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RESEARCH ARTICLE

Treatment Strategy for Pediatric Patients with Kawasaki Disease in Tertiary Referral Hospitals East Java Indonesia: A Retrospective Study

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Abstract

Objectives : Giving therapy to pediatric patients with Kawasaki syndrome is crucial in terms of healing and prevention of potential complications. This study aim to analyzed the treatment of pediatric patients with Kawasaki Syndrome at the Tertiary Referral Hospital in East Java, Indonesia. Methodology : This retrospective study involved 16 patients aged ≤ 18 years with a diagnosis of Kawasaki Syndrome in the 2013-2016 time series. Sampling uses a non random sampling technique. Medical record data related to the history of the disease, treatment, and the resulting outcome were analyzed descriptively. Results: Child patients receive treatment therapy in different amounts, types and doses based on the status of the patient and clinical manifestations that appear. The main therapy was given to patients namely acetosal (94%) and IVIG (50%), and corticosteroids ; methylprednisolone, prednisone (44%). Oral acetosal use is 80-100 mg / kg body weight as anti-inflammatory until the fever falls and 3-5 mg / kg body weight as platelet anti-aggregation as long as the patient does not show coronary artery abnormalities within 6 to 8 weeks, the IVIG dose is 2 g / kg weigth, and the dose of methylprednisolone is 10-30 mg / kg for 3 to 10 days. Conclusion: Giving treatment adapts to the patient's needs and is in accordance with the recommended standards.

Keywords: *Treatment strategy, Pediatric, Kawasaki syndrome, Referral hospital.*

Introduction

The case of Kawasaki Syndrome in developing countries is the most common cause of heart disease in children [1]. The incidence increases throughout the world, and varies greatly in different countries and in different ethnic groups [2]. In Indonesia, the development of this disease is estimated to reach 6,000 new cases per year, but most cases have not been clearly diagnosed [3]. Asian children have the highest incidence of Kawasaki Syndrome of all ethnic / racial groups. Siblings and children of Kawasaki syndrome patients are at higher risk [4].

This acute inflammatory disease is associated with vasculitis which occurs most in medium-sized arteries with causes that are not known with certainty [1]. However, there are clinical similarities between Kawasaki Syndrome and other toxin-mediated diseases such as scarlet fever and toxic shock syndrome [5].

Diagnosis of Kawasaki Syndrome requires a high index of suspicion. Infants and children can present with an incomplete clinical picture, but still experience significant coronary artery abnormalities [4]. The profile of drug use in the management of Kawasaki Syndrome needs to be assessed because it is associated with potential complications. Kawasaki Syndrome in the differential diagnosis of each child with fever for 4-5 days and compatible clinical and laboratory features.

Immediate therapy is needed, because delayed or unrecognized Kawasaki Syndrome can cause heart disease or lifelong death in previously healthy children [6]. Kawasaki Syndrome 20-25% develop into coronary artery aneurysm in children who are not properly treated . Other complications of Kawasaki Syndrome are myocarditis, pericarditis with effusion and lesion stenosis

at the end of the aneurysm [7]. In addition, this autoimmune disease is accompanied by systemic inflammation in children and can also cause coronary artery aneurysms, myocardial infarction, and sudden death. Giving therapy in Kawasaki Syndrome cases is a crucial part. Recommendations for initial evaluation, treatment in the acute phase, and long-term management of patients with Kawasaki Syndrome are needed in the management of patients with Kawasaki Syndrome. In addition, in the case and management trip, the final decision for clinical case management must be in accordance with certain conditions presented by each patient [6,9].

Various types of treatment are available in pharmaceutical practices. Immediate treatment with intravenous gammaglobulin and aspirin can save lives. Children who do not have resolution of fever with primary therapy have a higher risk of developing coronary artery abnormalities, and additional anti-inflammatory therapy must be given [4].

Treatment with intravenous immunoglobulin within ten days causes the onset of fever to improve. Clinical results show a reduction in coronary artery dilation to less than 5% given its severe morbidity [2].Treatment of non-respondent gammaglobulin consists of additional intravenous immunoglobulin, methylprednisolone, and or infliximab. Additional data on the pathogenesis of Kawasaki Syndrome are urgently needed to provide other targets for therapy for patients at the highest risk for developing coronary artery abnormalities [8].

