Review: Medical Nutrition in Diarrhea Management
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Medical Nutrition in Dairrhoea Management

Introduction

A third of the 2·5 billion people worldwide without access to improved sanitation live in India, as do two-thirds of the 1·1 billion practising open defecation and a quarter of the 1·5 million who die annually from diarrhoeal diseases. Diarrhoea accounts for the largest share of sanitation-related morbidity and mortality, causing an estimated 1·4 million deaths annually, including 19% of all deaths of children younger than 5 years in low-income settings. (Clasen, Boisson et al. 2014)

While childhood diarrhea mortality has declined steadily since the 1980s, diarrheal disease remains the third leading cause of death among children under-five globally. An estimated 800,000 under-five deaths were attributable to diarrhea in 2010, accounting for 11% of all under-five deaths, with about 80% of these diarrheal deaths occurring in the African and Southeast Asian WHO regions. (Liu, Johnson et al. 2012)

The comprehensive monograph “Interactions of Nutrition and Infection” stimulated many scientists to pursue further research on these issues. In general, the research conducted on this topic since 1968 can be categorized in one of three major areas:

1) The impact of diarrhea on nutritional status, particularly in young children;
2) Nutritional risk factors for diarrhea; and
3) Appropriate dietary therapy for patients during and after enteric infections.

Notably, the results of these studies prompted a number of changes in the clinical management of patients with diarrhea and in public health policies regarding its prevention.

Pathophysiology of diarrhea

Diarrhea is characterised by frequent evacuation of liquid stools, usually exceeding 300 ml, accompanied by an excessive loss of fluids and electrolytes, especially sodium and potassium. As per World Health Organization diarrhea is defined as a condition associated with three or more loose or liquid stools per day, or as having more stools than is normal for that person.

Acute diarrhea is defined as an abnormally frequent discharge of semisolid or fluid fecal matter from the bowel, lasting less than 14 days, by World Gastroenterology Organization.
Secretory

Secretory diarrhea means that there is an increase in the active intestinal secretion of electrolytes and water by intestinal epithelium, resulting from bacterial exotoxins, viruses and increased intestinal hormone secretion, or there is an inhibition of absorption. There is little to no structural damage. The most common cause of this type of diarrhea is a cholera toxin that stimulates the secretion of anions, especially chloride ions. Therefore, to maintain a charge balance in the lumen, sodium is carried with it, along with water. In this type of diarrhea intestinal fluid secretion is isotonic with plasma even during fasting. It continues even when there is no oral food intake. (Thiagarajah Donowitz wt al. 2015)

Osmotic diarrhea

Osmotic diarrhea occurs when osmotically active solutes are present in the intestinal tract and are poorly absorbed. (Gorkiewicz, Thallinger et al. 2013) If a person drinks solutions with excessive sugar or excessive salt, these can draw water from the body into the bowel and cause osmotic diarrhea. Osmotic diarrhea can also be the result of maldigestion (e.g., pancreatic disease or Coeliac disease), in which the nutrients are left in the lumen to pull in water. Or it can be caused by osmotic laxatives (which work to alleviate constipation by drawing water into the bowels). In healthy individuals, too much magnesium or vitamin C or undigested lactose can produce osmotic diarrhea and distention of the bowel. (Hill and Kamath 1982)

A person who has lactose intolerance can have difficulty absorbing lactose after an extraordinarily high intake of dairy products. In persons who have fructose malabsorption, excess fructose intake can also cause diarrhea. High-fructose foods that also have a high glucose content are more absorbable and less likely to cause diarrhea. Sugar alcohols such as sorbitol (often found in sugar-free foods) are difficult for the body to absorb and, in large amounts, may lead to osmotic diarrhea. In most of these cases, osmotic diarrhea stops when offending agent (e.g. milk, sorbitol) is stopped.

