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The effect of nutritional education program on micronutrient intake in children with chronic liver disease: A clinical trial

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Abstract:

BACKGROUND: Chronic liver disease (CLD) is one of the most common chronic diseases in the world that threatens the health of children due to its many complications such as malnutrition and problems related to growth and development. Paying attention to nutrition and lifestyle modification in these children is of special importance. Therefore, the aim of this study was to determine the effect of nutritional education program on micronutrient intake in children with CLD.

MATERIALS AND METHODS: The present study is a two-group randomized clinical trial that was performed by available sampling and referred to Ghaem Children's Hospital in Mashhad in 2016. In this study, 77 children with CLD who met the inclusion criteria (45 children in the intervention group and 32 children in the control group) were studied. The intervention included six workshops and training on proper diet, post-workshop phone calls, and regular face-to-face counseling sessions (first 4 weeks once a week and second 4 weeks once every 2 weeks) on adherence to the above diet. Patients in the control group received routine care. The collection tools in the study included demographic information questionnaires, body composition device, and diet plan form in the form of 24-h recall forms. Data analysis was performed using descriptive statistical tests and Mann-Whitney and Wilcoxon statistical tests using SPSS software version 16.

RESULTS: Based on the results of the study, the mean age of the research units was 7.8 ± 3.6 years. The mean duration of CLD was 4.6 ± 1.8 years in the intervention group and 5.1 ± 1.9 years in the control group. The mean crude intake of most minerals after the intervention was significantly higher than before the intervention, except for the crude intake of retinol, thiamine, riboflavin, folate, Vitamin C, iodine, and Vitamin B12. Furthermore, in relation to the modified intake of micronutrients, the mean modified intake of most micronutrients after the intervention showed a significant increase compared to before, except for retinol, Vitamin D, niacin, B12, and iodine.

CONCLUSION: Considering the effect of providing a nutritional education program to improve micronutrient intake in children with CLD and emphasizing the importance of adequate micronutrient intake in improving the health of children, special nutrition programs should be provided to these children with special attention. In this regard, nurses can play an important role in improving the quality of nutrition of children by providing nutrition programs with appropriate follow-up.

Keywords:

Children, chronic liver disease, education, micronutrients, nutrition

Introduction

Chronic liver disease (CLD) is one of the most common chronic diseases in the world that threatens the health of

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children. This disease is an abnormal activity of the liver with inflammation and necrosis (at least 6 months) caused by a series of disorders with variable causes and severity. CLD covers a wide range of diseases, from nonprogressive to severe forms. Severe forms are associated with scar formation and changes in liver structure and if progressed, eventually lead to cirrhosis.^[1] Contrary to popular belief that chronic illness is an adult illness, children and adolescents also get chronic illness. Chronic diseases occur in all age groups, socioeconomic classes, and different cultures.^[2] CLD and cirrhosis cause 44,000 deaths in the United States and 2 million deaths worldwide.^[3,4] In addition, the disease causes severe pressure on health-care systems and increases health care every year by creating disability.^[5] Worldwide, more than 1.5 billion people had CLD in 2017.^[6] It is estimated that by 2050, 167 million people will be chronically ill.^[1] According to the latest statistics, chronic diseases account for 47% of all diseases in the Middle East and 80% of deaths in low- and middle-income countries. In developed countries, chronic diseases are also a major cause of health problems. According to the American National Research Institute, 15%–18% of American children and adolescents currently have chronic illnesses, a rate that has nearly doubled in the past two decades.^[7] The progression of this disease can reduce the function of the affected person. In this way, by causing emotional and mood changes, it causes recurrent disorders of depressed mood. Depressed mood reduces the patient's performance by aggravating the symptoms of the disease and reduces the person's energy that needed to overcome the chronic illness. so physical symptoms become unbearable and the person's disability increases; and has a negative effect on the patient's quality of life.^[8] Studies show a decrease in quality of life in people with CLD, regardless of the type of disease.^[9,10] The quality of life of children with chronic autoimmune liver disease is impaired following symptoms such as abdominal pain, fatigue, and mood symptoms.^[11] On the other hand, this disease leads to complex pathophysiological lesions in the liver. Because the liver is a major organ of food metabolism and energy,^[12] damage to it impairs digestion,^[13] absorption, distribution, storage, and utilization of nutrients in children with chronic disease. Thus, whatever the underlying cause of CLD in children, it can lead to liver insufficiency and cirrhosis and may eventually lead to severe cholestasis with itching, malabsorption, malnutrition, and growth retardation. Malnutrition in CLD is complex and involves several mechanisms including decreased food intake, increased gastrointestinal wasting, malnutrition, increased energy consumption, and defective metabolism of various substrates.^[14] The effects of secondary malnutrition due to CLD vary and include deficiency of fat-soluble vitamins, impaired general growth, impaired gastrointestinal function, immunosuppression, and