Most children with Kawasaki Disease respond to a single dose of 2 grams / kg of intravenous gammaglobulin with oral aspirin, but a small portion requires additional therapy to deal with clinical diseases. The goal of therapy is to prevent or reduce inflammation of the coronary arteries and subsequent coronary artery stenosis from luminal myofibroblastic thrombosis and / or proliferation [4].

In addition to efforts to understand the pattern of Kawasaki Syndrome, efforts to increase the evidence base in acute management need to be done because it is related to children's health for life [1]. The care of patients with Kawasaki Syndrome is very important to optimize the quality of life related to health and it is hoped that the gap in care and diagnosis can be overcome in the future [6]. This study aims to analyze the treatment of pediatric patients with Kawasaki Syndrome in Referral Hospitals in East Java, Indonesia.

Material and Methods

Type of Study

This research was an observational study.

Study Population

Population in this study is patients aged ≤ 18 years with the final diagnosis of Kawasaki Syndrome both with and without complications

Study Approval

This study has been through a review of the Health Research Ethics Committee of Doctor Soetomo Hospital, Surabaya Indonesia and declared "ethical conduct" with Certificate of Ethical Worth No. 87 / Panke. KKE / II / 2017.

Inclusion Criteria and Exclusion Criteria

The research samples were taken by non-random sampling technique with purposive ampling method. Secondary data was obtained through medical health records on 16 pediatric patients who met the inclusion criteria. The data used by the complete medical record in these patients aged ≤ 18 years with the final diagnosis of Kawasaki Syndrome both with and without complications as well as having complete data regarding drug therapy given, history of disease, clinical data, and investigation if indicated.

Data Collection

This research use retrospective data during 3 years. This research is carried out through various stages. The initial stage of the medical record is obtained through hospital approval and medical record officers and is assisted by the recapitulation process. The next step is to examine the types of drugs given to patients, dosage regimens, frequency of drug administration, drug problems, monitoring of drug side effects, complications, and duration of therapy. In addition, a clinical data assessment related to Kawasaki Sydnrome patient clinical signs included blood morphology, erythrocyte sedimentation rate, C-Reactive protein,

serum albumin, white blood cell, urinalysis, sodium level. The discovery of incomplete data was clarified with the hospital. The data obtained are then analyzed descriptively.

Results

From the population obtained a sample of 22 people and those who met the inclusion criteria were 16 pediatric patients. Assessment of patient characteristics through gender, age, nutritional status according to the WHO Child Growth Standard in 2007 and clinical manifestations.

Most Kawasaki Syndrome sufferers are male, age range 1-12 years and good nutritional status. In this finding, there were no patients aged <4 weeks while patients aged 4 weeks-12 months were recorded as 5 patients. Not all patients experience the same clinical manifestations but a number of patients have fever (94%), rash (69%), red lips and rupture (50%), Left Main Coronary Artery (LMCA) and Right Coronary Artery (RCA) (50%), red eyes (44%), strawberry tongue (38%), flaking skin (38%) and lumps in the neck (19%). In addition to these symptoms, other symptoms were found: cough (56%), runny nose (38%), tightness (19%), itching (13%), nausea and vomiting (13%), canker sores (13%) and black bowel movements (6 %). In addition there were comorbidities, namely 2 patients suffering from sepsis, 2 patients with microcytic hypochromic anemia, 1 patient with ODS acute conjunctivitis, hypokalemia, acute kidney injury, urinary tract infection, bronchopneumonia, ascending and descending aortic stenosis. The drug use profile shows that patients make it possible to get several therapies in medical services. Most patients (94%) received Assetosal NSAID therapy to reduce inflammation of the coronary arteries and prevent platelet aggregation.

Half of the patients received IVIG immunoglobulin to reduce coronary artery inflammation in relation to autoimmune (50%). The types of methylprednisolone (38%) and prednisone (6%) corticosteroids are also used for immunosuppressant purposes and reduce coronary artery inflammation. Oral administration of acetosal is categorized into 2 functions, namely anti-inflammatory and anti-aggregation-platelets in Kawasaki Syndrome Patients. Most patients get acetosal as anti-inflammatory and half of the patients get platelet anti-aggregation. 6 patients received anti-inflammatory and anti-aggregation therapy. Oral acetosal use is presented in Table 1.

