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Effects of Curcumin Supplementation on Quality of Life of Cystic Fibrosis Patients

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Abstract

Background: Cystic fibrosis (CF) is one of the most common genetic disorders in children. CF patients are susceptible to chronic lung infections and malabsorption. Although patient longevity is increased by multidisciplinary care, patients still suffer from respiratory failure and low quality of life. In this situation, CF patients tend to use complementary treatments. To the best of our knowledge there is no research about curcumin supplementation in CF patients; thus, we decided to investigate the effects of curcumin supplementation on anthropometric indices, and quality of life in children with cystic fibrosis.

Materials and Methods

This randomized control-controlled clinical study was conducted in Tabriz University of Medical Sciences, Iran. Forty CF patients were randomly sorted into intervention (n=20), and control (n=20) groups. Patients received 3 curcumin nanoparticles (80 mg; total dose 240 mg/d) for six consecutive months. Before and after intervention, height and weight were measured and quality of life of patients was evaluated by the Pediatric Quality of Life Inventory (PedsQL) 4.0 (CITE).

Results: After intervention, the percentage of weight changes showed a significant increase in the curcumin group compared to the control group (7.48±4.68 vs. 4.15±4.68 kg, p=0.03). Following the intervention, only the percentage of change in emotional functioning scores was significant (p=0.01). Subjects in the curcumin group showed a trend towards more improvement in terms of percentage change in physical functioning (19.28±31.65 vs. 15.24±47.14), and school functioning scores (40.96±42.93 vs 23.90±14.82) compared with the control group.

Conclusion

Our findings suggest that curcumin may be a useful, inexpensive, and safe supplement in combination with conventional therapy to improve body weight in CF children.

Key Words: Anthropometrics indices, Curcumin, Cystic fibrosis, Quality of life.

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1- INTRODUCTION

Cystic fibrosis (CF) is one of the most common genetic disorders and involves several organs, particularly the pulmonary and gastrointestinal systems. In the United States, nearly 1,000 new cases of CF are reported annually. The median survival age of CF patients is 35 years in USA (1). CF is caused by mutations in the CF transmembrane conductance regulator (CFTR), the cAMP-activated Cl ion channel, resulting in the reduction of chloride transport in the ion channel (2-4).

This defect increases the concentration of secretions and abnormally thick mucus, causing lung adhesion; mucus plugs obstruct the pancreatic ducts and there is increased chloride in the sweat. Thus, CF patients are susceptible to chronic lung infections and malabsorption. Since infection leads to the activation of inflammatory and immune responses, therapeutic options focus on antibiotic and anti-inflammatory therapies and nutritional repletion (3, 5, 6). Although patient longevity is increased by multidisciplinary care, patients still suffer from respiratory failure and low quality of life. In this situation, CF patients tend to use complementary treatments (7-10).

Considering the role of inflammation and oxidative stress in the complications of the disease, researchers focus on the use of complementary therapies, especially those derived from natural sources that have anti-inflammatory and antioxidant properties (11). Turmeric is a dietary spice that has been widely used for centuries as an herbal medicine due to its antibacterial, anti-inflammatory, antioxidant, and wound-healing properties. Extensive studies have shown tumeric's therapeutic efficacy in treating various diseases such as asthma, ulcerative colitis, cancer, and rheumatoid arthritis (12, 13). There are numerous chemical compounds, including demethoxycurcumin, bisdemethoxycurcumin, volatile oils, sugars, proteins, and resins in turmeric's rhizome. Curcumin is the most important component and active ingredient of turmeric thought to exhibit pharmacological effects such as anti-inflammatory, anti-cancer, anti-oxidant, anti-atherosclerotic, anti-microbial, and healing properties (12). Furthermore, signs of oxidative stress have been observed in the CF respiratory tract due to increased inflammation and frequent infections. The presence of systemic inflammatory and oxidative processes is accompanied by increases in the incidence of certain diseases, including diabetes, insulin resistance, and cardiovascular disease (14). Clinical trials on diseases caused by inflammation or oxidative stress provide evidence for the therapeutic effects of curcumin (12, 15, 16).

