ACUTE GASTROENTERITIS IN MALAYSIAN CHILDREN: AETIOLOGICAL AND THERAPEUTIC CONSIDERATIONS

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INTRODUCTION

In recent years there have been a number of advances facilitating our understanding of the pathogenesis of acute gastroenteritis (AGE) in infancy and childhood. The discovery by Bishop *et al.* (1973) of the aetiological significance of the rotavirus has been confirmed by a number of other workers and it is now clear that the rotavirus is world-wide in distribution. The concept of toxigenic E. coli has replaced the unsatisfactory classification of pathogenicity of E. coli on the basis of serological types. Hopefully it should not be long before such toxigenic strains can be identified in routine diagnostic laboratories. The importance of acquired carbohydrate intolerance, complicating AGE is now well recognised. The ability to remove lactose enzymatically from cows' milk will hopefully provide a low cost palatable lactose-free milk acceptable to children in developing countries. In any event, proper management of sugar intolerance has reduced hospital admissions and reduced hospital stay in infants requiring admission for infective enteritis.

Despite these advances, there is still a group of infants with AGE who despite conventional treatment and exclusion of all carbohydrates from the diet continue to have diarrhoea. There is compelling evidence that a large proportion of these are the results of cows' milk protein sensitive enteropathy (CMPSE). This problem of course would be resolved with a lactose and cows' milk protein-free formula.

The present study of infantile diarrhoea was undertaken to determine prospectively the aetiological agents of infantile diarrhoea and their relationship to clinical presentation, course of the illness, response to treatment and outcome in Malaysian infants.

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Materials and Methods

All infants below the age of 2 years with loose stools for 2 weeks and with or without other symptoms admitted to the Department of Paediatrics, University Hospital, Kuala Lumpur, between 1974 and 1976 were studied. Following a clinical evaluation, the following investigations were carried out: stool cultures for the bacterial pathogens; identification of the rotavirus by electron microscopy; haemoglobin, haematocrit, total and differential white cell count, plasma sodium, potassium, glucose and urea on admission and 24 hours after therapy. Stools were tested for reducing sugars by the method of Kerry and Anderson (1964).

Initial management consisted of correction of fluid and electrolytes. Rehydration by the oral route with a glucose-polyelectrolyte solution was attempted in infants with dehydration up to 7%. Infants with dehydration exceeding 7% and those in whom oral rehydration was unsuccessful received intravenous fluids. No anti-diarrhoeal agent was used. Even when a bacterial cause was identified, antobiotics were not administered except in cases of Shigellosis (co-trimoxazole or ampicillin) and in those with evidence of tissue invasion.

Table I

Clinical Profile of the 150 Patients with acute gastroenteritis due to bacterial or viral entropathogens

Clinical Profile	Bacterial Enteropathogens No	(%)	Viral Enteropathogens No	(%)
Vomiting	37	(43)	56	(78.9)
Nature of stools				
Watery	62	(87.3)	67	(94.4)
Watery + mucus	6	(8.5)	2	(2.8)
Watery + blood + Mucus	3	(4.2)	2	(2.8)
Stool frequency				
4/day	14	(18.4)	15	(21.4)
5–9/day	35	(46.1)	30	(42.9)
10/day	27	(35.5)	25	(35.7)
Dehydration	43	(54.4)	46	(67.7)
Fever	41	(51.8)	51	(71.8)

In 79 patients bacterial enteropathogens were isolated while in 71 other patients viral enteropathogens were isolated.

Based on previous studies (Lifshitz *et al.* 1971; Harrison *et al.* 1976; Iyngkaran *et al.* 1978, 1979) infants with AGE were classified into high or low risk groups. The high risk group consisting of infants fed a cows' milk based formulae and having one or more of the following features:

(1) age $<$ 2 months
(2) malnutrition
(3) diarrhoea persisting for $>$ 7 days
(4) presence of reducing sugar in the stools

The high risk infants were offered a lactose and CMP-free formula while the low risk group were regraded on to a conventional cows' milk formula. If diarrhoea persisted or if there was reducing sugar in the stools of these infants, they were managed as in the high risk group. Infants on special milk were maintained so for 4-6 weeks when they were re-admitted for milk challenge studies as reported previously (Iyngkaran *et al.* 1979).