Table 1: Acetosal administration orally

Initials Patients	Body Weight Dosage	frequency and duration of anti-inflammatory Doses	frequency and duration of anti-aggregation	Number of platelets [g / dL]	
				Early	End
SKA	6.2	4x130 mg/ 6 days	1x35 mg/ 8 days	594,1	
MAA	7.2	4x250 mg/ 6 days	1x75 mg/ 1 days		
BAM	7.5	3x250 mg/ 2 days	1x25 mg/ 1 days	790	156
MZH	8	4x160 mg/ 10 days			
RB	10	4x200 mg/ 9 days			
MAR	12	4x250 mg/ 6 days			
DA	13	4x300 mg/ 5 days			
JNM	14	4x280 mg/ 7 days	1x70 mg/ 3 days	556	
CKL	16.5	4x450 mg/ 9 days	1x50 mg/ 8 days	855	
DRA	18	4x350 mg/ 8 days	1x40 mg/ 1 days	524	
KAPP	18	4x450 mg/ 7 days			
BPA	27	4x500 mg/ 4 days			
KA	21		1x100 mg/ 3 days	395	357
MS	37		1x100 mg/ 10 days	563	

The use of IVIG in Kawasaki Syndrome patients is carried out using a syringe pump for 12 hours with a dose based on body weight which is 2 g / kg body weight. This use is for 8 children namely An. MZH, An. RB, An. JNM, An. MAA, An. BPA, An. MS, An. BAM and An. DRA. In addition to the use of IVIG, corticosteroids are also used in the tapering-off pattern in patients with Kawasaki Syndrome. An SKA (6.2 kg) received methylprednisolone therapy by pulse IV at a dose of 650 mg (H6), PO prednisone 1x13 mg (H10-15) and 1x10 mg (H 16-19). This is due to the condition of the patient with a 0.32 cm LMCA dilatation with pericardial effusion. Corticosteroid doses can differ in Kawasaki Syndrome patients based on body weight. An. CKL (16.5 kg) received 2x62 mg (H5) of Methylprednisolone IV with LMCA and RCA dilatation, cardiac abnormalities (dilated LCMA and RCA) but did not receive IVIG.

The pulse route has a faster effect and is given to patients with cardiac abnormalities that

have the potential to become more severe or not respond to IVIG.

Table 2: Use of corticosteroids

Patient Initials	Drug name Route	Route	Patient Condition	Dosage and Frequency
MFA [8 kg]	Metilprednisolon	Pulse IV	Aneurismatic Dilatation of LMCA and RCA	250 mg [D2-11]
CKL [16,5 kg]	Metilprednisolon	IV	Dilatation of LMCA and RCA	2x62 mg [D5]
				2x16 mg [D6-9]
				2x4 mg [D10-12]
		PO		2x4 mg [D13-14]
DRA [18 kg]	Metilprednisolon	IV	Dilatation of LMCA	3x24 mg [D2-3]
KAPP [18 kg]	Metilprednisolon	Pulse IV	Does not look dilated	1x375 mg [D4-6]
		IV		3x12 mg [D7-9]
MS [37 kg]	Metilprednisolon	IV	Dilatation of LMCA and RCA	3x 8 mg [D7-9]
				3x2 mg [D4]
		PO		3x6 mg [D5-6]
				3x4 mg [D7-10]
				3x2 mg [D11]

Description: The dose of methylprednisolone 10-30 mg / kg weight for a days. Hx shows the provision of x-day Pulse IV given for 30 minutes to 1 hour

Corticosteroid Tapering-off patterns in Kawasaki Syndrome Patients should not be stopped immediately because they can cause steroid withdrawal, therefore the dose is lowered slowly called tapering-off. The tapering-off pattern of corticosteroids in Kawasaki Syndrome patients can be seen in Table 3.

Table 3: Pattern of tapering-off of corticosteroids in Kawasaki Syndrome patients

