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Research Progress on Malnutrition and Nutritional Intervention in Children with Leukemia During Chemotherapy

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***A*bstract:** This study systematically analyzed the primary causes of malnutrition in children with leukemia during chemotherapy, clarified the status of malnutrition and specific nutritional intervention measures, and comprehensively evaluated the research progress. The research indicates a shift from basic supportive care toward precision intervention strategies. Immunonutrition approaches, such as omega-3 fatty acid supplementation and probiotics for gut microbiota modulation, significantly mitigate chemotherapy-related side effects and enhance nutritional status. These targeted novel regimens demonstrate clear clinical advantages. The success of nutritional management depends on a multidisciplinary collaboration mechanism. The organic integration of innovative nutritional protocols with standard treatments from hematology, pediatrics, and nutrition departments significantly optimizes treatment outcomes and long-term quality of life for children with leukemia. This interdisciplinary synergy is reshaping contemporary medical models.

Keywords: Childhood leukemia; Chemotherapy period; Malnutrition; Nutritional intervention

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1. Introduction

The average annual incidence of childhood leukemia in China is 42.33 per million, making it the most common pediatric malignancy. Survey data indicate that the prevalence of malnutrition among children with leukemia is as high as 47% [1]. Chemotherapy serves as the cornerstone of treatment for pediatric leukemia; however, its cytotoxic effects lack target specificity. While effectively eliminating tumor cells, it also causes extensive damage to rapidly proliferating normal tissues, with particularly prominent adverse effects on the digestive system. Due to damage to gastrointestinal mucosal epithelial cells, disruption of intestinal microbiota, and neuroendocrine dysregulation, patients often experience a range of clinical symptoms, including severe anorexia, intractable nausea, frequent vomiting, and diarrhea. These side effects directly compromise the nutritional status and quality of life of affected children. Malnutrition during chemotherapy reduces tolerance to chemotherapeutic agents, exacerbates

myelosuppression, and increases the risk of complications and infections [2]. These risk factors significantly impair treatment efficacy and jeopardize patient survival. For pediatric leukemia patients undergoing chemotherapy, effective nutritional intervention has emerged as a critical dimension of comprehensive care. Provision of adequate energy and essential nutrients consistently optimizes physiological reserves, strengthens immune barriers, and markedly alleviates chemotherapy-induced toxicities such as myelosuppression and mucosal injury. Such systemic improvements are directly reflected in enhanced survival outcomes.

2. Causes of malnutrition in children with leukemia during chemotherapy

2.1. Adverse effects of chemotherapeutic drugs

VDLD Regimen (Vincristine, Daunorubicin, L-Asparaginase, and Dexamethasone) is a standard chemotherapeutic protocol for pediatric leukemia. Its mechanism of action involves direct irritation and damage to the gastrointestinal mucosal lining. Following standardized treatment, more than 45% of children with acute leukemia develop malnutrition, leading to an increased risk of complications and mortality [3].

Pathophysiological analysis reveals that chemotherapeutic agents can trigger inflammatory responses in the mucosa, resulting in epithelial cell damage, impaired gastrointestinal motility, and disruption of digestive enzyme secretion. This manifests clinically as frequent nausea and vomiting. Specifically, vincristine interferes with enteric nerve conduction by inhibiting microtubule polymerization, while daunorubicin disrupts DNA replication and concurrently causes abnormal mucus secretion. These processes establish a vicious cycle: nutritional deficits exacerbate drug toxicity, and metabolic disturbances lower the threshold for chemotherapy tolerance.

2.2. Impact of the disease

Leukemia, as a hematologic malignancy, induces metabolic dysregulation and imbalances in energy expenditure in children, significantly elevating the risk of malnutrition [4]. The malignant proliferation of leukemia cells occupies bone marrow space, and their abnormal division process requires the uptake of large amounts of glucose, amino acids, and lipids, creating metabolic competition with normal hematopoietic cells. This material deprivation directly impairs organ physiological function. During the body's response to leukemia, the immune response is activated, producing cytokines such as interleukin-6 and tumor necrosis factor-alpha. These molecules persistently accelerate the basal metabolic rate through both central nervous and peripheral tissue pathways.