Exudative

Exudative diarrhea result due to mucosal damage and are always associated with the presence of mucus, fluid, blood and plasma proteins, with a net accumulation of electrolyte and water in the gut. This occurs with inflammatory bowel diseases, such as Crohn's disease or ulcerative colitis, and other severe infections such as E. coli or other forms of food poisoning. Prostaglandins and cytokines release may be involved. (Tisourdi, Heidrich et al. 2014)

Medication induced

Diarrhoea is a relatively frequent adverse event, accounting for about 7% of all drug adverse effects. More than 700 drugs have been implicated in causing diarrhoea;
those most frequently involved are antimicrobials, laxatives, magnesium-containing antacids, lactose- or sorbitol-containing products, nonsteroidal anti-inflammatory drugs, prostaglandins, colchicine, antineoplastics, antiarrhythmic drugs and cholinergic agents. Certain new drugs are likely to induce diarrhoea because of their pharmacodynamic properties; examples include anthraquinone-related agents, alpha-glucosidase inhibitors, lipase inhibitors and cholinesterase inhibitors. Antimicrobials are responsible for 25% of drug-induced diarrhoea. The disease spectrum of antimicrobial-associated diarrhoea ranges from benign diarrhoea to pseudomembranous colitis. Several pathophysiological mechanisms are involved in drug-induced diarrhoea: osmotic diarrhoea, secretory diarrhoea, shortened transit time, exudative diarrhoea and protein-losing entero-pathy, and malabsorption or maldigestion of fat and carbohydrates. Often 2 or more mechanisms are present simultaneously. In clinical practice, 2 major types of diarrhoea are seen: acute diarrhoea, which usually appears during the first few days of treatment, and chronic diarrhoea, lasting more than 3 or 4 weeks and which can appear a long time after the start of drug therapy. Both can be severe and poorly tolerated. In a patient presenting with diarrhoea, the medical history is very important, especially the drug history, as it can suggest a diagnosis of drug-induced diarrhoea and thereby avoid multiple diagnostic tests. The clinical examination should cover severity criteria such as fever, rectal emission of blood and mucus, dehydration and bodyweight loss. Establishing a relationship between drug consumption and diarrhoea or colitis can be difficult when the time elapsed between the start of the drug and the onset of symptoms is long, sometimes up to several months or years. (Chassany, Michaux et al. 2000)

Broad spectrum antibiotic can greatly reduce the number of colonic bacteria that normally convert osmotically active molecules to gases and short chain fatty acids (SCFA). The SCFA are normally absorbed from the lumen of the colon as long as the amount is close to normal. Absorption of SCFA facilitate the absorption of electrolytes and water in the lumen, therefore reduction in the colonic bacteria leads to accumulation of osmotically active molecules and reduce absorption of water and electrolytes.

Antibiotics can also have direct adverse effect on the colonic function. For example erythromycin increase gut motility; clindamycin and clarithromycin may also increase secretions. Moreover some antibiotic allow the opportunistic pathogenic bacteria overgrowth which is normally suppressed by the normal gut flora as it is destroyed by the antibiotics. The organisms or the toxin produced by them reduce the absorptions or increase the secretion of the water and electrolytes. (Alam and Mushtaq 2009) Clostridium difficile is most commonly associated with antibiotic related diarrhea. C. perfringens, Salmonella, Shigella, campylobacter, Yersinia enterocolitica and Escherichia coli organisms have also been implicated in antibiotic associated diarrhoea. Clindamycin, penicillin and cephalosporins are associated more often with the development of C difficile infection.
Increased opportunistic infection is also associated with the use of anti-neoplastic agents and severe malnutrition. Antacids (especially magnesium salts), H₂-receptor blockers, and proton pump inhibitors have also been implicated in cases of diarrhea.

**Malabsorptive diarrhea**

Lipid malabsorption and maldigestion of other macronutrients or micro nutrients is associated with diarrhea. Malabsorptive diarrhea occurs when there is inadequate healthy absorptive area or there is rapid transit of chime, such as what occur in inflammatory bowel disease or after extensive bowel resection. *(Juckett and Trivedi 2011)*

**Dysentery**

Visible blood lose in the stools is referred to as dysentery. The blood is trace of an invasion of bowel tissue. Dysentery is a symptom of bacterial infections such as Shigella, Entamoeba histolytica, and Salmonella. *(Marie and Petri 2013)*

**Health impact of Diarrhea**

Diarrheal disease have a negative impact on both physical fitness and mental development. Early childhood malnutrition resulting from any cause reduces physical fitness and work productivity in adults, and diarrhea is a primary cause of childhood malnutrition. *(Giannattasio, Guarino et al. 2016)* It has been shown that children who had experienced severe diarrhea had significantly lower scores on a series of tests of intelligence. *(Richard, Black et al. 2014)*

**Differential diagnosis**

Acute diarrhea is most commonly due to viral gastroenteritis with rotavirus, which is generally seen in children under five years of age. In travellers however bacterial infections predominate. Various toxins such as mushroom poisoning and drugs can also cause acute diarrhea.