hypoxia. Malnutrition is now known to be a major risk factor for liver transplantation and increased morbidity and mortality.^[15] Children with reduced oral intake or functional/structural dysfunction in the gut (such as fat malabsorption, port hypertension, or atrophic changes associated with protein-calorie malnutrition) are prone to micronutrient deficiencies such as calcium, magnesium, iron, zinc, and selenium.^[12] In extensive hepatic failure, plasma branched-chain amino acid concentrations (leucine, isoleucine, and valine) decrease and aromatic amino acid concentrations (phenylalanine and tyrosine) increase, which can be associated with hepatic encephalopathy. As a result, branched-chain amino acids (valine, leucine, and isoleucine) prevent hepatic encephalopathy, whereas aromatic amino acids (tyrosine, phenylalanine, and methionine) accelerate it. Branched-chain amino acids are metabolized independently of the liver and mostly through the muscles, and after their breakdown, excretory material does not accumulate because they are excreted by the kidneys. Nutrition therapy is performed with the aim of improving quality of life; Through preventing malnutrition; catabolic status; improving protein metabolism by providing higher levels of branched-chain amino acids; and preventing or controlling ascites and edema with fluid restriction, sodium restriction, and adequate potassium intake.^[14] Therefore, it seems that in this disease, the intake, digestion, and absorption of micronutrients are impaired, and it is necessary to consider appropriate dietary measures to provide optimal care in children with liver disease.^[12,16] Measures should be individual and consistent with existing manifestations, interpretation of child nutrition studies, and treatment measures. Nutritional measures should be planned based on the nature and degree of malnutrition of the infant or child with CLD.^[17] So far, no effective treatment for this disease has been known. Therapies typically focus on lifestyle changes (including weight loss and adherence to appropriate nutritional strategies to reduce the severity and severity of the disease).^[18] Unfortunately, patients do not pay enough attention to nutritional instructions.^[19] One study reported that 35% of patients with metabolic syndrome had no healthy eating plans and diets for self-care, and only 7% of patients fully implemented the recommended nutritional self-care behavioral aspects.^[20] In another study that presented a diet plan to diabetic patients, the results showed that many patients did not adhere to the diet provided alone.^[21] In this regard, the study of Tehrani *et al.*, which examined the effect of nutrition education on nonalcoholic fatty liver disease, showed that nutrition education is more cost-effective than other treatments. Patients can also prevent the severity of the disease by observing nutritional tips and choosing better and more appropriate foods and knowing how much to consume.^[22] Therefore, in addition to prescribing diets

and dietary programs, focusing on nutrition education and follow-up sessions in vulnerable groups using the latest available resources and correcting eating habits can lead to changes in patients' diets.^[23] To provide training and nutrition program, nurses as a nutrition consultant, by assessing the status of micronutrient intake through selected foods, examine the balance between nutrient intake and the amount needed for it and thus play a role in facilitating nutritional care. In other words, the nurse helps the patient by intervening and educating the patient about nutrition and advising him to consume enough of the required micronutrients as well as monitoring the patient's performance.^[24-26] In this way, nurses can play an important role in determining the nutritional needs and diet of the patient through nutrition education and empowerment.^[25,27,28]

This disease is one of the health problems of the country, and due to the chronic and irreversible nature of the disease, it needs care and treatment education programs, lifestyle modification, and diet change.^[29,30] On the other hand, unfortunately, proper nutrition in providing micronutrients for children with liver disease is not well known. As a result, proper nutritional measures are essential in providing optimal care to children with CLD because early and appropriate dietary interventions bring many benefits to these children; considering the effect of CLD on micronutrient intake and the interaction between CLD and nutritional status, the present study was conducted to determine the effect of nutritional training program on micronutrient intake in children with CLD.

Materials and Methods

Study design and setting

The present study is a two-group randomized clinical trial with the code of clinical trial IRCT2015091424019N1 in Mashhad University of Medical Sciences. Sampling was done by available and by referring to Ghaem Children's Hospital in Mashhad in 2016. Inclusion criteria were as follows: children 2–18 years old with liver disease who have been ill for at least 6 months; have Iranian citizenship and live in Mashhad; in addition to CLD, the child should not have any other physical health restrictions; and in addition to CLD, the child should not have mental health restrictions. Exclusion criteria were as follows: do not want to continue to cooperate, need TPN feeding, and need tube feeding.

Study participants and sampling

The number of samples in the present study was calculated using the following formula, taking into account the 95% confidence level and 80% test power and 79 people (including 45 people in the intervention group and 34 people in the control group). However,

after dropping the sample, two patients from the control group were excluded from the study due to the severity of the disease and hospitalization. Finally, data analysis was performed on 45 people in the intervention group and 32 people in the control group.

$$N = (z_{[1-\alpha/2]} + z_{[1-\beta]})^2 \times (S_1^2 + S_2^2) / (m_1 - m_2)^2$$

The subjects were randomly divided into control and intervention groups (45 in the intervention group and 34 in the control group). Variables such as sex, age, weight, height, body mass index, and duration of the disease were statistically controlled. Therefore, the two groups were completely similar in terms of these variables, and as a result, these variables were not confusing.

