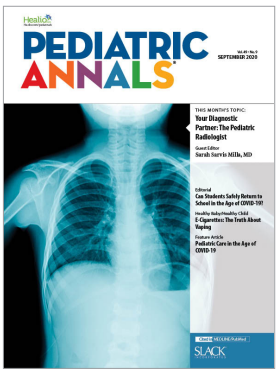
Corticosteroids May Be Indicated in Children with Severe COVID-19 Disease

To the Editor:

We read with interest the article "SARS-CoV-2 Infection in Children: Special Considerations"[1] in the September 2020 issue of *Pediatric Annals*. The article states that "corticosteroids should be avoided unless their use is indicated for another reason." As discussed below, we believe corticosteroids may be indicated in children with severe coronavirus disease 2019 (COVID-19).



Although COVID-19 has created an unprecedented health crisis, time has showed us that pediatric patients are relatively spared from the worst respiratory scenarios created by COVID-19, but they seem to be more prone to cardiac involvement, even when these cases are still rare. Unfortunately, this has not allowed us to determine the best course of action for the few patients who end up in the hospital or in the pediatric intensive care unit requiring respiratory support.[2,3] This forces us to rely on indirect evidence coming from well-known pediatric conditions with similar presentation.

Glucocorticoids have been shown to decrease mortality in adult patients with COVID-19 requiring supplemental oxygen or ventilatory support. The use of glucocorticoids is supported by a meta-analysis of randomized controlled trials (at low to moderate risk of bias) comparing glucocorticoids with placebo or usual care.[4] (This meta-analysis includes the RECOVERY [Randomised Evaluation of COVid-19 thERapY] trial,[5] which had a small number of pediatric patients). This is considered to be a strong recommendation when using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach,[6] which gives the results of this review a high level of certainty (**Figure 1**).

Unfortunately, it seems unlikely that we will be able to obtain a similar quality of evidence for the pediatric population in the near future. Under these circumstances, once again, we should rely on indirect evidence, which in this case is coming from the same condition in adult population. Due to serious indirectness (adult population), the certainty of the evidence has to be downgraded (no other changes in the certainty assessment are required), resulting in moderate certainty (**Figure 2**). Based on this, and the fact that the safety profile of short-term use of steroids is well known, we believe that steroids are a safe option that could provide significant benefit

Critically ill adult patients with COVID-19

Author(s): The WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT)Working Group
Question: Glucocorticoids compared to Placebo or usual care for Critically Ill Patients With COVID-19
Setting: Hospital (General ward and ICU)
Bibliography: WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group, et al. Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19: A Meta-analysis. JAMA. 2020.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Glucocorticoids	Placebo or usual care	Relative (95% CI)	Absolute (95% CI)		
28 Day All Cause Mortality (follow up: mean 28 days)												
7	randomised trials	not serious	not serious	not serious	not serious	none	222/678 (32.7%)	425/1025 (41.5%)	**OR 0.70** (0.48 to 1.01)	**83 fewer per 1,000** (from 161 fewer to 2 more)	⊕⊕⊕⊕ HIGH	CRITICAL
Serious Adverse Events												
6	randomised trials	not serious	not serious	not serious	not serious	none	64/354 (18.1%)	80/342 (23.4%)	**OR 0.72** (0.50 to 1.05)	**54 fewer per 1,000** (from 101 fewer to 9 more)	⊕⊕⊕⊕ HIGH	IMPORTANT

CI: Confidence interval; **OR:** Odds ratio

Figure 1. Use of corticosteroids in adult patients who are critically ill.

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Critically ill pediatric patients with COVID-19

Author(s):
Question: Glucocorticoids compared to placebo or usual care for critically ill pediatric patient with COVID 19
Setting: Hospital (General ward and ICU)
Bibliography: WHO Rapid Evidence Appraisal for COVID-19 Therapies (REACT) Working Group, et al. Association Between Administration of Systemic Corticosteroids and Mortality Among Critically ill Patients With COVID-19: A Meta-analysis. JAMA. 2020.

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Glucocorticoids	placebo or usual care	Relative (95% CI)	Absolute (95% CI)		
Mortality												
7	randomised trials	not serious	not serious	serious [a]	not serious	none	222/678 (32.7%)	425/1025 (41.5%)	**OR 0.70** (0.48 to 1.01)	**83 fewer per 1,000** (from 161 fewer to 2 more)	⊕⊕⊕◯ MODERATE	CRITICAL

CI: Confidence interval; **OR:** Odds ratio

Explanations

a. Studies were developed in adult patients. One of the studies included a small percentage of pediatric patients

Figure 2. Use of corticosteroids in pediatric patients who are critically ill.

to pediatric patients with COVID-19 infection requiring oxygen or ventilatory support. Decisions should be made on an individual basis, and risk and benefits should be discussed with family members as we continue to wait for better quality of evidence.

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Reply:

I would like to express my appreciation to Dr. Prutsky and Dr. Kamat for their interest in the article, "SARS-CoV-2 Infection in Children: Special Considerations," which was published in the November 2020 issue. They have expressed concern over the statement, "corticosteroids should be avoided unless their use is indicated for another reason" in reference to treatment of children with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The original article was written early in the pandemic with the goal of providing an overview of the ever-evolving pool of information we had available regarding coronavirus disease 2019 (COVID-19) and the pediatric population. At the time, many treatment options were still experimental and there were few data to support the use of any of them in pediatric patients. As time has gone on and we have been able to observe the effects of SARS-CoV-2 and its treatments in both adult and pediatric patients, it has become clear that corticosteroid use can be quite helpful in the treatment of children who are hospitalized with COVID-19. I agree with the statement that although we do not (and will likely not in the near future) have significant data on treatment options in the pediatric population, we can extrapolate from adult studies and similar pediatric diseases and consider the safety profile of different treatment options, with corticosteroid use being one of those options. Data that are available now suggest that corticosteroids are an important tool for the treatment of COVID-19 and are a reasonable option in the pediatric population.

Again, I thank Dr. Prutsky and Dr. Kamat for their input and agree with their update to the article.

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