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"Real food" enteral formulas in everyday clinical practice

Diety *real food* w żywieniu enteralnym w codziennej praktyce klinicznej

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Abstract

Enteral nutrition is a component of therapy for children whose ability to take in food by the natural route is impaired but whose gastrointestinal tract capacity still allows for nutrient digestion and absorption. According to guidelines, the optimum types of food for enteral feeding are ready-to-use commercial formulas (food for a special medical purpose, FSMP), which are classified into polymeric, oligomeric and amino acid/elemental. Using a blended kitchen diet as a sole food source is currently not universally recommended due to the higher risk of nutritional deficiencies and contamination with pathogenic microorganisms. However, in everyday practice, given isolated reports indicating their beneficial effects on gastrointestinal function, blended diets are attracting increasing interest and popularity. The so-called "real food" diets, available in some European countries and the USA, are a step towards the standardised and microbiologically safe use of natural nutrients in enteral nutrition. These fall into the category of industrial diets but, in addition to cow's milk protein, they contain various other natural foods. This article summarises current knowledge on the efficacy and safety of "real food" diets. A small number of studies with limited reliability have been identified, making a joint summary of the obtained results impossible. Despite the limited scientific evidence, the descriptions of various clinical situations presented in the literature show a good clinical response in patients receiving "real food" diets. This suggests that such treatment should be attempted for children with significant gastrointestinal complaints and poor tolerance to standard enteral formulas.

Keywords: enteral nutrition, blended diet, "real food" diets

Streszczenie

Żywienie dojelitowe stanowi element terapii u dzieci, których zdolność do przyjmowania pokarmu drogą naturalną jest zaburzona, jednak wydolność przewodu pokarmowego nadal umożliwia trawienie i wchłanianie składników odżywczych. Zgodnie z wytycznymi optymalnym rodzajem pokarmu w żywieniu dojelitowym są gotowe kompletne diety przemysłowe (żywność specjalnego przeznaczenia), które są klasyfikowane na polimeryczne, oligomeryczne i aminokwasowe/elementarne. Stosowanie blendowanej diety kuchennej jako jedynego źródła pokarmu nie jest obecnie powszechnie zalecane ze względu na wyższe ryzyko niedoborów pokarmowych oraz zanieczyszczenia drobnoustrojami chorobotwórczymi. Jednak w codziennej praktyce, wobec pojedynczych doniesień wskazujących na ich korzystny wpływ na funkcjonowanie przewodu pokarmowego, diety miksowane wzbudzają rosnące zainteresowanie i zyskują popularność. Krokiem w kierunku wystandaryzowanego i bezpiecznego mikrobiologicznie stosowania w żywieniu dojelitowym naturalnych składników pokarmowych są tak zwane diety *real food*, dostępne w niektórych krajach europejskich i w USA. Mieszczą się one w kategorii diet przemysłowych, ale zawierają w swoim składzie oprócz białka pochodzącego z mleka krowiego dodatkowo różne inne naturalne składniki w postaci liofilizowanej. W artykule przedstawiono podsumowanie dotychczasowej wiedzy na temat skuteczności i bezpieczeństwa diet *real food* na podstawie systematycznego przeglądu piśmiennictwa. Zidentyfikowano nieliczne badania, o ograniczonej wiarygodności, dlatego łączne podsumowanie uzyskanych wyników nie jest możliwe. Mimo ograniczonej jakości dowodów naukowych dostępne w literaturze opisy różnych sytuacji klinicznych wskazują na dobrą odpowiedź kliniczną pacjentów otrzymujących dietę typu *real food*, co sugeruje podjęcie próby takiego leczenia u dzieci z istotnymi dolegliwościami żołądkowo-jelitowymi, źle tolerujących standardowe diety przemysłowe.

Słowa kluczowe: żywienie dojelitowe, diety blendowane, diety *real food*

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INTRODUCTION

Enteral nutrition (EN) is a recognised element of therapy in children with an impaired ability to take in food by the natural route but with gastrointestinal capacity still allowing for nutrient digestion and absorption. Both international and national guidelines (European Society Pediatric Enteral Nutrition, ESPEN; European Society of Paediatric Gastroenterology Hepatology and Nutrition, ESPGHAN; Polish Pediatric Society of Clinical Nutrition – Polskie Towarzystwo Żywienia Klinicznego Dzieci, PTŻKD)[1–4] define enteral nutrition as the delivery of foods for special medical purposes, which are a source of calories, nitrogen (protein, protein hydrolysate or amino acids) and electrolytes, calcium, phosphorus, trace elements and vitamins, via a feeding tube inserted into the stomach, duodenum or small intestine or, via the oral route in selected cases. Detailed indications for EN are presented in Tab. 1.