Chronic diarrhea can be the part of the presentations of a number of chronic medical conditions affecting the intestine. Common causes include ulcerative colitis, Crohn's disease, microscopic colitis, celiac disease, irritable bowel syndrome and bile acid malabsorption.

**Infections**

There are many causes of infectious diarrhea, which include viruses, bacteria and parasites. Infectious diarrhea is frequently referred to as gastroenteritis. Norovirus is the most common cause of viral diarrhea in adults, but rotavirus is the most
common cause in children under five years old. Adenovirus types 40 and 41, and astroviruses cause a significant number of infections.

Campylobacter spp. are a common cause of bacterial diarrhea, but infections by Salmonella spp., Shigella spp. and some strains of Escherichia coli are also a frequent cause.

In the elderly, particularly those who have been treated with antibiotics for unrelated infections, a toxin produced by Clostridium difficile often causes severe diarrhea.

Parasites, particularly protozoa (e.g., Cryptosporidium spp., Giardia spp., Entamoeba histolytica, Blastocystis spp., Cyclospora cayetanensis), are frequently the cause of diarrhea that involves chronic infection. The broad-spectrum antiparasitic agent nitazoxanide has shown efficacy against many diarrhea-causing parasites.

Other infectious agents, such as parasites or bacterial toxins, may exacerbate symptoms.

**Inflammatory bowel disease**

The two overlapping types here are of unknown origin:

Ulcerative colitis is marked by chronic bloody diarrhea and inflammation mostly affecting the distal colon near the rectum.

Crohn's disease typically affects fairly well demarcated segments of bowel in the colon and often affects the end of the small bowel.

**Irritable bowel syndrome**

Irritable bowel syndrome (IBS), which usually presents with abdominal discomfort relieved by defecation and unusual stool (diarrhea or constipation) for at least 3 days a week over the previous 3 months.

**Other diseases**

Diarrhea can be caused by other diseases and conditions, namely:

- Chronic ethanol ingestion
- Ischemic bowel disease: This usually affects older people and can be due to blocked arteries.
- Microscopic colitis, a type of inflammatory bowel disease where changes are only seen on histological examination of colonic biopsies.
- Bile salt malabsorption (primary bile acid diarrhea) where excessive bile acids in the colon produce a secretory diarrhea.
- Hormone-secreting tumors: some hormones (e.g., serotonin) can cause diarrhea if excreted in excess (usually from a tumor).
- Chronic mild diarrhea in infants and toddlers may occur with no obvious cause and with no other ill effects; this condition is called toddler's diarrhea.
- Environmental enteropathy
- Radiation enteropathy following treatment for pelvic and abdominal cancers.
- Toddler's diarrhea (TD) is ascribed in children who have normal growth and no evidence of malabsorption or enteric infections. TD is common in developing countries like India too and accounts to 16% of diarrhoea in children. (Poddar, Agarwal et al. 2013)

Medical Nutrition therapy

The management of diarrhoea should being with the replacement of the necessary fluids and electrolytes. (Sack 1991), (Thiagarajah, Donowitz et al. 2015) Electrolyte solutions, soups, and broths, vegetable juices and other isotonic fluids can be used for this purpose, which should be followed by starchy carbohydrates such as cereals, bread, low fat meats, and small amounts of vegetables and fruits can be added, then lipids can be introduced. In most cases minimum residue diet (a diet that results in decreased fecal volume) similar to as described below may be initiated as the acute episodes resolves:
- Foods that is completely digested, well absorbed
- Foods that do not increase GI secretions
- Foods to limit in a Low- or Minimum Residue Diet is as follows:
  - Lactose (in lactose malabsorbers): 6-12 g may be normally tolerated in healthy lactase deficient individuals, but may not be in some individuals
  - Fiber not more than 20 g/day. Modest amount (10-15 g) may help maintain normal consistency of GI contents and normal colonic mucosa in healthy states and GI disease
  - Resistant starches
  - Raffinose, stachyose in legumes
  - Sorbitol, mannitol, xylitol >10g/day
  - Fructose (excess, not more than 20-25 g/meal),
  - Sucrose (excess, not more than 25-50 g/meal), well tolerated in moderate amounts; large amounts may cause hyperosmolar diarrhea or decreased fecal pH with fermentation to short chain fatty acids.
  - Caffeine, Alcohol (esp. wine and beer) increase GI secretion
The amount of hyperosmotic carbohydrates should be limited as they may be mal-digested and mal-absorbed leading to increased secretion of fluids in the intestinal lumen. Also the foods that increase the rate of gastrointestinal transit should be avoided. (Hammer and Hammer 2012) (Krause’s 2008)