2.3. Psychological factors

The protracted and arduous treatment cycle for pediatric leukemia imposes significant psychological stress on children, inducing various psychological disorders and negatively impacting feeding function. Persistent illness, periodic chemotherapy procedures, and the stimulation of confined hospital spaces directly trigger states of anxiety, low mood, and depression in patients [5]. Such stress states act on digestive tract function through the neuro-endocrine regulatory network, inhibiting the contraction rhythm of gastrointestinal smooth muscle and decreasing pepsinogen secretion levels, ultimately leading to impaired nutritional intake and metabolic dysregulation syndrome in the subjects.

2.4. Diet and metabolism

The European Society for Parenteral and Enteral Nutrition (ESPEN) noted in 2016 that the negative energy

balance and skeletal muscle loss in cancer patients result from the combined effects of reduced intake and metabolic dysregulation, which differs significantly from simple malnutrition [6]. Specifically, reduced intake is directly caused by tumor- and treatment-related factors such as anorexia, taste alterations, and gastrointestinal symptoms, leading to inadequate dietary consumption. Metabolic dysregulation refers to the systemic metabolic reprogramming triggered by the release of inflammatory cytokines (e.g., TNF-α, IL-6) and tumor-derived factors from the tumor-bearing host. Its key features include: (1) elevated or abnormally fluctuating resting energy expenditure; (2) insulin resistance, resulting in impaired glucose utilization; (3) persistently enhanced lipolysis; (4) heightened protein catabolism alongside suppressed anabolism.

3. Nutritional intervention measures for children with leukemia during chemotherapy

3.1. Dietary adjustment strategies

Assessing a child's nutritional requirements involves parameters such as age, weight, height, disease severity, chemotherapy phase, and basal metabolic rate. Utilizing tools like SCAN (Screening Tool for Childhood Cancer Nutritional Risk), individualized nutritional assessments should be conducted. This systematic analysis of nutritional and metabolic indicators, combined with clinical treatment progress and growth curve parameters, forms a quantitative diagnostic conclusion, ultimately clarifying the degree of nutritional deficiency and energy supply standards.

Adjusting dietary structure is an indispensable component of nutritional intervention for children undergoing chemotherapy [7]. It is recommended to follow the principles of high protein, high calorie, high vitamin, low fat, and easy digestibility. Priority should be given to ensuring the intake of high-quality protein, with lean meat, fish, poultry, eggs, dairy products, and legumes serving as ideal sources. Legume products combine plant protein with bioactive components while offering high digestibility and absorption rates. Dairy products provide composite nutrition, with outstanding content of high-quality milk protein, calcium, and other trace elements.

Wang et al. [8] pointed out in their study that as induction remission chemotherapy continues, children's intake significantly decreases across various nutrients. Therefore, nutritional intake deficiency can occur early in treatment. In such cases, individualized nutritional intervention is needed to improve prognosis and enhance the long-term quality of life for children. Energy supply should maintain the proportion of carbohydrates, with rice, noodles, steamed buns, and sweet potatoes constituting the foundational energy choices. Vitamin supplementation relies on fresh fruits and vegetables: spinach, broccoli, and carrots form the vegetable category; kiwifruit, oranges, and apples are included in the daily fruit list.

Nutrient supplementation can also be tailored to the child's specific condition [9]. For anemic children, supplementation with iron-rich foods such as animal liver, red dates, and spinach can be considered, with iron supplements under medical guidance if necessary. For children with compromised immunity, nutrients with immunomodulatory functions, such as vitamin C, vitamin D, and zinc, can be supplemented. If deficiencies in vitamins or minerals are present in the child, timely and appropriate supplementation should be implemented.

3.2. Nutritional support methods

Enteral nutrition is implemented via two pathways: Oral Nutritional Supplements (ONS) and tube feeding. Oral nutritional supplementation builds upon regular meals by adding special medical formula foods containing

protein, carbohydrates, fats, and trace elements. These products come in various flavors, such as chocolate and fruit, and can be customized based on children's preferences to enhance compliance. Tube feeding is suitable for children unable to eat orally. Gastrointestinal access includes nasogastric tubes, nasojejunal tubes, and surgical interventions such as ostomy placement. The choice of enteral route depends on individual tolerance and treatment goals for situations of insufficient oral intake. The infusion rate and temperature of the nutritional solution should be controlled within physiologically appropriate ranges. Xing et al. [10] proposed that compared to oral diets, the use of short-peptide enteral nutritional support yields better outcomes.

