Blood Xylose Concentrations in Protein Energy Malnutrition

RELATIONSHIP TO SERUM ALBUMIN AND JEJUNAL HISTOLOGY

F. C. M. SCHWARTZ, M. LUNAT, J. WOLFSDORF

SUMMARY

One-hour blood xylose concentrations have been advocated as screening tests for coeliac disease in childhood. It was therefore postulated that this test might be useful as a diagnostic index of the degree of malabsorption associated with protein energy malnutrition (PEM) and that it might indicate the type and severity of the nutritional abnormality. In addition, it was hypothesised that this test might be useful to document response to therapy.

Seventy-six children with PEM were divided into 3 groups (marasmic (M), marasmic kwashiorkor (MK) and kwashiorkor (K)) and 1-hour blood xylose concentrations and serum albumin levels were estimated on admission, and in 45 and 43 patients respectively, on day 7 and on clinical recovery. Blood xylose levels were correlated with type of PEM, severity of oedema, serum albumin levels and response to treatment. An assessment was also made to elucidate whether gastro-intestinal infection influenced blood xylose concentrations. In addition, 22 patients (3 M, 9 MK and 10 K) had jejunal biopsies within 3 days of admission, with repeat biopsies in 13 (2 M, 5 MK and 6 K) before discharge from hospital.

Results show, on admission, a significant difference in blood xylose and albumin levels between the marasmic and the two oedematous groups (MK and K), no significant difference existing between blood xylose levels in the 3 study groups by day 7, or on recovery. Gastro-intestinal infection did not alter this. Serum albumin levels were highest in the M group, on admission and throughout the study. Decreased xylose and albumin concentrations were associated with gross oedema. Further, no correlation was found between blood xylose and serum albumin levels in any group, nor between blood xylose concentrations and jejunal histology grade.

It is suggested that low blood xylose concentrations in PEM are the result of dilution rather than malabsorption. The test does not indicate the degree of small-bowel atrophy, nor does it provide significant additional information to the clinical appraisal.

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Intestinal malabsorption in protein energy malnutrition (PEM) is well documented,[1] and associated diarrhoea with or without intestinal pathogens is common.[2,3] In the past, the intestinal abnormality has been attributed to malabsorption associated with intestinal mucosal atrophy,[4-6] disaccharidase deficiency,[7] pancreatic enzyme deficiency[8] or abnormal small-bowel flora.[9]

D-xylose, a pentose sugar, is widely used in the study of intestinal absorption.[10] Though the urinary excretion of an oral dose of xylose is more extensively employed, recently Rolles *et al.*[11] advocated the use of 1-hour blood xylose concentration as a screening test for coeliac disease in children.

It was therefore postulated that this test might be useful as a diagnostic index of the degree of malabsorption associated with PEM, and possibly be used to indicate the type and severity of the nutritional abnormality. In addition, it was hypothesised that this test might be useful to document response to therapy.

Blood xylose and serum albumin concentrations were estimated to ascertain (*i*) whether any difference existed in 1-hour blood xylose levels in various types of malnutrition during the first 24 hours after admission to hospital and during recovery; (*ii*) whether any correlation existed between blood xylose/serum albumin levels and oedema to indicate severity of disease; (*iii*) whether gastro-intestinal infection affected blood xylose levels, and (*iv*) whether any correlation could be detected between blood xylose levels and jejunal histology.

PATIENTS AND METHODS

Seventy-six malnourished children, selected in a random manner, were classified clinically according to the Wellcome classification[12] into marasmic (M)—21, marasmic kwashiorkor (MK)—25 and kwashiorkor (K)—30, groups. The average age in each group was 13 months (range 2 - 26), 18 months (range 9 - 33) and 23 months (range 11 - 54) respectively. Children suffering from MK and K were further divided, on clinical grounds, into those with mild, moderate and severe oedema, depending on whether the swelling was confined to the feet, the lower limbs, or whether the whole body was involved. During the first 24

Department of Paediatrics and Child Health, Godfrey Huggins School of Medicine, University of Rhodesia, Salisbury, Rhodesia

F. C. M. SCHWARTZ, M.B., M.R.C.P., D.C.H., *Lecturer*
M. LUNAT, M.B. B.CH., B.SC., D.C.H., *Registrar*
J. WOLFSDORF, B.SC., M.B. B.CH., DIP. PAED., F.R.C.P., *Professor*

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Reprint requests to: Professor J. Wolfsdorf, Harare Central Hospital, Box ST 494, Southerton, Salisbury, Rhodesia.

