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Opinion Article

Kawasaki Disease in Children

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STUDY DESCRIPTION

Kawasaki Disease (KD), a systemic vasculitis first reported by Dr. Kawasaki in 1974 in English from Japan, mainly affects children less than 5 years old worldwide. Notably, Asia, Japan, Korea and Taiwan have the highest KD incidence worldwide. In 2010 alone, KD incidence ranged from 239.6/1000,000 to 264/100,000 in children less than 5 years old [1,2]. At present, Intravenous Immunoglobulin (IVIG) is the standard treatment for KD, and has been shown it lower the risk of Coronary Artery Aneurysm (CAA) from 3 to 5% [3]. However, studies have shown that 10-15% of KD patients exhibit persistent fever despite high dose IVIG treatment (2 g/kg). Moreover, they do not respond to IVIG, while children with IVIG non-response were found to have significantly higher incidence of Coronary Artery Lesions (CALs) than those who responded to IVIG [4]. Between 3 and 4% of children with KD fail to respond to IVIG after initial treatment failure [5]. In the past, IVIG non-responsive KD was also known as refractory KD, but with the increasing number of cases of treatment failure of KD, refractory KD tended to be separated from the definition of IVIG non-responsive KD. Previous studies have reported persistence or recurrence of fever (≥ 38.0°C), at least 36 hours after the last of more than 2 doses of IVIG therapy and high-dose aspirin, condition known as refractory KD [6].

Kawasaki Disease, also called mucocutaneous lymph node syndrome, is one of the most common vasculitides in children. Typically, this self-limited condition manifests as fever and acute inflammation that last for an average of 12 days without therapy. High doses IVIG have shown efficacy in suppressing inflammation and reducing prevalence of coronary artery abnormalities when administered during early stages of KD development.

In the present study, about 1.6% of children with KD still exhibited fever even after two IVIG treatments, which was lower than the 3-4% reported in previous studies. These children are at a high risk of developing coronary artery disease and long-term sequelae. Previous studies have shown that the main risk factors for KD coronary artery disease are C-reactive protein, duration of fever and time course of gamma globulin use.

Laboratory test data revealed that they had elevated levels of white blood cells, C-reactive protein, and erythrocyte sedimentation rate, suggesting that children with refractory KD not only have severe inflammatory reactions, but also exhibited thrombocytosis, hypoalbuminemia, and anemia [6].

At present, no unified standard for treatment of refractory KD has been developed. In fact, the choice of medicine is based on efficacious drugs against other vasculitis, including glucocorticoids, TNF inhibitors, other immunosuppressants, and plasma exchange. The use of glucocorticoids for treatment of Kawasaki disease remains controversial, although they are generally used as a remedy for IVIG resistance. Functionally glucocorticoids suppress KD-induced inflammations by inhibiting production of inflammatory mediators, inhibiting migration of white blood cells and reducing capillary permeability. To date, several glucocorticoid treatment options for children with refractory KD have been suggested, including high-dose methylprednisolone sodium succinate (30 mg/kg.d) intravenous pulse therapy for up to 3 days.

In Japan, intravenous or oral administration of prednisolone (1-2 mg/kg.d) for at least 15 days has been reported. Numerous studies have reported the use of infliximab for treatment of refractory Kawasaki disease.

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