Data collection tool and technique

The tools used in this study included demographic information, body composition device, and diet plan form which was in the form of 24-h recall forms. Diet plan form that is completed 24 h of a day. There are a variety of diet plan forms that contain tables of the amount and type of food consumed by a person within 24 h. For the validity of the form and the questionnaire, the validity of the content was used. After reviewing the existing forms and reviewing the latest studies and evidence, the draft form was prepared and provided to 10 respected professors of Mashhad School of Nursing and Midwifery for review and comment. After correcting and inserting the suggested comments, the tool was reviewed and then used. Children's personal and demographic information included 17 questions in the form of 4 questions with closed answers and 13 questions with open answers and inclusion and exclusion criteria. This questionnaire was completed by interviewing the mother and referring to the children's file. To measure weight, an electric bioimpedance device was used, which is a valid tool for measuring weight. Children without shoes and with minimal clothing were placed on it, and their weight was carefully calculated. Meanwhile, the accuracy of the device was checked by placing a weight of 2 kg. The method consisted of three stages (before the workshop, workshop, and after the workshop).

The stage before the workshop, including the nutrition adjustment guide, was developed by studying the articles and valid scientific sources in the integrative method at both specialized and general levels by the Delphi method. After finalizing the guidelines, their validity was reevaluated by experienced professors of pediatric gastroenterology, pediatric nursing, research method, and nutrition by content validity method. Then, training slides based on the guideline for training in the workshop and the educational content of the workshops were prepared separately for the sessions.

An educational brochure on CLD was developed for patient use. At the first visit of the research units to the nutrition and diet therapy clinic of Ghaem Hospital, they were visited by a nutritionist. The demographic information questionnaire was completed based on the statements of the competent caregiver and the patient file. The researcher then reviewed the 3-day food intake of the research unit and developed a 24-h, 3-day reminder by asking the competent caregiver. After sampling, the workshops began. The workshop consisted of six sessions over 2 weeks. The contents of the sessions were as follows: presentation of materials related to liver function and nutrition; introduction of various micronutrients and CLD; clinical findings of CLD, malnutrition, intolerance, and damage related to digestion; changes in micronutrient metabolism; useful understanding of micronutrient intake; expected contribution for children with CLD; specific calculation of contribution for the child; and how to calculate vitamins, minerals, and micronutrients. The follow-up phase consisted of 12 weeks,^[12] in which the patient's caregiver was evaluated by telephone, 3-day regular counseling sessions, and 24-h recall, and 24-h record forms. During the first 4 weeks once a week and during the second 4 weeks every 2 weeks, caregivers attended the counseling session. In these meetings, their questions about following the above regime were answered. After a 12-week follow-up phase, reassessment was performed in terms of adherence to a specific diet and calculation of minerals and micronutrients. A summary of the execution method is given in the form of a diagram [Figure 1]. After data collection, the data were analyzed by SPSS software version 16 statistical software package

IBM SPSS version 16 (IBM, USA, 2005). To describe the characteristics of the research units, descriptive statistics including absolute and relative frequency distributions (for qualitative variables) and mean and standard deviation (for quantitative variables) were used. In addition, Kolmogorov–Smirnov and Shapiro–Wilk statistical tests were used to evaluate the normality of the distribution of quantitative variables. Independent *t*-test was used to evaluate the homogeneity of the two groups in terms of quantitative normal variables and Mann–Whitney test was used for quantitatively abnormal variables. For before and after comparisons within the group (intervention and control), paired *t*-test was used, and when the variable did not have a normal distribution, nonparametric Wilcoxon test was used. In all tests, a confidence interval of 95% was considered. A significance level of 0.05 was considered; therefore, in cases where it was $P < 0.05$, a statistically significant difference was reported.

Ethical consideration

To observe the ethical considerations of the research, children and parents who for any reason at any stage did not want to continue to participate in the research could leave the research. Furthermore, a training workshop was held for the control group with the same content of the intervention group.

Results

Based on the results of the study, the mean age of the research units was 7.8 ± 3.6 years, which were homogeneous in both intervention and control groups. Furthermore, most of the subjects in both intervention (27; 0.60%) and control (18; 60%) groups were boys, who were homogeneous according to Chi-square test. Regarding anthropometric data, the mean height was 122.5 ± 23.1 cm in the intervention group and 135.2 ± 29.3 cm in the control group. The mean weight was homogeneous in the intervention group (26.0 ± 13.9 kg) and in the control group (28.3 ± 18.5 kg). The mean duration of CLD in the intervention group (4.6 ± 1.8 years) and in the control group (5.1 ± 1.9 years) was homogeneous. Mann–Whitney test showed that before the intervention, the mean crude intake of Vitamin D ($P = 0.181$) and Vitamin E ($P = 0.565$) was not statistically significant. However, the mean crude retinol intake was statistically significant ($P = 0.044$). Furthermore, after the intervention, the difference between the means of crude intake of Vitamin D ($P = 0.048$) and Vitamin E ($P = 0.021$) between the two groups was statistically significant. However, the mean crude retinol intake after the intervention between the two groups was not statistically significant ($P = 0.275$). Mann–Whitney test showed that there was no statistically significant difference between Vitamin D ($P = 0.186$) and Vitamin E ($P = 0.328$) before

