Diarrhoea and malnutrition

Nel ED
Department of Paediatrics and Child Health, Faculty of Health Sciences, University of Stellenbosch and Tygerberg Hospital, Cape Town, South Africa.
Correspondence to: Dr E Nel, e-mail: edn@sun.ac.za

Abstract

The relationship between diarrhoea and malnutrition is bidirectional: diarrhoea leads to malnutrition while malnutrition aggravates the course of diarrhoea. Many factors contribute to the detrimental effect of diarrhoea on nutrition. Reduced intake (due to anorexia, vomiting, and withholding of feeds), maldigestion, malabsorption, increased nutrient losses, and the effects of the inflammatory response are some of the factors involved. High volume stool losses (greater than 30 ml/kg/day) are associated with a negative balance for protein, fat, and sugar absorption. Enteric infections often cause increased loss of endogenous proteins, particularly after invasive bacterial infections. Initially, the major emphasis of treatment of acute diarrhoea in children is the prevention and treatment of dehydration, electrolyte abnormalities and comorbid conditions. The objectives of diarrhoeal disease management are to prevent weight loss, to encourage catch-up growth during recovery, to shorten the duration and to decrease the impact of the diarrhoea on the child's health. Addressing only diarrhoea or only food security is unlikely to be successful in decreasing the prevalence of malnutrition. Existing evidence provides some guidelines as to the optimal nutritional management of children with diarrhoea and novel treatments may prove to be valuable in future.

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Introduction

The burden of diarrhoea and malnutrition in developing countries are both high, and, as these conditions frequently coexist, it is attractive to hypothesise a causal association between them. The review, "Interactions of Nutrition and Infection" by Scrimshaw, Taylor and Gordon in 1968,[1] first drew attention to the relationship between infection and nutrition. Following this publication, studies attempted to quantify the contribution of diarrhoea to childhood malnutrition, to define the pathophysiology, to determine the appropriate nutritional therapy, and, more recently, to investigate the role of intestinal disease in HIV infected children. In this paper the interaction between diarrhoea and malnutrition in children will be reviewed briefly.

Epidemiology

The relationship between diarrhoea and malnutrition is bidirectional: diarrhoea leads to malnutrition while malnutrition aggravates the course of diarrhoea. On the one hand, severe and prolonged episodes of diarrhoea cause malnutrition in individual patients; on the other hand, malnourished children are more likely to develop complications with diarrhoea. Many studies, addressing the relationship between diarrhoea and malnutrition, have demonstrated a detrimental effect of diarrhoea on nutritional status.

Some of the first evidence of the association between diarrhoea and malnutrition was the graphical representation of the interaction between growth and infection in children in South America. Mata and co-workers[2] observed cohorts of infants born in Santa Maria Cauquè in Gautemala. Intestinal as well as other infections and growth parameters were recorded from birth to three years. Episodes of diarrhoea, upper and lower respiratory tract infection, measles and other infections were associated with progressive growth faltering: children with poor growth (growth in the lower quartile of the study) had more infections than those who grew the best (growth in the upper quartile). Especially dysentery and bronchopneumonia occurred more frequently in the lower growth quartile.

Subsequent studies assessed the impact of diarrhoea on the growth of large groups of children. The contribution of diarrhoea to growth failure in children in developing countries was estimated to be as high as 25–30%. The same effect is, however, not seen in children in developed countries. This lack of effect may be due to the lower burden of disease in developed countries, the better nutrition of children in these countries, and bias in measuring episodes of morbidity.[3]

Martorell[3] measured growth and episodes of infection in children in eastern Guatemala from shortly after birth to seven years. Diarrhoea was associated with reduced growth rate while there was no significant association between fever or respiratory illness and growth. Children with a low prevalence of diarrhoea (less than or equal to 5% of time with diarrhoea) grew 6,3% more in length and

11% more in weight than those with a high prevalence of diarrhoea (more than 5% of time with diarrhoea). This effect occurred independently of the type of nutritional supplement that the children were receiving (some were on a high and others on a low energy supplement).

Diarrhoea had a similar effect on the growth of children in The Gambia. Rowland[4] found that there was a negative correlation between weight and height gain and diarrhoea prevalence in children younger than three years. Malaria was the only other disease for which there was also a significant association in this study. The regression coefficient for the diarrhoea versus weight gain was -95+/- 8,5 g/kg body weight per month.

A more recent study from northern Brazil[5] analysed surveillance data collected between August 1989 and December 1998. The number of episodes of diarrhoea, days of diarrhoea and episodes of persistent diarrhoea (longer than 14 days), helminth infections and height-for-age Z-score were reported. There was a inverse relationship between the number of episodes of diarrhoea and growth: an average burden of diarrhoea of 9,1 episodes of diarrhoea before two years was associated with a 3,6 cm decrease in longitudinal growth at age seven years. There was also a negative association between intestinal helminth infections and height for age Z-score. These associations remained significant after controlling for nutrition during infancy, other parasitic infections, diarrhoea in later childhood, and socioeconomic status.

