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Current Management of Persistent Diarrhoea and Malnutrition in Developing Countries

S.K. Roy[1,2] A.M. Tomkins and [1]S.M. Akramuzzaman
[1]International Centre for Diarrhoeal Disease Research, Bangladesh,
[2]Institute of Child Health, London

Introduction

With the advancement of management and investigations, acute diarrhoea is not considered to be dreadful when rehydration fluid and appropriate antibiotics are available. But considerable difficulty is encountered to manage a case of persistent diarrhoea (PD) because of multiple pathophysiological changes occuring in gastrointestinal system and metabolism of the patients. In earlier studies mortality in persistent diarrhoea was as high as 50%.[1] Although the proportion of persistent diarrhoea patients is much lower than acute diarrhoea, death due to persistent diarrhoea is more than half (52%) of total diarrhoeal deaths.[2] In Bangladesh, it has been shown that mortality risk is 67 times higher in patients with PD and severe malnutrition.[3] In a study in Brazil, Victora et al[4] found that death due to persistent diarrhoea was 62%, acute diarrhoea 28% and dysentery was 10%. Risk of death increases many fold if persistent diarrhoea patients are malnourished.[5] It is now generally agreed that diarrhoea which continues for more than 2 weeks may be defined as persistent diarrhoea.[6] Without appropriate understanding of the underlying pathophysiology, it is difficult to recommend a general outline for the management of persistent diarrhoea.[7]

Epidemiology

Community based studies have showed that in Ethiopia about 27% of acute diarrhoea continued for more than 3 weeks in children between 12-23 months.[8] In Bangladesh, Guatemala and some parts of Ethiopia, the incidence is around 7%. During hospital treatment of acute diarrhoea, quite a good number of children goes on to persistent diarrhoea (> 14 days).

Factors that Determine Persistent Diarrhoea

To date there are only a few studies on identifying the predisposing factors for chronic diarrhoea. But it is known that malnutrition has strong relationship with increased duration and severity of diarrhoea, reduced intestinal enzyme activity and loss of normal mucosal integrity. Prolonged intestinal mucosal injury has been postulated to maintain a vicious cycle of malabsorption-osmotic diarrhoea-malnutrition.[9] Supplementary feeding, bacterial con-

tamination and environmental unhygienic conditions are also thought to be important factors for continuation of diarrhoeal episodes.

Diarrhoea can persist in conditions where pathogens of acute diarrhoea persist and cause diarrhoea.

a. Parasitic:

Giardiasis is a frequent cause of chronic diarrhoea in developing countries. Prolonged adherence to duodenojejunal mucosa, mucosal damage, mechanical barrier, competition for nutrients and toxin secretion may be the mechanism of diarrhoea due to giardiasis. Small intestinal bacterial overgrowth is frequently associated with malabsorption of nutrients[10] during giardiasis.

Cryptosporidium has been identified to be associated with few cases of persistent diarrhoea.[11]

Amoebiasis is a known cause of mucoid diarrhoea which may continue more than 2 weeks.

Strongyloides stercoralis can cause protracted diarrhoea with protein losing enteropathy.[12]

b. Bacterial:

Recent studies show that acute diarrhoeal pathogens can be isolated in about 60% of the persistent diarrhoea patients but two studies have shown that only 1% of acute diarrhoea pathogens continue at 2 weeks of persistent diarrhoea in Bangladesh.[13,15] This means the diarrhoeal duration may be a consequence of acute diarrhoea in some 6-8% of patients who don't spontaneously recover from acute diarrhoea.

Shigellosis, *Salmonella enteritis*, ETEC, EPEC, *Campylobacter jejuni*, *Yersinia enterocolitica*, *Aeromonas hydrophilia and Clostridium defficile* have been identified in children with persistent diarrhoea. The view that some of the acute bacterial pathogens may be significantly more common in persistent diarrhoea patients compared to acute diarrhoea patients or healthy controls has been unconvincing in recent reviews and studies.[14] Among those cryptosporidium[15] enteradhesive *E Coli*, enteroagrregative *E Coli* were isolated more frequently.[16]

