

EVALUATION OF AN ALGORITHM FOR PERSISTENT/CHRONIC DIARRHEA IN CHILDREN AT A COMMUNITY HOSPITAL ADJOINING SLUMS IN AGRA, NORTH INDIA

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Abstract. The objective of this study was to evaluate an algorithm for the management of children with persistent/chronic diarrhea at a community level hospital. The study was carried out in the pediatric OPD of a 150 bed trust hospital catering to children from poor, rural and urban slums. Fifty clinically stable children (6 months-5 years old, mean = 19.7 months) with persistent or chronic diarrhea refusing admission, being managed on an outpatient basis, were enrolled prospectively. A detailed history and physical examination were done for each child to ascertain the cause of diarrhea. They were managed using a pre-tested simplified algorithm and monitored for symptom improvement using a questionnaire 15 days, 1 month and 3 months after initiation of therapy. The average cost for treatment of each child was also calculated. Twenty-one (42%) children had persistent diarrhea. Seven (14%) infants with a typical history of lactose malabsorption responded to a trial of WHO feeding protocols or lactose/sucrose free milk. Four (8%) infants had chronic non-specific diarrhea. A total of 71.8% (28/39) of children were treated satisfactorily with albendazole or metronidazole and Cotrimaxazole along with hematinics and multivitamins. Three (6%) children were diagnosed with abdominal tuberculosis. Four (8%) had raised anti-tissue transglutaminase antibodies (age 18-34 months). The algorithm used was successful in managing all the children with chronic diarrhea. The average cost per managed case was US\$10. Further, multi-center evaluations of similar algorithms are needed to validate the observations in the present study.

INTRODUCTION

Chronic diarrhea in the tropics has entirely different etiological considerations than those observed in Western countries. Most of these factors are associated with poor sanitary and living conditions and gastrointestinal infections (Mittal, 1999; Rastogi *et al*, 1999). The diagnostic possibilities of chronic diarrhea are vast, and complicated algorithms for management in the Western literature are difficult to remember. These do not have any practical utility for management at primary health centers, rural based doctors and community health centers in developing nations (Donowitz *et al*, 1995; Berman, 2003). Development of management algorithms for community hospitals is an important research priority (Bhutta *et al*, 2004). It is important for

child health care providers in resource poor nations to know the profile, which investigations to order first and when to refer children with persistent/chronic diarrhea to higher centers. The present study was planned to evaluate a simplified algorithm approach with minimal dependence on investigations in the management of children with persistent/chronic diarrhea.

MATERIALS AND METHODS

Study set up

The study was carried out in Shanti-Mangalick Hospital, Agra, North India. The region is crippled by poor sanitary and environmental conditions and has many slums. Yamuna is the major river in the city and the only source of water, which has been badly contaminated by industrial and city waste. The efforts of the Yamuna Action Plan with collaboration from Japan have not yielded desired results (Yamuna Action Plan, 2005). Agra has a very large slum population in 513 slums. The integrated Child

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Services Program of government of India has very poor coverage in only 95 slums. There are many more unrecognized slums (Nayar *et al*, 1998; Agarwal and Taneja, 2005; Anonymous, 2005). This had led to a very high prevalence of persistent and chronic diarrhea in the region. The study site was a community hospital run by a registered public charitable trust with support of the United States Aid Foundation (USAF) with the sole aim of providing care to the underserved community. The charge for a specialist outpatient consultation is less than US\$ 0.25. It can be compared to a government community health center, which provides specialist services in medicine, surgery, obstetrics and gynecology, pediatrics, ophthalmology and orthopedics. The hospital caters mostly to the poorer sections of society and slum areas. About 6,000 children utilize the outpatient services of the hospital per year. It has been recognized as an important health care provider in the local region and has recently established a college of nursing recognized by the Indian nursing council. Basic laboratory investigations for phase I evaluation of chronic diarrhea (CBC, stool examination for ova and parasites, culture, pH, urine examination, and electrolytes) are available at the hospital. A D-xyloste test and stool for *C. difficile* are not available.