Checkley and co-workers[6] performed a multi-country analysis of the effect of diarrhoea on childhood stunting. Nine studies performed in South America, Africa, and Bangladesh between 1978 and 1998 were included. After correction for socioeconomic status, the odds of stunting by 24 months increased with every episode of diarrhoea and with each day of diarrhoea. Using pooled data, the proportion of stunting that could be attributed to more than or equal to five episodes of diarrhoea was 25% and for having diarrhoea more than or equal to 2% of the first 24 months of life was 18%.

The preceding data suggests that reducing the incidence and prevalence of diarrhoea in children in developing countries will lead to a reduction in malnutrition. This conclusion has been challenged by studies from Bangladesh, The Gambia, and Egypt.

Briend[7] challenged the importance of diarrhoea as a cause of malnutrition in communities. This challenge was based on concerns that there was inadequate epidemiological evidence to support causality. Briefly, the concerns were related to: temporal ambiguity; lack of consistency between short and long term studies (in terms of magnitude); poor strength of association; inadequate evidence for biological plausibility; and lack of evidence of a sustained effect of diarrhoea. A few epidemiological studies seem to support this position.

Poskitt and co-workers[8] reviewed data collected from 1979 through 1993 in The Gambia. Clinic visits for diarrhoea and growth parameters of 1190 children aged 0–2 years were analysed. During the study period the number of clinic visits for diarrhoea decreased. There was, however, no improvement in weight gain or longitudinal growth in this period.

A longitudinal study from Egypt[9] found that diarrhoea was unlikely to have a major impact on the prevalence of malnutrition. Diarrhoea was associated with a small increase in the risk of low height-for-age and children showed some catch-up growth in the following observation period. There was no effect on the weight-for-age or weight-for-height. On the other hand, children with a low weight for height (as well as those with poor sanitation and previous episodes of diarrhoea) had an increased risk of diarrhoea. Few children in this study however had persistent diarrhoea (1%) and the prevalence of malnutrition in this population was lower than in other populations that have been studied. The results of this study may thus not be applicable to poorer populations.

Although no organism has consistently been identified as a cause of persistent diarrhoea, in certain geographic areas entero-aggregative *E. coli,* cryptosporidium, and giardia lamblia have been identified as important causes of persistent diarrhoea and malnutrition. In a Peruvian study[10] children infected with cryptosporidium had faltering both in weight and height gain for months after the initial infection. Stunted children and infants younger than six months did not have catch-up growth during the study period. In HIV infected children cryptosporidium infection was especially severe, often causing severe malnutrition, monosaccharide intolerance, and death.

Pathophysiology

Many factors contribute to the detrimental effect of diarrhoea on nutritional status. Reduced intake (due to anorexia, vomiting, and with-holding of feeds), maldigestion, malabsorption, increased nutrient losses, and the effects of the inflammatory response are some of the factors involved.

Intake

Childhood infections are frequently associated with reduced dietary intake. This effect is most prominent in children with diarrhoea. A study from Gautemala[11] has found that diarrhoea was associated with a reduction of daily dietary intake of 160 calories and 3 g of protein for children between the ages of 12 and 60 months. The reduction in children with respiratory infections was considerably less (67 calories and 1 g of protein per day). Other studies from Costa Rica, Guatemala, Bangladesh and Uganda also found significant reductions in dietary intake in children with diarrhoea.

Absorption and digestion

Acute diarrhoea causes increased losses of fluid and electrolytes. These are accompanied by varying degrees of nutrient maldigestion, malabsorption and losses. Children with high stool losses have significant malabsorption of protein, carbohydrates, and fat. Additionally, enteric protein losses are often increased. Studies of children with acute and persistent diarrhoea in developing countries have increased our knowledge of these effects.

High volume stool losses (greater than 30 ml/kg/day) are associated with a negative balance for protein, fat, and sugar absorption. Balance studies conducted in Cape Town[12] found that increasing volumes of stool losses lead to decreasing nutrient absorption. Once stool volume exceeded 30–50 g/kg/day, children were unable to achieve a positive nutrient balance with normal infant formula. Apparent nitrogen absorption decreased by 0,86% and apparent fat absorption 0,4% for each gram increase in stool weight. A stool weight of 50 g/kg/day led to an apparent nitrogen absorption of 59% and fat absorption of 52 %. Sugar malabsorption also increased with increasing stool losses. In these studies the effect was less in children receiving a soya based formula.

Enteric infections often cause increased loss of endogenous proteins, particularly after invasive bacterial infections. Hoffman[13] measured alpha-1-antitrypsin in stool of infants with diarrhoea in Cape Town; losses were increased in children with enteric infections. Other studies have similarly documented increased protein loss during infectious diarrhoea[14] and after measles.[15]

Inflammatory response

The inflammatory response that accompanies enteric infections contributes to the detrimental effects of diarrhoea on nutritional status. Energy requirements are increased, appetite is suppressed by cytokine release, and catabolism and loss of nutrients is accelerated.

