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Management of acute diarrhoea in diabetic patients using oral rehydration solutions containing glucose, rice, or glycine

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Abstract

***Objective*—To assess the risk of hyperglycaemia with two standard oral rehydration solutions that contain carbohydrate compared with a carbohydrate free solution during rehydration of diabetic patients with acute diarrhoea.**

***Design*—Prospective randomised allocation to one of three oral rehydration solutions (World Health Organisation (glucose), rice, or glycine) groups after admission to hospital with acute diarrhoea.**

***Setting*—Dhaka hospital of the International Centre for Diarrhoeal Disease Research, Bangladesh.**

***Subjects*—45 diabetic patients aged between 15 and 60 who had had diarrhoea for fewer than three days on admission.**

***Main outcome measures*—Fluctuation of blood glucose concentrations measured three times a day, daily stool output, and time taken for recovery from diarrhoea.**

***Results*—There were no significant differences in blood glucose concentrations, stool output, and duration of recovery from diarrhoea among the three groups.**

***Conclusions*—Oral rehydration solutions containing glucose, rice powder, or glycine can be safely administered to diabetic patients with acute diarrhoea and some dehydration.**

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Introduction

The role of oral rehydration solutions in the management of acute watery diarrhoea is well established.[1] What is not known, however, is whether there is any risk of hyperglycaemia if these solutions are consumed by diabetic patients during episodes of acute diarrhoea. Although it is unlikely that 2-4 litres a day of oral rehydration solution that contains glucose 20-40 g/l would produce any problems, diabetic patients are reluctant to take these solutions. Thus we carried out a study to evaluate the effects of standard oral rehydration solutions that contain carbohydrate (World Health Organisation oral rehydration solution and rice oral rehydration solution) with a solution that does not contain carbohydrate but does contain amino acid (glycine oral rehydration solution) on blood glucose concentrations during the mangement of acute diarrhoea.

Patients and methods

SAMPLE SIZE

Based on preliminary data from a small pilot trial in diabetic patients (mean (SD) difference of 3·8 (4·2) mmol/l in blood glucose concentration) we estimated that a sample size of 20 in each group was needed to detect a difference in patients given rice and WHO oral rehydration solutions ($\alpha = 0{\cdot}05$, $\beta = 0{\cdot}2$).

SELECTION OF PATIENTS

Men and women aged 15 to 60 years who had previously been diagnosed as having diabetes mellitus[2] at the Bangladesh Institute of Endocrine and Metabolic Disorders and who had had diarrhoea for 72 hours or less were selected for the study. They came to the Dhaka hospital of the International Centre for Diarrhoeal Disease Research directly or were referred by the institute for management of diarrhoea.

The first group was allocated to WHO oral rehydration solution, containing glucose 20 g/l, sodium chloride 3·5 g/l, potassium chloride 1·5 g/l, and trisodium citrate dihydrate 2·9 g/l. The second group took rice oral rehydration solution, containing rice powder 50 g/l and salts as in the WHO solutions. The third group took glycine oral rehydration solution, containing glycine 15 g/l and salts as in the two other solutions.

Allocation was carried out with random number tables. The names of the randomised treatment groups were written on slips of paper and kept in sealed envelopes in the hospital pharmacy. Patients were allocated to treatment groups according to the serial number on admission and observed for volume and character of stools over four hours in the ward while receiving the assigned oral rehydration solution for rehydration. If stools were seen to be soft during this period this could not have been a result of management. Similarly, if stools were seen to contain blood or mucus, or both, the patients were not included in the study because specific antimicrobial drugs and not oral

rehydration solution are required for management after the initial watery phase is over. If a patient was not finally included in the study for the above reasons, the next patient selected for observation was assigned to a randomised group (glucose, glycine, or rice) according to the serial number. This was done to avoid any bias in selection (such as the tendency to avoid giving glucose oral rehydration solution to diabetic patients receiving insulin or with a high blood glucose concentration on admission) because rice oral rehydration solution is white unlike the two other watery solutions.

After we received written consent for the study from the ethical review committee patients were weighed and their dehydration assessed according to guidelines of the WHO.[3] Blood glucose and serum electrolyte concentrations and leucocyte counts were determined. Patients with severe dehydration were treated with an intravenous solution of sodium 133 mmol/l, chloride 98 mmol/l, potassium 13 mmol/l, and acetate 48 mmol/l for initial rehydration followed by the assigned oral rehydration solution. Analysis of serum electrolyte concentrations was repeated 24 hours after admission and before discharge from hospital.

