Hydrocortisone plus fludrocortisone: Taichi of risk hedge for improving adults with septic shock

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To the editor:

We read with interest the work presented by Annane *et al.* (1) in which the authors reported that hydrocortisone plus fludrocortisone therapy significantly improved 90-day all-cause mortality in patients with septic shock compared with placebo. Interestingly, recent work presented by Venkatesh *et al.* (2) did not favor hydrocortisone therapy alone in patients with septic shock undergoing mechanical ventilation.

Hydrocortisone has both glucocorticoid and mineralocorticoid effects, just like Chinese Taichi reconciling Yin and Yang. The former suppresses damaging, excessive inflammatory immune responses in sepsis; the latter results in sodium retention with plasma volume expansion and an increase in vascular sensitivity to catecholamine with increased peripheral resistance correcting hypotension. In addition, mineralocorticoid effects may cause metabolic alkalosis by excessive potassium release (3). However, with respect to septic shock, the mineralocorticoid effects of hydrocortisone alone seem not strong enough. Additional fludrocortisone enhances mineralocorticoid potency and therefore strengthens the antagonism of hypotension and metabolic acidosis in sepsis, especially in septic shock. Glucocorticoid and mineralocorticoid effects are likely to balance more perfectly in this combination strategy. Previous clinical trials also demonstrated that only corticosteroids with a relatively high potency of mineralocorticoid effects reversed

shock symptoms in patients with sepsis (3).

It is reasonable to speculate that compared with hydrocortisone alone, hydrocortisone plus fludrocortisone therapy improves mortality in patients with septic shock, especially with severe septic shock, by reversing shock symptoms faster and reducing fluid infusion. Reduction in fluid infusion is currently considered to be associated with better prognosis of sepsis. Moreover, patients who are vasopressor-dependent or who develop early severe acute respiratory distress syndrome benefit more from this combination strategy (4). In the light of this, hydrocortisone plus fludrocortisone may be more promising in treating patients with severer septic shock.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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