Review article

Huntington Disease – Principles and practice of nutritional management

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ABSTRACT

Huntington disease (HD) is a degenerative brain disease clinically manifested by the characteristic triad: physical symptoms involving involuntary movements and poor coordination, cognitive changes with less ability to organize routine tasks, and some emotional and behavioral disturbances. For patients with HD, feeding is one of the problems they have to face. People with HD often have lower than average body weight and struggle with malnutrition. As a part of therapy, good nutrition is an intervention maintaining health and functional ability for maximally prolonged time. In the early stages of HD, small amounts of blenderized foods given orally are recommended. In more advanced stages, enteral nutrition is essential using gastric, or jejunal tubes for short term. Most severe cases require gastrostomy or gastrojejunostomy. Although enteral feeding is well tolerated by most of the patients, a number of complications may occur, including damage to the nose, pharynx, or esophagus, aspiration pneumonia, sinusitis, metabolic imbalances due to improper nutrient and fluid supply, adverse effects affecting gastrointestinal system, and refeeding syndrome.

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1. Introduction

Huntington disease (HD), is a progressive neurodegenerative disease caused by genetic defect on short arm of chromosome 4 associated with the expansion of a CAG trinucleotide repeat in a novel gene. The clinical diagnosis is based on the presence of typical symptoms, positive family history, and genetic tests confirming HD mutation. The duration of the disease from the time the first symptoms appear is extremely variable, but typically ranges from 15 to 18 years [1]. Neuronal degeneration causes patients with HD to have problems with movement, cognition and psychiatric symptoms [2]. As disease progresses the vital functions including coordination, self-care, eating and eventually swallowing efficiency may decline significantly. For this reason affected individuals may suffer from unbalanced

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nutritional status, weight loss and require increasing levels of care. In patients with HD both energy consumption and expenditure could be involved in the development of malnutrition. Inadequate caloric intake usually results from: swallowing incoordination, choking on liquids, coughing on foods, mastication difficulties, solid food dysphagia, or food-preparation difficulties [3,4]. Patients with increased appetite and high calorie intake also present with lowered body weight. Because there is no evidence they have problems with malabsorption, the increased energy expenditure is suggested mostly due to the hyperkinetic movement disorder [5,6]. The overall mechanisms responsible for malnutrition in patients with HD could be multifactorial and more complex than energy intake-expenditure imbalance caused by major motor disabilities. Reports indicate degeneration of orexigenic neurons that synthesize neuropeptides (neuropeptide Y, agouti-related peptide, and GABA) stimulating hypothalamic hunger center [7], suggest energy metabolic deficits leading to generalized body mass loss [8,9], or underline association between higher CAG repeat number and faster rate of weight loss [10].

There is no successful cure for HD and medications are for calming symptoms that accompany progression of the disease. In 2003 The European Huntington’s Disease Network (EHDN) was formed, to provide a platform for clinicians and families to work together to find a cure for HD, and to coordinate worldwide research. Considering the proper care in a holistic way, nutritional support is one of the basic interventions that may prolong patient’s life and improve life quality. For people coping with HD, support can come from variety organizations, societies and home care services e.g. Turning Point Scotland, and SHAPE project (Supporting Huntington’s and Promoting Equality), Polish Society of Huntington Disease, International Huntington Organization and many others. The home care services provide varying levels of domestic help, meal programs, and nursing assistance.

2. Symptoms

Patients with HD experience movement, cognitive and psychiatric disorders. The symptoms usually are discrete or not present until people are in their thirties and forties.

An early-stage manifestations are not very obvious and include motor clumsiness, fidgeting, excessive restlessness, less ability to organize routine tasks. Intellectual and emotional symptoms often occur prior to the motor dysfunction and may include difficulty organizing and focusing on tasks, problems with attention and judgment, irritability and depression [11]. Some of the individuals develop schizophrenia-like psychosis. If physical symptoms have not yet begun, these patients might be misdiagnosed as having schizophrenia [12]. As HD progresses the early physical, intellectual and emotional symptoms become more evident.