Patient initial name	Drug name	Route	Dosage and frequency	Patient condition
SKA [6,2 kg]	Metilprednisolon	Pulse IV	650 mg	Fever, strawberry tongue, tightness, cough, runny nose, CHAPTER blackish green, red mouth and broke, Echo peeling skin: 0.32 cm LMCA dilatation with pericardial effusion
	Prenison	PO	1 x 13 mg	
			1 x 13 mg	
			1 x 13 mg	
			1 x 13 mg	
			1 x 13 mg	
			1 x 13 mg	
			1x10 mg	
			1x10 mg	
			1x10 mg	
			1x10 mg	
CKL [16.5 kg]	Metilprednisolon	IV	2x62 mg	Fever, cough, swelling left neck, red eyes, broken lips, nausea & vomiting, runny nose, Strawberry tongue Dilated LMCA and RCA
			2x16 mg	
			2x16 mg	
			2x16 mg	
			2x4 mg	
			2x4 mg	
			2x4 mg	
		PO	2x4 mg	
			2x4 mg	
			2x4 mg	
			2x4 mg	
KAPP [18 kg]	Metilprednisolon	Pulse	1x375 mg	Fever, red lips and ruptured, swollen left neck, peeling skin Does not look dilated
			1x375 mg	
			1x375 mg	
		IV	3x12 mg	
			1x375 mg	
			1x375 mg	
MS [37 kg]	Metilprednisolon	IV	3x8 mg	Fever, rash, itching, skin peel off Dilated LMCA and RCA
			3x8 mg	
			3x8 mg	
			3x2 mg	
		PO	3x6 mg	
			3x6 mg	
			3x4 mg	
			3x4 mg	
			3x4 mg	
			3x4 mg	
			3x2 mg	

Therapy in Kawasaki Syndrome patients is one of them is the use of acetosal and corticosteroids which have side effects on the gastrointestinal tract such as gastritis and intestinal bleeding, to reduce the risk of side effects on the use of acetosal andcorticosteroids are given H2-receptor antagonists and those used are ranitidine and antacids.

Almost all use of Ranitidine in IV method with certain doses, except for use in 1 child with IV and oral doses. SKA (6.2 kg) receives 2 doses of 2x10 mg and 2x6 mg intravenously. MZH (8 kg) and RB (10 kg) received a dose of 2x10 mg / IV. JNM (14 kg) received 2x15 mg / IV. DRA (18 kg) and KAPP (18 kg) received different doses even though the weight was the same ie 2x20 mg and 2x18 mg.

BPA (27 kg) gets 2x30 mg / IV and is oral. Antacids were also used in addition to ranitidine in 2 children, RB (10 kg) received antacids orally 4x1 cth and MS (37 kg) PO 3x 1 tablet. Effective Kawasaki Syndrome therapy must address existing clinical manifestations as well as factors that can cause comorbid disease to appear and overcome physiological changes that occur.

Other therapies needed by Kawasaki Syndrome patients are adjusted to the patient's condition. Some patients get antipyretics with different doses as follows; RB (10 kg) 3x100 mg / PO / 9 days, MZH (8 kg) 3x80 mg / PO / 7 days, JNM (14 kg) 4x150 mg / PO / 10 days, BPA (27 kg) 3x270 mg / PO / 9 days. DA (13 kg) 3x140 mg / PO / 2 days. BAM (7.5 kg) 3x50 mg / PO / 6 days.

KMA (10.5 kg) 3x105 mg / PO / 6 days. SKA (6.2 kg) 3x70 mg / PO / 19 days CKL (16.5 kg) 4 x 165 mg / PO / 17 days. DRA (18 kg) 4x180 mg / PO / 8 days. KAPP (18 kg) 3x80 mg / PO / 9 days. One patient received paracetamol with 3 different doses, namely MFA (8 kg) obtained 3 doses of paracetamol namely 80 mg / IV / 1 day, 4x80 mg / PO / 5 days and 4x 100 mg / PO / 5 days, MS (37 kg), DRA (18 kg) and MAR (12 kg) does not get antipyretics.

Antibiotics are also used in most patients. 5 children namely RB (10 kg), MZH (8 kg), JNM (14 kg), MS (37 kg) and DRA (18 kg) received different doses of Cloxacillin, both oral and intravenous, including RB 2x250 / IV / 12 days, MZH 2x120 / IV / 9 days and PO / 1 days, JNM 2x225 / IV / 6 days and PO / 4 days, 4x 4x mg / IV / 3 days and PO / 4 days and DRA 3x 250 mg / IV / 7 days.