The National Health Fund reimbursement criteria for home enteral nutrition (HEN) are limited and include:

- **exclusive enteral nutrition (EEN)**, in which at least 50% of the daily caloric requirements are met by an industrial diet administered via a feeding fistula or a feeding tube;
- **partial enteral nutrition (PEN)**, in which less than 50% of the daily caloric requirements are met by an industrial diet; PEN can be combined with oral feeding or parenteral nutrition.

EPIDEMIOLOGY

As opposed to several European countries and the United States, there are no HEN registers in Poland. However, an analysis of the National Health Fund years 2010–2018 databases has shown that HEN was used in this period in a total of 3,865 children, with 1,875 patients registered at the end of 2018 (a 2.5-fold increase compared to the beginning of 2010[5]). Children with central nervous system (CNS) damage followed by those with gastrointestinal (GI) disorders account for the majority of patients put on HEN reimbursed by the National Health Fund, which is comparable to global registry data.

Chronic gastrointestinal disorders
• Intestinal failure (complications and treatment) • Inflammatory bowel disease • Chronic diarrhoea • Chronic liver diseases (cholestasis – biliary atresia; combined malabsorption due to cholestasis and hepatitis) • Cystic fibrosis • Anatomical defects of the upper gastrointestinal tract (oesophageal atresia, tracheoesophageal fistula) • Oesophageal dysphagia (severe form of reflux disease, oesophageal stenosis, achalasia)
Chronic nervous system conditions
• Oropharyngeal dysphagia: – neurodegenerative diseases – cerebral palsy – neuromuscular diseases – encephalopathies (including epileptic, post-traumatic, other) – consciousness disorders due to CNS tumours

Tab. 1. Indications for enteral nutrition

TYPES OF ENTERAL NUTRITION

The choice of the diet and the route and method of its delivery depend on the gastrointestinal motor (oropharyngeal motor function, oesophageal patency and function, gastric emptying, intestinal motor function), digestive and absorptive (enzymatic efficiency of the pancreas, secretion of bile, contact digestion in the small intestine) functions.

According to the current ESPGHAN guidelines, readymade, nutritionally complete enteral formulas (industrial diets), classified as food for special medical purposes [FSMP; Commission Delegated Regulation (EU) 2016/128 of 25 September 2015 supplementing Regulation (EU) No 609/2013 of the European Parliament and of the Council as regards the specific compositional and information requirements for food for special medical purposes, in force in Poland from 22 February 2019] are the optimal type of EN food. Depending on the level of protein processing, industrial diets are classified as:

- polymeric – containing intact protein (usually cow's milk); starch, oligosaccharides and maltodextrin as the source of carbohydrates, and vegetable oils as the source of fat;
- oligomeric – containing hydrolysed cow's milk proteins (oligopeptides with 20 to 50 amino acids in the chain); disaccharides and glucose as the source of carbohydrates; and fats partly in the form of medium-chain fatty acids (medium-chain triglyceride, MCT);
- amino acid-based/elemental – containing protein in the form of free amino acids, disaccharides and glucose as the source of carbohydrates; and fat partly in the form of MCTs.

These categories are further subdivided into diets intended for various age groups, characterized by different caloric density, osmolarity, content of fibre and additional ingredients, for example formulas with immune properties. Enteral formulas do not contain gluten and are lactose-free or low-lactose in most cases (except for selected diets intended for infants). Special formulas, intended for patients with specified nutritional needs resulting from the underlying disease, e.g. liver and kidney diseases, metabolic dysfunctions, constitute a separate class of enteral diets.