Small amount of lipids can be used if the digestive mechanisms of the lipids are unaffected. (Lapillonne, Pastor et al. 2014) Generally sugar alcohol, lactose fructose and large amount of sucrose may worsen osmotic diarrheas. This is because the activity of disaccharidases and transport mechanisms may be decreased during inflammatory and infectious intestinal diseases, Sugar may need to be avoided especially in children.

**Prebiotics**

Use of limited quantity of foods or dietary supplements containing prebiotic component such as pectin, fructooligosaccharides, inulin, oats, banana flakes, chicory may actually help in control of diarrhea. Prebiotics are non-digestible food ingredients that have a specific stimulatory effect upon selected populations of gut friendly bacteria. The usual target microorganisms for prebiotic approaches are bifidobacteria and lactobacillus microbes. (Rastall and Gibson 2015) These friendly microbes prevent the over growth of potentially pathogenic organism.

Short-chain fatty acids (SCFAs), produced by bacterial fermentation of carbohydrates in the colon, influence gastrointestinal motility. However, caecal infusion of SCFAs as well as colonic fermentation of lactulose induce a relaxation of the proximal stomach in humans, indicating that SCFAs can affect motility at a distance from their site of production. Moreover, this suggests that SCFAs may be involved in the so-called ‘ileocolonic brake’, i.e. the inhibition of gastric emptying by nutrients reaching the ileo-colonic junction. In the terminal ileum, where their concentration may increase following a colo-ileal reflux, SCFAs stimulate contractions and shorten ileal emptying, which may protect ileal mucosa against the potentially harmful effects of the reflux of colonic contents. Small chain fatty acids (SCFA) in physiologic quantities serve as substrate for coonocytes, facilitate the absorption of fluids and salts. (Cherbut, Aubé et al. 1997)

**Probiotics**

Probiotics are often recommended on the assumption that ingestion of ‘healthy’ bacteria will reduce the disturbance of gut microbiota and subsequent diarrhoea by re-establishing the gut flora. Use of cultured foods and supplements, with or without prebiotics have modestly been successful in antibiotic-associated diarrhoea (AAD), travellers diarrhea, bacterial diarrhea and several other types of paediatric diarrhea. (Kause’s 2008)

A number of clinical trials have evaluated the role of probiotics in the prevention of AAD. These studies have used a range of probiotics and have shown variable
results. Meta-analyses show equivocal results due to the lack of homogeneity between studies. Sub-group analyses of the meta-analyses showed a significant reduction in AAD with the use of probiotics, namely Lactobacillus rhamnosus GG (LGG) and Saccharomyces boulardii. A number of methods have been used to administer these probiotics, including capsules, tablets and yogurts. The organisms used vary from a single species to multi-species cocktails, and the doses vary between studies, from 107 to 1010 colony-forming units (CFU). (Fox, Ahuja et al. 2015)

A review of 6 trials with 3562 patients evaluated the efficacy of probiotic interventions in prevention of AAD and Clostridium difficile diarrhoea (CDD) in older patients. Only 1 trial showed that Bacillus licheniformis was effective for preventing AAD in older patients. However, there was no preventive effect for AAD and CDD with Lactobacillus acidophilus (Florajen), Lactobacillus casei Shirota, Saccharomyces cerevisiae (boulardii) lyo, mixture of Lactobacillus acidophilus and Bifidobacterium bifidum (Cultech strains), and mixture of Lactobacillus acidophilus CUL60, CUL21, Bifidobacterium bifidum CUL20 and B. lactis CUL34. This indicates that probiotics may not reduce the risk of AAD and CDD in older patients. However, with current published data, it is difficult to draw concrete conclusions. (Xie, Li et al. 2015)