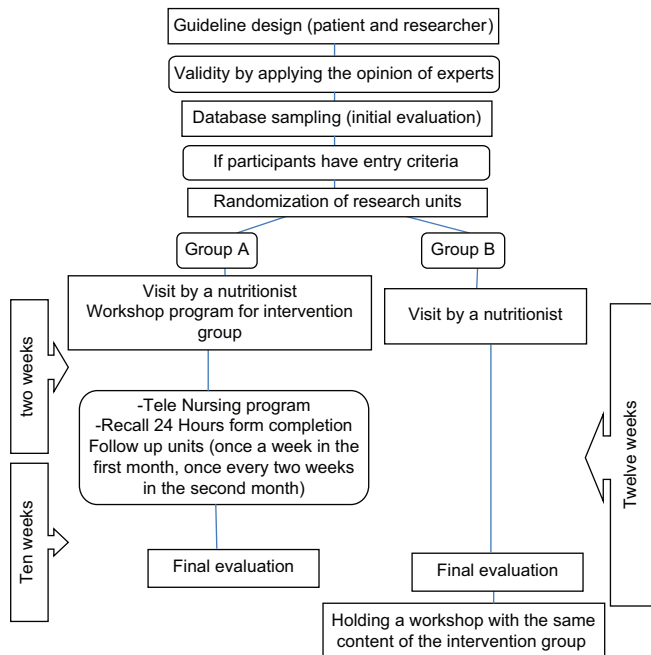


Figure 1: Algorithm of research implementation stages

the intervention. However, the mean intake after retinol energy adjustment was statistically significant ($P = 0.021$). Furthermore, after the intervention, the difference between the means of energy intake after adjustment of Vitamin D ($P < 0.001$) and retinol ($P = 0.002$) between the two groups was statistically significant. The mean intake of Vitamin E after energy adjustment after the intervention between the two groups was not statistically significant ($P = 0.021$) [Table 1].

In the intervention group, the results of Wilcoxon statistical test showed that the mean score of crude retinol intake ($P = 0.461$) and Vitamin D ($P = 0.169$) in the postintervention phase was not significant compared to before the intervention. However, the mean crude intake of Vitamin E ($P < 0.001$) in the postintervention stage compared to before the intervention was statistically significant. In the control group, the mean crude intake of retinol ($P = 0.064$), Vitamin D ($P = 0.668$), and Vitamin E ($P = 0.555$) in the postintervention stage compared to before the intervention was not statistically significant. The results of Wilcoxon statistical test showed that the mean score after retinol energy adjustment ($P = 0.434$) in the postintervention stage compared to before the intervention was not statistically significant; however, the mean score after energy adjustment of Vitamin D ($P = 0.017$) and Vitamin E ($P = 0.001$) in the postintervention stage compared to before the intervention was statistically significant. However, in the control group, the mean intake after retinol energy adjustment ($P = 0.668$) and Vitamin D ($P = 0.80$) in the next stage compared to before the intervention was not statistically significant. However, the mean intake of Vitamin E after energy adjustment ($P < 0.001$) in the postintervention stage compared to before the intervention was statistically significant [Table 2].

Mann–Whitney test showed that the mean crude intake of thiamine ($P = 0.818$), riboflavin ($P = 0.605$), niacin ($P = 0.908$), pantothenic ($P = 0.646$), B6 ($P = 0.774$),

B12 ($P = 0.167$), folate ($P = 0.472$), and Vitamin C ($P = 0.652$) was not statistically significant before the intervention. However, after the intervention, the difference between the means of crude intake of thiamine, riboflavin, pantothenic, B6, folate, and Vitamin C ($P < 0.001$) and niacin ($P = 0.007$) between the two groups was statistically significant. However, the mean crude B12 intake after the intervention between the two groups was not statistically significant ($P = 0.931$). Before the intervention, Mann–Whitney test showed that the mean intake after energy adjustment were not statistically significant. So that the amount of P values were as follows: thiamine ($P = 0.863$), riboflavin ($P = 0.301$), niacin ($P = 0.455$), pantothenic ($P = 0.527$), B6 ($P = 0.206$), B12 ($P = 0.605$), folate ($P = 0.358$) and Vitamin C ($P = 0.121$). However, after the intervention, the difference between the mean of thiamine, pantothenic, B6, folate ($P < 0.001$), riboflavin ($P < 0.002$), Vitamin C ($P < 0.001$) between the two groups was statistically significant. However, the mean intake after energy adjustment of niacin ($P = 0.301$) and B12 ($P = 0.328$) after the intervention between the two groups was not statistically significant [Table 3].

In the intervention group, the results of Wilcoxon statistical test showed that the mean scores of crude intake of thiamine, pantothenic, Vitamin B6, folate, and Vitamin C ($P < 0.001$) and riboflavin ($P = 0.001$), niacin ($P = 0.004$), and Vitamin B12 ($P = 0.042$) in the postintervention stage compared to before the intervention were statistically significant. In the postintervention stage compared to before the intervention in the control group, the mean crude intake of thiamine ($P = 0.829$), riboflavin ($P = 0.253$), B6 ($P = 0.829$), B12 ($P = 0.308$), folate ($P = 0.068$), and Vitamin C ($P = 0.975$) was not statistically significant. However, the mean crude intake of niacin ($P = 0.001$) and pantothenic ($P = 0.009$) in the postintervention stage compared to before the intervention was statistically significant. In the postintervention group compared to before the intervention, the results of Wilcoxon statistical