Various markers of inflammation (e.g. CRP, IL6, IL8, and TNF-α) are increased in diarrhoea:

1. Entero-aggregative *E. coli* infection, an important cause of both acute and persistent diarrhoea in developing countries, leads to a pronounced increase in IL8.[16]
2. Serum CRP is higher in children with bacterial than viral diarrhoea: a Taiwanese study[17] found that CRP as well as IL6 and IL8 were more elevated in children with bacterial than those with viral diarrhoea. Rotavirus, however, also caused a significant systemic inflammatory response.
3. Bacteraemia, a severe complication of diarrhoea in children, is also associated with a systemic inflammatory response.[18]
4. Cytokine activation (CRP, IL6, interferon (IFN)-gamma) in HIV infected patients predicts poor survival.[19]

HIV, intestinal disease and malnutrition

Diarrhoea and malabsorption are important complications of HIV infection that contribute to the high morbidity and mortality. Episodes of diarrhoea are often complicated by severe malabsorption.

Lactose malabsorption is a common complication in young HIV-infected children with diarrhoeal disease.[14,20,21] Thirty to sixty percent of these children have evidence of lactose malabsorption. In the presence of persistent diarrhoeal disease, it is advisable to use low lactose feeds. In the absence of diarrhoea however lactose-containing feeds are usually tolerated.

Fat malabsorption is also detected in up to 30% of children with HIV infection.[22] Exocrine pancreatic insufficiency[23,24,25] and mucosal factors contribute to the steatorrhoea. Despite the high proportion of children with increased faecal fat there is presently no clear association with malnutrition. At this stage, it seems prudent to provide pancreatic enzyme supplementation to HIV infected children with documented or suspected exocrine pancreatic insufficiency.

Management

Initially the major emphasis of treatment of acute diarrhoea in children is the prevention and treatment of dehydration, electrolyte abnormalities and comorbid conditions (e.g. pneumonia, bacteraemia). Nutritional management is, however, not delayed and is an integral part of their management. Objectives are to prevent weight loss, to encourage catch-up growth during recovery, to shorten the duration and to decrease the impact of the diarrhoea on the child's health.

Feeds are only interrupted for a few hours to allow correction of severe dehydration and shock.[26] There is no indication for "regrading" of feeds in infants. Giving diluted or low volumes of feeds aggravates the weight loss that follows an episode of diarrhoea and does not reduce the duration or severity of the diarrhoea significantly. Breastfeeding should not be interrupted; it shortens the duration of the diarrhoea and improves energy intake.

Initially children continue with their normal feeds and specialised formulae are indicated for those with malabsorption. Lactose free formulae are given to children with suspected lactose intolerance; this occurs more frequently in malnourished children and those whose diarrhoea persists longer than 3–4 days. Hydrolysed infant formulae are used for those with suspected protein sensitive enteropathy and may be of value in some children with severe malnutrition or HIV infection.[27]

Zinc

Zinc, a cofactor for many enzymes and required for cell division, has a number of potentially beneficial effects on the intestine. It reduces intestinal permeability in malnourished children with diarrhoea[28,29] and, in animal models, tight junction morphology is improved and paracellular permeability decreases after zinc supplementation.[30]

Clinical benefits of zinc supplementation include reduction of the severity and duration of diarrhoea in children at high risk of zinc deficiency. A recent meta-analysis[31] of randomised, placebo controlled trials of zinc supplementation in children with diarrhoea found that zinc supplementation reduced the duration of acute diarrhoea by 15% and the duration of persistent diarrhoea by 15,5%. Duration of diarrhoea was also reduced by 18,8% and 12,5% for acute and persistent diarrhoea respectively. Weight and length gain is also improved in children after zinc supplementation. A more recent South African study,[32] however, did not find the same benefit in children with diarrhoea. The implication for clinical practice in South Africa still needs to be determined.

Vitamin A

Studies from developing countries have found that vitamin A supplementation reduces the number of episodes of severe diarrhoea and diarrhoeal disease deaths in children. However, there is less evidence that vitamin supplementation will benefit children once they have diarrhoea. Supplementation with vitamin A also reduces intestinal permeability in children in developing countries supporting the role of vitamin A in maintaining the intestinal barrier function.[33,34]

Novel Agents

The role of glutamine and its derivatives and arginine in the management of acute infectious diarrhoea are not well established. These agents promote mucosal recovery and may accelerate recovery from diarrhoea.

Conclusions

The detrimental effects of diarrhoea, in particular persistent diarrhoea, on the nutrition of individual children are well recognised. The effects of diarrhoea on the prevalence of malnutrition in a population, however, are complex. Addressing only diarrhoea or only food security is unlikely to be successful in decreasing the prevalence of malnutrition. Existing evidence provides some guidelines as to the optimal nutritional management of children with diarrhoea and novel treatments may prove to be valuable in future.

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