HOMEMADE BLENDED FORMULA (HBF)

The use of HBFs was a common practice in the 20th century (1960s and 1970s), before the development of

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sterile and nutritionally complete commercial EN formulas. The 2021 guidelines of the PTŻKD[4] do not currently recommend the routine use of a mixed kitchen diet due to the higher risk of complications, nutritional deficiencies and contamination with pathogenic microorganisms. Additionally, HBFs are not reimbursed by the National Health Fund. ESPGHAN also recommends caution when deciding to include HBFs in children with neurological diseases due to concerns about their nutritional adequacy and safety[6].

However, in everyday (real life) practice, many children receive a home-blended diet as a supplement to commercial formulas; it also happens that it is the only source of nutrients as a result of parental decision. Blended diets are currently gaining popularity due to individual reports indicating their beneficial effect on gastrointestinal function. Caregivers often decide to introduce a homemade blended diet with various compositions due to the occurrence of unfavourable symptoms in children when using ready-made commercial formulas[4]. Furthermore, a home-blended diet is perceived by caregivers as "real food", the preparation and use of which increase the sense of parental fulfilment and reduce the discomfort associated with ready-to-use commercial formulas, which may be perceived more like a medicine than food[5].

HAZARDS ASSOCIATED WITH ENTERAL NUTRITION

When properly composed, administered and monitored, EN is generally safe and well-tolerated. However, some patients may experience complications related to the creation/insertion and functioning of a feeding ostomy/tube, as well as to the diet itself.

Functional GI disorders manifesting as abdominal pain, diarrhoea, constipation, nausea, belching, and vomiting are the most common undesirable symptoms related to the diet and/or the method of its delivery. The occurrence of these complications also largely depends on the multimorbidity of patients qualified for EN and the accompanying ailments. This problem is particularly complex in children with chronic nervous system impairment, in whom gastrointestinal motility disorders are secondary to gross and oropharyngeal motor dysfunction, combined with severe skeletal and muscular deformations and adverse effects of pharmacotherapy. It is estimated that regurgitation (which is not the same as reflux disease) occurs in up to 70% of children with nervous system damage. Constipation is reported in 26–74% of children with cerebral palsy, with 60% of these patients put on laxatives[7].

Complications of EN also include metabolic disorders, nutritional deficiencies, body composition disorders, gastrointestinal infections and overweight/obesity resulting from overnutrition.

NEW PERSPECTIVES IN ENTERAL NUTRITION – COMMERCIAL "REAL FOOD" FORMULAS

The limitations and sometimes poor tolerance of EN formulas prompted the search for new solutions. The so-called "real food" enteral formulas, available in some European countries and the USA, which also fall into the category of industrial diets, but contain, in addition to cow's milk protein, various other natural ingredients in freeze-dried form, are a step in this direction. We conducted a systematic literature review to make the most objective assessment of the effectiveness and tolerability of a real-food enteral formulations in the paediatric population (<18 years of age). A review of two databases: Medline and Embase until August 2023, using the same search strategy as the one used by Peers et al.[8], allowed the identification of eight studies (Tab. 2) assessing commercial formulas enriched with blended food ingredients in children. None of these studies was a randomized trial, which already indicates the limited credibility of the available scientific evidence on this issue.

The identified publications are listed and characterised in Tab. 2 by the strength of credibility and evidence (from the strongest to the weakest). The first four papers are prospective studies[9–12], whereas the next two are retrospective[13,14], and the last two are case series including a total of 8 patients[15,16].

A US study by Hron et al. (2019) is the only identified cohort study[9]. The authors of this study compared two groups of chronically ill tube-dependent children (n = 70) aged 1 to 18 years: a group on blenderised diets (60%) and a group on conventional EN formula. Participants were classified in the blenderised diet group if at least 50% of their nutritional needs were met by a homemade food or commercially prepared blenderised diets supplemented with "real" (natural) food. Children were classified in the conventional formula diet group if they had the majority of their caloric and protein requirements met via standard milk-based or elemental formulas. The authors planned a one-year follow-up. Detailed dietary records/analyses with assessment of nutrient intake (including vitamins and micronutrients), anthropometric indicators (body weight and height), number of hospital admissions and emergency room (ER) visits (with particular focus placed on respiratory symptoms), quality of life of parents/guardians and children, and the occurrence of reflux and gastrointestinal (GI) symptoms in children (details in Tab. 2) were assessed as the endpoints. The results obtained after one-year follow-up showed no significant differences between the groups in terms of energy distribution and demand for basic macro- and micronutrients. Higher fibre and lower vitamin D intake was found in the blenderised diet group.