In Bangladesh, Henry et al[3] reported that incidence of persistent diarrhoea was 0.8 per child per year in young children. Isolation of pathogens revealed that Enteroaggeregative *E Coli* was 24.4% in PD patients compared to 17.9% in acute diarrhoea patients. Enteroaggregative type of *E Coli* has been identified as a significant pathogen of persistent diarrhoea in children of East London.[17] There were 7% *C.jejuni* in PD patients compared to 1% in acute diarrhoea patients. In Lima peru, Lanata and his collegues reported no difference in proportion of enteropathogens between acute or persistent diarrhoea.[11] Baqui et al reported from Bangladesh that diffuse type of enteroadhesive *E Coli* was higher in PD patients (16.4 vs 10.3%). In Brazil, Wanke[18] reported that Aggregative type of adherent *E Coli* was present in 38% of PD patients compared to 18% in acute diarrhoea. Penny[14] reported from Peru that there was no difference in proportion of pathogens similar to the findings in the Gambia and South Africa. Bhatnagar et al[19] from India showed that aerobic bacterial isolation from duodenum was significantly higher in children with PD compared to controls (93.1 vs 71.4%, $p<0.05$).

In Bangladesh, a cohort of hospitalized patients with persistent diarrhoea, pathogens were identified in 57% patients compared with 67% in patients with acute diarrhoea during 1987-89 in Bangladesh.[20] Entertoxigenic and enteropathogenic *E Coli* were isolated in 20% of PD and 8% of acute diarrhoea patients. In these patients, 37% had single enteropathogens,

20% had multiple pathogens and 43% had no pathogens.

c. Viral

Rotavirus diarrhoea is very frequent in children. The isolation rate is as high as 50% among the acute diarrhoea patient between age 6 months to 2 years in ICDDR,B. 3% of rotavirus diarrhoea lasted more than 3 weeks in Bangladesh.[21] Astrovirus has been isolated in UK.[22] Measles infection may be followed by prolonged diarrhoea due to mucosal damage and secondary infection with enteropathens following the immune depression after measles infection.

Among other factors, malnutrition defined as less than 2 z-score of wt/ht had almost twice the higher risk for persistent diarrhoea.[23] In Brazil children less 75% wt/age had significantly higher attack rate of PD (15/18 vs 22/44, $p<0.02$) and shorter children <85% ht/age had higher (9/10 vs 28/50, $p< 0.04$) attack rate.[24] Depressed immune status has also been shown to be a significant risk factor for persistent diarrhoea.[24,25] Malnourished children have been shown to have frequent attacks of diarrhoea and more prolonged diarrhoea.[26] Malnourished children also suffer a longer from persistent diarrhoea.[27]

There are some studies showing environmental sanitation and feeding modes significantly related to incidence of persistent diarrhoea. Unmodified cows milk and buffalo milk have caused prolonged diarrhoea in children and appeared as a risk factor for persistent diarrhoea.[28,29]

Intestinal Mucosal Lesion in Persistent Diarrhoea

In a Gambian study, Sullivan et al[30] described several types of mucosal lesions. There was a "hyperplastic" type of lesion where villus was normal but crypt hypertrophy was present. Infiltration of submucosa with lymphocyte was predominent with CD8 and T lymphocytes. There was another "infiltrative" type, where small lymphocytes occupied villuos epithalium. The other type was a "destructive" type where villi were completely destroyed and lymphoid infiltration was seen in the crypts. All these mucosal changes did not correlate well with clinical presentation or nutritional status of the children. Much of these lesions could possibly relate with previous feeding status or enteropathogenic infection in diarrhoeal episodes.

Malabsorption of Nutrients

During diarrhoea or as a consequence of diarrhoea, digestion of food ingredients such as carbohydrate, protein and fat and their absorption can be partially or severely impaired and produce either osmotic or secretory diarrhoea and be a casual factor for persistence of diarrhoea.

Carbohydrate

Digestion can be impaired due to reduced exocrine pancreatic function leading to reduced luminal amylase which helps to hydrolyse oligosaccharides of more than 10 monosaccharide molecule. Decrease in brush border enzyme alpha-glucoamylase leads to inability of breaking oligosaccharide bonds of carbohydrates of less than 10 sugar molecules.