In a clinical trial, Hanai et al. reported that 2gr/d of curcumin over six months in colitis patients reduced the relapse rate of the disease. Additionally, consumption of curcumin significantly decreased clinical symptoms such as diarrhea and abdominal pain (17). In line with these findings, studies using cell cultures and animal models have shown that curcumin influences a variety of ion channels and transporters (18, 19). In this regard, Zhang et al. reported that curcumin affects the activities of different types of ion channels and transporters, especially the Cl^- channel, through various mechanisms. This finding is of interest for the treatment of CF and researchers have suggested that clinical trials are needed (18).

Management of pulmonary and pancreatic disorders has improved CF patients' life expectancy and quality of life. To the best of our knowledge, there is no research about curcumin supplementation in CF patients; thus, we decided to investigate the effects of curcumin supplementation on weight and quality of life in children with cystic fibrosis.

2- MATERIALS AND METHODS

2-1. Study design and population

This randomized control-controlled clinical study was conducted with patients who attended the Children's Cure and Health Hospital of the Tabriz University of Medical Sciences, Iran. Forty-five patients from January 2017 to February 2018 who were diagnosed with cystic fibrosis (CF) through clinical examination were selected. Sample size was calculated based on quality of life using G-power software. We estimated an alpha of 0.05 and power of 90% to calculate the sample size. The sample size for each group, with a probability of a 20% dropout rate, was computed at 20. CF children aged between 5 - 18 years old were recruited for the study group.

2-2. Inclusion and exclusion criteria

Patients were diagnosed with CF through clinical examination (steatorrhea, nasal polyps, rectal prolapse and frequent pneumonia), and laboratory testing (sweat test greater than or equal to 60 mmol/L) were selected for this study. Patients with diabetes, liver cirrhosis, hypoalbuminemia, severe oxygen-mediated pulmonary disorder or any side effects caused by supplementation were excluded.

2-3. Ethical consideration

After noting the inclusion criteria and obtaining informed consent, the patients were entered into the study. Children under the care of a pediatric gastroenterologist received conventional therapy and were asked not to change their usual diet, physical activity, or medication during the study. This study was approved by the Ethics Committee of the Tabriz University of Medical Sciences and registered in Iranian registry clinical trials (IRCT2016022826798N1).

2-4. Intervention

Forty-five subjects were enrolled in the study; however, five subjects were excluded due to lack of referral to the clinic. The remaining 40 participants were randomly divided into curcumin (n=20) and control (n=20) groups and matched based on age and sex. Curcumin group received 3 curcumin nanoparticles (80 mg; total dose 240 mg/d) and controls received placebo for six consecutive months. Curcumin and control capsules were prepared by Minoo Pharmaceutical Co., Iran (Sina curcumin 80), and were similar in appearance. The subjects were asked to return their packages every month and consumption of the supplement was assessed based on the number of capsules returned. Participants were also asked to report on side effects. If fewer than 90% of the capsules were consumed, the participants were then excluded from the study.

2-5. Data collection

Before and after intervention, anthropometric indices (including height, weight), and quality of life were noted. The height and body weight was measured by mounted tape (0.1 cm accuracy) and a Seca scale (0.1 kg accuracy), without shoes and with light clothes, respectively. Before and after intervention, children or their parents were asked to answer the PedsQL 4.0 questionnaire which is a valid and reliable tool to assess quality of life children (20, 21). Moreover, findings of studies that evaluated Iranian version of the PedsQL 4.0 questionnaire support the initial reliability and validity of the Iranian version of the PedsQL™ 4.0 as a generic instrument to measure health-related quality of life of children in Iran (22, 23). The 23-item PedsQL 4.0 consists of child (ages 5-8 years) and parent proxy-report (ages 2-18 year) formats to assess pediatric quality of life. The core scale includes physical functioning (8 items), emotional functioning (5 items), social functioning (5 items), and school functioning (3 items).

Questionnaires utilize a 5-point response scale from 'not at all' (1) to 'a lot' (5) that indicate problems during the past 1 month. Responses are reverse scored and linearly transformed to a 0–100 scale (0=100, 1 =75, 2 = 50, 3 =25, 4 = 0), where higher scores indicate higher quality of life. All investigators and patients were blind to group assignments.

2-7. Data Analyses

Data analysis was performed using SPSS software version 16.0. Results are reported as mean ± standard deviation (SD). Mean scores were calculated according to PedsQL 4.0 guidelines (21). According to Kolmogorov–Smirnov test and descriptive test, data were normally distributed. Differences between pre- and post-intervention were analyzed using a paired t-test. Differences between two groups were compared using an independent t-test. Changes between the two groups after adjustment for baseline values were compared using ANOVA. A p-value of <0.05 was considered significant in all statistical evaluations.