Results

Of the 300 infants studied, 150 had enteropathogens in their stools. Of the 150 infants with enteropathogens, 71 (47%) were viruses, 32 (21%) Salmonella, 18 (12%) Shigella and 29 (20%) E. coli; and of the 71 cases of viral aetiology, 58 were due to rotavirus and 13 adenovirus. The relevant clinical and laboratory findings are summarised in Table I–VI.

Discussion

Stool isolates showed a high rate of rotavirus identification, equalling that of Salmonella and Shigella combined (Table II). Although the maximal incidence of bacterial and viral identification occurred between the months of June and November when it doubled that of the other two four-month periods, infections with both types of agent occurred throughout the year. The ethnic incidence however certainly did not follow the population distribution within the country. Probably the distribution seen

Table II

Stools isolates and epidemiological data

Characteristics	No (%) of patients with:			
	Bacterial Enteropathogens		Viral Enteropathogens	
Total isolations	79		71	
Specific isolations	32 Salmonella		58 Rotavirus	
	18 Shigella		13 Adenovirus	
	29 E. coli			
Ethnic group	16 Malay		22 Malay	
	31 Chinese		15 Chinese	
	29 Indian		31 Indian	
Maximal seasonal incidence	June-November		June-November	
Per capita income	No	(%)	No	(%)
M$20/month	7	(8.7)	9	(12.6)
M$20-100/month	44	(55.7)	50	(70.4)
M$100/month	21	(26.6)	12	(16)

here reflected the site of the hospital and patient preference. As would be expected, the disease reflected low family incomes, although an unusually high bacterial incidence occurred in the higher income bracket, 16 of whom grew Salmonella.

Isotonic dehydration was by far the commonest (Table III). Eleven percent of the infants were hypernatraemic. For reasons difficult to explain, hypertonic dehydration was commoner in the viral group. It did not relate to family income, but all the infants were artificially fed from birth and the majority were offered solids before 8 weeks of age. In viral diarrhoea, there is proportionately greater loss of water. This is futher aggravated by sugar intolerence where osmotic mechanisms favour greater loss of water (Hamilton 1975). These factors may in part explain the higher incidence of hypernatraemic dehydration in viral diarrhoeas. Disturbances in potassium levels were unusual in both groups. It is perhaps surprising to find the lower levels in the viral group but the figures are small. Urea levels reflected the degree of dehydration quite closely and in this series was commoner in the viral group.

Total white cell counts were identical in both groups and in no way could they be used to predict the aetiology of diarrhoea.

Only 4 infants were being breast fed on admission (Table IV). It is of interest that the incidence of bacterial infection was much lower in those infants breast fed in the neonatal period than those artificially fed at that time. The neonatal feeding did not appear to be important in respect to the frequency of viral diarrhoea after the weaning period.

All cases recovered in both groups, although the viral group appeared to recover rather more quickly (Table V). Sugar intolerance occurred in approximately 1/3 of both groups.

This study emphasizes the importance of a viral aetiology in acute gasteroenteritis in infants and young children. The clinical features, the nature of the stools, and the outcome of the disease are similar irrespective of whether the organism implicated is of viral or of bacterial origin. The presence of fever (Table VI) and of blood in the stools does not neces-

Table III

Laboratory data

Characteristics	No (%) of patients with:			
	Bacterial Enteropathogens		Viral Enteropathogens	
	No	(%)	No	(%)
Sodium (mmol/L)				
130	10	(14.2)	4	(6.1)
130 – 149	55	(79.6)	51	(77.3)
150	5	(7.2)	11	(16.6)
Potassium (mmol/L)				
3	3	(4.4)	8	(12.3)
3 – 6	62	(92.5)	56	(86.1)
6	2	(3.0)	1	(1.5)
Urea (mg/100 ml)				
40	49	(74.2)	35	(59.3)
40 – 100	13	(19.6)	18	(30.5)
100	4	(6.1)	6	(10.2)
W.C.C. (/cmm)				
4,000	3	(3.8)	1	(1.4)
4 – 9,000	20	(25.3)	18	(25.7)
9,000	56	(70.8)	51	(72.8)
Sugar intolerance	25	(32.5)	21	(30.4)

sarily point to a bacterial diarrhoea and even the total white counts are similar.