The most characteristic are the uncontrolled body movements that occur spontaneously and develop gradually in different parts of the body. At early stages facial grimacing and pouting may occur together with rapid leg and arm movement. The gait is swaying and “dancing” from side to side, and may be disrupted by characteristic for HD sudden hyperextension at hips with a resulting danger of falling backwards. Ocular motor abnormalities present in a form of inability to suppress reflexive glances to suddenly appearing novel visual stimuli and delayed initiation of voluntary saccades. Problem with movement is most evident during the daily activity and disappears when the individual is asleep [13].

Patients in the mid-stage of HD present with more evident motor disabilities, swallowing difficulties and involuntary movements create dysphagia. Problems with impulse control and acting without thinking, difficulty memorizing and significant intellectual decline make them less productive and often individuals have to cease the work at that time. Memory deficits, and apathy tend to appear as HD progresses, often in the late phase of the disease [14].

Late-stage occurs when the patient cannot live without professional help and when self-care is no longer possible. Individuals experience deep cognitive impairment with apathy and even dementia, severe generalized motor disturbance and often malnutrition [15].

Low weight and unintentional weight loss are common and recognized throughout all stages of HD and, as mentioned before, etiology is multifactorial.

To classify the most common signs of HD into progression stages Kirkwood et al. prepared a survey of individuals with symptomatic HD completed by a first-degree relative. The study included 1238 individuals with a minimum of a 6-year history of symptomatic HD [16]. Classification of major symptoms according to the six onset periods from the beginning to the late stage of HD according to Kirkwood et al. presents Table 1.

3. Dysphagia

By the middle stage of HD patients may experience trouble chewing, drinking and swallowing which are called dysphagia. The warning signs associated with dysphagia include decreased alertness (e.g. playing with food, or taking to large or repeated bites without swallowing), coughing or choking on food and drink, gurgly voice especially after eating/drinking, food or liquid left in the mouth after swallow, recurrent respiratory infections [17]. Difficulty with swallowing usually occur in all three phases: oral (difficulty chewing or forming bolus), pharyngeal and esophageal. The pathomechanism is mostly based on deregulation of throat smooth muscle function, food aspiration around epiglottis and glottis, and esophageal motor dysfunction. If the esophageal phase is affected then the esophageal transit time is much longer than normally, and esophageal peristalsis is impaired and often reversed (reflux). In some cases asymptomatic food aspirations (“silent” aspiration) from piriform sinuses may occur leading to aspiration pneumonia and even death [18].

Many symptoms in patients with HD may interfere with eating. Worsening of neurological condition may cause an individual to become distracted and overwhelmed by mealtime activity. In 2014 Heemskerk et al. developed a valid and reliable 11-item scale to measure the severity of dysphagia in HD [19]. This Swallowing Disturbance Questionnaire could be very helpful when making decision about referral to a speech-language therapist (SLT) and further assessment including
clinical observation for signs of aspiration when different consistencies of food/liquids are consumed, or instrumental assessment like video fluoroscopy. Based on the assessment results, SLT recommends specific strategies for safe swallowing or proposes changes in food and liquid consistency to reduce risk of silent aspiration [20].

4. Malnutrition

The World Health Organization (WHO) defines malnutrition as the cellular imbalance between the supply of nutrients and energy and the body’s demand for them to ensure growth, maintenance, and specific functions. In HD long lasting problem with eating, changed cellular energy metabolism, increased energy expenditure, and impaired hypothalamic food intake control may finally change the patient’s nutritional status from lowered body weight to malnutrition. This, in turn, directly increases morbidity and mortality rate, length of hospitalization and costs of treatment, and as a factor contributing to the severity of the disease markedly decreases efficiency of the pharmacological and surgical management [21]. Consequences of malnutrition could be classified as primary and secondary. The primary are: reduced body mass caused by loss of muscles and adipose tissue, lowered muscle strength and immunity, hypochromic anemia, decreased serum protein concentration, disturbances with absorption and digestion, and finally impairment of all organs function. Secondary consequences of malnutrition include: increased vulnerability to infections, impaired wound healing, intestinal anastomotic leakage, increased morbidity and mortality rate, and high costs of treatment [22]. The assessment of malnutrition degree is based on nutrition interview, physical examination and biochemical, immunological and anthropometric parameters. Obtained results, when considered together, help to identify malnourished patients and prepare an optimal strategy for nutritional management. The EHDN Dietitians Group suggests nutritional support in malnourished patients with HD to maintain optimal healthy weight (BMI 23–25) [23]. Detailed indications are summarized in Table 2.

