Dietary intervention for low free sugars in children with non-alcoholic fatty liver disease: a randomized controlled trial

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Study design and participants

This study is a randomised, two-arm, parallel dietary intervention trial. A 48-week dietary intervention programme was conducted in children aged 5-14 years with a diagnosis of NAFLD. The study participants were randomized into a low free sugar diet group and a regular diet group. As this was a dietary intervention study, the participants could not be double-blinded for the grouping and intervention. The primary objective of this study is to determine whether a low free sugar dietary intervention improves liver function, fasting glucose, fasting insulin, lipid profile and hepatic steatosis in children with NAFLD. The effects of the intervention will be analysed and compared at weeks 12, 24 and 48.

Overweight and obese children and their guardians who attended Shengjing Hospital of China Medical University between October 2018 and April 2020 were selected as study subjects. All guardians signed an informed consent form before participating in the intervention. Out of 150 subjects initially included, 146 were eligible for analysis after excluding those missing key variables.

Intervention

After baseline data collection, the intervention group received a 30-60 minute educational session with a dietitian and clinicians, including a health education prescription. Interventions occurred at weeks 1, 12 and 24, with routine evaluations of disease, diet, physical activity, and adherence. Follow-ups at 48 weeks assessed NAFLD extent, dietary profile, and health knowledge for both subjects and guardians.

Blinding was not possible due to the researchers' roles in the intervention.

However,laboratory and imaging tests were conducted by separate hospital departments, with physicians unaware of group assignments, minimizing potential bias.

Statistical analysis

The questionnaire and laboratory examination data were entered into a database using EpiData 3.1 software, and the disputed data were determined by looking at the original data. The statistical descriptions of continuous variables were expressed as mean±standard deviation (Mean±SD), and after the normality test, t-test or analysis of variance (ANOVA) was used to compare the groups; the paired t-test was used to determine the differences between baseline and post-intervention hepatic fat scores, body composition, and serum analytical variables in the groups; the statistical descriptions of the categorical variables were expressed in the form of frequency (rate) and analyzed by the $\chi 2$ (chi-squared) test; the post-intervention versus baseline indices were analyzed by the $\chi 2$ (chi-squared) test.) test was used for analysis; the difference between the post-intervention and baseline indicators was used as an evaluation index of the intervention effect. The data were processed and analyzed using SPSS 23.0 software, and the two-sided P value of less than 0.05 was statistically different, with a test level of $\alpha=0.05$.

In the present study, the physical and laboratory indicators of children with NAFLD were measured longitudinally by repeated measures over a 48-week period, and generalized estimating equations (GEEs) were used to deal with the internal correlation, to test for the interactions between time and subgroups and the potential

subgroup-time interactions, and to obtain a generalized estimating equation (GEE). potential subgroup-time interactions to obtain valid estimates of intervention effects [105]. The dependent variable of this study is denoted as Yij, representing that there are i individuals (i= 1,..., n), each with j observations (tj = 1,..., p), and the covariate is denoted as Xij. The constructed models are: (1) $E(Yij) = \mu ij$, $g(\mu ij) = X'ij \beta = \beta 0 + \beta 1Xij1 + \beta 2Xij2 + ... + \beta jXijp$, g(μij) is the linkage function, the dependent variables in this study include continuous variables, ordered categorical variables, and the linkage function is selected as a linear function, Logit function, to establish a functional relationship between Yij and Xij; (2) Var(Yij) = v(μij) - φ, to establish a functional relationship between the variance of Yij and the mean, where v(μij) = v(μij) - φ, to establish a functional relationship between the variance of Yij and the mean. relationship, where v(μij) is the known variance function and φ is the estimated discrete parameter; (3) Ri (α) is a p × p dimensional operational correlation matrix of Yi = (Yi1, ..., Yip) 's indicating the magnitude of the correlation between repeated measurements of the dependent variable. The generalized estimating equation constructed is: $S (\beta; \alpha,\varphi) = \sum i \, Vi\text{-}1 \, (ui; \alpha) \, (yi - ui) = 0$, where Vi is the covariance matrix of Yi, $Vi = \varphi A \, i \, 1/2 Ri \, (\alpha) \, A \, i \, 1/2$. Based on the given estimates of α and φ, the above equations are solved by iteratively repeating the weighting to finally arrive at a covariance estimate of β. The covariance of α and φ is estimated by the following equation.