Does Synbiotic Supplementation Affect the Quality of Life in Children with Cystic Fibrosis? A Pilot Randomized Controlled Clinical Trial

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Abstract

Background There is no clinical trial that assesses the effect synbiotic supplementation on HRQOL in CF children. Considering the importance of HRQOL as an essential primary outcome and determinant of therapeutic benefit in chronic diseases like cystic fibrosis, the present clinical trial aimed to determine the efficacy of synbiotic supplementation on HRQOL in children with CF.

Methods In the present double-blind randomized clinical trial, 40 CF children were randomly allocated to the two groups. The intervention group was supplemented with synbiotics supplements and the patients in the placebo group received maltodextrin for six months. Demographic data and information about antibiotic use were recorded using the questionnaire. The health-related quality of life was assessed using the Persian version of quality of life inventory questionnaires. Paired t-test and ANCOVA were used for statistical analysis.

Results Totally, 36 participants completed the trial. The mean score of HRQOL was 76.34 ± 17.33. There were no significant differences between synbiotic and placebo groups regarding baseline demographic and quality of life characteristics. Compared with baseline values, the mean total score and subscores of quality of life did not change significantly after probiotic and placebo supplementation ($p > 0.05$). Moreover, the results of ANCOVA showed that there were no significant differences between the two groups regarding the post-trial value of HRQOL total score and subscores.

Conclusion According to results, six-month supplementation with synbiotic did not have a significant effect on the HEQOL in children with CF. However, further studies with larger sample sizes and using more disease-specific questionnaires are needed for a more precise conclusion.

Background:

Cystic fibrosis (CF) is a multi-organ and life-limiting disease [1] that is associated with respiratory infections and gastrointestinal inflammation with a possible association with intestinal dysbiosis [2, 3]. According to earlier reports, treatment interventions, special dietary regimen, and also intestinal dysfunction usually resulted in gastrointestinal dysbiosis in CF children that may contribute to different complications [4]. Considering the effect of probiotic bacteria on pathogen bacteria, different studies were conducted to assess the effect of probiotics supplementation in CF patients and some of them reported promising results [5–9]. However, only limited data is available about the effect of this supplement on health-related quality of life (HRQOL) in CF children. The only previous study that examined the effect of one-month supplementation of probiotics (2×10^9CFU/d) on quality of life in CF children showed that there was no significant difference between intervention and placebo groups regarding children report of HRQOL. However, the parents' report indicated significant improvement in the physical and total score of quality of life [10]. Supplementation duration in this study was limited and it seems that a study with longer treatment duration would be of value. On the other hand, previous studies showed that synbiotic supplements (have both prebiotic and probiotic properties) may have a synergistic

effect on the intestinal microbiota [11, 12]. However, there is no clinical trial that assesses the effect synbiotic supplementation on HRQOL in CF children. Considering the importance of HRQOL as an essential primary outcome and determinant of therapeutic benefit in chronic diseases like cystic fibrosis, the present clinical trial aimed to determine the efficacy of synbiotic supplementation on HRQOL in children with CF.

Methods:

In the present double-blind randomized placebo-controlled clinical trial, the CF patients were selected from Tabriz Children's Hospital affiliated with Tabriz University of medical sciences. The diagnosis of CF was confirmed by a pediatrician according to clinical signs and two sweat chloride test (> 60 mmol/L). The children were included if they aged 5–12 years with Tiffeneau-Pinelli index > 40% and the absence of recent acute exacerbation. The exclusion criteria were: having other related diseases such as liver or endocrine diseases, having ventilator-dependent respiratory failure, or had regular use of probiotics and probiotic fortified food were excluded from the study. Forty children with CF met inclusion/exclusion criteria and entered the study.

Written informed consent was obtained from all children's parents. This study was approved by The Ethics Committee of Tabriz University of Medical Sciences) IR.TBZMED.REC.1395.919). The protocol was registered at Iranian registry clinical trials (IRCT2017011732004N1).

Experimental Design

Forty patients were randomly divided into intervention and placebo groups according to their age and sex. The randomization was done using a computer-generated random table by a researcher who was not involved in the other part of this research. Patients and the assessor were blind to treatment allocation.

The patients in the intervention and placebo groups were instructed to consume two synbiotic or maltodextrin capsules per day for six months. The synbiotic supplement was purchased from Zist Takhmir company and its content was provided in our previous study [13]. The patients were asked to take capsules at least 2 hours apart from antibiotics. Patients were instructed to return the unused capsules. The patients who did not adhere to study protocol (consume less than 80% of prescribed supplements) or changed their medicines were excluded.

The health-related quality of life was assessed using the Persian version of quality of life inventory questionnaires. The validity of the Iranian version of this questionnaire was investigated previously[14]. The questionnaires had 23 items and include physical (8 questions), emotional (5 questions), social (5 questions), and school functioning (5 questions). Final HRQoL scores were computed out of 100. The questionnaire was completed before and six months after supplementation.

