Short Communication

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Dexamethasone In Acute Respiratory Distress Syndrome: A Successful Story

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Abstract

No proven effectivepharmacological therapies for the acute respiratory distress syndrome (ARDS) based on the results of randomized clinical trials (RCTs) had been reported until the publication in 2020 of DEXA-ARDS1 and RECOVERY2 trials, testing the effects of dexamethasone in patients with established ARDS and in hospitalized patients with COVID-19, respectively. Paradoxically, the anti-inflammatory and antifibrotic effects of dexamethasone had been tested successfully in hospitalized patients with bacterial meningitis, community-acquired pneumonia, and chemotherapy-induced lung injury, but never evaluated in a randomized trial in patients with ARDS or with severe acute hypoxemic respiratory failure. Dexamethasone is 20-30 times more potent than the naturally occurring hormone cortisol, and 4-5 times more potent than prednisone. Dexamethasone has pharmacological effects that are long lasting, allowing for a regimen of one dose per day. .

Introduction

In the DEXA-ARDS trial (published in February 2020)1, 277 mechanically ventilated patients with established moderate-to-severe ARDS from multiple etiologies were randomized within 24 h of diagnosis to receive conventional treatment or conventional treatment plus intravenous dexamethasone for 10 days (20 mg/day during the first 5 days followed by 10 mg/day from day 6 to day 10). Patients in the dexamethasone group had a greater mean number of ventilator-free days (between-groups difference 4.8 days, $p<0.001$) and lower 60-day mortality (between-groups difference 15.3%, $p<0.005$) than patients in the control group. These findings suggested that early therapy with dexamethasone could change the pulmonary and systemic immune responses, and thereby could reduce the duration of mechanical ventilation and overall mortality.

In the RECOVERY trial (release of results on June 16, 2020)2, 6425 hospitalized patients with coronavirus disease 2019 (COVID-19) were randomized to 6 mg/day of dexamethasone for 10 days or usual care. Overall, dexamethasone resulted in an absolute reduction in 28-day mortality of 2.8% (22.9% vs. 25.7%). The benefit was greatest for 1007 patients who were receiving invasive mechanical ventilation at the time of randomization with an overall mortality of 29.3% for dexamethasone vs. 41.4% for usual care (an absolute risk of death reduction by 12.1%). The signal seen in this trial led to all ongoing RCTs of corticosteroids in COVID-19 to suspend enrollment. Although there are no data on ARDS in the RECOVERY trial, is plausible that most intubated patients had acute hypoxemic respiratory failure and that a significant proportion of patients met criteria for ARDS.

Biography:

I was a Research Fellow and obtained intense and excellent scientific training in Toronto, under the supervision of Arnold Aberman and Arthur Slutsky in Respiratory and Critical Care Medicine from the University of Toronto, Canada. Trained as a pediatric and adult critical care medicine specialist. Then, I worked as a full-time staff at the Intensive Care Unit, Hospital del Pino (Las Palmas de Gran Canaria, Spain) from 1980 to 1987. He is Chief, Research Group, Multidisciplinary Organ Dysfunction Evaluation Research Network, Research Unit, Hospital Universitario Dr. Negrin, Las Palmas de Gran Canaria, Spain; (ii) Group Head, Centro de Investigación Biomédica en Red (CIBER), Instituto de Salud Carlos III, Madrid, Spain; (iii) Adjunct Scientist, Keenan Research Center for Biomedical Research at the Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, Canada.

Recent publication data:

1. Villar J, Ferrando C, Martínez D, et al. Dexamethasone treatment for the acute respiratory distress syndrome: a multicentre, randomised controlled trial. Lancet Respir Med 2020; 8:267–76.
2. RECOVERY Collaborative Group, Horby P, Lim WS, Emberson JR, et al. Dexamethasone in hospitalized patients with Covid-19—preliminary report. N Engl J Med 2020. https://doi.org/10.1056/NEJMoa2021436
3. Sterne JC, Murthy S, Diaz JV, et al. Association between administration of systemic corticosteroids and mortality among critically ill patients with COVID-19. A meta-analysis. JAMA 2020; 324:1330-41.

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