3- RESULTS

Forty-five patients were initially enrolled according to inclusion and exclusion criteria and five were subsequently excluded due to lack of referral to the clinic. The remaining forty patients were randomized to one of two groups (curcumin and control; n=20 in each group). After starting the study, no other patients were excluded, as shown in **Figure.1**. No patients indicated side effects or intolerance related to the use of treatment and all forty participants completed the study. The mean age of the participants in curcumin and control group was 11.60±4.53 (between 5-18 years old) and 11.30±4.07 years (between 6-18 years old), respectively. Of the 40 participants who received treatment, 18 patients (45%) were male and 22 (55%) were female. Fifty percent (10 patients) of patientsin curcumin group and forty percent (8 patients) in placebo group were males. There was no significant difference in the baseline characteristics of patients between the two groups regarding sex, age, or weight.

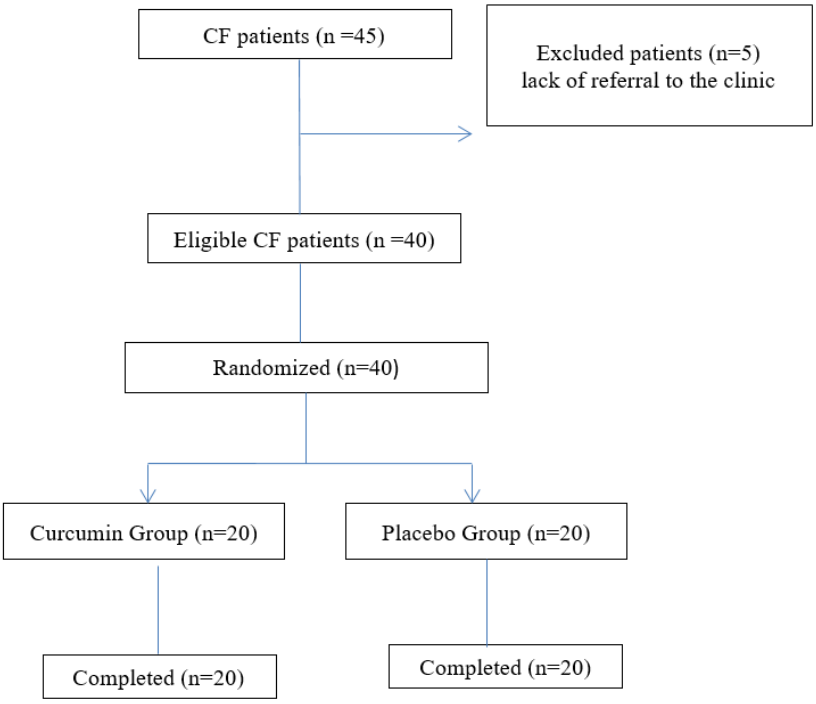

Fig.1: Flow chart of the study.

The mean body weight and scores related to quality of life at the beginning and end of the study for both the curcumin and placebo groups are presented in **Table.1**. There was no significant difference in body weight at the beginning of the study between the two groups. After intervention, the mean body weight of patients increased significantly within each group (**Table.1**). However, the percentage of weight changes showed a significant increase in the curcumin group compared to the placebo group (7.48±4.68 vs. 4.15±4.68 kg, p=0.03).

Table1: The patient's anthropometric measures and quality of life, before and after intervention in study groups.

Variables	Curcumin group(n=20)		P-value	Control group (n=20)		P-value
	Mean± SD			Mean± SD		
	Before	After		Before	After	
Weight (kg)	27.34±12.16	29.25±12.56	<0.001	29.30±12.65	30.44±12.89	<0.001
Physical functioning	52.10±14.68	60.52±17.53	0.007	41.00±9.48	44.22±14.78	0.43
Emotional functioning	58.25±17.49	71.25±16.37	<0.001	57±12.71	66.00±12.41	<0.001
Social functioning	71.5±14.96	78.02±15.97	0.002	54.70±14.83	63.57±18.76	<0.001
School Functioning	55.97±20.58	73.46±16.88	<0.001	55.88±12.77	68.52±14.97	<0.001
Psychosocial health	61.52±11.95	73.57±13.62	<0.001	56.47±7.79	68.13±10.13	<0.001

*P: Paired t –test. SD: Standard deviation.

