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Literature Research

MANAGEMENT OF DIARRHEA IN CHILDREN AND ITS RELATION TO STUNTING

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ABSTRAK

Diare adalah suatu kondisi dimana seseorang buang air besar dengan konsistensi lembek atau cair, atau dapat berupa air saja dengan frekuensi diare tiga kali atau lebih dalam satu hari. Angka kejadian dan kasus kematian akibat diare di Indonesia masih sangat tinggi dan membutuhkan perhatian khusus, terutama bagi para klinisi. Kejadian diare ini berkaitan erat dengan stunting. Diare yang berkepanjangan dapat menyebabkan pertumbuhan terhambat, sementara anak-anak dengan pertumbuhan terhambat lebih rentan mengalami diare. Oleh karena itu, pemahaman yang lebih mendalam diperlukan sebagai referensi dalam mengatasi diare. Penelusuran literatur diperoleh dari berbagai portal online seperti Medscape, Pubmed, Google Scholar, dan Science Direct dengan menggunakan kata kunci "diare," "anak," dan "stunting" Tatalaksana diare dilakukan dengan rehidrasi, mikronutrien (vitamin A, asam folat, zat besi, vitamin B12, dan seng), probiotik, antisecretory, dan antibiotik. Pendekatan terapi yang komprehensif diperlukan untuk menghindari komplikasi diare serta opsi pengobatan khusus untuk kasus diare pada anak-anak dengan pertumbuhan terhambat.

ABSTRACT

Diarrhea is a condition of changing bowel movements accompanied by an increase in the frequency of diarrhea. Currently, the incidence and death cases due to diarrhea in Indonesia are still very high and need special attention, especially for clinicians. The conditions of diarrhea and stunting are related to each other. Prolonged diarrhea will cause stunting, while children with stunting will easily experience diarrhea. Therefore, further understanding is needed as a reference in managing diarrhea. Literature searches were obtained from various online portals such as Medscape, Pubmed, google scholar, and science direct using the keywords "diarrhea" "children" and "stunting". Management diarrhea is mainly by rehydration, micronutrients (vitamin A, folic acid, iron, vitamin B12, and zinc), probiotics, antisecretory, and antibiotics. A comprehensive therapeutic approach is needed to avoid diarrhea complications as well as treatment options specifically for cases of diarrhea in children with stunting.

INTRODUCTION

Diarrhea is a condition with a mushy, liquid, or watery consistency defecation, with a frequency of diarrhea three or more times in one day[1]. This diarrheal disease has become a worldwide problem. It is estimated that more than 2 million children younger than 5 years die each year from diarrheal infections. In Indonesia, the morbidity rate of diarrhea is 270 children per 1000 population, where diarrhea is one of the leading causes of death for children[2].

Clinically, diarrhea is divided into acute diarrhea, dysentery, and persistent diarrhea. Persistent diarrhea can lead to malnutrition, micronutrient deficiencies, and increased mortality risk of other diarrhea-related diseases. Deficiencies in these nutrients and macronutrients can adversely affect the growth and development of a child[3]. Diarrhea and malnutrition are synergistically interrelated, forming a vicious circle. Malnutrition can lead to impaired immune function and increase the risk of infection. Gastrointestinal infections, in this case diarrhea, can eventually disrupt intestinal function, decrease nutrient absorption, and cause or worsen malnutrition conditions. The long-term effect of diarrhea is stunting[4].

Stunting is a failure of growth and development in children under five years old (toddlers) due to chronic nutritional deficiencies and recurrent infections, especially during the First 1000 Days of Life. This is indicated by the z-score value of height according to age (TB / U) which is below -2SD. Based on data from Basic Health Research, the prevalence of stunting was 30.8%. Stunting can further hinder physical growth, increase a child's vulnerability to diseases, impede cognitive development, and affect future productivity of the child[5–7].

Prompt and appropriate diarrhea treatment of in children can prevent death or long-term side effects such as stunting. Diarrhea therapy is done by giving rehydration fluids and drugs such as antibiotics, antiemetics, or antisecretory. In malnourished children, there is an increase in total sodium levels so rehydration can be at risk of excess fluid and heart failure. Therefore, this article will discuss more deeply about the treatment of diarrhea in children and its relation to stunting.