5. Oral nutrition

5.1. General considerations

An adequate dietary guidance that provides for individual patient’s needs and strategy for family/guardian support is

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**Table 1 – Classification of major symptoms according to the six onset periods from the beginning to the late stage of HD according to Kirkwood et al [16].**

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Earliest reported symptom</th>
<th>Early symptom</th>
<th>Early-Middle symptom</th>
<th>Middle symptom</th>
<th>Middle-Late symptom</th>
<th>Late symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Involuntary movements</td>
<td>Within 1st year</td>
<td>Less than 5 years into disease progression, equally represented between the within-1-year category and the 2-to-5-year category</td>
<td>2–5 years after HD onset</td>
<td>In the 2- to 5-year and 6- to 10-year range in approximately equal percentages</td>
<td>Typically 6–10 years after disease onset</td>
<td>More than 10 years</td>
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</tbody>
</table>

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**Table 2 – Indications for nutritional support in patients with HD according to European Huntington’s Disease Network (EHDN) Dietitians Group [18].**

<table>
<thead>
<tr>
<th>Malnourished patients</th>
<th>Patients at risk of malnutrition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unintentional weight loss</td>
<td>Patients who have eaten little or nothing for more than 5 days and/or are likely to eat little or nothing for 5 days or longer</td>
</tr>
<tr>
<td>&gt; 10% within the last 3–6 months</td>
<td>Patients who have food intake below 50–75% in preceding week</td>
</tr>
<tr>
<td>BMI &lt; 20 kg/m² and unintentional weight loss &gt; 5% within the last 3–6 months</td>
<td>Patients who have poor absorptive capacity and/or high nutrient losses and/or increased nutritional needs from causes such as catabolism</td>
</tr>
</tbody>
</table>
one of the most important steps in HD therapy. The goals for nutritional management are: reduction of protein and calories deficiency, maintenance of electrolyte and fluid balance, control of body weight avoiding rapid weight loss, lowering of catabolic rate and excessive protein breakdown [24,25].

5.2. Calorie intake, protein and fat supply

According to the evidence-based recommendations summarized by the EHDN Dietitians Group, patients with HD should receive 25–35 kcal/kg/day total energy (including that derived from protein). The daily calorie intake should be gradually elevated until the target calorie intake for patients with HD is reached. Ratio of fat and carbohydrate should stay at the same level as normal population. The recommended protein supply should be at the level of 0.8–1.5 g protein (0.13–0.24 g nitrogen)/ kg/day and at least 50% of ingested proteins should be of an animal origin. The baseline fluid intake should oscillate at the level of 30–35 ml fluid/kg (with allowance for any extra requirements, input of fluid from other sources and any additional losses), however, in some individuals fluid requirements may be higher. The diet may be supplemented with oral protein supplements, which appear to have high clinical benefits resulting in improvements in patients’ anabolic rate. Normally, 25% of daily energy requirement is covered by dietary lipids (daily intake of fats equals 1.5 g per kg of body weight). Some types of fats have specific health benefits, while others are detrimental. Trans fats from processed foods, saturated fats and heating to the very high temperature fats can evoke production of harmful free radicals. The types of potentially helpful dietary fat are mostly unsaturated and they include monounsaturated and polyunsaturated fats, and omega-3 fatty acids. The examples are oils (olive oil, sunflower oil, peanut oil and corn oil, avocado oil, walnut oil, evening primrose oil, borage seed oil, and flax seed oil) and fishes (salmon, tuna, trout, mackerel, sardines and herring) [23].

5.3. Nutrition in different stages of HD

Nutritional assessment and care planning for individuals with HD must take into account the stage of the disease and the feeding difficulties individuals may experience.

In the early stages of HD lowered mood of an individual may contribute to the changes in eating habits with cravings for carbohydrates. If the diet is well balanced then frequent and smaller meals are recommended without any other noticeable changes. Fruits and vegetables are a rich source of antioxidants, micronutrients and vitamins, moreover they help to improve visual appeal that enhances flavor experiences. Thus, the diet should incorporate colored and healthy plant foods.