Quality of life results were evaluated in five subscale scores, including physical functioning, emotional functioning, social functioning, school functioning, and psychosocial health. Following the intervention, both groups showed significant increases in the quality of life associated with pedSQL 4.0 questionnaire scores. Comparison of the changes in quality of life scores between the two groups showed no significant differences (**Table.2**). After adjustment for baseline scores, only the percentage of change in emotional functioning scores was significant (p=0.01) (**Table.2**). Subjects in the curcumin group showed a trend towards more improvement in terms of percentage change in physical functioning and school functioning scores when compared with the placebo group (p > 0.05).

Table-2: Comparison of changes in weight and quality of life scores between the study groups.

Variables	Curcumin group, (n=20), Mean ± SD	Placebo group, (n=20), Mean ± SD	P-value*	P-value**
Weight (kg)	7.48±4.68	4.15±4.68	0.03	0.03
Physical functioning	19.28±31.65	15.24±47.14	0.75	0.08
Emotional functioning	25.73±21.63	17.74±17.87	0.21	0.01
Social functioning	9.81±12.63	16.16±19.89	0.23	0.41
School Functioning	40.96±42.93	23.90±14.82	0.13	0.06
Psychosocial health	20.12±12.13	20.79±10.09	0.86	0.91

*P independent t- test. **P ANCOVA (adjusted for baseline of variable). SD: Standard deviation.

4- DISCUSSION

The aim of the present study was to investigate the effects of curcumin supplementation on anthropometric indices and quality of life in children with cystic fibrosis. Our findings revealed significant positive effects of curcumin on body weight in CF children (p=0.03). Furthermore, after six months of intervention, one aspect of quality of life (emotional functioning) improved significantly in the curcumin group compared with the placebo group (p=0.01). However, in vitro/in vivo studies have reported that curcumin may assist in correcting cystic fibrosis defects (24).

Based on our knowledge, this is the first clinical trial study to assess the effects of curcumin supplementation on anthropometric indices and quality of life in children with cystic fibrosis. Therefore, these results had to be compared with similar *in vitro* or animal studies. CF children usually experience pulmonary and gastrointestinal complications that lead to poor growth and, often, failure to thrive that can lead to postponed treatment. Attention to growth of CF children is very important for effectiveness of treatment. One study has shown that curcumin administration led to weight gain in mice that were homozygous for the CFTR-ΔF508 mutation (25).

He et al. demonstrated curcumin supplementation in colorectal cancer patients after diagnosis and before surgery increased body weight, and concluded curcumin can improve the general health of CRC patients (26). Consistent with above studies, our study results showed that percentages of weight changes were significantly high in the curcumin group compared with the control group (p=0.03). Several studies examined common complementary therapies, such as vitamin A, vitamin C, vitamin E, zinc, and omega 3 fatty acids, in cystic fibrosis patients and found that general conditions, symptoms, and signs improved after intervention (11, 27, 28). Recently, assessment of quality of life is an important indicator in clinical trials to show the impact of treatment. The results of our study also demonstrated significant improvements of quality of life in the curcumin group in emotional functioning after intervention (p=0.01). In addition, subjects in the curcumin group showed a trend towards improvement in the percentage of mean changes in physical functioning and school functioning scores when compared with the placebo group. Recent studies have shown many beneficial effects of curcumin on inflammatory and oxidative conditions (12, 13). Furthermore, studies have shown that curcumin can affect a variety of ion channels and transporters, especially CFTR. It seems that chronic infections, lung damage and gastrointestinal complications play an important role in health and functional status. Therefore, it has been proposed that curcumin supplementation might improve the quality of life in CF patients.

4-1. Limitation and Strength

One limitation of the current study was the small sample size; thus, results cannot be generalized. The high acceptance of curcumin in CF children is one strength. Another strength is that this study is the first clinical trial to investigate the effect of curcumin supplementation on anthropometric indices and quality of life in children with cystic fibrosis.

5- CONCLUSION

In conclusion, our findings suggest that curcumin may be a useful, inexpensive, and safe supplement in combination with conventional therapy to improve body weight in CF children. As result, further large-scale studies with multiple doses of curcumin and long-term supplementation are indicated to examine therapeutic effect of curcumin in CF children. Another area of interest is to

examine the effects of curcumin supplementation on inflammatory markers in these patients.

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7- CONFLICT OF INTEREST: None.

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