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REVIEW PAPER

Consensus Committee of experts on Kawasaki Disease and *Chinese Journal of Contemporary Pediatrics* – the expert consensuses on intravenous immunoglobulin, aspirin, and glucocorticoid

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ABSTRACT

Introduction and aim. Kawasaki disease (KD) is an acute vasculitis with unknown etiology, usually occurring in children under 5 years old. This article will summarize the three consensuses formulated in China about KD.

Material and methods. English databases for consensus search include UpToDate, BMJ Clinical Evidence, National Guideline Clearinghouse, Joanna Briggs Institute Library, Cochrane Library, and PubMed, etc.; Chinese databases include China Biomedical Literature Service, China Knowledge Network, Wanfang database, etc. All literature searches ended on February 28, 2022.

Analysis of the literature. KD is a common acquired heart disease in children and can lead to severe complications such as coronary injury. However, intravenous immunoglobulin (IVIG) combined with oral aspirin (Asp) is currently recognized as the most effective treatment in KD acute stage and the first-line treatment to prevent cardiovascular complications. Glucocorticoid (GC) is mainly used for KD patients with a high risk of coronary artery aneurysm (CAA), no immunoglobulin response, and confirmed CAA. There are already consensus guidelines on diagnosing and treating KD in different countries. This article summarizes the relevant expert consensus on aspirin, glucocorticoids and IVIG for the treatment of Kawasaki disease in China.

Conclusion. Still, there are inconsistent opinions in the literature on the mechanism, optimal timing, and dosage of medication for KD.

Keywords. aspirin, children, glucocorticoid, intravenous immunoglobulin, Kawasaki disease

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The list of abbreviations

Asp – aspirin, **CAA** – coronary artery aneurysm, **CAL** – coronary artery lesion, **Fc** – fragment crystallizable, **GC** – glucocorticoid, **GRADE** – grading of recommendations assessment, development, and evaluation of evidence, **IVIG** – intravenous immunoglobulin, **KDSS** – Kawasaki disease shock syndrome, **MAS** – macrophage activation syndrome, **KD** – Kawasaki disease

Introduction

Kawasaki disease (KD), also known as cutaneous mucosal lymph node syndrome, is a common febrile disorder in children, commonly seen in children under 5. The main pathological feature is systemic vasculitis, and the clinical features include terminal changes in the extremities, bilateral bulbar conjunctival congestion, lip and oral changes, non-purulent enlargement of the cervical lymph nodes, and fever. KD is mainly complicated by damage to the cardiovascular system, such as coronary artery dilation and thrombosis. In addition, KD can also cause multi-system complications such as pulmonary nodules, arthritis, hepatitis, urethritis, Kawasaki disease shock syndrome (KDSS), etc.[1-2]

The prevalence of KD varies widely among countries. The prevalence of KD is 10-30 times higher in East Asian countries, including Japan, Korea, and China than in the United States or Europe, and the prevalence is increasing year by year.[3] In 2015, the prevalence of KD among children under five years old was 19.1/100,000 in the United States and 19.6/100,000 in Canada in 2014.[4] The countries of Japan, Korea, and China have the highest KD prevalence rates in the world (>50/100,000 among children under five years old) and are increasing gradually.[5-7] Japan is reported to have the highest KD mortality rate in the world, estimated at approximately 264/100,000 deaths in children under five years old; the recurrence rate of KD is 3.5%, the mortality rate is <0.02% and 17.0% of children develop resistance to IVIG.[7] In China, the incidence of KD is on the rise, with a prevalence of approximately 7.06-55.1/100,000 children <5 years of age, and in Taiwan was 82.8/100,000 in 2010.[8-10] Hong Kong has the highest prevalence of KD in China (74/100,000 among children <5 years of age).[11]

Epidemiological studies in some regions of China have shown that the incidence of KD combined with coronary artery lesion (CAL) is as high as 15.9%, and the incidence of combined coronary artery aneurysm (CAA) is 1.8%.[12] Standardized treatment with intravenous immunoglobulin (IVIG) can reduce the risk of CAL occurrence from 15–20% to 3–5%.[13,14] Medications are currently the main treatment options for KD and its complications, among which the preferred treatment option IVIG combined with aspirin (Asp) has been widely used, and GC is used as a complementary treatment for IVIG non-response and KD combined with CAA.