Ampiciliin is used by 4 children, namely BPA (27 kg) 4x700 mg / IV / 8 days, SKA (6.2 kg) 4x300 mg / IV / 12 days and 4x500 mg / IV / 7 days, MFA (8 kg) 4x200 mg / IV / 11 days and CKL (16.5 kg) 4x450 mg / IV / 12 days. SKA obtained 3 types of antibiotics, Ampiciliin and 2 other types, namely Gentamicin 1x50 mg loading dose 1x40 mg / IV / 12 days and Kotrimoksasol 2x25 mg / PO / 7 days. Besides Ampicillin, MFA received Gentamicin therapy 1x50 mg / IV / 10 days. Ceftriaxon is used by 2 children with different doses, namely KAPP (18kg) 2x1 g / IV / 8 days and MAR (12 kg) 2x600 mg / IV / 8 days. DA (13 kg), BAM (7.5 kg) and KMA does not get antibiotics.

Some children getting other drugs included giving Ambroxol a dose of 3x6.5 mg / PO / 1days at RB (10 kg) and an dose of An. CKL (16.5 kg) 3x5 mg / PO / 9 days. Ezerra doses 4x sedays / tropical / 1 day on JNM (14 kg). Ventolin is given to SKA (6.2 kg) and An, MS (37 kg) at a dose of 0.6 cc / nebulizer / 1 day in SKA and 1cc / nebulizer / 1 day in MS. Furosemide is given to SKA (6.2 kg) 1x6 mg / IV / 1 day and MAR (12 kg) at a dose of 12 mg / IV / 5 days. MFA (8 kg) obtained metamizole 1x80 mg / IV / 5 days and onsdansetron 1x1 mg / IV / 2 days. Transfusion of albumin 1x20% / IV / 5 days and Fe 3x250 / PO / 2 days in MAR patients (12 kg). SKA obtains the most types of drugs and antipyretic 1 dose, 3 types of antibiotics, and other therapies such as ranitidine, furosemide and ventolin.

The drugs used by Kawasaki Syndrome patients have the potential to cause potential drug interactions. Potential drug interactions between corticosteroids and acetosal as many as 38% of patients risk increasing side effects in the digestive tract. Acetosal and Furosemide in as many as 13% of patients cause a decrease in the diuretic effect of furosemide. After being given therapy, the therapeutic outcome was assessed from Kawasaki Syndrome patients.

Outcomes include clinical manifestations that are reduced or dilated coronary arteries that disappear. The therapeutic outcomes of Kawasaki Syndrome patients can depend on the patient's symptoms, the outcomes of

which are, among others, reduced clinical manifestations and dilated coronary arteries. At the end of the study it was known that the patient's status after receiving therapy. Almost all patients have improved conditions (94%]. About 6% of patients recover. The therapeutic outcome in Kawasaki Syndrome patients can be seen in Table 4.

Tabel 4 : Outcome terapi pada pasien Kawasaki Syndrome

Clinical condition		Number of patient	Laboratory data	Number of Patient
Early	End			
Fever	Fever falls	15 [94%]	CRP falls	9 [56%]
Rash	Missing rash	9 [56%]	Leukocytes falls	7 [44%]
Red eyes	Red eyes lost	7 [44%]	Haemoglobin naik	5 [31%]
Strawberry tongue	*Strawberry tongue* lost	6 [38%]	Platelet falls	4 [25%]
Red lips and broken	Normal lip	5 [31%]	LED down	3 [19%]
Dilatation of LMCA and RCA2	Normal Echo2			
Skin peeling	skin is no longer peel off	3 [19%]		
The lump on the neck	The lump is gone	3 [19%]		

Discussion

Giving therapy to children with kawasaki syndrome is carried out according to the diagnosis and clinical manifestations that appear. Management of Kawasaki Syndrome according to the American Heart Association in 2004 is using IVIG therapy. The aim is to reduce the inflammation of high-dose coronary arteries and acetosal arteries as anti-inflammatory, which is then lowered as anti-aggregates when the fever has gone down.

IVIG and acetosal are the main therapies in Kawasaki Syndrome because acetosal can act as an antiinflammatory coronary artery and also as an antiagregation to prevent clot formation. The mechanism of action of IVIG is that it can regulate cytokine production in Kawasaki Syndrome patients found to be higher than normal and can also prevent coronary artery abnormalities [9].

The use of IVIG is prioritized for patients with coronary artery abnormalities such as LMCA and RCA dilatation because IVIG is thought to regulate differentiation T cells that will increase the number of regulator T cells and reduce the pro-inflammatory effects of the effector function of T cells and reduce the release of cytokines [10]. The dose used in patients with Kawasaki Syndrome is 2 g / kg for 12 hours and the dose is given can be said to be appropriate because in some cases rounding of doses is obtained.