When children exhibit gastrointestinal dysfunction, such as intestinal obstruction, perforation, or severe diarrhea, and cannot receive enteral nutrition support at all, intravenous nutrition intervention is required. Various nutrients—glucose, amino acids, fat emulsions, vitamins, and electrolyte solutions—are continuously infused via peripheral or central veins. This mode of nutritional supply encompasses two main categories: Total Parenteral Nutrition (TPN) and Partial Parenteral Nutrition (PPN), meeting the metabolic needs of children through different formula combinations [11]. Total parenteral nutrition is suitable for children who cannot receive nutrition via the gastrointestinal tract or have gastrointestinal dysfunction, supplying all essential nutrients. Partial parenteral nutrition is used for children whose enteral nutrition does not meet full requirements, serving as a supplement to enteral nutrition.

3.3. Nutritional education and support

Nutritional knowledge education is a core component of clinical nutritional therapy [12]. The medical team must systematically explain to families the mechanisms and clinical hazards of malnutrition in children with leukemia during chemotherapy, encouraging parents to understand the decisive impact of scientific diet on the child's prognosis. Nutritional intervention must be integrated throughout the entire chemotherapy process.

Psychological intervention should not be neglected. During chemotherapy, children and their families commonly experience negative emotions such as anxiety and fear. These emotions can lead to loss of appetite and impaired nutrient absorption. Nursing staff should establish regular psychological assessment mechanisms, listen to needs, and provide emotional support. Timely sharing of successful treatment cases helps boost confidence in treatment. For individuals with significant psychological distress, referral to psychiatric departments for professional intervention is warranted.

In addition to nutritional education, psychological support for children and their families is essential. Zhang et al. [13] confirmed through research that the combined application of nutritional education and psychological intervention in leukemia chemotherapy can effectively improve the psychological status of patients with acute leukemia undergoing chemotherapy, enhance compliance and satisfaction, and reduce adverse reactions. During chemotherapy, children and parents often bear immense psychological pressure, prone to anxiety, fear, depression, and other adverse emotions that can affect the child's appetite and nutritional intake. Healthcare workers should care about the psychological state of children and parents, proactively communicate with them, listen to their concerns, and offer comfort and encouragement. Sharing successful treatment cases can strengthen their confidence in overcoming the disease. For children and parents exhibiting psychological issues, referral to a psychologist for professional counseling may be necessary.

4. Intervention mapping methods and research advances in nutritional support for children with leukemia during chemotherapy

Intervention mapping is a multi-step design process based on health behavior theories (such as the Theory of Planned Behavior and Social Cognitive Theory) and empirical research evidence. It ensures that intervention programs align with the actual needs of the target population while precisely addressing specific health problems (e.g., chronic disease management, infectious disease control, health risk behavior intervention). During chemotherapy for pediatric leukemia, children often face issues such as malnutrition, immunosuppression, and chemotherapy-related adverse effects (e.g. mucositis, infections). The latest nutritional intervention mapping encompasses new concepts and methods in nutritional intervention, special dietary management, and multidisciplinary collaboration models.

4.1. New concepts and methods in nutritional intervention

Precision nutritional intervention is becoming a prominent frontier field. Leveraging high-throughput gene sequencing and metabolomics technologies, it reveals children's gene polymorphisms and metabolic pathway characteristics, providing a scientific basis for personalized dietary ratios. Upon detection of mutations in genes related to specific nutrient metabolism, adjustments to the types and dosages of corresponding supplements can be made to enhance bioavailability. Jiang et al. [14] confirmed that precision nutritional intervention helps improve the nutritional status of patients post-chemotherapy and reduces the incidence of chemotherapy-related adverse reactions.