The commonest problem in brush border disaccharidase deficiency include reduction of lactase, sucrase, maltase, and isoimaltase activity. Lactase is the most vulnerable enzyme white sucrase is next to it. Lactose malabsorption is frequently seen after gastrointestinal infection like Rotavirus diarrhoea when villous tip cells are partially damaged. This phenomenon is called secondary disaccharidase defi-

ciency or transient lactose malabsorption. In most occasion the repair of the villous is quick and malabsorption of carbohydrate improves. Some of these patients especially the malnourished ones can not have effective repair of mucosal damage leading to malabsorption of lactose which may aggravate diarrhoea. In these event lactose from cow' milk cannot be adequately digested or absorbed and passes on to colon, resulting in lactose induced osmotic diarrhoea. Moreover, in colon, bacterial fermentation produces lactic acid and gas. Similarly other carbohydrates are fermented in colon into short chain organic acids with secretory properties. The character of lactose malabsorption is some what unique in the sense that lactase activity is early to reduce and late to return to normal level. Sucrose malabsorption can also be a cause of persistent diarrhoea which is less frequent than lactose malabsorption. Monosaccharide malabsorption has been reported in persistent diarrhoea but it is very rare and the origin may be congenital.

Ineffective villous repair or prolonged mucosal injury in malnourished children can be potential cause for persistent diarrhoea. Even in absence of diarrhoea, malnourished children have been found to have significantly reduced level of lactase deficiency in Bangladesh[31] and in India.[32] Studies in children with PEM have shown that mucosal damage with brush border and pancreatic enzyme deficiency is common[33] in children with oedematus malnutrition. A study by Jain et al[34] have shown significantly reduced level of pancreatic enzyme levels especially lipase and amylase in children with severe malnutrition. Interestingly, this study showed that protein splitting enzymes are not so severely depressed inspite of severe malnutrition.

The extent of the malabsorption in persistent diarrhoea during feeding of diet has only recently been described from Bangladesh.[35] This study also showed that severity of persistent diarrhoea i.e. purging rate per kg body weight and total gut transit time (TGTT) has significant positive relationship with absorption of energy, protein and fat.[36] In the above mentioned metabolic balance study of persistent diarrhoea during feeding of an efficient diet, median coefficient of absosrption of carbohydrate was 81%, nitrogen 53% and fat 60% with a total energy asorption of 68%.[35] Highly significant role of nutritional status of the persistent diarrhoea patients was established in a subsequent study which showed that more malnorished patients (<65% wt/age, <80 wt/ht, <90% ht/age or muac <11 cm) showed further 30% reduction in nutrient absorption leaving only 50% of total energy absorption during persistent diarrhoea.[37]

Fat

Malabsorption of fat has been an important constraint for nutritional management during persistent diarrhoea. Steatorrhoea can be due to insufficient pancreatic lipase or absorptive defect of fatty acid from the gut due to disturbance in bile acid metabolism. Below a critical concentration of bile salt (2 mmol/L) micelle formation cannot happen thereby reducing long chain fatty acid transport across the mucosa. Malnourished children have been shown to have severely reduced output in pancreatic enzymes and the most of it is in lipase activity.[33] In persistent diarrhoea, dietary fat absorption may be decreased to 60% and specially among the malnourished, this may be as low as 44% in children with lower (<11 cm) mid upper arm circumference (MUAC).[37] During malnutrition, due to reduced bile acid pool fat absorption is incomplete in addition to the fact that absorption in young children below one year of age is 80% at it's best.

Protein

Net absorption of protein in persitent diarrhoea is seriously compromised. Compared to controls, it goes to down to a 53% of median ,[35] and among those with MUAC less than 11 cm, protein absorption goes down to 33%.[37] During malnutrition protease activity in pancreatic secretion is reduced. Reduced trypsin, chymotrypsin and carboxypeptidase A have been reported from patients with exocrine pancreatic disorder other than cystic fibrosis. In cystic fibrosis and other exocrine deficiency lipase is consistently decreased.[38] In a series of malnourished children in India, it was found that luminal proteolytic enzymes were less impaired.[39]