Table 1: Mean and standard deviation of fat-soluble vitamins in children with chronic liver disease studied in two groups of intervention and control

Fat-soluble vitamins	Studied groups					
	Intervention			Control		
	Before intervention	After intervention	P	Before intervention	After intervention	P
Retinol (mg)						
Crude	473.43±14.39	438.45±86.91	0.461	1898.665±50.53	626.94±70.93	0.064
Justified	347.69±43.62	318.62±70.23	0.434	1708.658±87.93	652.71±28.82	0.688
Vitamin D (mg)						
Crude	5.0±78.51	4.0±43.48	0.169	6.0±92.66	6.0±54.65	0.688
Justified	5.0±15.47	3.0±98.58	0.017*	5.0±93.37	6.0±68.51	0.180
Vitamin E (mg)						
Crude	40.6±31.39	58.4±18.31	<0.001*	42.4±21.51	41.3±29.57	0.557
Justified	34.4±99.38	51.2±21.84	0.001*	34.4±52.16	45.3±46.21	<0.001*

*Mann-Whitney statistical test

Table 2: Mean and standard deviation of fat-soluble vitamins in children with chronic liver disease studied before and after intervention in two groups

Fat-soluble vitamins	Studied groups					
	Intervention			Control		
	Before intervention	After intervention	P	Before intervention	After intervention	P
Retinol (mg)						
Crude	473.43±14.39	438.45±86.91	0.461	1898.665±50.53	626.94±70.93	0.064
Justified	347.69±43.62	318.62±70.23	0.434	1708.658±87.93	652.71±28.82	0.688
Vitamin D (mg)						
Crude	5.0±78.51	4.0±43.48	0.169	6.0±92.66	6.0±54.65	0.688
Justified	5.0±15.47	3.0±98.58	0.017*	5.0±93.37	6.0±68.51	0.180
Vitamin E (mg)						
Crude	40.6±31.39	58.4±18.31	<0.001*	42.4±21.51	41.3±29.57	0.557
Justified	34.4±99.38	51.2±21.84	0.001*	34.4±52.16	45.3±46.21	<0.001*

*Wilcoxon statistical test

Table 3: Mean and standard deviation of water-soluble vitamins in children with chronic liver disease studied in two groups of intervention and control

Water-soluble vitamins	Studied groups					
	Intervention			Control		
	Before intervention	After intervention	P	Before intervention	After intervention	P
Thiamine (mg)						
Crude	2.0±87.36	3.0±24.48	0.818	6.0±93.76	3.0±10.41	0.0002
Justified	2.0±68.16	2.0±72.15	0.863	4.0±79.25	3.0±42.22	0.00001
Riboflavin (mg)						
Crude	2.0±72.32	2.0±62.30	0.605	4.0±35.31	2.0±36.32	0.00004
Justified	2.0±37.23	2.0±90.19	0.301	3.0±51.35	2.0±55.20	0.002*
Niacin (mg)						
Crude	45.6±20.59	43.5±12.48	0.908	61.5±31.47	48.6±45.32	0.007*
Justified	39.5±61.46	33.2±89.04	0.455	46.3±64.44	54.3±55.40	0.301
Pantothenic (mg)						
Crude	9.1±31.00	9.0±33.83	0.646	14.0±74.69	8.0±32.78	0.00002
Justified	7.0±58.90	7.0±13.50	0.527	11.0±65.83	8.0±40.46	0.00001
B6 (mg)						
Crude	3.0±66.36	3.0±42.27	0.774	6.0±74.34	3.0±37.26	0.00005
Justified	3.0±31.31	2.0±90.13	0.206	8.0±19.35	6.0±70.15	0.00001
B12 (mg)						
Crude	10.1±60.40	14.1±18.83	0.167	11.0±75.99	11.1±99.26	0.931
Justified	9.1±66.27	12.1±52.53	0.605	10.1±80.27	13.0±11.90	0.328
Folate (mg)						
Crude	410.42±62.84	4766.51±40.74	0.472	1503.134±86.46	424.44±0.59	0.00003
Justified	342.27±93.82	375.23±21.07	0.358	1220.120±40.70	489.41±28.92	0.00001
Vitamin C (mg)						
Crude	165.27±50.01	126.18±30.39	0.652	406.52±0.83	132.25±20.50	0.00004
Justified	152.23±69.53	107.17±47.73	0.121	360.55±13.18	144.25±30.12	0.002*

test showed that the mean score after energy adjustment of thiamine, Vitamin B6, and folate ($P < 0.001$) and riboflavin ($P = 0.002$), niacin and Vitamin B12 ($P = 0.042$), pantothenic and Vitamin C ($P = 0.001$) that were statistically significant; however, in the control group, the mean score received after energy adjustment for thiamine was ($P = 0.001$), riboflavin ($P = 0.010$), niacin and Vitamin B6 ($P < 0.001$), pantothenic ($P = 0.018$), folate ($P = 0.004$), and Vitamin C ($P = 0.017$) and that were statistically significant. However, the mean intake of Vitamin B12 after energy adjustment ($P = 0.308$)

in the postintervention stage compared to before the intervention in the control group was not statistically significant [Table 4].