Current studies suggest that KD pathogenesis may involve pathogenic infections, environmental factors, immune dysregulation, and genetic predisposition. However, definitive conclusions are still deficient, making individualized treatment for different etiologies particularly important.[15,16] Studies on the dosage, duration, and timing of drug treatment for KD have been inconsistently reported in many countries.2021 The KD Treatment Center in Shaanxi, China, the Shaanxi Clinical Medical Research Center for Pediatric Internal Diseases, the Children's Hospital of Shaanxi Provincial People's Hospital, the Pediatric Capacity Building Committee of the National Society for Research on Maternal and Child Health, and the General Pediatrics (General Practice) Group of the Pediatricians Branch of the Chinese Medical Association, formed a KD expert group, including more than 100 scholars. Through several online video conferences, they discussed the mechanism, treatment dose, course, optimal timing, and safety of IVIG, Asp, and GC for KD. Finally, they formed three consensuses, all published in the Chinese Journal of Contemporary Pediatrics.[17-19] The consensus aims to provide a basis for the standardized clinical management of KD in China, ultimately achieving effective prevention of complications and sequelae in children with KD and reducing the risk of cardiovascular events and death in children with KD.[20,21]

Aim

This article will summarize the three consensuses formulated in China about KD.

Material and methods

These consensuses apply to children under 18 years old with all types of initial and retreatment KD, except those with a history of allergy to IVIG, GC, or Asp or with drug contraindications.[17] The population of use includes all pediatric rheumatologists, pediatric cardiovascular physicians, and general practitioners. All these consensus items have been registered on the International Practice Guideline Registrable Platform (http://www.guidelines-registry.cn) under the registration numbers IPGRP-2021CN183, IPGRP-2021CN183, and IPGRP-2021CN321, respectively.

English databases for consensus search include UpToDate, BMJ Clinical Evidence, National Guideline Clearinghouse, Joanna Briggs Institute Library, Cochrane Library, and PubMed, etc.; Chinese databases include China Biomedical Literature Service, China Knowledge Network, Wanfang database, etc. All literature searches ended on February 28, 2022. Nearly 200 papers were finally included, including seven guidelines, nine expert consensus and standards, 2 BMJ Best Practices, 12 UpToDate, 41 Meta-analyses and systematic reviews, 18 randomized controlled trials, and 102 observational studies.

The development of these consensuses is based on the current research progress and relevant research data on the medication of KD in children, as well as concerning domestic and international guidelines and experience in diagnosing and treating KD, and was developed after many discussions. The consensus follows the following principles:

(1) Participation of professionals from multiple centers, including pediatric specialty physicians, pediatric cardiovascular physicians, and experts in evidence-based medicine.

(2) Adopting the Grading of Recommendations Assessment, Development, and evaluation method, GRADE while guided by the GRADE manual, the recommendation level of a specific clinical issue in this consensus is determined based on the credibility level of the literature or data (guideline recommendation intensity are shown in Table 1, grade quality of evidence and strength of recommendation are shown in Table 2).[22]

Table 1. Guideline recommendation intensity

Grade	Content
Strongly recommended (1)	Effective measures that are clinically accepted and supported by curative cases
Weak recommendation (2)	Treatment with conflicting effectiveness and usefulness

Table 2. Grading quality of evidence and strength of recommendations in clinical practice guidelines[22]

Rank	Explanation	Examples
High	Further research is improbable to change our confidence in estimating the effect.	Randomized trials without severe limitations Well-performed observational studies with substantial effects (or other qualifying factors)
Moderate	Further research will likely significantly impact our confidence in the effect estimate and may change the assessment.	Randomized trials with severe limitations Well-performed observational studies yielding significant effects
Low	Further research will likely significantly impact our confidence in the effect estimate and may change the assessment.	Randomized trials with severe limitations Observational studies without particular strengths or significant limitations
Very low	Any estimate of the effect is very uncertain	Randomized trials with severe limitations and inconsistent results Observational studies with severe limitations Unsystematic clinical observations (e.g., case series or case reports)

Analysis of the literature

Chinese expert consensus on IVIG for KD

Mechanism of IVIG for the treatment of KD

The main objectives of treatment in the acute phase of KD are to control and terminate the inflammatory response, reduce the incidence of CAA, and prevent coronary thrombosis.[23] IVIG is an immunoglobulin preparation isolated from the blood of healthy people, of which IgG is the most abundant immunoglobulin, accounting for more than 95%. The IgG molecule is hydrolyzed to obtain a Fragment crystallizable (Fc); IgG Fc can bind to harmful complement components in the body and block their deposition in target tissues, thus avoiding immune damage, while IgG Fc can bind to Fc receptors and regulate immune function by activating intrinsic immunity.[24,25] Although the therapeutic regimen of IVIG applied to Kawasaki disease has been gradually refined and matured, its specific mechanism has not been elucidated in detail, and it is currently believed that IVIG treatment of Kawasaki disease may be through the following pathways:

(1) Modulates macrophage activity by inhibiting autoantibodies that bind to Fc receptors; inhibits endothelial cell activation, adhesion molecule expression, and secretion of soluble mediators; neutralizes antibodies to cytokines, chemokines, and activated complement proteins that activate inhibitory Fc receptors on macrophages; and blocks the transport of adhesion molecules critical for inflammatory cells to vascular endothelial cells; produces anti-liposomes to reduce inflammation and attenuate endothelial cell injury.[26]

(2) Immunoglobulins stimulate an adaptive immune response that can bind to bacteria or viruses and their toxins, and interact with unique type determinant clusters on pathogenic autoantibodies (and autoantibody-producing B cells), allowing direct neutralization of pathogens and thus their clearance; IVIG may also affect the number and function of regulatory T cells that help control inflammation.[27]

(3) IVIG can also bind to the Fc receptor. Still, the Fc receptor is not directly involved in regulating immune cell activation, but acts as a protective receptor by preventing the catabolism of immunoglobulins.

(4) Analysis of serum cytokine levels in children with Kawasaki disease treated with IVIG revealed that the levels of interferons-γ and IL-10 decreased rapidly. In contrast, IVIG treatment enhanced the Treg transcription factor FoxP3 expression. In IVIG, IgG monomers accounted for more than 95%, with the remainder being dimeric or multimeric IgG. Clinically, large doses of IVIG are often more effective in treatment, suggesting a better anti-inflammatory effect of IgG dimers or multimers. The specific mechanism is unclear, and it is speculated that the IgG dimer structure may enhance the binding ability of Fc to Fc receptors, thus effectively inhibiting the activation of intrinsic immune cells and reducing autoimmune damage.[28]

Summary of expert consensus recommendations for IVIG

Application in Kawasaki disease

The recommendations of IVIG for the treatment of KD are shown in Table 3.

Table 3. The recommendations of IVIG for the treatment of KD

Items	Recommendations	Recommendation strength and evidence level
Timing of IVIG application	1. The best time is 5-10 d after the onset of the disease, and the best within 7 d	1A
	2. The use within 5 d after onset may lead to an increased incidence of IVIG resistance (1B); in severe cases, such as combined hypertension, shock, hemodynamically unstable myocarditis, paralytic intestinal obstruction, etc., should still be applied promptly (1A)	1B; 1A
	3. Children with an onset of more than 10 d, excluding other causes of persistent fever with elevated ESR or CRP or elevated inflammatory markers combined with CAL, still need to be treated with sub-IVIG	2B
IVIG application dose and rate	A single dose of IVIG (2g/kg) is usually administered intravenously by drip over 12-24 hours.The recommended initial infusion rate is 0.01mL/(kg.min) [5% IVIG 30mg/(kg.h)] for 15-30min, then increase the dose to 0.02mL/(kg.min), if well tolerated, adjust to 0.04mL/(kg.min), and finally adjust to the maximum rate of 0.08mL/(kg.min)	1B
IVIG application protocol	1. Complete Kawasaki disease, incomplete Kawasaki disease, recurrent Kawasaki disease: IVIG dose is 2g/kg, single intravenous infusion in 12~24h, with oral aspirin	1A
	2. Non-responsive Kawasaki disease (IVIG-resistant Kawasaki disease): early reapplication of IVIG at a dose of 2g/kg, single intravenous infusion over 12 to 24h is recommended. For those who still have a fever, glucocorticoids can be used in combination with IVIG	1B
IVIG application safety	1. Infants and children with fluid restriction need to avoid low-concentration preparations	1A
	2. Infants and children with cardiovascular disease should be careful to avoid IVIG with high sodium content	1B
	3. Preparations using maltose or glucose as stabilizers are not recommended for use in patients with diabetes and risk of renal injury	1B
	4. Amino acid-containing preparations need to be used with caution in patients with specific genetic metabolic abnormalities	2A
IVIG adverse reaction management	1. Headache is a common adverse reaction, usually occurring during or 2-3d after infusion, and mild cases can be treated with NSAIDs for pain relief	1A
	2. Transient asymptomatic neutropenia after IVIG treatment usually occurs 2-4 d after infusion and recovers within two weeks; generally, no treatment is needed, but some scholars believe that glucocorticoids can prevent it	2B
	3. IgG subclass deficiency and high IgM syndrome are not contraindications to IVIG. For patients with severe allergic reactions, anti-IgA antibodies can be detected, and if the anti-IgA antibody titer is high (>1/1000), 1gG replacement therapy should be applied with caution.	2A
	4. Renal impairment is firstly manifested by elevated blood urea nitrogen or creatinine, followed by oliguria and renal failure, which peaks 5-7 d after high-dose infusion. In patients with existing renal impairment, IVIG should be infused slowly and hydrated appropriately, and IVIG products containing sucrose should be avoided	1B
	5. The estimated incidence of thrombotic events ranges from 1% to 16.9%, with risk factors including first high-dose IVIG, previous/current thrombosis, previous atherosclerotic disease, hyperviscosity syndrome, hereditary hypercoagulability, rapid infusion rate, pre-hydration, a rate less than 50 mg/(kg. h), hypotonic IVIG products (3% to 6%) and prophylactic use of aspirin or Low-molecular-weight heparin and other measures to reduce the incidence of thrombosis in high-risk patients, and patients with thrombotic complications need to receive antithrombotic therapy	2B