This, therefore, means that clinical features and simple blood tests can in no way be used as reliable ways to predict the aetiology of diarrhoeas. Fortunately, however the principles of treatment of acute gastroenteritis, irrespective of the aetiological agent is the same. The sheet anchor of therapy is still replacement of fluid and electrolytes by the oral of intravenous route using appropriate solutions. In most bacterial diarrhoeas, antibiotics is very rarely prescribed, even if a bacterial pathogen is subsequently isolated, because acute gastroenteritis is usually a self-limiting disease. However, antibiotics are definately useful in Shigellosis in that their use shorten the clinical course of the illness and rapidly reduce stool positivity for the organisms. The drug of choice is Co-trimoxazole but Ampicillin is also effective. In E. coli and Salmonella diarrhoeas, antibiotics are only indicated if there is evidence of tissue invasion. However, the injudicious use of antimicrobials have been implicated in the genesis of protracted diarrhoea, by causing alterations of the microbial flora in the gut. Antimotility agents are not recommended (Dupont and Hornick *et al.* 1973) because they slow down intestinal peristalsis causing pathogens and their toxins to remain longer in the gut and thereby

Table VI

Causative Organism and Fever

Organism	Incidence of Fever (%)
Salmonella	56
Shigella	66
E. coli	66
N.P.I.	66
Rotavirus	72
Adenovirus	38

Table V

Clinical Course

Clinical Course	No (%) of patients with:			
	Bacterial Enteropathogen		Viral Enteropathogen	
	No	(%)	No	(%)
Duration of stay				
10 days	55	(72.4)	58	(82.8)
10–28 days	11	(14.5)	10	(14.2)
28 days	10	(13.1)	2	(2.8)
Recovery	79	(100)	71	(100)

contributing to a prolongation of the diarrhoeal symptoms. In addition, other serious side effects like altered sensorium abdominal distension and para -lytic ileus are seen with diphenoxylate and kaolintincture opii mixtures.

The mainstay of therapy must therefore be effective and safe rehydration. In recent years rehydration has been simplified with the availability of glucose polyelectrolyte solutions. In determining the composition of the solution, the following factors have to be taken into consideration: (1) the optimal glucose-sodium ratio to promote satisfactory water movement across the gut mucosa in the different diarrhoeas, (2) the electrolyte losses in diarrhoeal stools which require replacement, (3) the potential complication of hypernatraemic dehydration and its avoidance, (4) the correction of acid-base balance, (5) the high incidence of sugar intolerance (30%) in infants in this country, (6) the majority of infantile diarrhoea in this country is of the non-choleragenic type.

Based on these considerations, it appears that the ideal oral glucose electrolyte solution is one that contains in mmol/L: Glucose 110-140, Na^+ 50-60, K^+ 20, Cl^- 50-60 and HCO_3 20 (Zainal, Iyngkaran and Royan 1980).

Table IV

Feeding Data

Characteristics	No (%) of patients with:			
	Bacterial Enteropathogen		Viral Enteropathogen	
	No	(%)	No	(%)
Feed on admission				
Breast	21	(2.5)	2	(2.8)
Artificial	77	(97.5)	69	(97.2)
Feed on discharge				
Cow's milk	47	(60.2)	49	(72)
Special formula	31	(39.8)	19	(27.9)
Neonatal feed				
Breast	21	(29.2)	29	(41.4)
Artificial	45	(62.5)	33	(47.4)
Mixed	6	(8.3)	8	(11.4)

Protracted diarrhoea seemed less common in the viral group – 10 of the bacterial group were still in hospital after 28 days. Approximately 1/3 of infants were discharged on lactose and cows' milk protein-free formulae because of sugar and/or CMP protein intolerance. More infants (31) from the bacterial group required a special formula compared to the viral group (19 infants). The possible inter-relationships between enteropathogens, sugar intolerance, cows' milk protein sensitive enteropathy and protracted diarrhoea have been previously dealt with elsewhere (Iyngkaran *et al.* 1978; 1979).

Summary

In a prospective study of 300 infants with acute gastroenteritis (AGE), 150 infants had enteropathogens in the stools, 58 being due to rotavirus, 130 to adenovirus, 32 to Salmonella, 18 Shigella and 29 E. coli. Hypernatraemic dehydration was present in 11% and acquired carbohydrate intolerance in 30% of the infants. Protracted diarrhoea was observed in 8% of infants and was commoner in the bacterial than viral group. The study shows that clinical features and simple blood tests cannot be used as reliable indices of predicting the aetiology of AGE. Despite the diverse aetiology of acute gastroenteritis, rehydration by the oral or intravenous route remained the mainstay of therapy.

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