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Tab. 2. Identified studies and their characteristics

Author	Study design	Characteristics of the population	Intervention	Comparator	End-points	Results and conclusions
Prospective studies						
Hron et al. (2019)[10]	United States, cohort study	70 tube-fed children aged 1 to 18 years: • blenderised diet group (60%) • conventional feed group (40%)	Blenderised diet: ≥50% of caloric requirement met by a homemade blended diet and/or a commercial blenderised feed (in this subgroup, blenderised feed with the addition of a conventional formula was used in 41%, a commercial "real food" formula in 33%, and a home-blended diet in 26% of patients). One-year follow-up	Conventional feed: most caloric requirements covered by commercial formula (in this subgroup, standard formula was used in 36%, elemental diet in 57%, various formulas in 7%)	1. Detailed dietary records/ analyses with assessment of vitamin and micronutrient intake 2. Anthropometric indicators (body weight and height) 3. Number of hospital admissions and ER visits (with particular attention to respiratory symptoms) 4. Parental quality of life (Likert scale) 5. Reflux and gastrointestinal (GI) symptoms – validated tools*	Fiber intake was higher in children on the blenderised diet (14.6 ± 7.3 vs. 4.6 ± 5.1 g/day, $p < 0.001$) ER visit rates (0.8 ± 1.5 vs. 1.4 ± 2.7, $p = 0.05$), hospital admissions (0.8 ± 1.2 vs. 1.7 ± 2.3, $p = 0.01$), including respiratory admissions (0.2 ± 0.5 vs. 0.6 ± 0.8, $p = 0.04$), were significantly reduced in the blenderised feed group Patients on blenderised feed showed higher satisfaction scores (Likert 4.3 ± 1.0 vs. 3.3 ± 1.2, $p = 0.001$) Patients on blenderised feed showed improved GI symptoms (0.7 ± 0.8 vs. 1.2 ± 1.1, $p = 0.03$) reduced nausea and vomiting (64.0 ± 22.6 vs. 49.0 ± 37.9, $p = 0.02$), abdominal pain (65.0 ± 26.8 vs. 56.4 ± 33.9, $p = 0.04$), diarrhoea (87.9 ± 15.5 vs. 73.6 ± 26.3, $p = 0.004$) and less global symptoms (70.2 ± 16.3 vs. 62.3 ± 19.6, $p = 0.03$) The distribution of dietary calories and the requirement for macro- and micronutrients did not differ between the groups There were slight differences in the intake of folic acid, iron and zinc, but both subgroups met their basic needs Vitamin D intake was lower in the blenderised feed group vs. conventional formula (64 ± 42 vs. 96 ± 57% of reference intake, $p = 0.01$)
Gallagher et al. (2018)[11]	Canada, description of the cohort before vs. after switching	20 tube-dependent children aged 1 to 16 years (mean age 3.4 ± 2.2 years) ≥75% of daily nutritional needs met via a tube A heterogeneous group in terms of morbidity: genetic syndromes, congenital heart defects, neuromuscular diseases, neurological disorders	Homemade blended food based on a commercial formula according to a strict recipe Switch to a new formula over a 4-week period 6-month follow-up	Commercial EN feed	Parental questionnaire: 1. GI symptoms 2. Stool frequency and consistency 3. Oral-motor skills – assessment of oral feeding (a tool for assessing oral motor problems) 4. changes in the gut microbiota (16S rDNA sequencing method) Assessment at baseline, then at months 3 and 6	Transition to a blended diet was achieved in 17 participants Children on the blended diet needed 50% more calories to maintain their weight gain rates The micronutrient content of the blended diet exceeded that of the commercial diet Switching to a blended diet significantly reduced vomiting (from 76% to 53%) and the use of acid-suppressive agents (from 88% to 76%) The diversity and abundance of bacteria in stool samples increased significantly Caregivers were more satisfied with the blended diet and unanimously declared that they would recommend it to other patients Stool consistency and frequency remained unchanged Increased use of stool softeners (from 24% to 29%)
Thornton-Wood et al. (2020)[12]	Great Britain, multicentre study, description of the cohort before vs. after switching	19 (3 excluded) tube-fed children aged 1 to 14 years ≥75% of daily caloric need met via a tube A heterogeneous group in terms of morbidity: most children with psychomotor delay, cerebral palsy, epilepsy, Down syndrome	Isosource® Junior Mix – based on a commercial EN formula with the addition of fibre and a 14% content of food-derived ingredients 7-day intervention	Standard industrial preparations – based on whole milk or peptide diet	Symptoms reported by parents/ guardians Frequency of: 1. diarrhoea 2. constipation 3. GI symptoms (bloating, nausea, vomiting, regurgitation, abdominal pain, discomfort)	Resolution of reflux and gradual reduction of gagging ($n = 2$; 10%) Improved stool consistency in children with constipation ($n = 2$; 10%) Improved stool consistency and frequency in children with diarrhoea In 2 patients, an increase in the number of loose stools (from 1/day to 3/day) Worsening of GI symptoms (2 children were excluded due to constipation, 1 due to flatulence and abdominal pain)