Inclusion criteria

Fifty children (6 months-5 years, mean = 19.7 months) with persistent or chronic diarrhea (clinically stable) fulfilled admission criteria were not hospitalized since the parents refused admission. These were enrolled prospectively in the study after obtaining informed parental consent and if the parents were willing to have the compulsory follow-up.

A detailed history, with emphasis on the onset of diarrhea (acute or insidious), blood/mucus in stools, relation to feeds, socioeconomic status using a modified Kuppuswamy's scale, place of stay, source of water supply, family history of Koch's, appetite, history of pica and systemic diseases was recorded. A physical examination focusing on signs of vitamin deficiencies, ear/nose/throat examination, growth and development, anthropometry, and systemic diseases was done.

Definitions

Persistent diarrhea was defined as a history of >3 liquid stools/day (an acute onset after gastroenteritis either in a previously normal child or a malnourished child) for ≥ 14 days with no more than two days without diarrhea. Chronic diarrhea was defined when the onset was insidious and the duration of the diarrhea was more than 3 months.

Exclusion criteria

Children with associated systemic renal or hepatic disease, children requiring admission for severe infection, urinary tract infection, dehydration, abnormal electrolyte levels, seizures and grade IV malnutrition were excluded from the study.

Follow-up

Since the study was outpatient based, the children were monitored using a parent/caregiver card questionnaire with close-ended questions (a version in local language was provided). This was pre-tested on 10 children with chronic diarrhea prior to the study. Parents/relatives were asked to record the daily progress regarding

Table 1
Characteristics of study population.

| Characteristic | N=50 | Control group |
|------------------------------|-------------------------|-------------------------|
| Age (months) | 19.7 (6.8) ^a | 18.6 (6.3) ^a |
| Male : female ratio | 82:18 | 74:26 |
| Weight on enrollment (kgs) | 7.8 (1.3) ^a | 8 (1.3) ^a |
| Duration of diarrhea in days | | |
| 14-20 | 6 | 4 |
| 21-30 | 2 | 1 |
| 31-89 | 13 | 7 |
| >90 | 29 | 13 |
| Stool frequency | | |
| $\leq 7/d$ | 15 | |
| 8-11/d | 15 | |
| $\geq 11/d$ | 20 | |
| History of bloody stools | 10 | 3 |
| PEM | 34 (68%) | 15 (60%) |
| Wasted | 23 (46%) | 10 (40%) |
| Wasted and stunted | 11 (22%) | 5 (20%) |
| Signs of vitamin deficiency | 7 (14%) | 1 |

^aMean (SD)

