Diet

Calorie supplements in cystic fibrosis

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Background

In CF overall studies indicate that good nutritional status and its adequate monitoring impact favorably on disease progression and prognosis. Identification of most suitable parameters to define malnutrition and evidence-based practice recommendations have been historically accepted(Stallings VA et al. 2008) and recently outlined by an australasian group of experts (van der Haak N et al. 2020). Previously (Kalnins D et al. 2012) it was outlined what are the major nutritional parameters that have to be managed in patients with CF, including advances in oral intake of PERT and fat-soluble vitamin therapy. Reinforcement of adherence to diet, sodium and enzyme recommendations, using behavioral individualized modification or motivational interviewing may represent anticipatory guidance to maintain a good nutritional status, as suggested by the European Cystic Fibrosis Society Standards of care (Castellani C et al. 2018).

Recently a review focused on the current issues related to energy imbalance, dietary composition, adherence to nutritional recommendations, PERT, and the effects of modulators of CFTR for maintanence of adequate caloric intake (Colombo C et al. 2019). A regular surveillance, including age-specific individualized expert advice, particularly in difficult clinical situations, and a nutritional support, including a dedicated dietician as part of the CF team, is an integral part of the care of subjects with CF. Several factors could induce poor nutrition in people with CF.

Guidelines developed by an international multidisciplinary working group in accordance with officially accepted standards, reviewed by ESPGHAN and ECFS, are also available (Turk D et al , 2016).

Adequate calorie supplements are needed to maintain a good nutritional status a s an important prognostic factor in patients with CF prior and after lung transplantation.

The advent of new medications targeting defective CFTR protein has modified nutritional status, especially derived from the use of Ivacaftor, as well as control of specific factors including bile acid metabolism, pancreatic function, energy expenditure, and intestinal dysbiosis. Randomized clinical trials provided different results derived from triple combination. Early initiation of CFTR modulators as their use in younger patients probably will lead to correction of growth and partially restore pancreatic insufficiency (Bass R et al. 2021).

Issues

1. Oral caloric supplements

To establish whether there is evidence of benefit in using oral caloric supplements in terms of:

- increase in daily caloric intake
- improvement in nutritional intake
- improvement in nutritional indices
- improvement in lung function
- improvement in survival and quality of life

and to identify any adverse effect associated with using these supplements.

1. Enteral nutrition

To evaluate whether enteral tube feeding, when indicated:

- improves nutritional status
- improves respiratory function
- improves quality of life
- is not related to adverse effects

1. Parenteral nutrition (PN)

To evaluate whether PN in CF:

- improves nutritional status
- improves respiratory function
- improves quality of life
- is not related to adverse effects

What is known

A not-recent meta-analysis of the literature (Woestenenk JW, 2013) on treatment approaches to malnutrition in CF was conducted to compare the effect of oral supplementation, enteral nutrition, parenteral nutrition and behavioral intervention on weight gain before and after treatment. All interventions were effective in producing weight gain in patients with CF. Behavioral intervention appeared to be as effective in improving weight gain in patients with CF as a more invasive medical procedure.

1. Oral caloric supplements

1 CDSR (Smith Rosalind L, 2017) evaluated the effect of oral supplementations in children and adults with CF. The following outcome measures were evaluated: change in activity (% 24 hours); change in BMI (kg/m2); change in BMI centile (percentile points); change in lung function parameters; change in auxologic parameters; change in Kcal/day from supplement; change in mid-upper arm circumference (cm); change in total fat (g/day); change in total Kcal/day; change in total protein (g/day); change in weight (kg); change in weight centile (percentile points); change in weight for height (%). Three randomized controlled trials out of 21 trials, including 131 moderately malnourished patients aged between 2 and 15 years, were analyzed comparing use of oral calorie supplements for at least one month to increase calorie intake with no specific intervention or additional nutritional advice. Only one trial reported that people taking supplements consumed significantly at 12 months more calories than people receiving dietary advice alone.

There were no significant differences between people receiving supplements or dietary advice alone for any nutritional or growth measurements as weight, height, body mass index, z-score or other indices of nutrition or growth, as well as for lung function, adverse effects on the digestive system or levels of activity.

1 CDSR (Francis Damian K et al, 2015) evaluated the effect of oral protein calorie supplements in children with CF in three studies, but results were unable to draw any conclusions based on the limited data extracted. In children with CF who are moderately malnourished the use of dietary advice and monitoring alone could be an appropriate approach to management. Nutritional supplements may be used, but should not be regarded as an essential part of care, as also recently accepted (Turk D et al, 2016).