hours after admission, and after a 6 - 8-hour fast (during which an intravenous infusion of 10% dextrose solution was given to prevent hypoglycaemia), a standard 5-g oral loading dose of xylose was administered. Venous blood was taken 1 hour later for the estimation of blood xylose[13] and serum albumin[14] concentrations. Fifteen M, 13 MK and 17 K patients had repeated blood xylose tests on day 7 after admission, and 10 M, 12 MK and 21 K children on clinical recovery (defined in this study as the time when the patient was fit enough to be discharged from hospital—average 21 days after admission, range 13 - 41 days). In order to observe and analyse the response to therapy in the same patients, 8 M, 10 MK and 14 K patients had their blood xylose and serum albumin estimated on admission, on day 7, and on clinical recovery (average 20 days, range 13 - 29 days).

All children admitted to the study had their stools cultured. Blood xylose concentrations performed as above were compared on admission and on day 7 in the patients with intestinal pathogens.

Within 3 days of admission, jejunal biopsy and blood xylose estimations were performed on 22 patients (3 M, 9 MK and 10 K). A Paediatric Watson Biopsy Capsule with a Kifa-red tube was used.[15] In 13 children (2 M, 5 MK and 6 K) the biopsy was repeated before discharge from hospital (mean 26 days later). The histological features of the biopsy specimens were graded according to a modification of the method of Doniach and Shiner.[16]

Statistical analyses and correlation coefficients were sought between blood xylose and albumin levels in relation to time, to each other, and between these levels and differing degrees of oedema, in the various PEM groups. In addition, these parameters were examined in relation to improvement on treatment, gastro-intestinal infection and jejunal biopsy histology.

RESULTS

Table I gives the xylose and albumin levels of all groups of patients studied on admission, on day 7, and on recovery.

On admission, the blood xylose concentration was significantly higher in the M compared to the MK or K groups ($P<0,001$), but no difference was discernible between the oedematous groups. However, by day 7 and on recovery no significant difference in blood xylose concentrations between the 3 PEM groups could be demonstrated.

On admission, serum albumin levels in M were also significantly higher than in the oedematous groups ($P<0,001$) and this pattern remained throughout recovery ($P<0,001$ and $<0,05$ for day 7 and recovery, respectively).

No significant correlation was found between blood xylose and serum albumin concentrations on admission, on day 7, or on recovery, in any of the groups:

M r = 0,3175 0,1581 and 0,0771 (admission/day 7/recovery)

MK r = 0,3715 0,2607 and 0,0733 (admission/day 7/recovery)

K r = 0,2345 0,4495 and 0,1158 (admission/day 7/recovery).

Table II illustrates blood xylose and albumin concentrations in MK and K patients combined, when classified according to degree of oedema. The blood xylose concentrations were significantly higher when comparing the mild with the moderate and severe groups ($P<0,01$ and $<0,001$ respectively); however, no significant difference was found between moderate and severely oedematous patients. Albumin levels were only significantly different between the mild and severely oedematous groups.

Table III demonstrates the response of the blood xylose and serum albumin concentrations to therapy. In M there was no difference between the blood xylose concentrations on admission, day 7 and recovery, although albumin levels improved between admission and recovery ($P<0,01$). In MK and K the blood xylose levels rose significantly between admission and day 7 ($P<0,05$ and $<0,01$ respectively), but in neither group was there a change between the results on day 7 and on recovery. Albumin levels in these groups improved with each period.

Table IV gives the blood xylose concentrations in marasmic and oedematous patients, on admission and on day 7, when gastro-intestinal infection was present (an epidemic of *S. heidelberg* occurred during the period of this study). The results show no adverse effects on blood xylose levels.

Table V indicates the number of children biopsied, their blood xylose values, and the corresponding histo-

TABLE I. MEAN (± SD) BLOOD XYLOSE (mg/100 ml) AND ALBUMIN (g/100 ml) CONCENTRATIONS IN THE THREE GROUPS OF PATIENTS STUDIED, PLUS STATISTICAL ANALYSES

