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Ulinastatin: is it worth using in severe sepsis?

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Dear Editor,
Severe sepsis and septic shock are progressively severe stages of the host's systemic inflammatory response to infection and are associated with high mortality. The inflammatory response to infection is complex; repeated failed efforts have been made in the last decade to block the activity of these biochemical triggers such as endotoxin, tumor necrosis factor alpha, cytokines, and others [1]. In the same quest, Karnad et al. [2] have used the molecule ulinastatin.

The authors have chosen less sick patients, 65 % of whom had single organ failure [2]. The mean APACHE II score was 13.4, which suggested that the subjects selected were not ideal intensive care unit (ICU) patients. The sequential organ failure assessment (SOFA) score, which is a better score for organ dysfunction, was not revealed. Another anti-inflammatory molecule, activated protein C (APC), was specifically

advocated in patients with severe sepsis and APACHE II score ≥ 25 [3]. It was also recommended that APC should not be given to patients with APACHE II score ≤ 20 or one organ failure [3]. The drug was ultimately banned in 2012 after the PROWESS shock trial [3]. The recruitment of patients with mean APACHE II score of 13.4 in the current study raises questions about the utility of ulinastatin.

The use of netilmicin and colistin, which are used specifically for multidrug-resistant (MDR) bugs, is twice as common in the placebo group (12 versus 6), suggesting that the presence of more MDR organisms in the placebo group could be responsible for higher mortality [2]. Recently published randomized controlled trials (RCTs) in *The New England Journal of Medicine* have shown that neither protocol-based resuscitation nor the use of albumin has shown any mortality benefit in patients with severe sepsis [4, 5]. At the end of the day, in management of severe sepsis, early recognition and immediate initiation of effective antibiotic therapy holds the key not the use of any magic drug. The health scenario in India is different from in developed countries. The majority of ICUs in India are in private sector and above all the cost of treatment is borne by the patient's family. This is unlike in the UK and Australia where the cost of treatment is borne by the government. In India the cost of ICU treatment per day is US\$300–400; burdening patients with expensive medications would further increase the cost of treatment. A large RCT involving at least 1,000 patients with

strict criteria like APACHE II ≥ 25 is warranted and those results should be extrapolated in a clinical setting.

Conflicts of interest Nil.

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