Before the intervention, Mann–Whitney test showed that the mean intake of crude zinc ($P = 0.626$), copper ($P = 0.158$), selenium ($P = 0.697$), manganese ($P = 0.242$), iodine ($P = 0.173$), and iron ($P = 0.080$) did not have a statistically significant difference. However, after the intervention, the difference between the mean intakes of crude zinc, copper, selenium,

manganese, and iron ($P < 0.001$) and iodine ($P = 0.002$) between the two groups was statistically significant. Mann–Whitney test showed that before the intervention, the mean intake of zinc ($P = 0.922$), copper ($P = 0.436$), manganese ($P = 0.144$), and iron ($P = 0.064$) was not statistically significant. However, the mean intake after modulation of selenium ($P = 0.003$) and iodine ($P = 0.006$) before the intervention between the two groups was statistically significant. After the intervention, the differences between the means of zinc ($P = 0.058$); copper, manganese, and iron ($P < 0.001$); selenium ($P = 0.001$); and iodine ($P = 0.010$) between the two groups were statistically significant [Table 5].

The results of Wilcoxon statistical test showed that the mean scores of crude zinc, copper, selenium, manganese, and iron ($P < 0.001$) in the postintervention stage compared to before the intervention in the intervention group were statistically significant. However, in the postintervention stage compared to before the intervention in the intervention group, the average crude iodine intake ($P = 0.636$) was not statistically significant. In the control group, in the postintervention stage compared to before the intervention, the average intake of crude zinc ($P = 0.146$), selenium ($P = 0.147$), manganese ($P = 0.477$),

iodine ($P = 0.440$), and iron ($P = 0.089$) was not statistically significant. However, the mean score of crude copper intake ($P = 0.045$) in the postintervention stage compared to before the intervention was statistically significant. In the postintervention stage compared to before the intervention in the intervention group, the results of Wilcoxon statistical test showed that the mean scores of zinc, copper, selenium, manganese, and iron ($P < 0.001$) were statistically significant. However, the mean score of iodine intake ($P = 0.751$) in the postintervention stage compared to before the intervention in the intervention group was not statistically significant.

In the control group, in the next stage, compared to before the intervention, the mean intake of zinc, selenium, manganese, and iron ($P < 0.001$) was statistically significant. However, in the postintervention stage, compared to before the intervention in the control group, the mean intake of copper ($P = 0.404$) and iodine ($P = 0.440$) was not statistically significant [Table 6].

Discussion

CLD is one of the most common chronic diseases. The first line of intervention at any age is lifestyle

Table 4: Mean and standard deviation of water-soluble vitamins in children with chronic liver disease studied before and after intervention in two groups

Water-soluble vitamins	Studied groups					
	Intervention			Control		
	Before intervention	After intervention	<i>P</i>	Before intervention	After intervention	<i>P</i>
Thiamine (mg)						
Crude	2.0±87.36	3.0±24.48	<0.001*	6.0±93.76	3.0±10.41	0.829
Justified	2.0±68.16	2.0±72.15	<0.001*	4.0±79.25	3.0±42.22	0.001*
Riboflavin (mg)						
Crude	2.0±72.32	2.0±62.30	0.001*	4.0±35.31	2.0±36.32	0.253
Justified	2.0±37.23	2.0±90.19	0.002*	3.0±51.35	2.0±55.20	0.010*
Niacin (mg)						
Crude	45.6±20.59	43.5±12.48	0.004*	61.5±31.47	48.6±45.32	0.001*
Justified	39.5±61.46	33.2±89.04	0.042*	46.3±64.44	54.3±55.40	0.00001
Pantothenic (mg)						
Crude	9.1±31.00	9.0±33.83	<0.001*	14.0±74.69	8.0±32.78	0.009*
Justified	7.0±58.90	7.0±13.50	0.001*	11.0±65.83	8.0±40.46	0.018*
B6 (mg)						
Crude	3.0±66.36	3.0±42.27	<0.001*	6.0±74.34	3.0±37.26	0.829
Justified	3.0±31.31	2.0±90.13	<0.001*	8.0±19.35	6.0±70.15	0.00004
B12 (mg)						
Crude	10.1±60.40	14.1±18.83	0.042*	11.0±75.99	11.1±99.26	0.308
Justified	9.1±66.27	12.1±52.53	0.042*	10.1±80.27	13.0±11.90	0.308
Folate (mg)						
Crude	410.42±62.84	4766.51±40.74	<0.001*	1503.134±86.46	424.44±0.59	0.068
Justified	342.27±93.82	375.23±21.07	<0.001*	1220.120±40.70	489.41±28.92	0.004*
Vitamin C (mg)						
Crude	165.27±50.01	126.18±30.39	<0.001*	406.52±0.83	132.25±20.50	0.975
Justified	152.23±69.53	107.17±47.73	0.001*	360.55±13.18	144.25±30.12	0.017*

modification through changes in diet and physical activity.^[30] The liver plays an important role in the metabolism of micronutrients, and this metabolism is often altered in CLD.^[31]