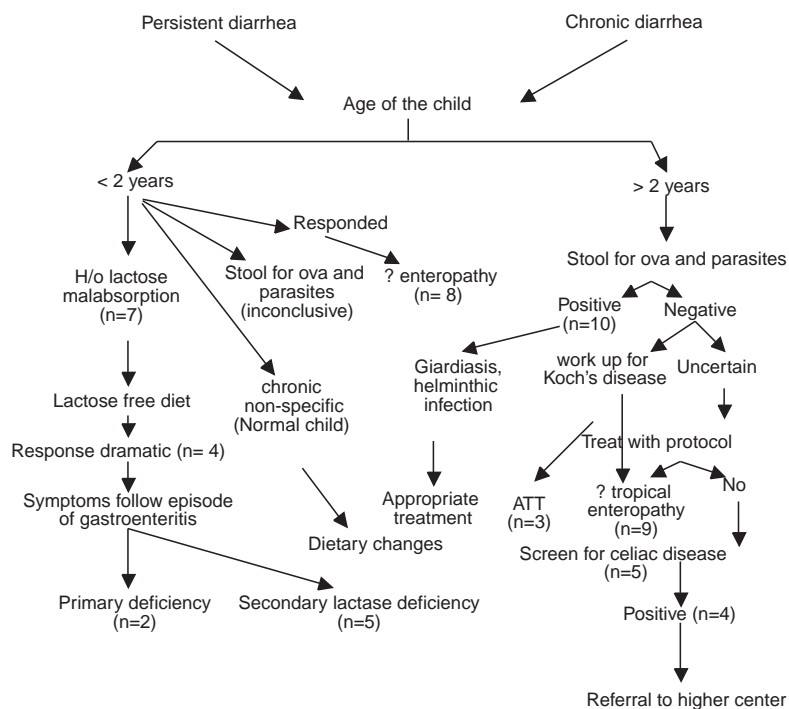


Fig 1-Algorithm for management of children with persistent/chronic diarrhea at a community hospital.

these items themselves. The card was designed in such a manner so that even illiterate parents could record symptom improvement. They were asked to bring this to each follow-up visit at 15 days, 1 month and 3 months (Table 2).

Algorithm

After considering the causes of chronic diarrhea in Indian children a simplified algorithm was developed by the author. In order to substantiate the protocol and algorithm, a control

group of 25 children, 12 with chronic and 13 with persistent diarrhea were used to define the microbiological organisms prevalent in the region prior to the study. The control group was comparable in terms of mean age, nutritional status, place of residence, income group and the clinical diagnosis of diarrhea. The etiological organisms isolated in the control group were probable Enterococci in 6, probable Enteroinvasive *E. coli* in 2 (*E. coli* 8), mixed growth of *Salmonella typhi* and *E. coli* in 4, giardiasis in 5, *Entamoeba histolytica* in 1 and hookworm in 2. In 5 children no microorganism was identified. Thus the algorithm with treatment protocol was developed. This was pre-tested for its reliability and validity in 10 children with chronic/persistent diarrhea

(reliability coefficient 0.87 and validity coefficient 0.7) and evaluated for success in management. The components of the algorithm along with the disposition of the children at various stages of the study are summarized in Fig 1. For infants with a history of lactose intolerance or cows milk hypersensitivity (which was only a corroborative diagnosis) a trial of WHO diets A/B or lactose free milk was given. For each child age 1-5 years old a stool microscopic examination was done. Irrespective of the stool findings (unless any other

Table 2
Patient symptom monitor questionnaire card^b.

| Question | No | Yes | | |
|---|--------|------------------------|--------------------|----------------|
| Is there improvement in the child? ^a | No | Yes | | |
| What is the frequency of stools now? ^a | Normal | ≤7 | >7 | Same as before |
| What is the consistency of the stools? ^a | Same | Better, but still soft | Firm | |
| How is the odor? ^a | Same | Some improvement | Marked improvement | |
| Has the irritability decreased? ^a | No | Some improvement | Marked improvement | |
| Is there improvement in the appetite? ^a | No | Some improvement | Marked improvement | |

^a Please circle your response

^b Hindi (local language) version of the card was used for the study

Table 3
Diagnosis.

| | |
|------------------------------------|---|
| Persistent diarrhea (n= 21) | |
| Lactose malabsorption | 7 |
| Secondary lactase deficiency | 5 |
| Primary lactase deficiency | 2 |
| Hookworm infestation | 2 |
| Chronic non-specific diarrhea | 4 |
| Tropical enteropathy | 8 |
| Chronic diarrhea (n=29) | |
| Abdominal tuberculosis | 3 |
| Suspected celiac disease | 5 |
| ? Tropical enteropathy (responded) | 9 |
| Giardiasis | 8 |
| Lost to follow-up | 4 |

cause was obvious) all children received a trial of albendazole for 5 days and/or metronidazole 20 mg/kg in three divided doses for 10 days, Clotrimoxazole (6 mg/kg of the trimethoprim component q 12 hrly), hematinics (if pallor on examination), multivitamin supplementation (containing zinc 20 mg/day and other micronutrients at the daily recommended dose) and a single oral dose of 20,000 units of vitamin A. All the children were followed up at 15 days, 1 month and 3 months of therapy for evaluation of improvement in symptoms. If there was no improvement the child was investigated for Koch's disease and /or screened for celiac disease using anti-tissue transglutaminase (tTG) antibodies.