METHODS

The literature review is using conventional methods, this is not a systematic review or meta-analysis. The strategy employed is to search for relevant articles related to the topic. Source searches were conducted on various online portals such as Medscape, Pubmed, google scholar, and science direct using keywords “diarrhea”, “children”, “treatment”, “management” and “stunting” with Boolean connectors “AND” and “OR”. This article's content was derived from various sources with total 33 review sources (31 scientific articles, 1 guideline, and 1 book) provided by relevant institutions.

RESULTS

Definitions of Diarrhea

Diarrhea is still one of the leading causes of illness and death, especially in developing countries[8]. Diarrhea is defined as defecating more than three times a day with a mushy or liquid consistency. Diarrhea can be classified into liquid acute diarrhea, dysentery, persistent diarrhea and diarrhea with poor nutrition. The World Health Organization (WHO) defines acute diarrhea as liquid bowel movements with a mushy or liquid consistency, three or more times per day, for 3 days more and less than 14 days. Dysentery is recognized as a liquid bowel movement accompanied by the presence of blood. Meanwhile, persistent diarrhea is a condition in which episodes of diarrhea persist for more than 14 days[9–11].

Epidemiology

Worldwide, there are about 1.3 million people who die from diarrhea and almost half

of them are children younger than 5 years. Indonesia's health profile shows that 731 children under the age of 5 died from diarrhea. Acute diarrhea highest prevalence occurring between the ages of 3 to 24 months. This is attributed to the fact that the immune system of children aged 3 to 24 months is not yet fully mature[12–15].

The most common ways of transmission of enteropathogens are through the person-to-person, fecal-oral route, or by ingesting contaminated food or water. The incubation period varies depending on the diarrhea-causing pathogen, it can range from 1 hour (toxin-producing bacteria: S. aureus), 1-3 days (*Rotavirus*), or 7 days (invasive bacteria such as *Shigella spp*). However, for some bacteria, the incubation period can be up to 14 days (*Salmonella spp*.), and for some parasites up to several weeks or months (*E. histolytica*)[11].

Etiology

Diare terjadi karena adanya infeksi, alergi, malabsorpsi, keracunan, obat dan defisiensi imun. Acute diarrhea is generally caused by acute infection either by viruses, bacteria, or parasites, in developing countries, diarrhea more often arises due to bacteria and parasites than viruses. Bacteria that cause diarrhea include *Escherichia coli, campylobacter, shigella, Vibrio cholerae*, *Salmonella* and *H. pylori*. *H. pylori* will lower the concentration of stomach acid which can then increase the colonization of intestinal bacteria. *Rotavirus, Human caliciviruses, Adenovirus, Norwalk Virus*, *Astrovirus*, and *Coronavirus* are viruses that generally cause diarrhea. Cryptosporidium parvum, Giardia intestinalis, Entamoeba histolytica, and Cyclospora cayetanensis are parasites that often cause acute diarrhea in children. Chronic diarrhea is generally caused by non-infectives such as malabsorption, inflammatory bowel disease, celiac disease, pancreatic insufficiency, or medication side effects[11,16–19].

Broadly speaking, there are two basic mechanisms of diarrhea: (1) due to an increase in intraluminal osmotic pressure, leading to the inhibition of water and electrolyte reabsorption, and (2) due the result of an increased capacity for the secretion of water and electrolytes. The mechanism of diarrhea caused by viruses involves the entry of the virus into the gastrointestinal tract, infecting enterocytes, and causing damage to the small intestinal villi. The damaged enterocytes are replaced by cuboidal or flattened epithelium that is structurally and functionally immature. This results in villous atrophy, which prevents optimal absorption of nutrients and fluids. Unabsorbed food and fluids lead to an increase in intestinal osmotic pressure and heightened intestinal motility, ultimately resulting in diarrhea[20].

Meanwhile, the pathogenesis of bacterial diarrhea occurs through the gastrointestinal tract contaminated by unhygienic food. When a sufficient amount of bacteria enters, the infection process continues into the duodenum. In the duodenum, bacteria multiply to around 100 million colonies. Within the cell membrane, bacteria secrete toxin subunit A and subunit B. Subunit B attaches to the subunit A membrane and eventually contacts the cell membrane. This leads to stimulation of secretion and inhibition of fluid absorption, resulting in an increased volume of fluid in the intestinal lumen. If the fluid exceeds 4500 ml or its capacity for absorption, diarrhea occurs[20].