Vranešić Bender *et al.*, by examining the nutritional status, macronutrients, and micronutrients in people with nonalcoholic liver disease, concluded that people with nonalcoholic fatty liver disease are deficient in

calcium, magnesium, iron, zinc, and Vitamins B1, A, and B2. As a result, they need specific dietary modifications.^[32]

The results of the present study, which aimed to investigate the effect of a specific nutritional program on children with CLD, showed that after the intervention, there was a significant difference in micronutrient intake of children with the disease. The difference between the means of raw Vitamin D and Vitamin E intake between

Table 5: Mean and standard deviation of micronutrient intake in children with chronic liver disease studied in two groups of intervention and control

Micronutrients	Studied groups					
	Intervention			Control		
	Before intervention	After intervention	P	Before intervention	After intervention	P
Zinc (mg)						
Crude	24.2±97.43	26.2±70.78	0.626	44.3±42.01	27.3±76.03	0.00001
Justified	22.1±29.51	20.1±26.19	0.922	35.2±87.47	30.1±88.41	0.058
Copper (mg)						
Crude	2.0±10.21	3.0±40.44	0.158	7.0±34.71	2.0±15.21	0.00002
Justified	3.0±46.12	4.0±12.39	0.436	6.0±55.42	3.0±38.29	0.00001
Selenium (mg)						
Crude	87.7±85.15	82.7±24.58	0.697	155.11±21.32	83.9±8.16	0.00001
Justified	77.3±24.76	62.2±37.46	0.003*	116.7±99.16	90.2±17.35	0.001*
Manganese (mg)						
Crude	3.0±65.36	4.0±83.65	0.242	14.1±79.65	4.0±61.53	0.00003
Justified	0.2±23.17	2.0±76.14	0.144	10.0±42.60	5.0±24.52	0.00001
Iodine (mg)						
Crude	253.25±0.49	190.18±40.33	0.173	266.28±64.96	184.28±16.70	0.002*
Justified	231.0±56.50	148.11±70.29	0.006*	231.33±29.77	192.24±43.16	0.010*
Iron (mg)						
Crude	20.1±69.78	26.3±80.16	0.080	62.5±80.52	24.2±90.88	0.00002
Justified	16.0±59.64	19.0±38.87	0.064	46.4±55.04	26.1±95.29	0.00001

Table 6: Comparison of mean micronutrient intake in children with chronic liver disease before and after the intervention in the two groups

Micronutrients	Studied groups					
	Intervention			Control		
	Before intervention	After intervention	P	Before intervention	After intervention	P
Zinc (mg)						
Crude	24.2±97.43	44.3±42.01	<0.001*	24.2±70.78	27.3±76.03	0.146
Justified	22.1±29.51	35.2±87.47	<0.001*	20.1±26.19	30.1±88.41	0.00001
Copper (mg)						
Crude	2.0±10.21	7.0±34.71	<0.001*	3.0±40.44	2.0±15.21	0.045*
Justified	3.0±46.12	6.0±55.42	<0.001*	4.0±12.39	3.0±38.29	0.404
Selenium (mg)						
Crude	87.7±85.15	155.11±21.32	<0.001*	82.7±24.58	83.9±8.16	0.147
Justified	77.3±24.76	116.7±99.16	<0.001*	62.2±37.46	90.2±17.35	0.00002
Manganese (mg)						
Crude	3.0±65.36	14.1±76.65	<0.001*	4.0±83.65	4.0±61.53	0.477
Justified	2.0±23.17	10.0±42.60	<0.001*	2.0±76.14	5.0±24.52	0.00003
Iodine (mg)						
Crude	253.25±10.49	266.28±64.96	0.636	190.18±40.33	184.28±16.70	0.440
Justified	231.20±56.50	231.33±29.77	0.751	148.11±70.29	192.24±43.16	0.147
Iron (mg)						
Crude	20.1±69.87	62.5±80.52	<0.001*	26.3±80.16	24.2±90.88	0.089
Justified	16.01±59.64	46.4±55.04	<0.001*	19.0±38.87	26.1±95.29	0.00001

the two groups was statistically significant. However, the mean crude retinol intake after the intervention between the two groups was not statistically significant. The mean intake after retinol energy adjustment was statistically significant. Regarding the role of retinoic acid in hepatic lipid metabolism, the Shiota study in transgenic mice lacking hepatic retinoic acid expression showed a deficiency in mitochondrial β -oxidation and impaired hepatic lipid metabolism regulation. Modified diets containing high retinoic acid are eliminated.^[33] In this regard, Gavaravarapu *et al.* in reviewing the meta-analysis showed that nutrition education interventions along with follow-up can be effective in improving children's micronutrient intake and improving children's health.^[34] The study by Chaves *et al.*, which examined retinoic acid deficiency in CLD patients, showed that due to the severity of liver disease, a gradual decrease in serum retinol and RBP was observed and a higher prevalence of severe VAD was observed in cirrhosis.^[35] Regarding the role of Vitamin D in CLD, Vitamin D deficiency is caused by malabsorption or reduction of dietary intake and exposure to sunlight and hydroxylation of the liver. This deficiency leads to rickets and fractures if left untreated. Babies are especially sensitive because their bone mineral can be rapidly depleted during the first 2 years of life.^[36,37] The difference between the means of crude intake of thiamine, riboflavin, pantothenic, B6, folate, Vitamin C, and niacin between the two groups after the intervention was statistically significant, but the mean crude intake of B12 after the intervention between the two groups was not statistically significant. The mean crude intake of niacin and pantothenic acid in the post-intervention stage compared to before the intervention was statistically significant. Furthermore, in the postintervention stage compared to before the intervention, in the intervention group the mean score after energy adjustment of thiamine, Vitamin B6, folate, riboflavin, niacin, Vitamin B12, pantothenic, and Vitamin C was statistically significant. However, the mean intake of Vitamin B12 after energy adjustment in the postintervention phase compared to before the intervention in the control group was not statistically significant. In a study in mice with liver disease, the addition of niacin significantly reduced hepatic and serum triglyceride levels and improved hepatic steatosis.^[38,39]