	Admission		Day 7		Recovery	
Type of PEM	Xylose	Albumin	Xylose	Albumin	Xylose	Albumin
Marasmus	**26,48 ± 6,40 (21)**	**3,41 ± 0,58 (21)**	**30,40 ± 6,34 (15)**	**3,84 ± 0,53 (15)**	**32,20 ± 5,63 (10)**	**4,37 ± 0,31 (10)**
Marasmic kwashiorkor	**19,04 ± 7,62 (25)**	**2,41 ± 0,55 (25)**	**24,62 ± 8,85 (13)**	**3,02 ± 0,80 (13)**	**30,08 ± 6,40 (12)**	**4,03 ± 0,43 (12)**
Kwashiorkor	**16,63 ± 6,28 (30)**	**2,19 ± 0,50 (30)**	**26,53 ± 8,43 (17)**	**3,11 ± 0,70 (17)**	**28,00 ± 7,64 (21)**	**3,96 ± 0,45 (21)**
M v. MK	$P<0,001$	$P<0,001$	NS	$P<0,001$	NS	$P<0,05$
M v. K	$P<0,001$	$P<0,001$	NS	$P<0,001$	NS	$P<0,01$
MK v. K	NS	NS	NS	NS	NS	NS

Number of patients in parentheses.

TABLE II. BLOOD XYLOSE (mg/100 ml) AND SERUM ALBUMIN (g/100 ml) CONCENTRATION IN THE OEDEMATOUS PATIENTS (MEAN ± SD) PLUS STATISTICAL ANALYSES

Degree of oedema	Xylose	Albumin
Mild (15)	**23,13 ± 8,61**	**2,58 ± 0,47**
Moderate (12)	**17,33 ± 5,58**	**2,33 ± 0,49**
Severe (28)	**15,00 ± 4,67**	**2,11 ± 0,52**
Mild v. moderate	$P<0,01$	NS
Mild v. severe	$P<0,001$	$P<0,01$
Moderate v. severe	NS	NS

Number of patients in parentheses.

logical grades on admission and on clinical recovery. Blood xylose levels improved in all oedematous patients, though no significant correlation between the histological grades and blood xylose concentrations was found. Histological abnormalities varied from mild to severe mucosal atrophy. However, when repeat biopsies were done, 6 of the 13 patients showed histological improvement during the study period.

DISCUSSION

Coeliac disease is associated with xylose malabsorption and intestinal mucosal atrophy, the diagnosis being confirmed by histological examination of a jejunal biopsy specimen.[17] In PEM, jejunal abnormalities of varying degrees are found,[4-6] thus malabsorption of D-xylose in this condition could logically be expected. As the result of the present study, at least three questions require an answer:

1. Why are the 1-hour blood xylose concentrations in the marasmics higher on admission than those of the oedematous PEM groups?

2. By what mechanism does the blood xylose concentration improve by day 7 in the oedematous groups?

TABLE III. MEAN (± SD) XYLOSE (mg/100 ml) AND ALBUMIN (g/100 ml) IN PEM — AN ANALYSIS OF RESPONSE TO THERAPY IN THE SAME PATIENTS

	Marasmus (8)		Marasmic kwashiorkor (10)		Kwashiorkor (14)	
Treatment interval	Xylose	Albumin	Xylose	Albumin	Xylose	Albumin
Admission to day 7	**28,87 ± 7,25**	**3,38 ± 0,62**	**18,5 ± 8,4**	**2,61 ± 0,53**	**14,50 ± 4,46**	**2,22 ± 0,46**
	31,62 ± 6,92	**3,81 ± 0,67**	**27,50 ± 7,57**	**3,25 ± 0,80**	**25,42 ± 8,50**	**3,09 ± 0,76**
	NS	**NS**	$P<0,05$	$P<0,05$	$P<0,01$	$P<0,01$
Day 7 to recovery	**31,62 ± 6,92**	**3,81 ± 0,67**	**27,50 ± 7,57**	**3,25 ± 0,80**	**25,42 ± 8,50**	**3,09 ± 0,76**
	33,50 ± 5,95	**4,45 ± 0,29**	**30,40 ± 7,33**	**4,01 ± 0,49**	**30,21 ± 7,24**	**3,88 ± 0,37**
	NS	**NS**	**NS**	$P<0,05$	**NS**	$P<0,01$
Admission to recovery	**28,87 ± 7,25**	**3,38 ± 0,62**	**18,50 ± 8,4**	**2,61 ± 0,53**	**14,50 ± 4,46**	**2,22 ± 0,46**
	33,50 ± 5,95	**4,45 ± 0,29**	**30,40 ± 7,33**	**4,01 ± 0,49**	**30,21 ± 7,24**	**3,88 ± 0,37**
	NS	$P<0,01$	$P<0,01$	$P<0,01$	$P<0,01$	$P<0,01$

Number of patients in parentheses.