Statistical analysis

All analyses were conducted using SPSS 22.0 and based on intention to treat (ITT) analysis. The Kolmogorov-Smirnov test was used for checking the normality. The within-group comparisons were performed by paired sample t-test. The between-group analysis was done using independent sample t-test and chi-square tests. One way ANCOVA was used to compare the quality of life score after intervention by adjusting to the baseline values. The significance level was considered P-value ≤ 0.05.

Results:

Figure 1 shows the patients` recruitment and analysis diagram. According to the figure, thirty-six participants completed the trial. The patient's mean age was 8.72 ± 3.23 years. About 52% of them were male. The mean Forced expiratory value in one second (FEV_1) (%) was 82.00 ± 28.49 and 79.42 ± 23.62 in synbiotic and placebo groups respectively. The mean score of quality of life was 81.10 ± 16.81. There were no significant differences between synbiotic and placebo groups regarding baseline demographic and quality of life characteristics.

Table 2 presents the mean total score and subscores of quality of life in synbiotic and placebo groups. As can be seen, compared with baseline values, the mean total score and subscores of quality of life did not change significantly after probiotic and placebo supplementation ($p > 0.05$). Moreover, the results of ANCOVA also showed that there were no significant differences between the two groups regarding the post-trial value of quality of life total score and subscores.

Table 1
Baseline characteristics of participants.

Variables	Synbiotic (n = 20)	Placebo (n = 20)	p-value*
Age (years)	8.29 ± 2.11	9.25 ± 3.99	0.35
Sex (M/F)	9/11	12/8	0.26**
FEV1 (%)	81.75 ± 27.51	80.29 ± 22.84	0.68
Quality of life (total score)	72.76 ± 17.96	79.92 ± 16.42	0.23
Physical score	67.64 ± 22.93	73.71 ± 19.48	0.41
Emotional score	66.47 ± 22.62	79.41 ± 22.63	0.10
Social score	79.41 ± 22.21	82.05 ± 10.61	0.66
School performance score	80.58 ± 19.43	88.23 ± 18.70	0.25
M: Male; F: Female; FEV: Forced Expiratory Volume			
*p-value of independent t-test			
**p-value of chi-square			

Table 2
Comparison of the quality of life score and subscores between two groups

Variables		Synbiotic (n = 20)	Placebo (n = 20)	p-value
Quality of life (total score)	**Before**	72.76 ± 17.96	79.92 ± 16.42	0.23**
	After	73.52 ± 16.74	79.95 ± 15.57	0.95¥
	p-value*	0.08	0.69	
Physical score	**Before**	67.64 ± 22.93	73.71 ± 19.48	0.41**
	After	69.30 ± 20.40	74.26 ± 18.37	0.58¥
	p-value*	0.07	0.48	
Emotional score	**Before**	66.47 ± 22.62	79.41 ± 22.63	0.10**
	After	66.17 ± 21.39	79.37 ± 21.28	0.74¥
	p-value*	0.57	0.61	
Social score	**Before**	79.41 ± 22.21	82.05 ± 10.60	0.66**
	After	80.00 ± 20.76	82.04 ± 9.69	0.75¥
	p-value*	0.33	0.91	
School performance score	**Before**	80.58 ± 19.43	88.23 ± 18.70	0.25**
	After	81.17 ± 19.08	89.11 ± 18.64	0.69¥
	p-value*	0.33	0.45	
*p-value of paired sample t-test				
**p-value of independent sample t-test				
¥ p-value of ANCOVA after adjusting for baseline values				

Discussion:

In the present study, we examined the effect of six-month supplementation of synbiotic on quality of life in CF children and the results showed that compared with placebo, synbiotic supplementation did not have a significant effect on the quality of life in these patients. To the best of our knowledge, only limited data is available regarding the effect of probiotic supplementation on quality of life in these patients. In line with the results of the present study, Jaffari et al also showed no significant difference between intervention and placebo groups regarding children's reports of health-related quality of life. However, the

parents' report indicated significant improvement in the physical and total score of quality of life [14]. In the present study, we did not assess the parents' report of child HRQOL. The observed effect of probiotic supplementation on parents' reports of HRQOL in the mentioned study may be attributed to the differences in disease severity. Although Jaffari et al, did not report the FEV1, none of their patients received antibiotics during the intervention period. However, in the present study 35.3% and 55% of patients in the intervention and placebo groups respectively received antibiotics during the study; this may be due to a longer duration of supplementation or higher severity of diseases in the present study.

The results of the present study should be interpreted according to the following limitations. We did not consider the parental report of quality of life. Moreover, the sample size was limited and we did not use the CF specific quality of life assessment questionnaire. Moreover, we did not have a follow-up period to assess the long term effect of synbiotic supplementation on quality of life. However, the duration of supplementation in the present study seems to be long enough to assess changes in quality of life.

Conclusion:

Briefly, According to the results, six-month supplementation with synbiotic did not have a significant effect on the quality of life total score and subscores in children with CF. To the best of our knowledge, this is the first study that assesses the effect of synbiotic in these patients and the data regarding the effect probiotic supplements on quality of life in these patients are also scarce. So, further studies with larger sample sizes and using more disease-specific questionnaires are needed for a more precise conclusion.