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Tab. 2. Identified studies and their characteristics (cont.)

Author	Study design	Characteristics of the population	Intervention	Comparator	End-points	Results and conclusions
Minor et al. (2020)[13]	United States, description of the cohort before and after switching	21 tube-dependent children with severe psychomotor and/or mental retardation aged from 1 to 13 years ≥90% of daily caloric needs met via a tube	Commercial Compleat® Pediatric: 1.0 kcal/mL, protein 15%, carbohydrates 51%, fats 34%, with added fibre and natural food ingredients (such as tomatoes, peas, green beans, peaches, chicken and cranberry juice) 7-day intervention	Conventional formula or previously used mixed diet The data recorded from day 1 before switching to the new formula was analysed	Parental assessment of: 1. tolerance (stool consistency and frequency, vomiting, flatulence) 2. adverse effects, including serious adverse effects (the doctor assessed whether they were study-related) 3. patient's anxiety/mood on a 5-point scale Dietician's assessment of: 1. daily calorie and protein intake 2. medications taken (whether they were associated with achieving the endpoints)	60% ($n = 12$) of children achieved ≥90% of target caloric needs 90% ($n = 18$) achieved ≥70% of calorie goal 90% ($n = 18$) achieved the recommended daily protein intake GI symptoms remained unchanged (unchanged mean number of stools, slight improvement in constipation and flatulence) 5 adverse effects were identified, but were not considered as related to the study by the doctor 3 children exceeded (>110%) the daily calorie requirement
Retrospective studies						
O'Connor et al. (2022)[14]	Great Britain, retrospective study, evaluation of the cohort before vs. after switching	43 tube-fed children, age: median 6 years (IQR 4–8) ≥80% of daily caloric needs met via a tube	Compleat® Pediatric – complete diet, with added fibre and 13.8% of food-derived ingredients (such as chicken, peas, green beans and orange juice) 1-month follow-up	Conventional EN diet	1. Tolerance of the diet (improvement, no change, deterioration) 2. GI symptoms (nausea, vomiting, flatulence and stool consistency and frequency) 3. Intake volume (before vs after switching). Number of calories consumed (before vs. after switching) 4. The use of medications to modify stool frequency and consistency	Good tolerance of a "real food" diet, with significantly improved GI symptoms: ↓ vomiting – 17/18 children (95%), ↓ flatulence – 6/8 (85%), ↓ loose stools – 10/11 (90%), improved constipation – 10 /11 (90%) (7/16 medicated children ↓ anti-constipation agents) Significant weight gain within 1 month (from a mean of 19.5 ± 9 kg to 20.1 ± 9 kg; $p = 0.002$) 1 child did not tolerate the new feed and developed FPIES 1 patient discontinued the feed due to persistent constipation
Samela et al. (2017)[15]	United States, retrospective study, evaluation of a cohort of 10 children before vs after switching	10 children with intestinal failure [short bowel syndrome: after necrotizing enterocolitis ($n = 6$), atresia ($n = 2$), gastroschisis ($n = 2$)], age >1 year EN patients with poor tolerance of commercial diet	"Real food" diet (Compleat® Pediatric – a tube-feeding formula with the addition of fibre and natural food ingredients) 12-month follow-up	Conventional EN diet	1. Tolerance of the formula – 100% switch to a new diet 2. The appearance, consistency and frequency of stools described by parents/guardians	9 out of 10 (90%) children tolerated 100% transition to the "real food" formula (intact colon in 7 children) Mean time to 100% switch was 67.3 days (range: 2–322) Improved diarrhoea (7 children): from >3/day (range: 3–8, mean: 5) to <3/day (range: every 2nd day to 2/day) Improved constipation (2 children): from 1–3 per week to 1 daily or every other day, with improved stool consistency and volume 1 patient (short bowel syndrome, without ileocecal valve and 2/3 of the large intestine) did not tolerate the formula (diarrhoea and perianal inflammation)
Case series						
Dipasquale et al. (2022)[16]	Italy, description of 4 patients	• Chronically ill tube-dependent children with multiple complications • Various reasons [poor tolerance of conventional formula, problematic GI symptoms (e.g. reflux disease/constipation), unsatisfactory weight gain]; they were switched to a "real food" diet • Good tolerance, reduced GI symptoms and improved growth parameters were achieved in most cases, but 1 patient required supplemental feeding with a semi-elemental formula with a higher caloric content to increase the general caloric content of the diet				
Siddiqui et al. (2021)[17]	Great Britain, description of 4 patients	• Chronically ill tube-dependent children with genetic disorders, complex congenital gastrointestinal defects • Due to severe reflux disease and co-occurring feeding problems, the patients showed poor weight gain, which was the reason for the constant search for optimal dietary solutions • The "real food" diet allowed for achieving better growth parameters, while at the same time it reduced reflux, normalized bowel movements and improved the quality of life in all patients and their families				