Stool microscopy, rectal swab cultures for *Vibrio cholerae*, salmonellas, shigellas, and urine analysis were performed on admission. Urinary glucose and ketone concentrations were determined daily by test strips (Medi-Test Glucose 3, Macherey-Nagel, Germany).

MANAGEMENT OF PATIENTS

Patients were encouraged to drink oral rehydration solution to match stool loss. The volumes of oral rehydration solution and water intake and output of stool, urine, and vomit were recorded every eight hours. Patients with cholera were treated with tetracycline capsules 500 mg every six hours for three days; those with shigellosis were treated with nalidixic acid 500 mg every six hours for five days. Breakfast (bread, egg, milk), lunch (boiled rice, fish or meat, lentils, vegetables) and supper (like lunch) were provided, with light snacks in between. Total energy provided was 8400 kJ a day, with carbohydrates constituting 55%, proteins 20%, and fat 25%. Presented food and leftovers were weighed to determine the amount eaten. Calorific value was calculated from the known values of the food offered as determined by adiabatic bomb calorimetry (adiabatic bomb calorimeter, Gallenkamp, United Kingdom).

Blood glucose concentration was checked in finger prick samples before breakfast, lunch, and supper by Haemo-Glukotest strips and Refloflux II (Boehringer Mannheim, Germany). The difference between concentrations determined by this method and those determined by assaying samples of venous blood (enzyme oxidase method) was only 0·2-0·4 mmol/l, tested on several occasions during the study. Doses of previously prescribed oral hypoglycaemic agents (either glibenclamide or chlorpropamide) or injected insulin were adjusted after monitoring blood glucose concentrations at these times. Recovery from diarrhoea was defined as the duration in hours from time of admission to passage of the last liquid stool.

DATA ANALYSIS

Clinical characteristics of patients were compared among the treatment groups. The major outcome variables were compared between groups by analysis of variance and Kruskal-Wallis non-parametric tests. Student's *t* test was used to test the significance of differences between two groups.

Results

During the four hour observation period four patients in the group taking WHO oral rehydration solution and five in the group taking rice oral rehydration solution passed soft stools; three in the group taking WHO oral rehydration solution and one in the group taking rice oral rehydration solution passed stools containing blood and mucus. They were not included in the study.

Clinical characteristics of the 45 patients who were finally enrolled in the study were comparable in all the treatment groups (table I). Two patients in the group taking WHO oral rehydration solution and glycine oral rehydration solution and three in the group taking rice oral rehydration solution had insulin dependent diabetes mellitus. Thirty three patients had not taken oral rehydration solution at home before coming to hospital, and 30 out of 34 (88%) of those prescribed hypoglycaemic agents stopped taking them after the onset of diarrhoea. The volume of intake of oral rehydration solution and stool output in all the groups was similar over the four days (table II). Serum electrolyte concentrations were comparable in all three groups on admission, 24 hours after rehydration, and before discharge from the hospital.

On the first day, when intake of oral rehydration solution was highest, blood glucose concentrations were higher before supper compared with admission values in the groups taking WHO oral rehydration solution and rice oral rehydration solution; but in the group taking glycine oral rehydration solution it was the reverse. Means of the differences between admission blood glucose concentration and before supper

TABLE I—*Clinical characteristics of diabetic patients with diarrhoea and stool pathogens isolated on admission according to allocated oral rehydration solution*

Variable	WHO (n=12)	Rice (n=13)	Glycine (n=20)
Mean (SD) age (years)	46·9 (11·6)	51·1 (15·7)	49·2 (10·4)
No (%) of men	7 (58·3)	7 (53·8)	12 (60·0)
No (%) of women	5 (41·7)	6 (46·2)	8 (40·0)
Mean (SD) body weight (kg)	56·3 (9·2)	54·8 (13·7)	56·0 (8·8)
Mean (SD) duration of diarrhoea (h)	24·7 (18·9)	29·8 (21·7)	23·2 (18·8)
Mean (SD) duration of vomiting (h)	19·8 (19·8)	23·0 (17·9)	16·1 (12·6)
Mean (SD) duration of diabetes months)	55·2 (72·5)	91·6 (78·9)	73·9 (69·1)
No (%) with treatment of diabetes before diarrhoea:			
Diet only	1 (8·3)	5 (38·5)	5 (25·0)
Oral hypoglycaemics	8 (66·6)	2 (15·4)	4 (20·0)
Insulin	2 (16·7)	5 (38·5)	7 (35·0)
Mixed/irregular	1 (8·3)	1 (7·7)	4 (20·0)
No (%) with dehydration:			
Mild	6 (50)	5 (38·5)	10 (50)
Moderate	6 (50)	7 (53·8)	8 (40)
Severe	Nil	1 (7·7)	2 (10)
No (%) with stool pathogens:			
Vibrio cholerae-01	2 (16·6)	3 (23·0)	5 (25)
Shigella spp	2 (16·6)	2 (15·4)	Nil
Salmonella (non-typhoidal)	0	1 (7·8)	Nil
Aeromonas spp	1 (8·3)	Nil	2 (10)

