Medicine by the Numbers

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Corticosteroids for the Treatment of Kawasaki Disease in Children

Robert A. Beck, MD, and Sara Spiva, DO

Details for This Review

Study Population: Children younger than 19 years diagnosed with Kawasaki disease (KD)

Efficacy End Points: The primary intervention outcome was any coronary artery abnormality found on cardiac angiography or echocardiography within three months of a KD diagnosis; abnormalities were defined by de Zorzi criteria (coronary lumen dimension 2.5 standard deviations or more above the mean for body surface area) or specified Japanese Ministry of Health criteria based on the patient's age and lumen diameter; secondary treatment outcomes included fever duration, length of hospitalization, and mortality

Harm End Points: Any serious adverse event attributable to the administration of corticosteroids

Narrative: KD (i.e., mucocutaneous syndrome) is a multisystem vasculitis that may be related to an abnormal host response to an infection.[1] Although KD is the leading cause of childhood-acquired heart disease in high-income countries, the incidence in children younger than five years varies, with 20.8 per 100,000 in the United States and 239.6 per 100,000 in Japan. Because there is no diagnostic test for KD, the diagnosis is based on clinical features or symptoms defined by the American Heart Association or the Japan KD Research Committee guidelines. Determining a diagnosis is challenging because clinical symptoms of KD are prevalent in common childhood viral illnesses (e.g., fever, rash, conjunctivitis, cervical lymphadenopathy).

The most significant complication of KD is a predisposition for coronary artery abnormalities, which can lead to aneurysm formation in up to 25% of untreated patients.[2] Prompt treatment decreases coronary complications. The mainstay of initial treatment is intravenous immune globulin and aspirin. Intravenous corticosteroids have been recommended for patients at high risk (e.g., history of cardiac abnormalities, diagnosis before 12 months of age, clinical features of shock) or if the initial treatment regimen fails (up to 20% of patients), although data are limited.

The Cochrane review analyzed eight randomized trials with 1,877 children (younger than 19 years) worldwide diagnosed with KD.[1] All forms of corticosteroids in conjunction with any combination of placebo, no treatment, intravenous immune globulin, aspirin, or infliximab were studied. Comparators included monotherapy or a combination of the previously mentioned interventions. Corticosteroid administration was broadly grouped into a single pulsed dose of intravenous methylprednisolone or a longer tapering course of oral prednisolone.

Moderate-quality evidence showed that when compared with no corticosteroid use, corticosteroids administered in the acute phase of KD reduced coronary artery abnormalities over a two- to six-week follow-up period (odds ratio = 0.32; 95% CI, 0.14 to 0.75); absolute risk difference = 10.7%; number needed to

THE NUMBERS

Benefits	Harms
1 in 10 patients were helped (reduction in coronary artery abnormalities)	No reported harms with corticosteroid use

The NNT Group Rating System

Green	Benefits greater than harms
Yellow	Unclear benefits
Red	No benefits
Black	Harms greater than benefits

treat = 10). There were no reported serious adverse events in the included studies.

Moderate-certainty evidence demonstrated a reduction in the length of hospital stay (mean difference = –1.01 days), and low-certainty evidence demonstrated a decrease in fever duration (mean difference = –1.34 days) in patients treated with corticosteroids compared with no corticosteroids. There were no deaths reported in the included studies.

Caveats: The Cochrane review considered trials involving children diagnosed with KD worldwide. Four of the eight trials had an unclear risk of selection bias, seven had an unclear risk of performance bias, four had an unclear risk of detection bias, and one had an unclear risk of attrition bias.

A subgroup analysis revealed that corticosteroids used as first-line therapy led to a reduction in coronary artery abnormalities, but this effect was not found in a subgroup analysis of corticosteroids used as second-line therapy (e.g., after the failure of intravenous immune globulin and aspirin).

Six of the eight included trials were performed in Japan or South China. The two North American studies involved children at lower risk and used single-dose corticosteroid regimens, limiting the overall applicability in the United States.

The subgroup analyses performed in the systematic review provided limited information because of the small sample sizes. Studies did not include long-term data involving outcomes more than one year after KD diagnosis. Larger studies are needed to target patient-centered outcomes such as mortality. The studies need to provide longer follow-up periods to properly assess the benefits and harms of this intervention.

Conclusion: A color recommendation of green (benefits greater than harms) was assigned for corticosteroid treatment in the acute phase of KD because of the promising moderate-certainty evidence supporting this intervention and possibly limited adverse events.

This series is coordinated by Christopher W. Bunt, MD, *AFP* assistant medical editor, and the NNT Group.

A collection of Medicine by the Numbers published in *AFP* is available at https://www.aafp.org/afp/mbtn.

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