Chinese expert consensus on Asp for KD

Mechanism of Asp for the treatment of KD

Asp can act on the hypothalamic thermoregulation center and cause peripheral vascular dilation, increasing skin blood flow, sweating, heat dissipation, and other cooling effects in children. In addition, Asp can cause the acetylation of serine at position 530 of a polypeptide chain, the active site of cyc-1 in children, to completely inactivate cyc-1, block the conversion of arachidonic acid to thromboxane A_2 and achieve the effect of anti-platelet aggregation, to effectively avoid embolism in children and affect blood pressure circulation. Therefore, Asp in treating KD children will play a role in antipyretic analgesia and preventing thrombosis.[16,29]

Summary of expert consensus recommendations for Asp application in KD

The recommendations of Asp for the treatment of KD are shown in Table 4.

Chinese expert consensus on GC for KD

Mechanism of GC for the treatment of KD

Vascular endothelial injury is a critical link in the pathogenesis of KD. Neutrophils, $CD8^+$ T lymphocytes, and mononuclear macrophages accumulate in the coronary artery mesothelium during the acute phase of KD, causing vascular endothelial injury is a critical link in the pathogenesis of KD. Disruption of the vascular barrier releases cytokines and adhesion molecules that diffuse into the vessel wall, leading to vessel wall edema, elastic fiber fracture, and destruction of the flexible layer, causing vascular remodeling and coronary artery dilation or CAA. GC can reduce the transcription of inflammatory mediators and decrease fever and inflammation in KD patients, thus reducing the incidence of coronary artery damage and future cardiovascular sequelae.[37,38]

Indications for GC application for KD

Indications for GC application for KD include the following :

(1) IVIG unresponsive KD remedial therapy;

(2) Children with combined CAA with persistently elevated inflammatory markers;

(3) KDSS;

(4) KD combined with macrophage activation syndrome (MAS);

(5) Children at high risk of IVIG unresponsiveness, including those with an age of onset less than 0.5 years, high levels of inflammatory markers, and a Kobayashi