RESULTS

Twenty-one (42%) children had a history of persistent diarrhea and 29 (58%) had chronic diarrhea. The mean age of the children was 19.7 months. All the children were from a lower socio-economic status on a modified Kuppaswamy scale. Twenty-three (46%) children had wasting and 11 (22%) had stunted growth. Four children admitted with moderate to severe dehydration were excluded from the study. Five children had bitot spots and 2 had rickets (Table 1). Table 2 shows that seven (14%) infants with a history of lactose malabsorption responded dramatically to

a lactose free diet or a WHO diet (symptomatic improvement in the form of a decrease in stool frequency, improved consistency and a recorded gain in weight). Five (10%) had secondary lactase deficiency (postgastroenteritis) and 2 (4%) had primary lactase deficiency. Four (8%) infants who were thriving well and developmentally normal responded to dietary interventions (decrease in fluid intake and appropriate weaning). Stool microscopy revealed 8 children with giardiasis and 2 with hookworm infestation. However, 71.8% (28/39) children responded dramatically to the discussed protocol. Three (6%) were diagnosed with abdominal tuberculosis (positive Mountoux with a suggestive chest X ray and /or abdominal ultrasound findings and a response to anti-tubercular therapy at follow-up. Anti-tissue transglutaminase antibodies were positive in 4 (8%) children (done in 5). These children were referred to tertiary centers. Four children were lost to follow-up at either second or third visits. The average cost per treatment for each child was around US\$ 10 (this included the cost of consultation, stool microscopic examination and cost of medicines).

DISCUSSION

Persistent and chronic diarrheas are a major causes of morbidity and mortality in developing countries (Bhan *et al*, 1989). This is increasing with an ever-growing population of urban slums (Agarwal *et al*, 2005). Though algorithms for management of hospitalized children with persistent diarrhea have been evaluated in multi-center trials, management algorithms for clinically stable children with chronic diarrhea have not been evaluated (Anonymous, 1996). This is extremely important for providers at the community level. Experts in international working groups on persistent and chronic diarrhea believe the development of algorithms for community hospitals for the management of chronic diarrhea is an important research priority (Bhutta *et al*, 2004). A large number of children with chronic diarrhea in rural and urban settings in India have to be managed as outpatients rather than admitted (Bhan *et al*, 1989). This is the reason why only children managed on an outpatient basis were enrolled in our study.

Malabsorption syndromes in Indian children can be broadly grouped into two groups according to age (Yachha *et al*, 1993). Protracted diarrhea and milk protein intolerance constitutes the major etiologies of malabsorption syndromes in children below 2 years of age, whereas celiac disease, parasitic infestations and intestinal tuberculosis are the common causes in children above 2 years of age. The starting limb of the algorithm in the present study was developed keeping this knowledge in mind. The spectrum of children with chronic diarrhea in the present study is consistent with the published Indian literature (Table 3) (Yachha *et al*, 1993; Mittal, 1999).

Lactose malabsorption in infants has been described as a cause of acute gastroenteritis and persistent/chronic diarrhea (Kumar *et al*, 1977; Yachha *et al*, 1989). Tropical enteropathy has been shown to be a major cause of chronic diarrhea in Indian children (Mittal *et al*, 2001). Enteroaggregative *E. coli* was associated with persistent diarrhea in a cohort in rural India and as an important organism in non-dysenteric diarrhea (Bhan *et al*, 1989). The spectrum of etiological organisms causing chronic diarrhea is wide (Mathan *et al*, 1968; Madan *et al*, 1981; Bhan *et al*, 1989; Shetty *et al*, 1990, 1992; Talwar *et al*, 1990; Jindal *et al*, 1995; Suganan *et al*, 1996). Parasitic infections especially amoebiasis and giardiasis, are the prominent organisms in Indian children (Madan *et al*, 1981). Amoebiasis is more frequent in infants than giardiasis (Shetty *et al*, 1992). Celiac disease has been well described in India (Thapa, 1999; Mohindra *et al*, 2001).