In relation to Vitamin C and other antioxidants, studies confirm that the effect of this vitamin balances the effects of reactive oxygen species in cells by inhibiting free radicals.^[40] Low levels of Vitamin C in children are associated with cases of NASH-proven biopsies, but in adults, there is no association.^[41]

The difference between the means of crude intake of zinc, copper, selenium, manganese, iron, and iodine between the two groups after the intervention was statistically

significant. Furthermore, the difference between the means of energy intake after adjustment of zinc, copper, manganese, iron, selenium, and iodine between the two groups was significant. Zinc reduces hepatic triglyceride accumulation and oxidative stress by increasing the secretion of low-density lipoprotein and activated receptor by proliferating proxies and liver factor-4a by mediating fatty acid oxidation, hepatic triglyceride accumulation, and oxidative stress.^[42] The liver plays an important role in copper metabolism, including the production of the ceruloplasmin transporter protein.

In a study of rats with nonalcoholic fatty liver disease, Aigner *et al.* compared three groups of diets rich in copper, free of copper, and with limited intake of copper for 8 weeks. The results showed severe hepatic steatosis and liver weight gain in copper-deficient and copper-free diet groups.^[43] Copper deficiency in liver patients may exacerbate oxidative stress and toxicity by impairing mitochondrial function and regulation. Therefore, various studies emphasize the importance of copper intake in the diet of liver patients.^[43-45] Iron plays an important role in liver disease. In this regard, the results of the study of Rao. agreed with the results of our study. The results of the Rao study showed that nutritional training intervention improved iron intake in girls aged 15–35 years, and girls who used more counseling sessions after training sessions received more iron intake.^[46] However, Kumar's study, which compared the effect of training on intake of iron-enriched salt, showed that receiving enriched salt is more effective in receiving iron than nutrition education.^[47] Regarding the effect of nutrition education and lifestyle modification on iodine intake in the diet, Ojeda-Rodríguez's study was also in line with our study and showed a significant effect of nutrition education on iodine intake.^[38]

Yang *et al.*, who looked at the nutritional status of children with end-stage liver disease, looked at the micronutrient status of these children. They stated that in order to improve these children, special diet programs that emphasize the intake of micronutrients should be considered, so that the complications of liver disorder affect the developmental stages of the child to a lesser extent.^[41] The results of many studies indicate the positive effects of nutritional interventions and lifestyle modification in patients with CLD and the need to provide specific dietary programs in children with treatment.^[30,48-51] In most studies, interventions are performed by the treatment team and nurses who play an important role in communicating with children. Lifestyle changes are the most important aspect in the prevention and treatment of CLD. In this regard, nurses play an important role, because patients are different in creating and maintaining lifestyle changes and weight loss.^[52] This requires trying to make patients fully aware of the disease and motivating them to

make lifestyle changes. Integrating the role of nurses in clinical management and care of patients with CLD has a great impact on better adherence to life changes and outcomes.^[53] Therefore, the use of educational intervention methods can lead to improving the health of children and adolescents in the future.^[54] In addition, nurses can be part of a multidisciplinary team (for example, dietitians, physiotherapists, and health educators to help the patient).^[55-57]

The most important strength of the present study was to pay attention to the follow-up of sustainability and adherence to diet and training tips that were done during face-to-face meetings with patients and the training method alone was not used. In several sessions, patients' questions about diet modification were answered and their adherence to the diet plan was considered.

Limitation and recommendation

The present study had a short follow-up period (which is the most important weakness of the present study). As a result, it seems that the sustainability of dietary reforms can have a greater impact on the course of the disease. For this purpose, it is suggested that the repetition of the current research with advanced review methods and a longer duration can be considered. Furthermore, considering the role of exercise along with diet modification, it is recommended to study the effect of dietary modification and exercise program in children with CLD.

Conclusion

The results of the present study indicate the effect of a specific nutritional program on the intake of most micronutrients in children with CLD. Due to the importance of providing a special diet in children to prevent malnutrition and growth and development problems and prevent the progression of liver disease to the final stages, it is recommended to pay special attention to special diets and provide to children with the disease. In this regard, nurses can play an important role in improving the quality of nutrition of infants by providing nutrition programs along with follow-up.

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Conflicts of interest

There are no conflicts of interest.

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