Clinical manifestations

Based on WHO, diarrhea is defined as the presence of liquid stools three or more times per day or the frequency of diarrhea is more frequent than normal. Diarrhea occurs due to the presence of excess intestinal secretions or because there is impaired absorption of fluids and electrolytes throughout the intestinal epithelium. In Rotavirus, virus will secrete toxic proteins that induce electrolyte

imbalance (sodium and potassium), inhibit water reabsorption, and interfere with enzyme activity. Disruption of enzyme activity triggers lactose intolerance that can last for weeks. Amobiasis is known to cause immune system disorders and decreased IgA antibodies. Other clinical manifestations can vary in the form of fever, vomiting, dehydration, abdominal distention, and lethargy. In children, the risk of dehydration is very high and can develop into hypovolemic shock and death. Assessment of dehydration degree can be done with skin turgor, mucous membranes, sunken eyes, urine output, and pulse. Diarrhea in highly endemic areas or in malnutrition conditions can cause chronic diarrhea that can interfere with the growth and development of children so that in the end it causes stunting[11,16–18,21].

Diarrhea and Stunting

Infection and malnutrition are always closely related. The relationship between infection and malnutrition (stunting) is like a vicious cycle that is difficult to break. Bacteria, parasites, and viruses that cause diarrhea are agent factors that contribute to the occurrence of stunting. The epithelial lining of the gastrointestinal tract acts as a protector throughout the body and regulates the absorption, secretion, and digestion of nutrients. Damage to the epithelium in gastrointestinal infections can lead to malabsorption of carbohydrates, fats, proteins, and micronutrients and ultimately malnutrition. Furthermore, malnutrition can also cause abnormalities of the gastrointestinal epithelium. Lymphoid tissue in the gastrointestinal tract such as Peyer's patch which contains immune cells will affect the immune response to the gastrointestinal tract. Children with malnutrition will experience changes in the production of immune responses including changes in the production of lymphocytes, T-cells, and cytokines Il-2, Il-4, Il-6 and Il-10. Changes in lymphocyte physiology are the cause of immune disorders in malnourished children so children will be at higher risk of recurrent infections. Previous reports have shown that malnourished children are >3 times more likely to be infected with diarrhea than children with normal nutrition. Malnutrition is a major predictor of persistent and prolonged diarrhea that lasts more than 14 days. This persistent diarrhea will further result in chronic malnutrition such as stunting. Stunting is a condition of failure to thrive in children due to chronic malnutrition and/or repeated infections so that children are too short for their age. There is a strong link between malnutrition, infection, and mortality. Infectious diseases duration experienced by malnourished toddlers is also longer than normal toddlers. Choiroh et al. reported that the frequency and duration of diarrhea can increase the risk of stunting by 1.4 times and 5 times, respectively. Desyanti et al. also demonstrated that toddlers who experiencing diarrhea are at a 3.6 times greater risk of experiencing stunting[7,8,16,22–24].

Risk Factors

Other diarrhea risk factors are availability of clean water and toilet facilities, personal hygiene of parents, parents' level of education, parents' economic status, living environment of the child, immunization status, and exclusive breastfeeding. The availability of clean water and toilet facilities is necessary to provide a healthy environment that meets health standards and emphasizes the monitoring of various environmental factors that influence the level of public health. Lestari et all reported toddlers who frequently experience diarrhea are those who use unprotected sources of drinking water[19,25,26].

Diarrhea Management

Management of diarrhea is divided into symptomatic therapy and causative therapy such as ORS, zinc and antibiotics.[21]

Rehydration

The first thing to do for a child with diarrhea is to assess hydration status. Dehydration is a