Micronutrients & Macronutrients

Severe and chronic diarrhea is accompanied by dehydration and electrolyte imbalance. Malabsorption of vitamins, minerals and proteins or lipids may also occur, and the nutrition may need to be replaced parenterally or enterally. In particular the loss of potassium alters bowel motility, encourages anorexia and can introduce a cycle of bowel distress. (Kause’s 2008)(Odey, Etuk et al. 2010)

Certain infectious diarrhea may lead to GI bleeding and loss of iron which may be severe enough to cause anemia. Nutritional deficiencies themselves cause mucosal changes such as decrease villi height and reduced enzyme secretion, further contributing to malabsorption. (Sherwani, Alam et al. 2008)

With the resolution of diarrhea, increased amount of fibre can be added to the diet to restore the normal mucosal function, fibre may increase electrolyte and water absorption and increase in firmness of stools.

Food in the lumen is required to restore the compromised GI tract after the disease and fasting period. Early feeding after rehydration reduces stool out and shortens the duration of disease. Micronutrient replacement and supplementation may be useful for acute diarrhea, probably because it accelerates the normal regeneration of damaged mucosal epithelial.
Treating diarrhoea in infants and children

Oral rehydration therapy (ORT) has been a major advance and has saved many lives from acute diarrhoea. However, persistent diarrhoea is now a major problem and is very significant because of its strong negative impacts on nutritional status. Persistent diarrhoea and dysentery are now major causes of infant and young child deaths. ORT provides clear and practical methods for replacement of fluid and electrolyte losses during diarrhoea. Rehydration salts can be made available as (i) a simple, easy-to-use package, complete with user instructions; (ii) cereal-based formulae based on widely available ingredients that can be prepared domestically or commercially; and (iii) home-made mixtures of sugar and salt which should be simple to prepare but are risky because of inadequate understanding about their preparation at home and the chance of mixing the ingredients inaccurately and giving them wrongly.

The oral rehydration therapy is the keystone of National Diarrhoeal Disease Control Programme. The packets of oral rehydration salts (ORS) are available at the Primary health centres as well as in chemist shops. There are depot holders of ORS packets in the community too. Most of the times the health care workers do not emphasise the role, benefits and method of preparation of ORS. As a result of this mothers do not know the right method of preparation of ORS and do not understand the need to give ORS to the child. Demonstration of correct preparation of ORS solution should be inbuilt in the health education package of the Oral Rehydration Therapy for diarrhoeal diseases. Health care providers must emphasise about the role of ORS in prevention of dehydration so that mothers give ORS to the child. (Kadam, Hadaye et al. 2013)

Table 1. Composition of the new ORS formulation

<table>
<thead>
<tr>
<th>Reduced osmolarity ORS</th>
<th>grams/litre</th>
<th>Reduced osmolarity ORS</th>
<th>mmol/litre</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium Chloride</td>
<td>2.6</td>
<td>Sodium</td>
<td>75</td>
</tr>
<tr>
<td>Glucose, anhydrous</td>
<td>13.5</td>
<td>Chloride</td>
<td>65</td>
</tr>
<tr>
<td>Potassium chloride</td>
<td>1.5</td>
<td>Glucose, anhydrous</td>
<td>75</td>
</tr>
<tr>
<td>Trisodium citrate dihydrate</td>
<td>2.9</td>
<td>Potassium</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>20.5</td>
<td>Citrate</td>
<td>10</td>
</tr>
<tr>
<td><strong>Total Osmolarity</strong></td>
<td><strong>245</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

The ORS composition (Table 1) has passed extensive clinical evaluations and stability tests. The pharmacokinetics and therapeutic values of the substances are as follows:
Glucose facilitates the absorption of sodium (and hence water) on a 1:1 molar basis in the small intestine.

Sodium and Potassium are needed to replace the body losses of these essentials ions during diarrhoea (and vomiting).

Citrate corrects the acidosis that occurs as a result of diarrhoea and dehydration.

Early refeeding during diarrhoea is another important principle to help to reduce its duration, severity and its nutritional impacts.