In the midstage, because of dysphagia the meals should be based on moist and soft foods. Before being blended food should be steamed as it helps to reduce a nutrient loss. The samples of recommended meals include: full fat milk shakes, fruit/vegetable mousse, mashed potatoes with butter, creamed soups and sauces, scrambled eggs, puddings, gelatins, creamed cereals, lean meat cut into small pieces, mayonnaise and full-fat salad dressings [26]. Patients should avoid eating when tired and upset, they should eat slowly and stay in the upright position during and 30 min after meal, when eating they should take small bites (1/2 teaspoon or less) and chew well.

Patients who have or are at risk of malnutrition can be managed with dietary modification, nutritional supplements and dietetic counseling. The amount of delivered proteins should be elevated above normal dietary limits and include all exogenous amino acids that stimulate human muscle anabolism. Fattening diet serves for an accumulation of the energy sources, which are depleted due to the intense catabolism in HD patients. Although dietary fats are the most concentrated source of calories in the diet, malnourished patients should avoid overloading their diet with fatty substances because a feeling of discomfort may occur. The person with HD may need to get more nutrition from a smaller volume of food, so the number of meals per day should be 6–8 and high-calorie snacks plus extra calories in regular recipes are necessary to maintain body weight. Additionally, to increase an appetite, everyday menu should be varied and meals should be nicely prepared [27].

In the advanced stages, when it is no longer possible to meet the patient’s nutritional needs with an oral diet, enteral feeding is considered. The decision on non-oral methods of feeding should be made in conjunctuon with the patient, family, dieticians and medical team. To agree the details of nutritional management patients must obtain sufficient information about their treatment in the context of quality of life. When the patient is still in a quite good mental condition it is worth discussing the future possibilities of therapy, explaining the profits and risks, and ensuring that patient makes informed decisions and gives consent based on good information. However, because of a decline in a cognitive ability and decision making skills, discussing enteral feeding with patients is very difficult. When the patient is legally incapacitated the decision, according to the Polish law, belongs to legal guardian and the court.

5.4. Enteral nutrition

Enteral nutrition (EN) is an administration of special food mixture containing protein, carbohydrates, fats, vitamins, and minerals through the tube directly to the stomach or intestines. Tube feedings may be used to supplement oral intake of food and fluids, or they may become the primary source of nutrition.

EN represents one of the nutritional management methods that, according to the ESPEN (European Society of Parenteral Nutrition and Metabolism), consists of specific liquid nutritional preparations given orally as a dietary supplements, through nasogastric or nasonetal feeding tube, and by gastrostomy or jejunostomy [28]. EN uses and maintains absorption and digestion in the gastrointestinal (GI) tract and is preferred to parenteral feeding as it is more physiological and has fewer side effects. When compared with parenteral nutrition, EN avoids bacterial translocation, prevents abnormalities of liver and biliary function, helps to prevent mucosal atrophy, gastroenteritis or ulcer disease. However, the upper part of GI system is not involved in the digestion process [29,30]. Although EN has a number of undisputed advantages, it can be considered only if the
gastrointestinal system is not affected, according to the adage “If the gut works use it”. Complete intestinal obstruction, failure of intestinal function, severe gastrointestinal inflammation, chronic diarrhea, or malabsorption represent major contraindications to EN. Selection of the enteral access device depends, among others, on expected duration of EN. Feedings are either “continuous” or “bolus” servings. Most patients who are just starting out on tube feedings are given continuous feedings, then gradually changed over to bolus feedings. For short term use (less than four weeks) the nasogastric/enteric tube is the most commonly used method. The tube can be placed in the stomach, duodenum or jejunum. In patients requiring long term (more than 4 weeks) EN tube enterostomies are used (gastro- or jejunostomy) [31]. The nasogastric tubes are used if there are indications to short-term EN. Before connecting the tube to administration set and start feeding, the position of the tube must be checked by X-ray control, fiber optics, aspiration of stomach juice, and stethoscope continuous gut drainage. Disorders with high risk of gastric juice reflux and regurgitation should be excluded from feeding by gastric tube. In these cases duodenal or jejunal tubes are more safe and recommended. Large bore tubes made from PCV may be helpful in home made diet administration. However, a number of complications may occur, including: bacterial contamination, nasal septum necrosis, esophageal necrosis and perforation, otitis media and sinusitis, gastroesophageal reflux, aspiration pneumonia. Therefore, tubes for gastric drainage and home made diets should not be used for more than 10 days. For longer EN (up to 6 weeks) small bore naso-enteric feeding tubes are usually preferred. Using tubes that are small in diameter requires liquid commercial enteral formulas administration [32,33]. Percutaneous endoscopic gastrostomy (PEG) is one of more permanent access routes for long-term EN, that can be performed nonsurgically with gastrointestinal guidance. For patients requiring long-lasting (months-years) enteral feeding, PEG is better alternative that avoids occurrence of adverse effects related with nasoenteral tubes (regurgitation, nausea, diarrhea). PEG feeding catheters, made from silicone, are hypoalergic, well tolerated and do not cause development of sores. If necessary they may be easily removed and replaced. The indications for PEG reflect difficulties with oral intake often where obstruction to the upper airway or gastrointestinal tract or makes passing a nasogastric tube difficult e.g. unsafe swallowing, problems with chewing [34].