* Reflux symptoms – Paediatric Gastroesophageal Reflux Disease Symptom and Quality of Life Questionnaire (PGSQ); quality of life – Paediatric Quality of Life Inventory (PedQL); gastrointestinal symptoms – Gastrointestinal Symptoms Scale (GI-PedsQL).
EN – enteral nutrition; **FPIES** – food protein induced enterocolitis syndrome; **IQR** – interquartile range; ***SD*** – standard deviation; **ER** – emergency room.

The rates of ER visits and hospital admissions, including consultations directly related to exacerbation of respiratory symptoms, were significantly lower in children receiving blenderised diets (0.8 ± 1.5 vs. 1.4 ± 2.7, $p = 0.05$ and 0.8 ± 1.2 vs. 1.7 ± 2.3, $p = 0.01$, respectively). Families using blenderised diets showed higher levels of satisfaction, which may be associated with a significant improvement in GI symptoms in this group of children. Summarising, based on the results obtained, the authors of the study concluded that the use of blenderised diets (with the addition of natural food products) in EN-dependent children is associated with decreased health care utilization, improvement of GI symptoms and increased patient satisfaction compared to conventional commercially available formulas based on cow's milk protein.

In the BLEND study, Gallagher et al. (2018) prospectively assessed switching from commercial formula based on cow's milk proteins to blenderised tube feeds (BTFs) containing natural food products[10]. A total of 20 G-tube dependent children aged 3.4 ± 2.2 years were followed-up for 6 months. Over 4 weeks, the children were slowly transitioned from commercial milk-based formula to BTF enriched in natural food (prepared and blended according to a recipe adjusted to the needs of these children). The study showed that the blenderised diet prepared in this way is safe and well tolerated (details in Tab. 2). Among other things, the prevalence of GI symptoms and use of acid-suppressive agents significantly decreased compared to baseline. This in turn improved oral-motor skills in children and increased their oral food intake. Stool consistency and frequency remained unchanged on BTF; stool softener use increased throughout the study (24% vs. 29%). BTF was observed to contribute to bacterial diversity and richness of intestinal microbiota. Parents/guardians rated BTF significantly higher than the conventional commercial enteral formulas, pointing to its positive aspects, such as the child's contact with "real" food and flavours, the ability to adapt recipes to the child's individual needs, improved GI symptoms, which translated into better feeding of children and potential cost savings. Most of them declared that they would definitely recommend this type of diet to other parents/guardians.