World Health Organization-recommended rehydration solution for malnourished children (ReSoMal) for rehydrating severe acute malnourished children may not be available. In a clinical study, 110 consecutive children aged 6-59 months with severely acute malnourishment and acute diarrhea were randomized to low-osmolarity oral rehydration solution (ORS) (osmolarity: 245, sodium: 75) with added potassium (20 mmol/l) or modified ReSoMal (osmolarity: 300, sodium: 45). In all, 15.4% of modified ReSoMal group developed hyponatremia as compared with 1.9% in low-osmolarity ORS, but none developed severe hyponatremia or hypernatremia. Both groups had equal number of successful rehydration (52 each). Both types of ORS were effective in correcting hypokalemia and dehydration, but rehydration was achieved in shorter duration with modified ReSoMal. (Kumar, Kumar et al. 2015)

Acute diarrhoea is most dangerous in infants and children, who are easily dehydrated by large fluid loses. In these cases replacement of fluids and electrolytes must be aggressive and immediate.

Newer reduced osmolarity solutions (= 130 to 200 mOsm/L) have been shown to be equally effective in the treatment of persistent diarrhea in children. Several commercial solutions typically contain less glucose and slightly less salt. Oral rehydration therapy is less invasive and less expensive than intravenous rehydration and, when used with children, allows parents to assist with their children’s recovery. (Krause’s, 2008)

A substantial proportion of children 9 to 20 months of age can maintain adequate intake when offered either a liquid or a semi-solid diet continuously during bouts of acute diarrhea. Even during acute diarrhea the intestine can absorb upto 60 % of the food eaten.

Some practitioners have been slow to adopt the practice of early feeding after severe diarrhoea in infants despite evidence that resting the gut is actually more damaging. A report from the working group of World Congress of Paediatric Gastroenterology, Hepatology and Nutrition suggests that strategies must be cohesive and uniform to address the problems of pediatric diarrhea and reduce the number of deaths worldwide. Prescription of the typical hospital full liquid and clear
liquid diet that is commonly high in fructose, lactose and other sugars is inappropriate for recovery from diarrhea. (Krause’s, 2008)

Continuation and encouragement of breastfeeding is an important strategy to prevent and control diarrhoea and as part of its management. Breast-feeding provides significant protection against many diseases including diarrhea in infancy. This is attributable to a complex of acquired and innate factors unique to human milk including immunoglobulins, oligosaccharides, glycoconjugates, lactoferrin, antimicrobial compounds, leukocytes, cytokines, and other agents. (Abdel-Hafeez, Belal et al. 2013)

The interactions between diarrhoeal disease and nutritional status are complex and synergistic. Despite intensive field-based and laboratory studies over three decades, many questions remain unanswered about the causes, pathophysiology and best approaches to management and prevention of this "diarrhoea-malnutrition" syndrome. (Gracey 1999)

**Nutritional supplementation**

Research has shown the positive effect of nutritional supplementation on child growth in diarrheal disease. Supplementation completely offset the negative effect of diarrheal disease on length. Targeting supplementation programs to the critical period of high diarrheal prevalence among infants and young children should increase the effectiveness of such programs in preventing growth retardation associated with diarrhea. (Lutter, Mora et al. 1989)

To combat diarrheal illnesses the World Health Organization recommends improved child nutrition and micronutrient supplementation. Zinc and vitamin A have been shown to reduce the incidence of diarrheal illnesses. Stemming from the immunologic properties of vitamin D, it represents an additional micronutrient that may have a role in the prevention of childhood diarrheal diseases.

Levels of 1,25(OH)2D, the active form of vitamin D, are increased by the enzymatic activities of CYP27B1-hydroxylase and reduced by CYP24A1-hydroxylase. It is postulated that the kinetics of that equilibrium control tissue-specific paracrine activities of vitamin D. Immunologic activation of toll-like receptors on macrophages by pathogens augments intracellular expression of CYP27B1-hydroxylase and vitamin D receptor (VDR) genes. Subsequently, with sufficient cytosolic concentrations of 25-(OH)D, CYP27B1-hydroxylase produces 1,25(OH)2D. Binding of the 1,25(OH)2D-VDR complex to DNA response elements upregulates expression of the antimicrobial peptides cathelicidin and -defensin, intracellular modulators that are ubiquitously expressed in the gastrointestinal tract. Thus in vitamin D-deficient individuals innate immune activity may be impaired, thereby enhancing susceptibility to intracellular diarrheogenic
Pathogens. Additionally, in vitro research of adaptive immunity has shown that the 1,25(OH)2D-VDR complex induces CCR10 expression in terminally differentiated B cells. CCR10 functions in cellular homing of immunoglobulin A-secreting cells to enteric tissues. Given the importance of immunoglobulin A in adaptive mucosal immunity, vitamin D deficiency could result in impaired host abilities to mount pathogen-focused immune responses to diarrhoegenic microbes.