The gut microbiota is a host-specific entity that develops throughout life. It is susceptible to exogenous and endogenous modifications and can be a fundamental driver or contributing factor in many diseases, affecting local and distant organ systems, with the potential to influence diverse processes, including hematopoiesis [15]. Strategies such as probiotic supplementation, prebiotic intake, and fecal microbiota transplantation are used to improve microbial balance and repair the mucosal barrier. Immunonutrition support is considered a novel nutritional intervention strategy, with core components including arginine, ω-3 polyunsaturated fatty acids, and nucleotides [16]. Arginine stimulates immune cell proliferation and promotes lymphokine secretion; ω-3 fatty acids lower IL-6 levels and modulate neutrophil activity; nucleotides accelerate immunoglobulin synthesis and maintain Th1/Th2 axis homeostasis, precisely regulating cellular immune responses.

Nutritional assessment and plan formulation are also indispensable. As indicated in the study, responsible nurses need to determine patients' daily dietary requirements and actual intake based on their condition and nutritional risk screening results. The daily caloric requirement is 83–125KJ/kg, protein is 1.5–2.0g/kg/day, and fat constitutes 50% of non-protein calories [17]. By accurately formulating and implementing nutritional plans, expected nutritional intervention outcomes can be achieved.

4.2. Special dietary management

Managing the side effects of chemotherapy in children with leukemia requires attention to dietary adjustment plans. L-asparaginase (L-asp) can potentially induce pancreatitis, a common and severe complication, making fat intake control a key intervention measure [18]. Daily diets should avoid high-fat categories such as fried foods and animal offal. Low-fat milk, fish, and lean meat are ideal choices, combining low-fat properties with high-quality protein supplementation, effectively reducing pancreatic metabolic stress.

Children with oral mucositis require special attention to food texture and temperature. It is recommended

to choose soft, easy-to-swallow foods like rice porridge, noodles, tofu pudding, and steamed eggs. Spicy and irritating foods such as chili peppers, Sichuan pepper, and ginger should be avoided to reduce secondary irritation to the oral mucosa. Food temperature should be controlled within a suitable range, as excessively hot food may burn oral lesions, while excessively cold food can trigger local sensitivity. Cooking methods such as steaming, boiling, and stewing are recommended to effectively enhance food softness and digestibility.

Children experiencing diarrhea require simultaneous implementation of dietary intervention plans. High-fiber food intake should be restricted to prevent intensified intestinal peristalsis. Cold foods like sashimi, ice cream, and cold salads are strictly prohibited to reduce the risk of intestinal infections.

4.3. Multidisciplinary collaboration model

In the field of nutritional management for children with leukemia during chemotherapy, the multidisciplinary collaboration model demonstrates its unique value. Nutrition departments, in alliance with hematology and pediatrics experts, form diagnostic and therapeutic coalitions to collaboratively develop and execute individualized nutritional support strategies. Zhong [19] proposed that receiving multidisciplinary collaborative nutritional intervention alongside chemotherapy can improve treatment efficacy and enhance overall nutritional status, making it worthy of promotion. Hematology specialists deeply understand the clinical characteristics of children, stage the chemotherapy process, and systematically assess the impact of tumor burden on body metabolism, laying a precise diagnostic foundation for nutritional management. Pediatricians master child growth patterns and physiological characteristics, systematically calculating nutritional needs based on parameters such as age, weight, height, and underlying diseases, allowing data from hematology and pediatrics to serve as the baseline for nutritional science intervention.

5. Conclusion

To optimize children's nutritional levels, enhance treatment efficacy, and improve quality of life, various intervention programs have been gradually implemented, involving dietary structure modification, personalized nutritional supplementation strategies, and professional education support systems. Currently, nutritional interventions for children with leukemia during chemotherapy still face certain practical bottlenecks and theoretical gaps. In-depth exploration in this field continues, with improving specific implementation pathways being a key focus of clinical practice. It is essential to deepen multidisciplinary collaboration mechanisms, enhance healthcare professionals' capabilities in nutritional diagnosis and therapy [20], and improve the comprehensive support system for children with leukemia and their families. Implementing systematic nutritional education and psychological counseling strategies can significantly improve treatment compliance. Promoting the clinical translation of new nutritional intervention models, proposing novel intervention mapping methods, and analyzing research progress will facilitate the application of scientific findings in practice, build precise nutritional support programs, ultimately optimize the survival prognosis of children during chemotherapy, and comprehensively enhance the quality of life for children with leukemia.

Disclosure statement

The authors declare no conflict of interest.

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