TABLE II—*Mean (95% confidence interval) intake and output of fluids over four days of study of diabetic patients with diarrhoea according to allocated oral rehydration solution*

Intake/output (ml/kg/day)	WHO (n=12)	Rice (n=13)	Glycine (n=20)
Stool output:			
Day 1	76 (30 to 122)	71 (23 to 119)	52 (29 to 74)
Day 2	28 (8 to 48)	44 (17 to 71)	48 (23 to 73)
Day 3	21 (6 to 36)	41 (26 to 56)	37 (17 to 57)
Day 4	19 (9 to 29)	22 (17 to 27)	21 (8 to 34)
Urine output:			
Day 1	43 (25 to 61)	40 (22 to 58)	32 (22 to 42)
Day 2	28 (15 to 41)	36 (18 to 54)	42 (28 to 55)
Day 3	42 (35 to 49)	35 (23 to 46)	41 (33 to 49)
Day 4	50 (36 to 64)	37 (29 to 45)	51 (40 to 62)
Intake of oral rehydration solution:			
Day 1	93 (55 to 131)	61 (54 to 68)	78 (64 to 92)
Day 2	39 (17 to 61)	40 (18 to 62)	51 (29 to 73)
Day 3	36 (9 to 63)	31 (15 to 47)	41 (23 to 60)
Day 4	34 (12 to 56)	19 (15 to 23)	38 (17 to 59)
Intake of water:			
Day 1	28 (19 to 37)	49 (31 to 67)	37 (17 to 57)
Day 2	35 (22 to 46)	43 (31 to 54)	43 (30 to 56)
Day 3	38 (30 to 46)	45 (33 to 57)	33 (26 to 40)
Day 4	52 (44 to 60)	58 (39 to 77)	39 (31 to 47)

(mmol/l) were compared between groups: the differences between the means (95% confidence intervals) were -1·13 (-5·98 to 3·75) for WHO oral rehydration solution and rice oral rehydration solution; 4·44 (-0·29 to 9·16) for WHO oral rehydration solution and glycine oral rehydration solution; and 4·44 (-0·17 to 9·04) for rice oral rehydration solution and glycine oral rehydration solution. These differences, however, were not significant (P=0·10), though a clear trend for lower blood glucose concentration before supper was seen in the group taking glycine oral rehydration solution. Over the next three days patients in all three groups had comparable blood glucose concentrations (table III). Only one patient with irregularly treated insulin dependent diabetes mellitus in the group taking rice oral rehydration solution had a blood glucose concentration greater than 15 mmol/l on five occasions. The mean (SD) daily energy intake was low in all groups: 5670 (2809) kJ to 7997 (3541) kJ.

TABLE III—*Mean (95% confidence interval) blood glucose concentrations (mmol/l) over four days of study of diabetic patients with diarrhoea according to allocated oral rehydration solution*