major complication of diarrhea. Therefore, dehydration management is the main basis for diarrhea therapy. According to the American Academy of Pediatrics (AAP), the Centers for Disease Control and Prevention (CDC), the European Society for Pediatric Gastroenterology and Nutrition and the World Health Organization (WHO), oral rehydration therapy is the first line for acute gastroenteritis[27]. Rehydration therapy can be given peroral or parenteral to prevent or correct dehydration. The composition of WHO's recommended oral rehydration fluid contains 75 mM glucose, 75 mM sodium, 65 mM chloride, 20 mM potassium, and 10 mM citrate with a total osmolarity of 245 mOSM/L. Oral rehydration therapy is contraindicated for severe dehydration, paralytic ileus, frequent and persistent vomiting (more than four times per hour), and the presence of moderate to severe oral disorders. For patients who have difficulty drinking or with clinical symptoms of vomiting, parenteral administration is given through a nasogastric tube or intravenously. In conditions of oral rehydration therapy failure or severe dehydration, the choice of therapy is intravenous rehydration. The provision of rehydration is divided into the first stage and the second stage. The first stage is given in the first 1 hour as much as 20 mL/kg. In the second stage, children < 1 year old are given for 6 hours and children 1-5 years old are given for 5 hours given as much as 80 mL/kg. During rehydration, assess the child's dehydration status every 1-2 hours. Rehydration of children with severe malnutrition accompanied by diarrhea is a new challenge. Signs of dehydration in children with diarrhea are difficult to recognize in children with this malnutrition. There are electrolyte and fluid disorders in children with malnutrition which if not considered in the provision of rehydration can have life-threatening consequences. Special liquid is needed for children with malnutrition consisting of glucose 125 mM, sodium 45 mM, chloride 76 mM, potassium 40 mM, and citrate 7 mM with a total osmolarity of 300 mOSM / L[21].

Nutrition

Breast milk contains antimicrobial properties and essential nutrients needed by children experiencing acute diarrhea. Breast milk is given to prevent weight lose and to replace lost nutrients. Children who are still breastfeeding should be breastfed more frequently. Providing breast milk has been proven to reduce the duration and frequency of acute diarrhea. Infants aged 6 months or older should be provided easily digestible foods, in smaller and more frequent portions (>6 times/day). After the diarrhea stops, the provision of extra food should continue for two weeks to aid in weight recovery. This nutritional provision helps prevent nutritional disorders, stimulates intestinal recovery, and reduces the severity of the disease[15,20,28].

Micronutrient

Micronutrients such as vitamin A, folic acid, iron, vitamin B12, and zinc are associated with the formation of antibodies and the development of the immune system. Vitamin A is one of the fat-soluble vitamins that is stored in the liver and adipose tissue. Vitamin A plays a role in maintaining the integrity of the epithelium of the respiratory tract and gastrointestinal tract. Vitamin A deficiency will increase the risk of diarrhea, malaria, measles, and mortality. Vitamin A supplementation can maintain intestinal integrity, reduce the incidence of respiratory tract infections, and reduce diarrheal mortality. Vitamin A requirements can be vary based on age groups. For children aged 1-3 years, the requirement for Vitamin A is 400 mcg. Meanwhile children aged 4-6 years need 450 mcg Vitamin A. Multivitamin and mineral supplementation should be given a minimum of two RDAs (Recommended Daily

Allowances) for two weeks[9,29]. Zinc is a cofactor in the formation of enzymes and nucleic acid and plays an important role in cell membrane structure and in immune cell function. Diarrhea leads to zinc deficiency, which in turn exacerbates the severity and duration of acute diarrhea. Zinc deficiency can reduce nonspecific immunity including neutrophils, natural killer cells, complement activity, reduce the number of T and B lymphocyte cells, and decrease antibody production. In diarrhea, zinc plays a role in the inhibition of second messenger-induced Cl secretion (cAMP, cGMP, calcium ions) increases sodium absorption, improves intestinal permeability, and enzyme function in erythrocytes, increases intestinal epithelial regeneration and local immune response by limiting bacterial overgrowth, and increases pathogen clearance. Zinc administration can reduce diarrhea prevalence by 34%, pneumonia incidence by 26%, acute diarrhea duration by 20%, persistent diarrhea duration by 24%, therapy failure or death due to persistent diarrhea by 42%.[9,15,30,31] One RDA for a 1-year-old child includes 50 micrograms of folic acid, 10 mg zinc, 400 micrograms of vitamin A, 10 mg iron, 1 mg copper, and 80 mg magnesium. WHO recommends zinc supplementation for children aged ≤6 months by 10 mg and for children aged >6 months by 20 mg, with a period of 10-14 days. All children with persistent diarrhea should get additional vitamin and mineral supplements daily for 2 weeks[9,30].