Cow's Milk Protein Sensitive Enteropathy (CMPE) and Soyprotein Allergy

Cow's milk allergy occurs usually before 6 months of age. β-lactoglobulin fraction in the milk shows frequent antigenic stimulation to cause protein induced hypersensitivity responsible in most cases. During malnutrition or diarrhoeal episodes mucosal permeability (paracellular) increases and in children with decreased secretory IgA in the gut, antigen uptake is enhanced and it causes local inflammation. It can lead to mucosal damage to deeper layer and inflammatory cells appear in submucosa. Circulatory milk protein antigen can stimulate further systemic manifestations. Soy protein has also been reported to cause such protein hypersensitivity in children. Withdrawal of milk responds with recovery. Milk antibody and IgE are increased in the mucosa in this milk protein enteropathy. In Malaysia and Indonesia milk protein enteropathy is frequently encountered.[39,40] Even in UK, CMPE was reported to be a cause of protracted diarrhoea.[41] Recently, Snyder[42] has reviewed results of several studies on role of cow's milk protein on persistent diarrhoea, and has casted doubts on the seriousness of the problem. It appears that unmodified milk protein has some relationship on the mucosal enteropathy and continued antigenic sensitivity to further milk protein.

Defective Bile Acid Metabolism

Bile acids can cause purgation and diarrhoea by stimulating fluid and electrolyte secretion from jejunum, ileum and colon. Dihydroxylated (chenodeoxycholic acid or deoxycholic acid) bile acids induce cholera like secretion through c-AMP mediated mechanism. It can increase membrane permeability and can damage the mucosal cells. Formation of dihydroxy bile acids reduces enterohepatic circulation of bile acids and leads to reduced bile acid pool. Increased presence of bile acid in the colon produces 'Choleric enteropathy' with diarrhoea and carries an additional risk of cholesterol gallstone disease, renal stone formation and steatorrhoea.[43,44] Obligate anaerobes are capable of 7 dehydroxylation of bile acids. In addition, deconjugation of bile acids catalysed by bacterial Cholylamidases liberates unconjugated compounds preventing micellar solubilization. However, there has not been no study on bile acid composition and concentration in persistent diarrhoea.

Abnormal Bacterial Colonisation of Intestine

An important aspect of the pathophysiology of chronic diarrhoea includes bacterial colonisation of the jejunum, ileum and colon. In breast-fed babies lactobacilli and bifidus bacteria are present which suppress over growth

of other abnormal bacteria. They are protective by bactericidal and neutralising capacity. With supplementary feeding or weaning process abnormal bacterial colonisation (*E Coli*, Klebesiella, Enterobacter, Staph Aureus, Streptococci) may occur. Aerobic organisms predominates in upper small intestine and anaerobic bacteria grows in colon. Among anaerobic bacteria *Clostridium defficile* and *bacteroides fragilis* are more common. The upper limit of bacterial population in upper GI. tract is below 105/ml, but in colon, 10^{7}-10^{9}/ml. Bacterial overgrowth and patchy mucosal lesions in the jejunum was well correlated.[6] Protracted diarrhoea can be due to this abnormal bacterial population through several mechanisms such as, competitive utilization of micronutrient, release of toxins, stimulation of secretion, deconjugation of bile salts, inhibition of nutrient absorption, enzymatic degradation of brushborder enzymes and mucosal structures. Malnutrition and depressed immune capacity are two predisposing factors of this process though congenital, surgical and infective causes are also important.

Recent reviews in this subject does not support any major role of bacterial overgrowth in persistent diarrhoea.[9,11,13]

Tropical Enteropathy and Tropical Sprue

Tropical sprue is characterised by chronic diarrhoea with severe weight loss, glossitis and anaemia but most studies have reported on adults. It seems likely that enteropathogens are responsible for abnormalities of intestinal structure and functions. Most of the western visitors have changed intestinal flora during their stay in tropical countries. This syndrome is again termed as post-infective tropical malabsorption.

Management issues

Diagnosis of the underlying causes in persistent diarrhoea

History:

Detailed history of mode of onset of diarrhoea in relation to age, previous diarrhoeal episodes including measles, use of drugs, previous dietary regime, introduction of supplementary feeds, history of diarrhoea in the family, duration of diarrhoea, character of stool, hygiene and sanitation of the family, socioeconomic status of the parents and breast feeding.

Physical Examination:

Assessment of nutritional status, signs of protein energy malnutrition, assessment of dehydration, vital signs, signs of deficiency diseases, systemic examination and presence of underlying infection.

Laboratory investigations: (Table I)

Stool: M/E for parasites, formol ether concentration (EEC) method for Giardia lamblia, Ziehl Neilsen stain for Cryptosporidium, Pus cells/HPF, RBC/HPF Sudan III stain for stool fat (Qualitative).