Table 4. The recommendations of Asp for the treatment of KD

Items	Recommendations	Recommendation strength and level of evidence
Asp suitable dosage form	1. Enteric-coated tablets or enteric-coated capsules are recommended for long-term use (swallowed whole)	1A
	2. Infant preferred drops and syrup agent, 2~5 years old can use solution agent, syrup agent, suspension agent, foaming agent, etc	1B
	3. Effervescent tablets are convenient for precise dosage and easy to take (but there are problems such as preservation and waste when taking them at different times)	2B
Asp dose and course of treatment	1. In the acute stage of KD children, as was given 30~50mg/(kg.d) orally 2~3 times and changed to 3 5mg/(kg.d) in 48-72h or 14 days after the onset of fever, and maintained in one dose.[30-33] Continued oral administration for 6-8 weeks; children with CAL need normal oral coronary arteries.	1A
	2. Children with undiagnosed KD and atypical KD before IVIG can usually receive Asp 3~5mg/(kg.d) in one dose at a time for 6~8 weeks.	2A
	3. Children with CAL must take it orally until their coronary arteries are normal.	2B
Application of Asp in KDSS	According to the dosage and usage of Asp in KD treatment.	2A
Asp adverse reactions and prevention	Common adverse reactions include nasal bleeding, gastrointestinal bleeding, gastrointestinal ulcer, subcutaneous bleeding, intracranial hemorrhage, asthma, liver and kidney failure, rash, loss of appetite, Rehmannia syndrome, tinnitus, hearing loss, toxic epidermal necrolysis/mucosa-ocular syndrome, etc.	1A
	If the above adverse reactions occur, the dose of Asp should be reduced, or the Asp should be discontinued.[34] Gastric mucosal protectants are also recommended during oral Asp treatment.	2A
Precautions for Asp use	1. Contraindication: allergy to Asp, active bleeding, liver, and kidney failure, digestive ulcer and frequent recurrence, hemophilia, other coagulation disorders, etc. 2. Caution: abnormal liver function, minor bleeding of subcutaneous mucosa, transient nosebleed, asthma, glucose-6-phosphate dehydrogenase deficiency, Reay's syndrome, genetic metabolic diseases similar to Reay's syndrome, ASP-related rash, gastrointestinal disorders, etc. 3. Other precautions: If liver transaminase increases in KD subacute or recovery stage, the Asp dose should be reduced and discontinued. As KD's acute phase often appears to be a persistent high fever, clinical use of ibuprofen can reduce fever. Ibuprofen combined with ibuprofen can counteract the irreversible platelet inhibition induced by Asp, so ibuprofen should be avoided for fever reduction in children with CAL, and acetaminophen can be used for fever reduction.[35] In the KD recovery period, it is still recommended that children taking low doses of Asp can be inoculated, but the relevant clinical symptoms need to be strictly observed.[36]	

warning score greater than or equal to 5 (Kobayashi score are shown in Table 5), or children with high-risk KD as judged by the IVIG high-risk warning score at each hospital.[39,40]

Table 5. Kobayashi score of high-risk Kawasaki disease[41]

Indicator	Critical value	Score
Serum sodium levels	≤133 mmol/L	2
Aspartate transaminase	≥100 IU/L	2
Start time of treatment	Day 4 or earlier	2
Percentage of neutrophils	≥80%	2
C-reactive protein	≥ 100mg/L	1
Blood platelet count	≤ 300×10^9/L	1
Age	≤12 months	1

Different kinds and methods of GC are applied to KD

Recommendation: The type of GC treatment for KD patients is methylprednisolone intravenous shock followed by oral prednisone sequential therapy (1A).[38]

Dose and course of GC applied to KD

Kobayashi early warning score suggests first-line treatment for children with IVIG non-responsive KD or persistently elevated inflammatory markers combined with CAA or peripheral vascular tumors inflammatory index

TNF-α is involved in the occurrence and development of KD inflammatory/immune response as a significant pro-inflammatory cytokine. It is positively correlated with CAL, so it has an essential clinical value in the prediction and prognosis evaluation of KD induced.

Table 6. The recommendations of GC for the treatment of KD

Items	Recommendations	Recommendation strength and level of evidence
The dose and course of GC applied to KD	Prednisone [1-2 mg/(kg.d)], taken in the morning, total dose <60 mg/d, or methylprednisolone [1-2 mg/(kg.d)], intravenously, once or twice a day, starting to be reduced when body temperature and CRP return to normal. After 15 days, it gradually decreased [1-2 mg/(kg.d)] for five days. 0.5 to 1 mg/(kg.d) for 5 days. 0.25-0.5 mg/(kg.d), 5 d].	1A
Different kinds and methods of GC are applied to KD	The type of GC treatment for KD patients is methylprednisolone intravenous shock followed by oral prednisone sequential therapy	1A

Recommendation: Prednisone [1-2 mg/(kg.d)], taken in the morning, total dose <60 mg/d or methylprednisolone [1-2 mg/(kg.d)], intravenously, once or twice a day, starting to be reduced when body temperature and CRP return to normal. After 15 days, it gradually decreased [1-2 mg/(kg.d)] for five days. 0.5 to 1 mg/(kg.d) for 5 days, 0.25-0.5 mg/(kg.d), 5 d (1A).[42-46]

Second-line treatment of IVIG non-responsive KD

Optional 2nd dose infusion of IVIG combined with prednisone (methylprednisolone).