Supplementation with specific dietary ingredients, such as vitamin A, zinc and folate, is rather contentious and drug therapy is of little value unless specifically indicated. Some patients may require enteral nutrition or parenteral nutrition but these require specialized equipment and skills that are usually beyond the reach of developing countries and infants and children who live in remote areas. (Aluisio, Maroof et al. 2013)

Zinc supplementation: diarrhoea prevention and treatment

It is estimated that zinc deficiency is responsible for 4.4% of childhood deaths in Africa, Asia, and Latin America. A review examined the impact of zinc supplementation, administered prophylactically or therapeutically, on diarrhoea. A total of 38 studies were included in this review, 29 studies examined the effect of prophylactic zinc and nine studies examined the effects of therapeutic use of zinc for treatment of diarrhoea in children under 5 years.

Prophylactic zinc has been shown to be effective in decreasing both prevalence and incidence of diarrhoea, reducing respiratory infections and improving growth in children with impaired nutritional status. There is less conclusive evidence of reduction in diarrhoea duration or diarrhoea severity. While prophylactic zinc decreases mortality due to diarrhoea and pneumonia, it has not been shown to affect overall mortality. Therapeutic use of zinc for the treatment of diarrhoea in children has been shown to reduce diarrhoea incidence, stool frequency and diarrhoea duration as well as respiratory infections in zinc deficient children. However, stool output is only reduced in children with cholera. Less conclusive evidence exists for therapeutic zinc reducing mortality due to diarrhoea and respiratory infections. (Liberato, Singh et al. 2015)

Daily zinc supplements (40 mg for 14 days) in children aged 5-12 years with acute dehydrating diarrhoea did not shorten the duration of diarrhoea or reduce subsequent episodes. (Negi, Dewan et al. 2015)

Lactose free diet

Secondary lactose intolerance is often a cause of prolongation of diarrheal episodes. Appropriate management includes elimination of lactose from diet. Weaning diet made from locally available cereals have been effective in the management of secondary lactose intolerance. Lactose free formulae are also available.
In a Cochrane review 33 trials enrolling 2973 children with acute diarrhoea were included. Fifteen trials included children aged below 12 months, and 22 excluded children who were being breast-fed. It was found that compared to lactose-containing milk, milk products, or foodstuffs, lactose-free products may reduce the duration of diarrhoea by an average of about 18 hours (MD -17.77, 95% CI -25.32 to -10.21, 16 trials, 1467 participants, low quality evidence). Lactose-free products probably also reduce treatment failure (defined variously as continued or worsening diarrhoea or vomiting, the need for additional rehydration therapy, or continuing weight loss) by around a half (RR 0.52, 95% CI 0.39 to 0.68, 18 trials, 1470 participants, moderate quality evidence). Diluted lactose-containing milk has not been shown to reduce the duration of diarrhoea compared to undiluted milk or milk products (five trials, 417 participants, low quality evidence), but may reduce the risk of treatment failure (RR 0.65, 95% CI 0.45 to 0.94, nine trials, 687 participants, low quality evidence). It was concluded that in young children with acute diarrhoea who are not predominantly breast-fed, change to a lactose-free diet may result in earlier resolution of acute diarrhoea and reduce treatment failure. Diluting lactose-containing formulas may also have some benefits but further trials are required to have confidence in this finding. (MacGillivray, Fahey et al. 2013)

Probiotics in antibiotic-associated diarrhea (AAD)

The use of several prebiotics was evaluated in AAD in children. The risk reduction of AAD ranged from 0.2 for Saccharomyces boulrdi, 0.3 for lactobacillu GG, 0.5 for L Bifidus and streptococcus termophilus. (Krause's, 2008)