Time of measurement	WHO (n=12)	Rice (n=13)	Glycine (n=20)
Day 1:			
On admission	11·2 (6·9 to 15·5)	12·9 (10·4 to 15·4)	13·4 (10·5 to 16·5)
Before lunch	8·2 (5·2 to 11·2)	10·9 (8·1 to 13·7)	15·0 (12·0 to 18·0)
Before supper	12·6 (8·9 to 16·3)	15·4 (11·3 to 19·5)	11·2 (9·1 to 13·3)
Before supper minus on admission	1·23 (-2·1 to 4·6)	2·36 (1·2 to 3·5)	-2·07 (-5·0 to 0·9)
Day 2:			
Before breakfast	11·3 (6·8 to 15·7)	10·8 (8·5 to 3·1)	9·7 (8·1 to 11·3)
Before lunch	10·5 (7·1 to 13·9)	12·9 (9·7 to 16·1)	11·5 (8·5 to 14·5)
Before supper	11·1 (9·0 to 13·2)	13·2 (10·7 to 15·7)	10·7 (8·8 to 12·6)
Day 3:			
Before breakfast	8·8 (6·9 to 10·7)	10·3 (6·9 to 13·7)	9·3 (7·8 to 10·8)
Before lunch	8·1 (6·6 to 9·6)	10·8 (7·8 to 13·8)	10·4 (8·2 to 12·6)
Before supper	9·8 (7·1 to 12·5)	13·3 (10·7 to 15·9)	9·7 (8·1 to 11·3)
Day 4:			
Before breakfast	8·3 (6·8 to 9·8)	10·6 (8·2 to 13·0)	8·1 (6·6 to 9·6)
Before lunch	8·7 (7·6 to 9·8)	10·3 (8·3 to 12·3)	11·3 (8·9 to 13·7)
Before supper	9·7 (6·8 to 12·6)	11·2 (5·6 to 16·8)	10·8 (9·5 to 12·1)

The mean (SD) recovery time from diarrhoea was shortest with rice oral rehydration solution; 50·5 (29·9) hours compared with 71·33 (42·3) hours with WHO oral rehydration solution and 57·63 (39·3) hours with glycine oral rehydration solution. This result, however, was not significantly different (P=0·39).

Discussion

The results of this study were not surprising since we did not expect the amount of glucose ingested with WHO oral rehydration solution or rice oral rehydration solution during an episode of acute diarrhoea to produce substantial hyperglycaemia. Some of our findings were, however, important. Most of the diabetic patients were quite reluctant to consume oral rehydration solution with carbohydrate; only 12 (26·6%) of them took it at home compared with 77-81 (85-90%) of adults without diabetes who took oral rehydration solutions before coming to the centre (unpublished observations from hospital surveillance data). Most patients stopped taking antidiabetic agents after the onset of diarrhoea and vomiting (fearing hypoglycaemia), which is reflected by the higher blood glucose values on admission.

Patients taking the WHO solution consumed the most and those taking the rice powder solution the least, probably because polydipsia would lead to an increased intake of the watery solutions. As rice oral rehydration solution is a thicker solution, the patients in this group drank more water on average than those in the two other groups. Blood glucose concentrations were higher (but not significantly so) in the group taking rice oral rehydration solution because two patients with insulin dependent diabetes mellitus had previously not received treatment regularly.

Clinical implications

- Diabetic subjects in the developing world are also prone to diarrhoea
- Oral rehydration solutions should be advocated for management of acute watery diarrhoea
- In this study blood glucose concentrations were similar in diabetic patients given oral rehydration solutions whether or not they contained carbohydrate
- Diabetic patients can safely take oral rehydration solutions at home during episodes of acute diarrhoea and avoid unnecessary admission to hospital

Although stool output was high in the group taking rice oral rehydration solution on the first day, which is different from results of previous studies,[4] recovery was also quicker in this group. Since the average time required for recovery from diarrhoea was three days we can assure diabetic patients that if hyperglycaemia does occur after intake of any of the above oral rehydration solutions, it will only be temporary and adverse effects such as ketoacidosis are unlikely.

The major limitations of this study were its small sample size and inability to withhold hypoglycaemic agents to enable assessment of fluctuations in blood glucose concentration due to oral rehydration solution alone. In any case diabetics are not advised to stop intake of usual food and prescribed hypoglycaemic drugs during a diarrhoeal episode but to adjust the dose as required. We further conclude that oral rehydration solution containing carbohydrate can be safely used for management of acute diarrhoea in diabetic patients. This information should be communicated to diabetic patients as part of health education so that they can start oral rehydration at home during a diarrhoeal episode, thus avoiding unnecessary admission to hospital.

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Correction

How effective is nicotine replacement therapy in helping people to stop smoking?

An author's error and two editorial errors occurred in this article by Tang *et al* (1 January, 21-6). The last sentence of the first paragraph of the Results section should read "among the 15 trials of invited subjects" (not 14 as given). In table IV, Blöndal's study had 28 subjects given placebo gum, and 1 (4%) quit smoking (these numbers are missing from the table).