Thornton-Wood and Saduera (2020) conducted a multicentre study in the UK, including a total of 19 tube-dependent children aged 1 to 14 years[11]. The majority of participants had global developmental delay, while other children were diagnosed with epilepsy, cerebral palsy and Down's syndrome (one child). Participants were given a new industrial formula (Isosource® Junior Mix 1.2 kcal/mL with 3.6 g protein, 70 g carbohydrate, 5 g fibre, osmolarity of 280 mOsm/L, and with 14% of natural food derived ingredients) for 7 days. The trial was completed by 16/19 participants (of the 3 excluded patients: feed was not stored in the correct conditions in 1 patient, parents reported poor tolerance of the new feed in the other 2 cases). At the end of the study, improvement in stool consistency and frequency (reduced diarrhoea) was observed in some children. Two patients experienced less reflux and a gradual decrease in gagging. One child showed improved mood, eye contact and concentration. Therefore, the blenderised diet, even though used for such a short period, showed some limited efficacy and good tolerance.

Minor et al. (2020) conducted a prospective observational study in a cohort of 21 enterally-fed children aged 6.4 ± 3.3 years, who were diagnosed with developmental delay and neurological impairment (NI), and had at least 90% of their caloric and protein needs met via EN[12]. Participants were transitioned from conventional EN feeds to a new formula (Compleat® Pediatric: 1.0 kcal/mL, protein 15%, carbohydrates 51%, fat 34%) with added fibre and natural food ingredients such as: tomatoes, peas, green beans, peaches, chicken and cranberry juice. A total of 20 children completed a 7-day trial. On average, 60% ($n = 12$) of children met at least 90% of calorie goals, and 90.0% ($n = 18$) met at least 70% of the calorie goals. Three children exceeded their calorie goal (intake >110%). There were no significant differences in GI symptoms or adverse effects (Tab. 2). The authors concluded that the new formula is nutritionally complete and allows for achieving nutritional goals in children with severe NI, with good dietary tolerance and no serious adverse events.

O'Connor et al. (2022) conducted a multicentre retrospective study to assess the tolerance of Compleat® Pediatric, which is a nutritionally complete feed enriched in fibre and 13.8% of food-derived ingredients (such as chicken, peas, green beans and orange juice)[13]. Children aged 1 to 17 years in whom this new enteral formula accounted for at least 80% of total energy requirements were included. The authors collected data on diet tolerance (improvement, no change, worsening) and GI symptoms (nausea, vomiting, flatulence, stool consistency and frequency) from 43 patients. The feed volume (before and after switching), the number of calories consumed, as well as the intake of agents modifying stool frequency and consistency were also analysed. The analysis showed that the new diet was well tolerated, with most children experiencing an improvement in GI symptoms, which translated into better growth parameters. Only 1 child did not tolerate the feed and developed food protein induced enterocolitis syndrome (FPIES) requiring a dairy-free diet, while the diet had to be discontinued in another patient due to persistent constipation.

Samela et al. (2017) conducted a retrospective analysis of 10 children >1 year of age with intestinal failure (IF) (Tab. 2) who, due to poor EN tolerance (diarrhoea, irregular bowel movements), were switched to a milk-based feed very similar in composition, but with

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End-points	Summary of the evidence
Vomiting	Most studies have shown a positive effect on reducing symptoms Stronger scientific evidence is needed
Bloating, nausea, reflux symptoms	Most studies have shown a positive effect on reducing symptoms Stronger scientific evidence is needed
Oral feeding	Insufficient data to reach final conclusions Some patients improved, but some required additional calories to meet their daily needs
Regurgitation, flatulence, abdominal pain	Insufficient data to reach final conclusions
Diarrhoea	There is some evidence suggesting improved stool consistency and frequency Stronger scientific evidence is needed
Constipation	Contradictory data from currently available studies – impossible to summarise the impact
Immunity/morbidity	Insufficient data to reach final conclusions
Modification of intestinal microbiota	Insufficient data to reach final conclusions

Tab. 3. Summary of primary end-points

the addition of natural food ingredients[14]. The contribution of the new formula to children's diet was increased very slowly (starting from 25%, then 50%, 75%, up to 100% of nutritional needs). The mean time to switch to a complete (100%) "real food" diet was 67.3 days (range: 2–322, median: 18). The study found that 90% of children tolerated the new enteral formula with "real" food ingredients and experienced improved bowel movements (both those with a history of diarrhoea and constipation). After 6 and 12 months of the diet, normal growth parameters were observed; only 1 patient did not tolerate the diet due to diarrhoea and perianal inflammation.

