

## Combo therapy may prevent blood vessel complications in children with Kawasaki disease

19 August 2020



Heart illustration with magnification of the artery. Credit: copyright American Heart Association

Adding corticosteroids to standard intravenous (IV) immunoglobulin treatment for children with Kawasaki disease judged to be at higher risk of developing blood vessel complications made initial treatment more successful and prevented these complications, according to new research published today in the *Journal of the American Heart Association*, an open access journal of the American Heart Association.

"Early diagnosis and prompt treatment are important for children with Kawasaki disease to prevent the development of cardiac complications," said lead author Ryusuke Ae, M.D., Ph.D., an assistant professor in the department of public health at the Center for Community Medicine at Jichi Medical University in Shimotsuke, Japan. The study was conducted during 2018-2019 when Dr. Ae was a guest researcher at the U.S. Centers for Disease Control and Prevention (CDC) and is a collaboration between the CDC and Jichi Medical

University.

Kawasaki disease, which occurs most often in children younger than 5 years old, causes inflammation of the blood vessels, particularly the coronary arteries that supply fresh blood to the heart muscle. In developed countries, Kawasaki disease is a leading cause of heart disease in children born without heart defects and the cause is unknown. The criteria for diagnosis is when a child has a fever for five days or longer (unless interrupted by treatment) along with multiple other defining symptoms that can include a rash over the abdomen, swollen and red hands and feet, bloodshot eyes, swollen lymph glands, and redness and swelling of the mouth, lips, throat and tongue. Kawasaki disease occurs in children of all races and ethnicities: however, it is more common among Asian children regardless of where they live.

"As the blood vessel wall becomes enlarged, the inside of the vessel may narrow. Blood clots may form, blocking the artery and potentially leading to a heart attack. Children who have such vessel wall complications may require long-term follow-up after the onset of Kawasaki disease," said Ae.

Standard treatment for Kawasaki disease includes IV immunoglobulin with aspirin. However, for an estimated 17% of Kawasaki disease patients, initial IV immunoglobulin treatment is not effective, increasing their risk of cardiac complications. In recent years, it has become more common to add corticosteroids to the <u>initial treatment</u> approach; however, researchers have reached different conclusions about which approach is best.

In this study, the largest of its kind to-date, researchers analyzed real-world data on children with Kawasaki disease in Japan to determine whether the more intensive combination approach



could heal children faster and prevent cardiac complications among those considered more vulnerable to treatment failure and long-term complications. In this study, patients were deemed at higher risk if initial treatment was predicted to be ineffective based on standing scoring systems, if the child was less than one year old or had elevated blood test results.

Researchers identified 1,593 Kawasaki disease patients under the age of 18 who were first treated with standard IV immunoglobulin with aspirin. Outcomes were compared with another set of 1,593 Kawasaki disease patients who were likely to have been initially treated with corticosteroids in combination with the standard therapy. Patients were matched for age, sex and how quickly treatment was started after symptoms appeared, with care taken to account for other factors that could bias results.

Compared with standard IV immunoglobulin treatment, the researchers found:

- Initial combination treatment (immunoglobulin plus aspirin and corticosteroids) reduced the need for a second course of therapy by 35%.
- Initial combination treatment reduced the risk of <u>coronary artery</u> abnormalities by 47%.
- Delivering a low-dosage of corticosteroids over many days was more beneficial than a high-dose pulse over fewer days or typically just one day.

"It was surprising to see the dramatic results of our analysis. Clinicians should consider initial combination treatment with multiple-dose corticosteroids for high-risk Kawasaki disease patients," Ae said.

Limitations of the study included that researchers did not have precise information on the type, dose and duration of corticosteroid therapy because of the way initial data was recorded.

The same combination treatment of immunoglobulin and corticosteroids has been recently used to treat children with multisystem inflammatory syndrome (MIS-C), a new condition associated with COVID-19 infection that has some symptoms like Kawasaki <u>disease</u>. While MIS-C is seen in <u>children</u> with COVID-19, it is rare.

**More information:** Ryusuke Ae et al, Corticosteroids Added to Initial Intravenous Immunoglobulin Treatment for the Prevention of Coronary Artery Abnormalities in High?Risk Patients With Kawasaki Disease, *Journal of the American Heart Association* (2020). DOI: 10.1161/JAHA.119.015308

Provided by American Heart Association



APA citation: Combo therapy may prevent blood vessel complications in children with Kawasaki disease (2020, August 19) retrieved 3 December 2022 from <u>https://medicalxpress.com/news/2020-08-combo-therapy-blood-vessel-complications.html</u>

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