The choice of adequate feed administered to the patient with HD decides about safety and efficiency of dietary treatment. A wide variety of feeds is available [35], the most common types of formulas are shown in Table 3.

The dietitian, in consultation with doctors and other health professionals, decides which type of feed and route of feeding is most suitable for the patient. Formulas are in a liquid form and contain high biological value proteins (usually from milk, cassein and soya), healthy fats (from vegetable oils), carbohydrates (glucose polymers, maltodextrin, starch). The content of electrolytes, minerals, micro-nutrients and vitamins is carefully calculated to avoid excess intake, and should reflect individual’s daily needs. When delivering enteral feeding patient’s medications should be in a liquid form or dispersible/soluble formulations and must be

<table>
<thead>
<tr>
<th>Table 3 – Enteral nutrition – general types of feed.</th>
<th>Composition</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of feed</strong></td>
<td><strong>Polymeric feeds</strong></td>
<td>Whole protein as a nitrogen source, oligosaccharides, maltodextrins or starch as a carbohydrate source, vegetable oil as a fat source and minerals, vitamins and trace elements.</td>
</tr>
<tr>
<td><strong>Oligomeric feeds</strong></td>
<td>Dipeptides, tripeptides and some free amino acids as a nitrogen source. Fat in the form of long and medium chain triglycerides. Carbohydrates, minerals, vitamins and trace elements. Lower osmolality than elemental diets.</td>
<td></td>
</tr>
<tr>
<td><strong>Predigested elemental feeds</strong></td>
<td>Protein in the form of partial hydrolysates and comprise a mixture of free amino acids, dipeptides, and tripeptides. Carbohydrate as a partially digested starch with various chain lengths of glucose polymers (maltodextrins). Variable amounts of fat in the form of medium chain triglycerides and/or essential fatty acids. Diet highly osmotic.</td>
<td>Patients with a degree of malabsorption</td>
</tr>
<tr>
<td><strong>Disease specific feeds</strong></td>
<td><strong>Liver formulas</strong></td>
<td>Branched chain amino acids enriched and aromatic chain amino AIDs deficient formulas. The formulas vary in protein, electrolyte, vitamin and mineral content. Generally they are lower in protein, caloriically dense and have lower levels of potassium, magnesium and phosphorus when compared to standard formulas.</td>
</tr>
<tr>
<td><strong>Renal formulas</strong></td>
<td>Modified carbohydrate and fat nutrition formulas (to reduce CO2 production from carbohydrates).</td>
<td>Kidney failure (except patients on dialysis, who require higher protein content in a diet)</td>
</tr>
<tr>
<td><strong>Pulmonary formulas</strong></td>
<td>Glutamine, arginine, omega-3 fatty acids, nucleotides and branched chain amino acids.</td>
<td>COPD, ARDS</td>
</tr>
<tr>
<td><strong>Immunomodulatory formulas</strong></td>
<td>Oligomeric feed plus supplementation of glutamine and fiber.</td>
<td>Hyperglycemic critically ill patients</td>
</tr>
<tr>
<td><strong>Gastrointestinal dysfunction formulas</strong></td>
<td>Standard feed or 15% of calories from protein, 30% from fat and 55% from carbohydrates.</td>
<td></td>
</tr>
</tbody>
</table>
considered to avoid possible drug/nutrient interactions and administration problems.