In 2022, Dipasquale et al. described 4 patients with various complex conditions (a patient with nemaline myopathy due to *TNNT1* mutation; a patient with congenital cytomegalovirus complicated by severe CNS damage, epilepsy and severe gastrointestinal motility disorders; a patient with complex cardiopathy and oesophageal atresia; a patient with laryngotracheal cleft, microgastria and partial pyloric stenosis), who were put on a new EN formula[15]. The inclusion of a commercially available EN formula with the addition of fibre and natural food ingredients improved the patients' nutritional status, reduced GI symptoms and improved their quality of life.

A similar case report was published a year earlier by Siddiqui et al. (2021), who described 4 patients with multiple genetic and metabolic disorders in whom the inclusion of Isosource® Junior Mix, a commercial EN feed available in UK (a complete diet with the addition of fibre and natural food products), resulted in improved functioning, especially in terms of tolerance of the new diet and minimization of adverse GI effects[17].

CONCLUSIONS AND RECOMMENDATIONS

The literature review identified few studies with limited reliability, therefore it is not possible to draw final conclusions from the obtained results (Tab. 3). The studies were conducted in different populations and the authors included extremely heterogeneous groups, which were small samples with multiple comorbidities and limitations directly affecting the processes of feeding, digestion and absorption in the gastrointestinal tract, which makes it impossible to reliably assess the efficacy of formulas and compare the studies. The follow-up period ranged from a few days to several/dozens of months. Furthermore, various endpoints were assessed and were very poorly defined in all studies. The final analysis was usually performed by parents/guardians, which may be related to their subjective (better) assessment of some symptoms occurring in their children.

The authors of all studies paid attention to the primary goals of choosing "real food" formulas in chronically ill tube-dependent children, which included:

- optimisation of the nutritional status and growth processes of the affected children;
- better taste of food and, as a result, improved oral and motor skills (with an increased intake of oral diet);
- improvement (alleviation) of GI symptoms, which are very common in this population, such as: reflux, nausea, vomiting, abdominal pain, flatulence, constipation;
- modification of gut microbiota, which may translate into improved digestive and motor functions, as well as the broadly understood immunity of patients;
- meeting the expectations of parents/guardians, who (even in the absence of strong scientific evidence) believe in additional benefits of a diet based on natural food ingredients;
- improving the quality of life of both the children and their families, including higher parental satisfaction.

The mechanisms contributing to better tolerance of "real food" formulas vs conventional enteral feeds remain unclear. However, it is believed that enteral diets containing "real" food ingredients support the gastrointestinal function[7–11,16]. Dietary fibre promotes, among

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other things, the growth of beneficial gut microbiota. Indigestible dietary fibre passes to the large intestine, where it undergoes anaerobic bacterial fermentation giving rise to short-chain fatty acids (acetic, propionic, butyric) – the major energy source for colonocytes. Short-chain fatty acids play a role in maintaining the integrity of the intestinal barrier, stimulate mucus production, inhibit the activity of pro-inflammatory mediators of the intestinal epithelium and reduce the risk of colorectal cancer. Fructo-oligosaccharides and galacto-oligosaccharides present in such a diet are a source of food for bifidobacteria, contributing to their growth, which may improve intestinal barrier function and the host's immunity. Changes in the composition of a diet based on natural food products may also stimulate gastrointestinal taste receptors, which in turn transmit sensory stimuli to effector systems involved in immune responses and gastrointestinal motility, stimulating the brain-gut axis and improving the overall functioning of the affected child.

Despite the limited quality of scientific evidence, the descriptions of various clinical situations presented in literature and the suggestions of good tolerance and satisfactory clinical response of patients to the "real food" diet based on these reports allow for such treatment to be attempted in children who present with severe gastrointestinal symptoms and poor tolerance of the available industrial diets despite the optimisation of their composition and method of delivery.

Furthermore, the identified gap in scientific research on this topic will help design of a multicentre randomised trial to provide the basis for developing treatment guidelines.

Conflict of interest

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