Another therapy in Kawasaki Syndrome patients is with acetosal, acetosal in Kawasaki syndrome is divided into two doses, namely the dose of 80-100 mg / kg weight sedays as antiinflammatory and then reduced to a dose of 3-5 mg / kg weight sedays as anti-aggregation platelets when the fever has gone down [9].

Acetosal is a non-selective group of NSAID drugs that works by acetylating serine residues on the active side of COX and causing COX enzymes to be unable to biotransform arachidonic acid into Prostaglandin-H2 [PGH2] thereby reducing prostaglandin production which is a proinflammatory compound [11].

this study not all patients received doses as anti-inflammatory or anti-aggregation. In patients who still have many doses of acetosal clinical manifestations starting at the dose as anti-inflammatory and then lowered if the fever has dropped and clinical manifestations have decreased. Some patients do not get a dosage as anti-inflammatory, which is a patient who at the time of admission is in a better condition such as a fever that is not too high or clinical manifestations that have been greatly reduced because even without Kawasaki

Syndrome therapy can improve on its own. Antiinflammatory doses are given because Kawasaki Syndrome patients experience swelling in the coronary arteries and platelet antiaggregation doses are given because there is an increase in platelet value in Kawasaki Syndrome patients in patients receiving doses as anti-aggregation platelets found an increase in platelet value but not all patients are rechecked after administration

Doses of acetosal as platelet antiagregation. Patients in this study received doses that

were in accordance with the dosage that should be as a dose as anti-inflammatory or dose as an anti-aggregation-platelet [12].

Another therapy if the patient cannot respond to the main therapy is to use corticosteroids as in patients who have heart abnormalities [LMCA and RCA dilatation] and suspected patients do not respond to IVIG because clinical manifestations are still quite visible even though the dilatation in the coronary arteries is no longer visible after 48 hours [9].

All Kawasaki Syndrome patients use methylprednisolone as corticosteroid therapy, when the patient's condition has improved, its use must be stopped slowly or called tapering-off as seen because if corticosteroids are stopped abruptly it will cause steroid withdrawal symptoms [steroid withdrawal] Corticosteroid doses can be reduced slowly before being stopped or the intravenous route can be replaced by an oral route before being stopped.

Not all patients who get corticosteroids will be tapered off because taperingoff does not completely prevent steroid withdrawal symptoms so it can be seen in advance whether the cessation of corticosteroids the patient will experience steroid withdrawal symptoms or because the time for corticosteroid administration is quite short [13].

Dosage given Kawasaki Syndrome patients in this study can be said to be appropriate but there are some that are not in accordance with the literature that are possible because the patient's condition is quite good, such as clinical manifestations that are not too much found or because the patient also receives IVIG therapy. Other alternative therapies such as corticosteroids also have potential side effects such as hypertension, cushing's syndrome, adrenal suppression, hyperglycemia to osteoporosis [14].

IVIG causes kidney damage but is reversible in addition immunoglobulins have a high enough molecular weight that causes blood viscosity to rise and cause kidney failure acute ischemic. IVIG also causes thromboembolism caused by administration at high doses or at high infusion rates, IVIG is thought to activate platelets, causing arterial vasospasm and high infusion rates thought to cause increased blood viscosity. Other side effects associated with the use of IVIG are not yet known exactly how the mechanism is but it is thought to be due to activation of a system of balancing immunoglobulin macroaggregates, IgG that crosses the blood brain barrier and IgG interactions with antigens in blood vessels that cause the release of proinflammatory cytokines [15]. Side effects from IVIG this does not always appear in each individual and is not clearly written on the medical record of the patient's Kawasaki Syndrome.

Acetosal inhibits COX-1 in the stomach which causes reduced mucosal blood flow, acetosal also damages specific defenses that require prostaglandins that protect the intestinal mucosa causing bleeding, gastric ulcers, even perforation of the intestinal wall [11]. Acetosal weak acid which when in acid the stomach has an ionized and fat-soluble form, acetosal in an un-ionized form will penetrate the membrane and accumulate in mucosal epithelial cells that have a pH of 7.4 which causes ionized acetosal and trapped in cells called ion trapping and cause cell and vascular damage.