There are three methods of formula administration: (1) bolus feeding (without usage of the pump), and (2) continuous feeding (feeding over 16–20 h). Continuous feeding requires a break of at least 4 h in 24 h to allow the stomach to re-acidify. In continuous feeding the formula can be delivered overnight or during the day depending on patient’s condition. Bolus feeding involves the delivery of 200–400 ml over a period of 15–60 min and can be given 4–6 times a day. In a gastric feeding the most optimal are small servings 200–300 ml administered within 30–40 min ensuring good emptying of a stomach. Before the next serving is administrated aspiration of the gastric content by enteral syringe is necessary to ensure if there is no retention of stomach content [36].

Detailed guidelines regarding equipment and procedure of administration of feed plus recommendations for staff training and practice are widely described in the literature [37].

The clinical and laboratory monitoring of nutritional treatment includes review of the indications, route, risks, benefits and goals of nutrition support at regular intervals. Feed and water flushes should be recorded on a daily fluid balance chart. The comprehensive protocols provided by National Institute for Health and Care Excellence in London (NICE) help to control nutritional, anthropometric and clinical condition monitoring of nutrition support and separately detailed laboratory monitoring. The time interval between reviews depends on the patient, care setting and duration of nutrition support [23].

In most cases enteral feeding is well tolerated, however an adverse effects may occur. The most common complications are summarized in Table 4.

Some of them are associated with refeeding syndrome (RS), which can be defined as the potentially fatal shifts in fluids and electrolytes that may occur in malnourished patients receiving artificial refeeding [38]. RS may develop in malnourished patients who start enteral feeding as a result of a sudden shift from fat to carbohydrate metabolism and increased insulin secretion. Insulin stimulates glycogen, fat, and protein synthesis. This process requires minerals such as phosphate and magnesium and cofactors such as thiamine. Cells absorb and use more potassium, magnesium, phosphate, and water follows by osmosis. Finally deficiency of serum phosphate, potassium, magnesium, and thiamine may lead to the clinical features of RS, including rhabdomyolysis, leukocyte dysfunction, respiratory failure, cardiac failure, hypotension, arrhythmias, seizures, coma, and sudden death [39,40].

6. Conclusions

In summary, there is no cure currently available for patients with HD, thus good nutrition appears to be one of the interventions maintaining health and functional ability for maximally prolonged time. The type of food and way of feeding differ according to the stage of disease and feeding difficulties individuals may experience. When oral feeding is no more possible enteral feeding is recommended. Based on the current clinical guidelines, standard formula should be the product of choice for the majority of patients requiring enteral feeding [41]. Optimal nutritional assessment and care planning must include appropriate feeding techniques, regular monitoring of nutritional intake, weight changes plus overall patient’s condition and effective communication between patient, family members and healthcare professionals.

Conflict of interest

None declared.

Acknowledgement and financial support

None declared.

Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

Table 4 – Most common complications of enteral nutrition.

<table>
<thead>
<tr>
<th>Gastrointestinal</th>
<th>Biochemical</th>
<th>Mechanical</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea or constipation</td>
<td>Deficiency of vitamins (e.g. Thiamine\textsuperscript{a}), minerals, trace elements</td>
<td>Pulmonary aspiration</td>
<td>Sinusitis, otitis media</td>
</tr>
<tr>
<td>Bloating</td>
<td>Hypo-/hypernatremia</td>
<td>Tube malposition</td>
<td>Oesophageal erosions, oesophagitis</td>
</tr>
<tr>
<td>Regurgitation</td>
<td>Dehydration</td>
<td>Tube clogging</td>
<td>Feed contamination and resulting infection</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>Hyperglycaemia\textsuperscript{a}</td>
<td>Gastrointestinal perforation</td>
<td></td>
</tr>
<tr>
<td>Reflux</td>
<td>Hypo-/hyperkalaemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interactions with drugs</td>
<td>Hypophosphataemia\textsuperscript{a}</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malabsorption/maldigestion</td>
<td>Hypomagnesaemia\textsuperscript{a}</td>
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<tr>
<td></td>
<td>Hypozincæmia</td>
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\textsuperscript{a} Symptoms that may indicate refeeding syndrome.