Abbreviations

ANCOVA
One-way Analysis of Covariance (ANCOVA)
CF
Cystic fibrosis
FEV1
Forced expiratory value in one score
HRQOL
Health-related quality of life

Declarations

Ethics approval and consent to participate

Written informed consent was obtained from all children's parents. This study was approved by The Ethics Committee of Tabriz University of Medical Sciences) IR.TBZMED.REC.1395.919)

Availability of data and materials

The dataset supporting the conclusions of this article is included in the article.

Consent for publication

Not applicable.

Competing interests

All authors declare that they have no competing interests.

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Authors' contributions

ZN, LN, and NB were responsible for the conception and design of the study. LN and EM were responsible for data acquisition. LN and MAF were responsible for data analysis. ZN, LN, EM, and NB were responsible for data interpretation. EM and ZN drafted the manuscript; all other authors revised and commented on the draft. All authors read and approved the final version of the manuscript.

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Figures

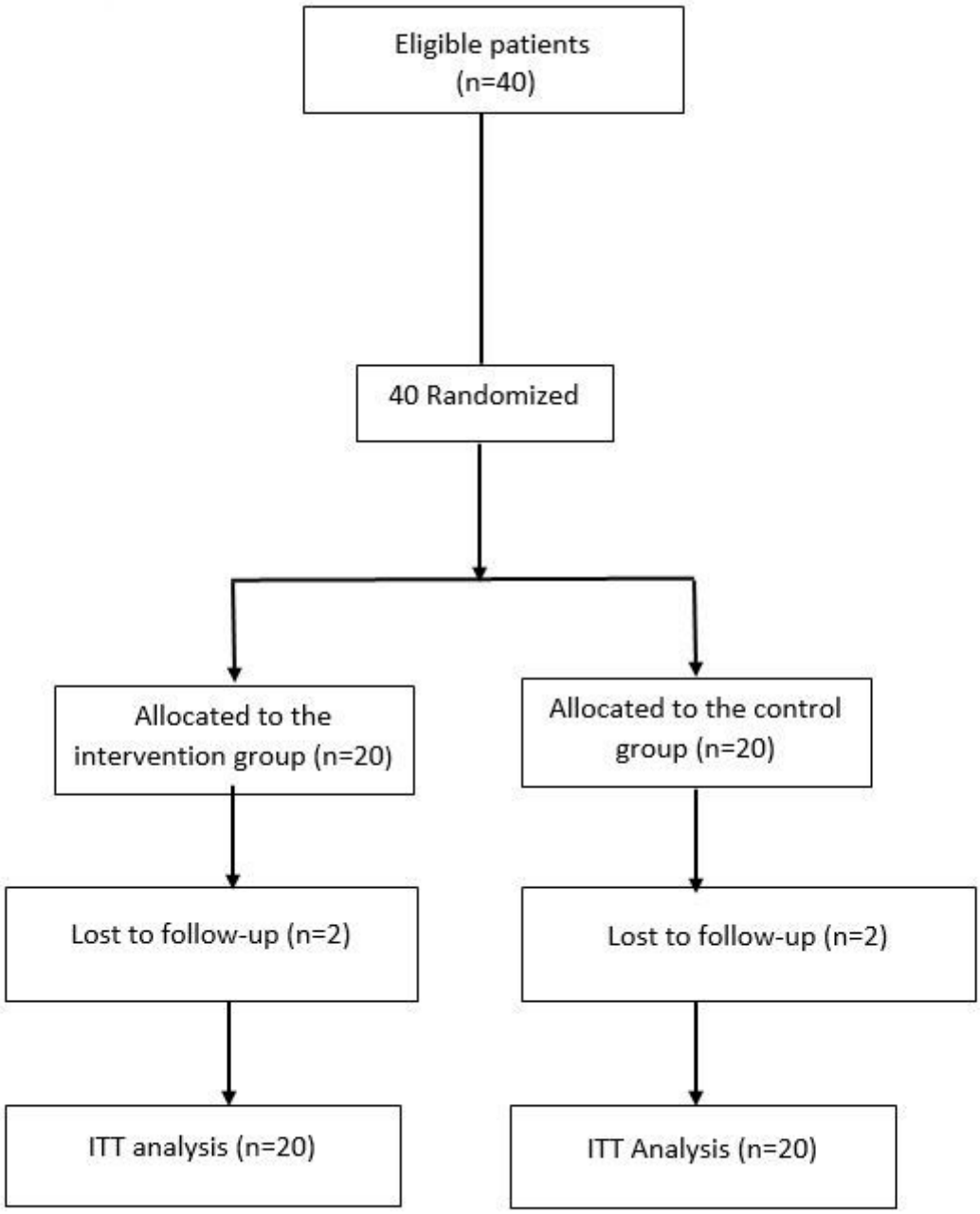

Figure 1

Flow chart of patients' recruitment and analysis

Supplementary Files

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- CONSORT2010Checklist.doc