Recommendation: Prednisone [1-2 mg/(kg.d)], taken in the morning, total dose <60 mg/d or methylprednisolone [1-2 mg/(kg.d)], intravenous drip, 1-2 times a day,

after body temperature and CRP returned to normal, the dose began to be reduced, and gradually stopped within 15 days [1-2 mg/(kg.d)], five days. 0.5-1 mg/(kg.d) for 5 days. 0.25-0.5 mg/(kg.d), 5 d] (1A).[42-46]

First-line treatment of KDSS

Recommendation: Methylprednisolone 10-30 mg/(kg.d) for 1 to 3 d with 2 to 3 h of each intravenous infusion. Heparin anticoagulation [10 U/(kg.d) of heparin concurrently two h before the start of methylprednisolone] for 24 h is recommended, or low-molecular heparin anticoagulation with coagulation, echocardiography, and blood pressure monitoring (2A).[47-50]

First-line treatment of KD combined with MAS

Recommendation: Methylprednisolone 10-30 mg/(kg.d) for 3 d, with each IV infusion for 2-3 h. Sequential prednisone orally [1-2 mg/(kg.d)] until complete control and remission of MAS with gradual dose reduction and discontinuation (2A)[51-53]

GC is not recommended as routine first-line therapy for KD. GC alone is unsafe and contraindicated as a first-line treatment for KD, as studies have shown that GC alone used as an initial treatment for KD can significantly increase coronary artery damage.[37,54]

Prevention of adverse reactions

During treatment with GC in children with KD, special attention should be paid to the prevention of Cushing's syndrome, infection, thrombosis, osteoporosis, aseptic necrosis of the femoral head, diabetes mellitus, hypertension, hormonal glaucoma, cataract, bradycardia, secondary adrenocortical insufficiency, and growth retardation. To prevent and treat osteoporosis, it is recommended to supplement vitamin D 600-800 U/d and calcium 1000-1200 mg/d while applying GC. Various infections, such as tuberculosis, fungus, and chickenpox, should be entirely excluded before high-dose methylprednisolone shock therapy, and blood pressure and blood glucose should be closely observed and tested to detect any of the above complications in time and deal with them actively. While applying CC, strive to minimize the adverse effects to improve the prognosis of children with KD.

Precautions

(1) Contraindicated: hypersensitivity to GC drugs, epilepsy, fractures, uncontrolled infections (e.g., chickenpox, fungal infections), active tuberculosis, etc.

(2) Caution: Cushing's syndrome, myasthenia gravis, hypertension, diabetes mellitus, intestinal disease or chronic malnutrition, infectious diseases, etc., must be combined with effective antibiotics.

(3) Other precautions: 1. Prevent cross-allergy; those who are allergic to one GC drug may also be allergic to other GCs. 2. When using GC, adopt low sodium, high potassium, high protein diet, supplement calcium, and vitamin D, and add drugs to prevent peptic ulcer and bleeding and other adverse reactions. 3. If there is an infection, antibiotics should be applied simultaneously to prevent the spread and aggravation of the disease. 4. The interaction between GC and other drugs should be noted; for example, excessive potassium loss can be caused when GC is combined with potassium-removing diuretics (e.g., thiazide or tab diuretics), and the incidence of gastrointestinal bleeding and ulcers increases when GC is combined with NSAIDs.[38,42,55-57]

Conclusion

After more than thirty years of clinical validation, concerning half a century of research results on KD, and combined with the treatment experience of hundreds of pediatric KD clinicians and experts in China, these consensuses standardize the use of IVIG, Asp, and GC in pediatric KD medication, which has important clinical significance in effectively reducing the incidence of complications in all systems of KD and preventing cardiovascular sequelae caused by KD. The limitations of consensuses include relatively few high-quality randomized controlled studies, fewer and more foreign references, and insufficient consideration of ethnic differences. Because the pathogenesis of KD is not fully understood, the medication for KD is constantly updated and researched. It is necessary to continuously update the consensus of KD medication according to the latest international studies and supplement the dosage and regimen of other complications in various medicines for myocarditis, acute inflammatory response syndrome, MAS, and other diseases.

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Author contributions

Conceptualization, R.S., X.L. and J.F.; Methodology, R.S. and X.L.; Validation, D.F., W.H. and J.F.; Formal Analysis, D.F.; Investigation, D.F.; Resources, D.Z.; Data Curation, D.Z.; Writing – Original Draft Preparation, D.Z.; Writing – Review & Editing, Y.X.; Supervision, Y.X. and X.L.

Conflicts of interest

The authors declare that the research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

Consent to publish

The authors affirm that the Chinese Journal of Current Pediatrics provided informed consent for the publication of this paper.

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