administration of epinephrine, norepinephrine, vasopressin, dopamine, or phenylephrine. Initiation of appropriate empirical antibiotics was defined by the start of antimicrobial regimens for which presumptive or definitive pathogens were susceptible to in vitro. In the case of culture-negative sepsis or severe sepsis, broad-spectrum antibiotics were deemed sufficient based on the presumptive source of infection and in accordance with local practice guidelines [21].

The primary outcome of the study was the need for vasopressor support between the 2 groups. Secondary outcome measures included absolute change in MAP, a greater than 20% decrease in MAP from baseline, maximum vasopressor infusion rates, the requirement for multiple vasopressor agents, and duration of vasopressor use. The duration of ICU and hospital length of stay as well as the incidence of hospital

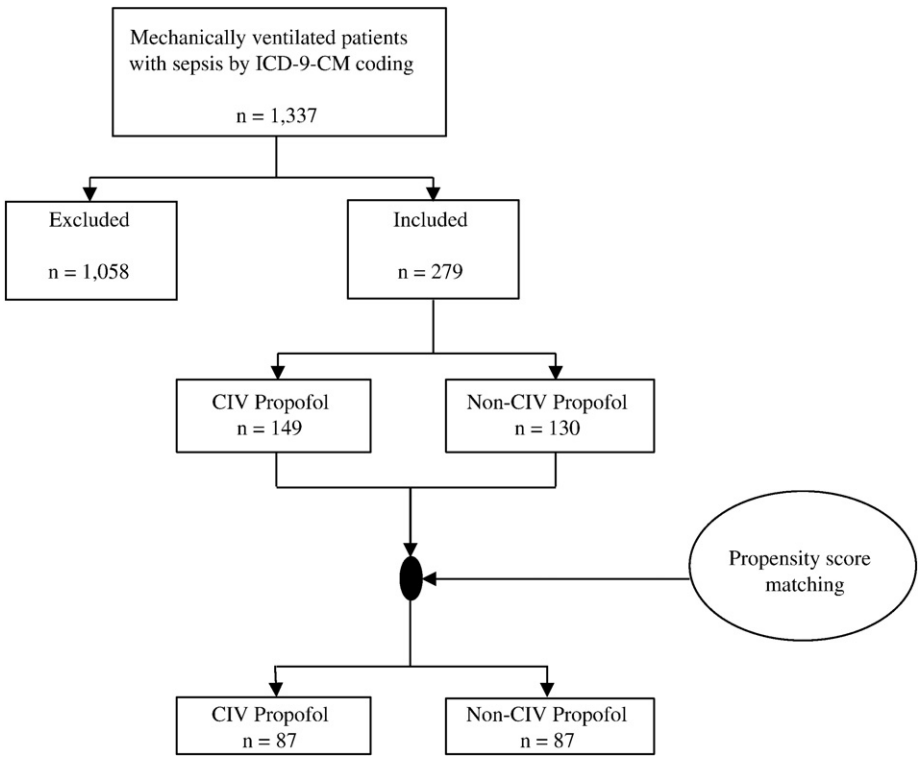

Fig. 1. Patients identified, analyzed, excluded, and propensity score matched.