Giardiasis infection has also been observed as an important confounding variable in celiac disease (Mastropasqua *et al*, 2003). This, along with a high prevalence of tropical enteropathy in India, justifies a trial of albendazole/metronidazole and Cotrimoxazole (*E. coli* was the commonest identified organism) in all children before screening for celiac disease at the primary and secondary levels of care. The efficacy of Cotrimoxazole for persistent diarrhea has already been evaluated in a randomized trial (Alam *et al*, 1995). Zinc has an established role in children with acute and persistent diarrhea. A pooled

analysis of randomized controlled trials of zinc supplementation performed in nine low income countries demonstrated that supplemental zinc led to an 18% reduction in the incidence of diarrhea and a 25% reduction in the prevalence of diarrhea (Bhutta *et al*, 2000). Vitamin A was included in the trial, as its deficiency has been linked to increased susceptibility to diarrhea and respiratory tract infections in children (Mishra and Kumar, 1993; Bhan and Bhandari, 1998). Anti-endomysium antibody and anti-tissue transglutaminase antibodies are sensitive with up to 90% positive predictive value for the diagnosis of celiac disease (Sblattero *et al*, 2000). Though one would have liked to screen all children for celiac disease it appears to be a futile expenditure in light of our observations. This algorithm approach proved to be very helpful as most children were managed without any invasive investigations. Most parents were satisfied with the improvement in symptoms in their children. Nutritional management of infants and children is rewarding in many cases (Mehta, 1996). Efficacy of WHO diets A/B, which are cost effective, has already been evaluated in infants with persistent diarrhea (Nizami *et al*, 1996). The initial diet (A) contained cereals, vegetable oil and yoghurt. Diet B was offered when the child did not improve with the initial regimen. These diets were helpful in managing infants with lactose intolerance in the present study.

It is important to highlight the limitations of the study. First, microbiological diagnosis of chronic/persistent diarrhea in the study group was not done. This was deliberate, as the aim of the study was to develop a management algorithm without dependence on stool culture so as to limit the investigations done in resource poor settings. The microorganisms identified in the control group of 25 children points towards tropical enteropathy as the most common cause of chronic diarrhea in the region, followed by giardiasis. The differentiation into enteroaggregative and enteroinvasive *E. coli* in the control group was presumptive. A diagnosis of enteroaggregative *E. coli* infection was made in infants with no inflammatory cells, whereas enteroinvasive infection was diagnosed in infants with inflammatory cells on stool microscopic examination. Molecu-

lar characterization on the basis of sequence analysis using PCR or DNA probes (gold standard) of *E. coli* into enteroaggregative and enteroinvasive *E. coli* could not be done due to a lack of laboratory facilities and funding. Second, one may argue that metronidazole has no effect in children with non-dysenteric persistent diarrhea in the community setting (Bahl *et al*, 1996). Either metronidazole for 10 days or albendazole for 5 days for the management of giardiasis was used. Metronidazole was used when there was a history suggestive of or stool microscopy revealed amebiasis. Third, some malnourished children may have responded primarily to the zinc and vitamin A supplementation rather than the antimicrobials. However, it is extremely difficult in clinical practice in the rural setting to differentiate rate between tropical enteropathy and nutrient deficiency. Nutrient deficiency may occur because of a combination of dietary inadequacies and tropical enteropathy (Ghosh and Shah, 2004). Thus this management protocol appears to be reasonable. Almost all children with chronic diarrhea in India can be managed at community level hospitals using a simple easy to remember and cost effective algorithm. Further, multi-center evaluations of such algorithms at community level hospitals in different developing nations is needed to validate the findings of the present study.

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