TABLE IV. MEAN (± SD) BLOOD XYLOSE (mg/100 ml) CONCENTRATION ON ADMISSION AND DAY 7 IN PEM PATIENTS WITH GASTRO-INTESTINAL INFECTION

	Admission	Day 7
Marasmus (6)	**27,16 ± 6,85**	**27,66 ± 6,15**
	NS	
Oedematous PEM (7)	**18,85 ± 6,15**	**29,57 ± 7,63**
	($P<0,05$)	

Number of patients in parentheses.

TABLE V. BLOOD XYLOSE CONCENTRATIONS (mg/100 ml) AND CORRESPONDING JEJUNAL HISTOLOGICAL GRADES ON ADMISSION AND ON RECOVERY

	Marasmus				Marasmic kwashiorkor				Kwashiorkor			
	Admission		Recovery		Admission		Recovery		Admission		Recovery	
	Xylose	Grade	Xylose	Grade	Xylose	Grade	Xylose	Grade	Xylose	Grade	Xylose	Grade
1	37	3^+	40	3^+	20	3-	37	3^-	21	3^-	33	3^-
2	24	5	26	3^-	38	3^-	42	3^-	10	3^-	33	3^-
3	24	4			28	3^-	35	3	16	3^-	18	3^-
4					11	6	21	3^-	12	3^-	38	4
5					19	6	39	4	12	4	39	3^+
6					16	5			12	6	21	3
7					31	4			19	3^-		
8					12	5			14	3^-		
9					18	6			12	3^-		
10									14	4		

3. Why does this not occur in the marasmic patients?

An obvious answer to the first question could be that in the marasmics, the jejunal histology is near normal, while in the oedematous children the mucosa is abnormal, giving rise to malabsorption. The findings of Brunser *et al.*[18] are in favour of this suggestion. Barbezat *et al.*,[6] however, could not separate the histological biopsy features of patients with marasmus and kwashiorkor, and though the number of marasmics biopsied was small, the data presented here support this. Clearly, then, the answer to question 1 must lie elsewhere. Bowie *et al.*[7] suggested that xylose absorption in PEM is slow, but that total amounts absorbed were within normal limits. In their study the maximal blood xylose concentration occurred at 120 minutes. In the series of Viteri *et al.*[1] in 9 out of 16 children the blood xylose peaked at 60 minutes, and in the rest of their study group at 90 minutes. In a study of 5 marasmic and 6 kwashiorkor patients conducted in this laboratory, no difference was found between the 60- and 120-minute blood xylose concentrations.[19] Slow absorption, therefore, does not appear to be the answer either.

It has been suggested that xylose absorption may be influenced by the presence of oedema[20] and/or an abnormal upper intestinal flora.[9,21] The results of this study suggest that the low blood xylose concentrations found, especially in the oedematous children, could be the result of dilution. This dilution hypothesis is favoured by the following points which emerged from the present study: (*a*) the higher blood xylose concentrations in the marasmic children on admission; (*b*) the inverse relationship between blood xylose levels and the severity of oedema; (*c*) that no correlation was found between blood xylose levels and serum albumin concentrations in any of the PEM groups, independent of the time at which the test was done; (*d*) the lack of correlation between blood xylose concentrations and the degree of jejunal atrophy; and (*e*) the lack of influence of intestinal pathogens on the blood xylose levels.

Total body water and extracellular fluid volumes are greatly increased in PEM.[22] In response to treatment, MK and K patients rapidly lose large amounts of fluid. This reduction in total body water could result in less and less dilution of the blood xylose, which would thus initially tend to improve rapidly, followed by stabilisation as fluid losses decreased. In the marasmics, since body fluid losses probably occur much more slowly and over a much longer period, blood xylose levels would tend, in the short term, to remain static. With feeding and normal protein absorption, however, albumin levels in all the subgroups of PEM would tend to rise slowly and continuously towards normal. The above would not only result in the lack of correlation between blood xylose and albumin levels found in this study, but would also answer the queries initially raised by the data.

When the blood xylose concentrations of the group as a whole, at recovery, are compared with those of a normal group of children, these levels are still decreased.[22] It is possible, therefore, that in addition to dilution, a minor degree of xylose malabsorption may also be present. This could be explained by the abnormal jejunal histology found in all the PEM patients.

It would have been of value had the blood xylose concentrations separated the different types of PEM and/or been related to their severity, particularly if they had differentiated mild from moderate disease. It appears, however, that blood xylose levels relate primarily to differing degrees of oedema. Since clinical examination allows one to separate M from MK and K, and since oedema itself is a poor prognostic parameter for judging the severity of PEM, the blood xylose test does not add any useful information to the clinical assessment of the malnourished patient, nor does it indicate the state of the small-bowel mucosa.

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