Oral caloric supplementations, usually in the form of either fortified milk or juice drinks or simple energy sources, are used to increase total daily calorie intake and improve weight gain. However, they are expensive and there are concerns they may reduce the amount of food eaten and not improve overall energy intake. Oral supplements should be used as additional calories in a time-limited trial or temporarily as meal replacement for ill patients with moderate malnutrition, as suggested by the European Cystic Fibrosis Society Standards of Care (Castellani C et al, 2018).

Recently (Staufer K et al, 2018) nutritional status has been assessed by BIA predicted lung function in CF transplant recipients in order to monitor patients' nutritional status with the aim to improve or maintain lung function.

1. *Enteral nutrition*

1 CDSR (Conway S et al, 2015) included thirty-eight trials; however, no studies were eligible for inclusion in this review, because of small number of enrolled participants, study design and incomplete data regarding primary and secondary outcomes.

No conclusions can be met regarding the role of this method on nutritional status. However, a few studies reported an increase in total energy intake resulting in significant improvements in body weight, height and height velocity, respiratory function (in particular, one study reported a slower rate of decline in respiratory function and reductions in the number of infections leading to fewer hospital admissions), and quality of life (all studies reported improvement in physical activity, but a negative impact about body image).

Few adverse effects were registered as transient nausea, vomiting (mainly associated with coughing), early morning fullness with loss of appetite, abdominal pain, loose stools, irritation of the nose and throat (in case of nasogastric feeding) and irritation of the gastrostomy site.

Enteral nutrition is routinely used in many CF centres by enteral tube feeding in different situations as weight for height percentage less than 85%, weight loss for longer than a two-month period or when no weight gain for two to three months (under five years old) or for six months (over five years old) has been registered. Temporary nasogastric (NG)/nasojejunal (NJ) feeds may be useful in individuals with moderate malnutrition.

In general, the papers report that both nasogastric and gastrostomy tube feeding are well-tolerated by people with CF.

One observational retrospective study (Shabbir S et al, 2014) was performed in Manchester (UK) to compare changes in weight and FEV1 in 53 CF adult patients receiving one of 3 interventions in order to prevent weight loss at 6 and 12 months: i) Percutaneous Endoscopic Gastrostomy (PEG), ii) oral steroid therapy (megestrol acetate- MA) or iii) nasogastric (NG) tube feeding. All 3 interventions were equally effective in improving nutritional status as measured by weight gain, and possibly to stabilize lung function. The small sample size and the lack of a control group cannot lead to strong conclusions.

One retrospective case-control study (Khalaf RT, 2018) comparing CF patients who received Percutaneous Endoscopic Gastrostomy (PEG) (n=20) and a control group who did not receive PEG (n=40) concluded that lung function trajectory showed a trend towards preservation among patients with CF who receive PEG despite lack of significant difference in BMI. There may be a favorable effect of PEG on lung function independent of changes in BMI.

1. *Parenteral nutrition (PN)*

Short term PN intervention may increase body weight, triceps skinfold thickness, and mid-arm muscle circumference. The effects of PN with high content of lipids and aminoacids were inconclusive regarding its impact on respiratory function, exercise tolerance, or recurrent infections. However, PN is recommended in severe malnourished patients with CF.

Unresolved questions

1. *Oral caloric supplements*

No studies reported outcomes measured daily, weekly or over some other time interval. No study reported outcome measures of eating behaviour.

Oral protein energy supplements in the short-term management of people with CF and acute weight loss should be assessed in prospective RCTs. It would be also defined the effect of oral caloric intake for the long-term nutritional management of adults with cystic fibrosis and/or advanced lung disease.

1. *Enteral nutrition*

Clinicians must balance possible potential benefit against the invasive nature and cost of procedures and products involved for each individual.

1. *Parenteral nutrition*

Indication for PN is based on anedoctal experiences of PN on short term. No conclusions can be made about the effect of PN on the long term intervention.

1 study enrollingin adult patients with CF(NCT03931252) started in 2020 will evaluate the thermic effect of food intake (TEF), which is the amount of energy expended to digest food, to overall energy expenditure in CF.

Keywords

Failure to Thrive; Nutrition Disorders; Caloric Intake; Supplementation;