VIEW POINT

Viewpoint: Weak Scientific Basis for the Recommendation of Executive Summary of Surviving Sepsis Campaign Guidelines 2021

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Abstract

The Executive summary of Sepsis 2021 was published recently, which for the first time, recommended that in septic shock, the vasopressor infusion should be commenced through a peripherally inserted venous catheter (PiVC) for up to 6 hours. We discuss the scientific basis for such a recommendation regarding the safety of vasopressor infusion through a peripherally inserted vascular catheter or the accepted duration.

Keywords: Peripherally inserted vascular catheter, Septic shock, Surviving Sepsis Campaign guidelines 2021, Vasopressors.

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Highlights

Inconsistencies in the Executive Summary of the Surviving Sepsis Campaign (SSC) guidelines 2021 and the weak scientific base of a particular recommendation are being discussed in this viewpoint.

The Executive summary: Surviving Sepsis Campaign: Guidelines for the management of sepsis and septic shock 2021 by Evans et al. was published recently.[1] The SSC guidelines had been considered sacrosanct by intensivists and are expected to be based on sound scientific evidence. The present write-up is regarding the suggestion to start vasopressor infusion in septic shock, where MAP <65 mm Hg. The executive summary mentions that peripherally administered vasopressor infusion is safe, provided it is infused through a PiVC *distal* to the antecubital fossa for a duration not exceeding 6 hours. There are two issues mentioned: the site of the peripheral cannula and the duration of vasopressor infusion by PiVC. In all likelihood, the "*distal*" to the antecubital fossa site mentioned for peripheral infusion of a vasopressor is an inadvertent typographical error as it is inconsistent with that mentioned in the sepsis guidelines 2021.[2] It was supposed to be "proximal" to the antecubital fossa, and the author's letter to the editor pointed out the discrepancy and a corrigendum to this effect was published subsequently.[3]

It is worthwhile to examine the evidence on which this recommendation was based. In the Executive summary, the authors have cited the following two systematic review articles to back this weak recommendation.[4,5]

Loubani et al., in their systematic review, included 85 studies, of which 80 included individual patient data (case reports and small case series), and five were aggregated patient data with a sole randomized control trial. They analyzed a total pooled data of 270 patients. 85.3% of all tissue injury events were reported when vasopressor was infused through a PiVC at distal sites (distal to the antecubital or popliteal fossa). They mentioned that most commonly, 12–24 hours (range 0.08–528 hours) of vasopressor-induced hypoperfusion was needed to trigger local tissue injury.[4] Indeed, the number of events rose significantly when the duration of vasopressor infusion exceeded 6 hours, but the incidence of events before that was also not negligible when millions of septic shock the world over were considered. Moreover, since the review mainly included case reports and case series, a reporting bias exists, and the results are not representative of the general clinical practice. They concluded that vasopressor infusion through PiVC for a short duration (i.e. less than 2 hours) and in proximal location (i.e. antecubital fossa or external jugular vein) was likely to be bereft of tissue injury events.[4]

Tian et al. included seven reports in their systematic review to assess the frequency of adverse effects following vasopressor infusion through a PiVC, with pooled data of 1,382 patients.[5] Contrary to the review of Loubani et al., even though the duration of vasopressor infusion ranged from 4.5 to 60.5 hours (mean 22 hours), there was a 3.4% incidence of extravasation with no case of limb ischemia or tissue necrosis. This review did not mention the site of the peripheral catheter at all! They conceded that due to the low incidence rate, the association between complications and PiVC site could not be evaluated, nor did they describe any association between the duration of infusion and onset of local complications. It may be noted that the Canadian Association of Emergency Physicians too forwarded a conditional recommendation of a vasopressor infusion through a PiVC for <1–2 hours.[6]

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The Surviving Sepsis Guidelines 2021 mention a few more studies to buttress this recommendation (number 44), though they do not mention the safe period of 6 hours, unlike the Executive summary.[2] Delaney et al. performed a *post hoc* analysis of the ARISE trial and compared patients of septic shock who received vasopressor through PiVC to those who received it through central venous catheters (CVC). The two groups were not comparable as those who received vasopressor infusion through PiVC weighed more, were sicker (higher APACHE II scores and serum lactate levels), and had lower blood pressure and faster respiratory rate. The authors reported that the odds ratio for mortality for those who received vasopressor through PiVC was 1.26, though they did receive vasopressor and anti-microbial earlier.[7]

Lewis et al. reported an extravasation rate of 4% when vasopressor was infused through a PiVC. They did not report a correlation of complications with PiVC with their insertion site. About 46% of those who received vasopressor infusion through PiVC had to be transitioned to CVC.[8] Ricard et al. reported a significantly higher incidence of complications when vasopressors were infused through PiVC than those associated with CVC.[9] In their study, too, about 50% of the patients who initially had a PiVC needed insertion of CVC.

The indisputable truth is that delaying starting vasopressor in septic shock heralds poor outcomes. It was demonstrated that every hour delay in vasopressor initiation was associated with a 7% increase in mortality (odds ratio 1.07 per hour, confidence interval 1.06–1.08).[10] The authors of the Surviving Sepsis Guidelines 2021 seem to have been too overwhelmed by this concern to make recommendations that are not backed by robust evidence and less so by the systematic reviews they claimed supported their contention.

Hence, we look forward to the authors revisiting the recommendation regarding the administration of vasopressor through a PiVC in septic shock as we believe that there is neither a solid scientific basis to recommend it nor the acceptable duration of 6 hours. Furthermore, this recommendation might unnecessarily promote vasopressor infusion through PiVC and discourage CVC insertion.

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