Acetosal also increases levels of TNF-α which is a potent modulator of caspase, an enzyme that causes apoptosis of gastric epithelial cells [16]. Side effects of acetosal can be reduced by using prostaglandin analogues or inhibiting gastric acid secretion using H2-receptor antagonists such as ranitidine, antacids or using proton pump inhibitors such as omeprazole and lansoprazole.

In this study all patients who received acetosal get either or both of them from drugs that reduce the side effects of acetosal, usually used ranitidine or antacids [11]. Corticosteroids can stimulate osteoclast activity in the first 6-12 months of therapy, accompanied by a decrease bone formation by suppressing osteoblastic activity in the bone marrow and causing osteoblast and osteocyte apoptosis.

In addition, prednisolone use ≥ 5 mg / days is associated with a significant reduction in bone mineral density and an increased risk of fracture by administering corticosteroid therapy 3-6 months [14]. From the patient's medical record data, the period of administration of corticosteroid therapy for a maximum of 14 days so that the side effects of osteoporosis can be minimized. Long-term

use of corticosteroids generally causes Cushing's syndrome [adrenal insufficiency] which is characterized by weight gain, redistribution of adipose tissue, and full moon face effect caused by corticosteroid administration of negative feed-back to corticosteroid receptors in the anterior hypothalamus and causing suppression of corticotrophin production -releasing hormone [CRH] and adrenocorticotropic hormone [ACTH], this emphasis can lead to atrophy of the adrenal cortex and secondary adrenal insufficiency [17].

The most common side effects of weight gain are reported in the use of long-term corticosteroids equivalent to prednisone dosage 16 ± 14 mg / days ≥ 60 days, while the administration of prednisone ≥ 20 mg for 3 months causes the incidence of Cushing's syndrome to be 61%. The recommendation to overcome this side effect is to stop corticosteroid use gradually or reduce the dose of corticosteroids because the risk of Cushing's syndrome increases with increasing doses [14].

Giving corticosteroid therapy less than one week generally does not require tapering-off, but corticosteroid administration between one week to one month needs to be tapered-off dose for 7-14 days until physiological doses are achieved. Therapy given for more than 1 month requires regular taperingoff doses every 15-30 days until physiological doses are achieved. This tapering is done to prevent steroid withdrawal symptoms such as lethargy, fever and myalgia after cessation of the use of corticosteroids [13]. The absence of specific guidelines that become a reference for tappering off corticosteroids so that in the therapy there are many variations of tappering off. Prone drug interactions occur in the provision of medical services.

The use of acetosal with furosemide will reduce the diuretic effect of furosemide because acetosal decreases the kidney response to the diuretic process but no replacement therapy is needed but monitoring of the diuretic effect of furosemide is still needed [18]. Acetosal and corticosteroids have gastrointestinal side effects such as gastritis and patients who use both at once so that the possibility of side effects that appear more severe and more frequent, for patients who get this therapy is necessary to provide additional antacid therapy, H2-receptor antagonists or proton pump inhibitors to reduce side effects of acetosal and corticosteroids [14]. Kawasaki Syndrome is a disease that can heal on its own without therapy, but the provision of therapy is beneficial to reduce complaints from patients and prevent further complications.

Kawasaki Syndrome therapy can be said to successfully reduce clinical manifestations but not all patients are re-examined besides Kawasaki Syndrome therapy successfully prevents other complications from appearing. Other outcomes obtained were laboratory data that returned to normal after administration of therapy such as CRP dropped, leukocytes dropped, HB increased, platelets dropped and LEDs dropped but not all patients were examined for related laboratory data.

The condition of pediatric patients with Kawasaki Syndrome that comes out of the hospital usually comes out with improved status because Kawasaki Syndrome cannot heal quickly and still needs monitoring regarding the development of dilatation of the patient's coronary arteries, but patients are allowed to go home with or without additional therapy such as acetosal and need to control to the doctor after 2 weeks out of hospital.

It is necessary to monitor and record periodically and systematically to monitor the provision of therapy, outcomes and possible emergence of side effects and drug interactions from Kawasaki Syndrome therapy and other therapies because so far drug related problems has not been recorded in the patient's medical record.

Conclusion

The strategy for administering drugs to pediatric patients with Kawasaki Syndrome is carried out in accordance with the policy regarding the patient's condition and recommended clinical manifestations. Some drugs such as IVIG and acetosal are still the main treatment and the addition of several drugs in accordance with the complaints experienced by patients.

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