Blood: Total and differential count of WBC, electrolytes, serum albumin, serum zinc and serum folate.

Stool culture for: (Where possible)
Salmonella, Shigella, Cholera, E Coli (ST, LT) *EPEC, Klebsiella, Campylobactor.*
Aeromonas hydrophilia, Yersinia enterocolitica.

Stool examination (Biochemical): pH and reducing substance or prehydrolysed and posthydrolysed glucose. Stool electro-

lytes and osmolality can reveal nature of diarrhoea whether osmotic or secretory.

Breath hydrogen test for lactose intolerance may exclude lactase deficiency.

Urine examination - routine analysis and culture to exclude UTI.

Assessment of present diet:

Present diet with persistent diarrhoea should be assessed for solute content, digestibility, osmolality, adequacy of major nutrients, fluid load as volume/kg/day, vitamins and minerals.

Management of Persistent Diarrhoea

A definite outline for management of persistent diarrhoea is yet to be agreed. Few simple principles may be followed for most of the persistent diarrhoea patients in developing countries.

1. Correction of dehydration

Mild to moderate dehydration can be rehydrated with oral rehydration solution. WHO ORS contains 111 mmol of glucose with a total osmolality of 330 mmol/L. In osmotic diarrhoea with malabsorption of nutrients (e.g., Lactose), administration of ORS may precipitate diarrhoeal severity. Rice powder containing oral rehydration solution (rice ORS) has low osmotic load and may be better.[46] But young infants who suffer from persistent diarrhoea with associated malnutrition may not be able to digest cereals due to reduced pancreaticamylase before 7 months of age, but brush border glucoamylase can split up oligosaccharides up to 10 molecules of monosaccharide if there is no severe damage in mucosal epithelium. Furthermore gastric hydrochloric acid helps in hydrolysis of carbohydrate. Infants below 4 months with severe PEM may require attention to this fact. A recent study has shown that infant below 6 month can be rehydrated with rice-based ORS in acute diarrhoea.[47] Intravenous rehydration can be an alternative approach to different cases. Children who are receiving carbohydrate diet may receive rice based ORS. There is however scope to investigate whether oral rehydration fluid of lower osmolality would reduce severity of persistent diarrhoea.

2. Control of systemic infection

Invariably patients with persistent diarrhoea present with many infections other than diarrhoea. Common infections encountered are: respiratory tract infection, bronchopneumonia, skin infection, urinary tract infection and septicemia. In a series of patients who were hospitalised in ICDDRB, Bangladesh, upper respiratory tract infection was present in 20% patients, lower respiratory tract infections in 3%, ear infection in 3%, urinary tract infection in 2%, TB in 5.3% and septicemia was clinically suspected in 2% of cases.[18] In this series of persistent diarrhoea patients, death occurred in 3% patients. The causes were bronchopneumonia, septicaemia and necrotising

Table I Laboratory Investigations for Persistent Diarrhoea patients

Routine:	Microscopy stool fat (qualitative by Sudan III stain)
1. Stool	Bacterial culture - for cholera, Shigella, Salmonella, *E Coli* Parasites - stool microscopy pH and reducing substance Electrolytes and osmolality
2. Blood	Full WBC counts, Hematocrit
3. Duodenal juice	Microscopy for Giardia and Strongyloides. Bacterial culture for aerobic and anaerobic organism

enterocolitis. Appropriate antibiotics should be used without delay in children with systemic infection. Underlying tuberculosis needs to be excluded in unexplained fever and malnutrition.

3. Nutritional management

Adequate energy, protein and fat intake should be ensured for recovery from malnutrition. But this can be very difficult during the early part of management due to compromised digestive ability. There are two aspects of the management plan:

a) To enhance recovery dietary ingredients are to be adjusted to help easy digestion and better absorption in persistent diarrhoea patients, many of whom are malnourished. Dietary quality needs to be ensured for better digestibility, absorption, low osmolality, protein quality, micronutrient content and provision of at least optimal energy for the catabolic stage. Appropriate dietary formulation is the key issue for management of persistent diarrhoea (Table II).

b) The major constraint of nutrient malabsorption in persistent diarrhoea is compounded by anorexia or reduced food intake thus making it difficult for giving adequate energy and protein for nutritional rehabilitation during persistent diarrhoea. Giving the ideal feeds with high energy and high protein diet in a child with limited digestive and absorptive capacity is likely to produce osmotic diarrhoea and further exaggeration of persistent diarrhoea. Recovery may be further delayed due to metabolic and pathological changes in malnutrition. Therefore a compromise is necessary to control of the episode of persistent diarrhoea and afterwards build up increased nutrient intake slowly to recover from malnutrition.

