Corticosteroid Treatment for Acute Respiratory Distress Syndrome

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Acute respiratory distress syndrome (ARDS) is a common life-threatening clinical syndrome characterized by severe respiratory failure caused by various etiologies (not cardiac dysfunction), and often associated with multiple organ failure. In 1994, the definition of ARDS was developed by the American-European Consensus Conference (AECC) (1). According to these criteria, ARDS is diagnosed based on a ratio of arterial oxygen tension (PaO₂) to the fraction of inspired oxygen (FiO₂) of < 200 mmHg; patients with a PaO₂/FiO₂ ratio of < 300 mmHg are considered to have acute lung injury (ALI). In addition, the possibility of cardiogenic lung edema should be excluded by the measuring pulmonary capillary wedge pressure (PCWP). In 2012, the Berlin definition of ARDS (2) was published, subsequently replacing the AECC definition. The major differences in the Berlin definition are that the term “ALI” was eliminated, minimal ventilator settings have been included and PCWP examinations are no longer considered necessary if no other findings of cardiac failure are present. The new definition proposed three categories of ARDS according to the degree of hypoxemia: mild, 200 mmHg < PaO₂/FiO₂ ratio ≤ 300 mmHg on ventilator settings consisting of a positive end-expiratory pressure (PEEP) or continuous positive airway pressure of ≥ 5 cm H₂O; moderate, 100 mmHg < PaO₂/FiO₂ ratio ≤ 200 mmHg on ventilator settings of PEEP ≥ 5 cm H₂O; and severe, PaO₂/FiO₂ ratio ≤ 100 mmHg on ventilator settings of PEEP ≥ 5 cm H₂O. The use of the Berlin definition may support future clinical studies of novel treatments by increasing diagnostic reliability and the enabling the more precise classification of patients according to the disease severity. However, it should be noted that most previously published research was based on the AECC definition.

Causes of death in ARDS patients include not only respiratory failure, but also complications of nosocomial infection and/or multiple organ failure. Persistent inflammation may result in these complications and may play a role in the mortality associated with ARDS. Previous studies have demonstrated that the mortality rate is higher among patients exhibiting large quantities of polymorphonuclear leukocytes (3), high levels of pro-inflammatory cytokines, and low levels of anti-inflammatory cytokines (4) in the lungs. Therefore, it is assumed that anti-inflammatory treatment has the potential to improve the prognosis of ARDS.

In the current issue of Internal Medicine, Horita et al. reported the results of a systematic review and meta-analysis that studied the impact of corticosteroid treatment in patients with ARDS (5). Although no benefits of corticosteroid therapy for ARDS were demonstrated statistically, the authors detected the presence of strong publication bias in this field of study. This is an important discovery that has not been noted previously.

Both the AECC (1) and Berlin (2) definitions of ARDS may have a weak point with respect to assessments of the efficacy of pharmacotherapies, as they specify no criteria regarding the underlying etiology of acute inflammatory lung injury. In the report by Horita et al., previously published articles were searched among four databases using the inclusion criteria “ARDS” or “ALI” and steroids for the systematic review and meta-analysis. Consequently, studies investigating ARDS in patients with leukemia and H1N1 influenza pneumonia were included, whereas reports investigating subjects with various interstitial lung diseases (6), AIDS-related pneumocystis pneumonia (7, 8) and/or fat embolism syndrome (9), all of whom have been reported to receive some benefits of corticosteroid treatment, were not. Perhaps these reports did not state a diagnosis of ARDS and were thus not included in the study. However, the limitations of the inclusion criteria were thoroughly discussed in the article.

The heterogeneity of ARDS may help to explain why most previous trials have failed to demonstrate the effectiveness of corticosteroid treatment. Furthermore, the Berlin definition of ARDS may account for the effects of corti-
costeroid treatment according to the classification of severity of the disease severity. Nonetheless, systemic corticoid treatment is not expected to become routine therapy for ARDS, as its effect on mortality remains uncertain and these agents may induce critical adverse events.

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References


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