Cochrane review included 23 studies (3938 participants) which treatment with either Bacillus spp., Bifidobacterium spp., Clostridium butyricum, Lactobacilli spp., Lactococcus spp., Leuconostoc cremoris, Saccharomycoses spp., orStreptococcus spp., alone or in combination. Eleven studies used a single strain probiotic, 4 combined two probiotic strains, 3 combined three probiotic strains, 1 combined four probiotic strains, 2 combined seven probiotic strains, 1 included ten probiotic strains, and one study included two probiotic arms that used three and two strains respectively. It was found there is moderate quality evidence suggesting a protective effect of probiotics in preventing AAD. It is premature to draw conclusions about the efficacy and safety of other probiotic agents for pediatric AAD. Although no serious adverse events were observed among otherwise healthy children, serious adverse events have been observed in severely debilitated or immuno-compromised children with underlying risk factors including central venous catheter use and disorders associated with bacterial/fungal translocation. Until further research has been conducted, probiotic use should be avoided in pediatric populations at risk for adverse events. (Goldenberg, Lytvyn et al. 2015)

A clinical study evaluated the efficacy of a probiotic yogurt compared to a
pasteurised yogurt for the prevention of antibiotic-associated diarrhoea in children. It was found that 200 g/day of either yogurt (probiotic) containing Lactobacillus rhamnosus GG (LGG), Bifidobacterium lactis (Bb-12) and Lactobacillus acidophilus (La-5) was an effective method for reducing the incidence of antibiotic-associated diarrhoea in children. (Fox, Ahuja et al. 2015)

Soya-based feeds

Ongoing acute diarrhoea in infancy may respond to a change from a cows' milk to a soya-based formula. This is usually ascribed to the change in carbohydrate content of the feed. There prompt cessation of diarrhoea and the disappearance of evidence of carbohydrate malabsorption suggests the response is due to the removal of lactose from the diet. (Bowie, Hill et al. 1988) Soy polysaccharide, significantly reduce the duration of liquid stool excretion. (Brown, Perez et al. 1993)

Early versus delayed refeeding for children with acute diarrhoea

Cochrane review evaluated the efficacy and safety of early versus late reintroduction of feeding in children with acute diarrhoea. Twelve trials involving 1283 participants were included; 1226 participants were used in the analysis (724 in the early refeeding group and 502 in the late refeeding group). Nine trials described their allocation sequence, but only two used concealed allocation. One trial reported single-blinding but did not clearly identify the person who was blinded. Early refeeding meant intake during or immediately after start of rehydration, while late refeeding meant intake only 20 hours to 48 hours after start of rehydration. Significant heterogeneity was noted in the data for the duration of diarrhoea. There was no significant difference between the two refeeding groups in the number of participants who needed unscheduled intravenous fluids (six trials with 813 participants), who experienced episodes of vomiting (five trials with 466 participants), and who developed persistent diarrhoea (four trials with 522 participants). There was no evidence that early refeeding increases the risk of unscheduled intravenous fluid use, episodes of vomiting, and development of persistent diarrhoea. (Gregorio, Dans et al. 2011)

Hypokalaemia is a common electrolyte abnormality in children with severe protein energy malnutrition and diarrhoeal diseases. (Odey, Etuk et al. 2010)

Conclusion

Identification and treatment of the underlying cause is critical in management of diarrhea. The fluid and electrolyte replacement should be managed by using oral glucose electrolyte solutions.
Minimum-residue diet should be initiated and avoid large amounts of sugars and sugar alcohols. Prebiotics in modest amounts including pectin, oligosaccharides, inulin, oats, banana flakes may be useful. Probiotics, cultured foods and supplements that are sources of beneficial gut flora may be helpful.

In infants and children with acute diarrhea, aggressive replacement of fluid and electrolytes should be priority. Continue a liquid or semisolid diet during bouts of acute diarrhea for children 9 to 20 months. Intestine absorbs up to 60% of food even during diarrhea, so early refeeding is helpful and gut rest is harmful.

References:


Dear Doctor,

Diarrhea is the third leading cause of childhood mortality in India, and is responsible for 13% of all deaths/year in children under 5 years of age. Information on diarrheal diseases, its determinants and preventive and control strategies need to be reviewed for better management of our patients. Nutrition plays an critical role in the management of diarrhea in both children and adults.

It gives me immense pleasure to present to you this QMR issue by Dr. Vidya Patil and Dr. Sunil Patil, renowned physician and pediatrician respectively. In this issue, they are enlightening us on ‘Medical Nutrition in Diarrhea Management’.

With best regards,

Dr. Balaji More
Vice President - Medical