Table II . Composition of Feeds Used for Persistent Diarrhoea in ICDDR,B

Diets		Indication
1. Lactose-free infant formula (soya-based)		<4month age Lactose intolerance
2. Milk, soya & sucrose free formula (rice-based)		>4 month age Milk and soya intolerance
Full-strength composition - per litre		
Rice powder	60 g	
Egg albumin	30 g	
Oil(coconut)	30 g	
Glucose	20.g	
$MgCl^2$	1 g	
Nacl	1 g	
Kcl	1 g	
Calcium lactate	0.5 g	
Energy	800 kcal	
3. Milk, soya, sucrose & complex carbohydrate free comminuted chicken diet:		
Ingredients		Very young and any age
Minced chicken	180 g	Severe PEM with
Glucose	30 g	prolonged (>1 month) diarrhoea
Oil(coconut & soya)	30 g	Failure with any diet
Onion	20 g	Intractable diarrhoa
Kc1	1 g	
$MgCl^2$	1 g	
Nacl	1 g	
Calcium lactate	2 g	
Energy	600 kcal	

4. Micronutrient in persistent diarrhoea

Folic acid help maturation and pro-

liferation of intestinal epithelial cells. In persistent diarrhoea and tropical enteropathy, diarrhoea has resolved more quickly if folate had been used in therapy (Unpublished observation at ICDDR,B ,1994).

Micronutrient such zinc has been well studied in diarrhoea. Zinc supplementation has shown earlier recovery and better weight and height gain in persistent diarrhoea specially in malnourished children.[48,49] Intestinal integrity in persistent diarrhoea has significantly improved by zinc supplementation and this has high correlation with malnutrition.[50] Zinc supplementation has been useful if the dose is more than twice the RDA. Sach Dev et al[51] have also reported that zinc supplementation has helped earlier recovery in persistent diarrhoea in zinc deficient Indian children.

5. Use of antibiotics to control small intestinal bacterial over growth

The recent studies don't support the view that it is a major problem as thought earlier. Yet there are suggestions that in particular patients, drugs may be used as following:

a. Anaerobes (e.g., by metronidazole)
b. Aerobes (by sensitive drugs)

Recent studies have shown that there is no significant advantage of broad spectrum antibiotics in persistent diarrhoea per se. A randomized trial with oral gentamicin in persistent diarrhoea showed no benefit in Peru[52] or in India.[53] Small bowel bacterial overgrowth in persistent diarrhoea has been recognised to be casual in a few cases. But well controlled epidemiological studies has been unable to identify this concept. However Entero adhesive *E Coli* and enteroaggregative *E Coli* has more association with persistent diarrhoea compared to acute diarrhoea. But they constituted a small proportion of the persistent diarrhoea patients. Cotrimoxazole-trimithoprim trial also have failed to result earlier recovery (unpublished result ICDDR,B). Therefore individual cases identified with proper diagnostic procedure should be treated with drugs with bacterial sensitivity tests. There is however no strong evidence that blindly antibiotic use would benefit children with persistent diarrhoea.

The diarrhoea may be secretory in nature with high sodium concentration in stool, small osmotic gap (anion gap), high purging rate (Table III).