Probiotic

Probiotics are living organisms with effective doses used to manage acute diarrhea in children. Probiotics that can be used in the management of diarrhea caused by Rotavirus in children include Lactobacillus GG, Saccharomyces boulardii, and Lactobacillus reuterii. Probiotics can be given both for acute and prolonged diarrhea. Gaon et al reported that feeding milk containing Lactobacillus casei, Lactobacillus acidophillus and Saccharomyces boulardi in patients with persistent diarrhea for 5 days can reduce the amount of stool, duration of diarrhea and duration of accompanying vomiting. The recommended dosage is 108-1010 CFU[9,20]. Probiotics can combat pathogenic microorganisms through various mechanisms. Probiotics compete with pathogens to attach to the gastrointestinal mucosa and acquire nutrients. Probiotics can synthesize short-chain fatty acids (SCFA), polyamines, and antioxidants, which are essential for maintaining the balance of gut microbiota ecology. Additionally, probiotics can prevent pathogenicity by disrupting inter-pathogen signalling and modulating the local mucosal immune system. Modulation of the immune system by probiotics involves the secretion of IgA in the gastrointestinal lumen, aiming to prevent colonization by pathogenic microorganisms. Probiotics are a group of bacteria capable of producing lactic acid from carbohydrates, thus it can lowering the pH of the gut environment. In this acidic environment, probiotic bacteria can thrive while pathogenic bacteria perish. Probiotics also produce bacteriocins and stimulate the production of intestinal epithelial mucus, which inhibits the attachment of pathogenic microorganisms to the gut mucosa. Several factors determine the efficacy of probiotics in therapy such as composition of probiotic strains, combination of probiotic strains in a dairy product, and individual patient characteristics[32].

Antisecretory

The administration of antimotility or antisecretory agents can be useful as an adjunct therapy aimed at lowering fecal secretion by slowing intestinal transit. However, long-term use is not recommended in children with persistent diarrhea. Antidiarrhea drugs in patients with dysentery

or high fever can aggravate intestinal infections[18].

Table 1. Antibiotics Based on Microbial Agent

Microbial Agent	Therapy
Cholera	Doxycycline Adult : 1x 300 mg Child : 2mg/kg (Not recommended) Azithromycin Adult: 1 g single dose Child: 20 mg/kg, single dose
Shigellosis	Ciprofloxacin Adult : 500 mg, 12 hours for 3 days or 2 gr single dose 1x/days Pivmecilinam Adult : 400 mg 3-4 x/days for 5 days Child : 20 mg/kg 4x/ days for 5 days Ceftriaxone Adult: 2-4 g, 1 x/days Child: 50-100 mg/kg 1 x/days i.m for 2-5 days
Amebiasis	Metronidazole Adult : 750 mg 3 x/ days for 5 days Child: 10 mg/kg 3 x / days for 5 days Can be given until 10 days in severe cases
Giardiasis	Metronidazole Adult : 250 mg, 3 x/days for 5 days Child: 5 mg/kg 3 x/days for 5 days
Camplyobacter	Azithromycin Adult: 500 mg 1 x/days for 3 days Child: 10 mg/kg/days, oral or iv (for child > 6 months old, <45 kg) 1x/days for 3 days Erythromycin Child: 40-50 mg/kg/days, 3-4 x/days for 5-7 days
Salmonella thyphimurium	Imipenem 30-60 mg/kg/days, on severe cases, can be increase until 100 mg/kg/days), 3-4 x/days iv Cefotaxime 50-100 mg/kg/days, 2-4 x, iv

Antibiotic

Antibiotics can be given in some cases such as tourist diarrhea, persistent diarrhea, and dysentery. In high-risk populations such as malnutrition, antibiotics may be considered. Antibiotics are aimed at lowering the intensity and duration of diarrhea. Antibiotics administration is adjusted according to fecal culture and sensitivity. Due to the low yield of fecal culture, the decision to conduct antimicrobial therapy for acute diarrhea can be based on clinical grounds, and the selection of antibiotics is selected empirically. The choice of antibiotics based on microbial agents can be seen in Table 1. Improper administration of antibiotics will lead to the risk of resistance or prolonged cases of diarrhea[9,17,21,27,30,33].

CONCLUSION

Diarrhea is a disease that we routinely encounter every day. Assessment of the history of the disease, physical examination and examination of stool cultures are performed to determine the cause of diarrhea. A comprehensive therapeutic approach is needed in dealing with diarrhea cases, it is important to avoid complications in children's growth and development such as stunting. Treatment for diarrhea in a stunted child from the rehydration, micronutrient, probiotic, and antibiotic needed to be handled differently than acute diarrhea.

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