6. Dietary management in persistent Diarrhoea

Appropriate feeding is an important tool for control of persistent diarrhoea and of fundamental importance for the recovery of the patients. The first line of management at current practice is dietary manipulation . Failure of dietary management and continued diarrhoea indicate use of total parenteral nutrition (TPN) which may be available in limited facilities and is expensive for most of the patients.

a) Dietary Manipulation

Children with persistent diarrhoea may respond promptly to dietary manipulations. Diet should be selected with consideration to the nutritional state of the patients and underlying cause of diarrhoea. Diets are given in small amount at frequent intervals. Appropriate dietary management helps to maximize the

Table III Features of Osmotic and Secretory Diarrhoea

Character	Osmotic	Secretory
Fasting	stops diarrhoea	continues
Stool Volume (ml)	<500	>500
Stool osmolality	400	280
Stool Na+	30	100
Stool K+	30	40
*Solute gap	280	0

* Osmotic gap= Osmolality - [(Na+K)X 2]
(Walker-Smith JA, 1986)

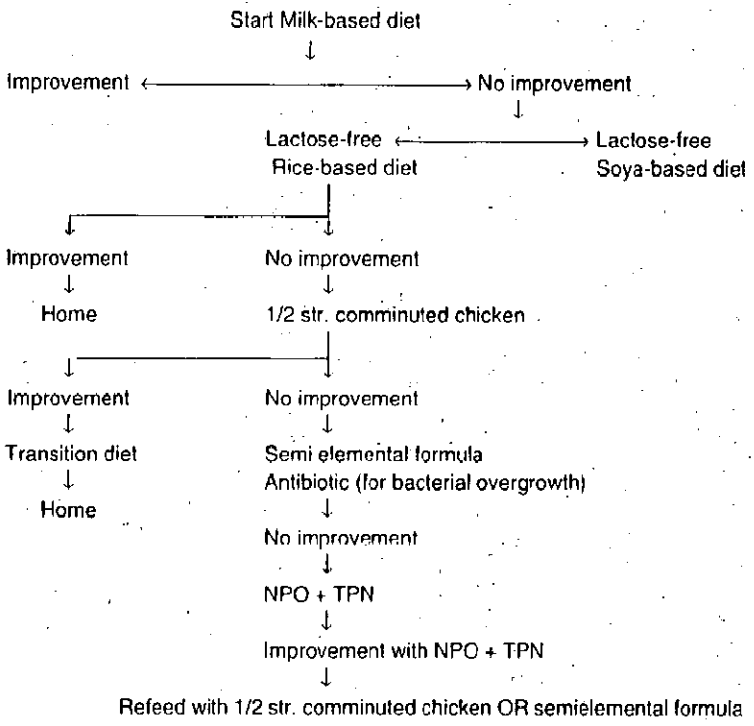
capacity of digestion and absorption by already reduced brush border enzymes and by subtotal villous atrophy due to mucosal injury and reduced pancreatic secretion in malnutrition.

Usual lactose load in milk based diet may be reduced and in a clean environment, child may recover early. About a quarter (24-26%) of children with more than 2 weeks diarrhoea have shown prompt recovery in Bangladesh[54,55] with this regime without total withdrawal of milk from their diet. An algorithm of dietary management (Fig.) has been proven to be simple, effective and inexpensive.[55]

Secondary lactase deficiency is most common type of enzymatic deficiency which can be easily managed with lactose free cereal based or soybased milk formula. Besides lactose, β-lacto globulin, present in the cows milk may also cause persistent diarrhoea from milk protein hypersensitivity. After introducing a milk free diet, recovery may be seen by 3 to 4 days and duration of feeding varies from 2-3 weeks before reversing to previous milk formula. Occasionally lactose intolerance may be prolonged to 2-6 months.[32] Infants who are less than 4 months, may be given complex carbohydrate free diets. Infants above 4 months of age may be given a cereal based diet. Rice based diet has been successfully used in ICDDR,B, Bangladesh. This therapeutic diet (rice suji) has been newly developed and successfully used (81% cure rate) in persistent diarrhoea patients. This has been formulated with rice powder, glucose, soya oil and egg-white.[54] A subsequent study on severely malnourished (<60% wt/Age) children with persistent diarrhoea has shown 88% cure rate within 4 days using rice based diet of the same composition.[55] The advantage of this diet is to avoid lactose, sucrose, milk protein and soy protein.

The above diets are to be introduced at a lower concentration and volume. It has been reported that excess fluid load from diet cannot be handled well by the compromised digestive capacity of the malnourished child having persistent diarrhoea. An optimal dietary fluid load of 100 ml per kg body weight per day may be given initially and can be increased up to 175 ml /kg/day in the recovering phase. With the re-

Fig. Algorithm of dietary management in persistent diarrhoea



duction of diarrhoeal stool volume and frequency, dietary feed volume and concentration can be increased gradually. The diet can provide adequate energy and protein for catch up growth.

Failure to recover with rice cereal diet, dietary modification can further be made with a chicken based diet where cereal and egg white is replaced with minced chicken meat. This formula may be made with minced chicken meat, glucose, soya oil, water, vitamins and minerals. This diet has also been able to improve more than 90 per cent of persistent diarrhoea patients. The infants who were less that 4 months of age and who failed to improve with rice based diet had improved with this chicken meat based diet.[54,55] The advantage of chicken meat based diet over the rice diet is that there are elimination of cows' milk ingredients, complex carbohydrates, and egg albumin for possible hypersensitivity. Commonly used in the west for intractable diarrhoea of infancy is comminuted chicken formula.[56] A full strength feed contains (per 100 ml) comminuted chicken 50 g, gastrocaloreen (glucose polymer) 10 g, prosparol (fat) 4 gm, metabolic mineral mixture 1 g, with added calcium (1.25 mmol/100 ml). In ICDDR,B this formula has been further simplified with remarkable success. Soybean oil and coconut oil are replaced for prosparol and glucose has been replaced for gastrocaloreen. Initially this formula is given as half strength (50 kcal/100ml) in small frequent feeds with complete vitamin and mineral supplements. The feed is then slowly build up over a week. Feed volume may slowly be increased to 175 ml/kg/day and energy 750 KJ/KG/day.

Semi-elemental formula can be used which are commercially available. But these formula are very expensive for poorer countries and the supply may be inconsistent. This formula has the advantage of being free of disaccharide, milk protein, soyprotein and long chain fatty acids.

Reintroduction of cows' milk after improvement with elimination diets

Infants and children may need to restart their usual feed which contains milk. This is done when lactose intolerance is no more present. Lactase is the slowest enzyme to return during recovery from mucosal injury. After 2 weeks of recovery, there is further improvement in enzyme status while milk may be introduced in small quantity. In some severely ill children it may take 8 weeks for reintroduction of milk.[32] Usually test feeds are given to find the appropriate time for reintroduction of milk.

b)Intravenous Alimentation

This is indicated in cases of intractable diarrhoea when diarrhoea continues despite nil by mouth. Intravenous alimentation should be continued for a period till the diarrhoea ceases. Prolonged total parenteral nutrition (TPN) feeding reduces recovery of mucosal enzymes and leads to atrophy of intestinal mucosa. Intravenous alimentation can be done by opening a central vein line using cannula (e.g., subclavian vein or superior vena cava). Parenteral fluid contains mixture of aminoacids providing 2-3g protein per kg body weight per day. Major amount of energy is supplied from emulsion of fat (e.g., intralipid) containing essential fatty acids and from 50% dextrose solution. Additional vitamins and minerals may be given in weekly schedules. This regime is difficult to manage in a general hospital set up. Frequent infection, requirement of additional manpower, maintenance of sterile environment and surgical help for opening intravenous line and isolation of the patient are the main constraints in addition to high expenditure. In spite of those technical disadvan-

tages there are severe cases of protracted diarrhoea who require TPN as a measure for saving their lives.

Energy and protein supplied should be at least 100 Kcal/kg per day and 1-5 gm/kg/day respectively. Protein calorie at 8% of the diet would provide growth and energy over 100 Kcal/kg will enhance growth above maintenance.

Home Follow Up and Transition Diet

Treatment of persistent diarrhoea patients is a continuous process for stopping diarrhoea and establish nutritional rehabilitation. The exclusion diet that improves diarrhoea should be continued with adequate micro nutrients. The child should be prepared to take home diet and gradually omit the exclusion diet. Such mechanism can be ensured when dietician works with mother. Mother is to be trained well how to prepare clean feeds and how the ingredients of diets are to be measured in right quantities. Nutritional follow up should be made at 2 weekly interval to make sure that weight gain or height gain has started after persistent diarrhoea is cured. Remarkable progress has been made in the last few years in respect of management of persistent diarrhoea with inexpensive available diet. With the above dietary management, most of the children suffering from persistent diarrhoea in the developing countries can avoid high risk of mortality and malnutrition due to persistent diarrhoea.

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Correspondence to:
Dr. S.K. Roy
Scientist
ICDDR,B
GPO Box-128
Dhaka.
Bangladesh.