Evaluation of Surface Area Corrected Peak Blood Xylose as a Screening Test of Intestinal Malabsorption in the Tropics

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Abstract

The 1 hour surface area corrected peak blood xylose as an indicator of xylose absorption has been compared with the 5 hour urine excretion test in a tropical population. Peak blood xylose concentration occurs at 1 hour in normals whereas in 76 per cent of patients with malabsorption the peak is delayed and a wide scatter in time is noted. However with correction to a constant body surface area the maximum discrimination between normal and abnormal values occurred at 1 hour. The reference range in the control group (1 hour surface area corrected blood xylose value) was found to be between 34.7 and 45.1 mg/dl (mean 39.9 ± 2.6). A good correlation was observed between the 5 hour urinary xylose excretion and 1 hour surface area corrected blood xylose value both in the controls (r = 0.92; P < 0.001) and in the patient group (r = 0.92; P < 0.001). In view of difficulties in obtaining accurate urine collection, it is recommended that 1 hour blood xylose (surface area corrected) should be adopted as a standard test of xylose absorption.

Key word: Peak blood xylose.

Introduction

Measurement of d-xylose absorption in a timed urine collection is a standard test of jejunal mucosal integrity. However, this test demands meticulous attention to urine collection and renal functions. False positive results may also be found in various conditions like increasing age, intestinal bacterial overgrowth, thyroid disease, in the presence of ascites, and administration of certain drugs like aspirin and indomethacin. Increased tubular reabsorption of d-xylose in some residents of tropical countries has been shown to cause a false positive urinary xylose excretion test.

An alternative method of estimation of blood xylose values could bypass many of these problems. The value of one hour blood xylose in children and adults with coeliac disease and with tropical sprue has already been established. The sensitivity of this test is further enhanced when the peak blood xylose values are corrected to a constant surface area to avoid variation in individual body volumes.

The present study aimed to establish the peak value of blood xylose in normal North Indian individuals and to evaluate its value in patients with malabsorption; assess and compare the validity of blood xylose levels with 5 hour urinary excretion as routine laboratory procedure; and investigate the value of adjusting the results to a constant surface area in order to exclude individual variations in the blood volume.

Material and Methods

The patient group included 25 patients with chronic diarrhea (9 males, 16 females; aged 16-20 years, mean 33.9). Two patients were aged 70 years. The duration of diarrhea, number of stools, their bulk, and presence or absence of froth, blood and mucus in the stools were noted. Weight loss was recorded in each patient. A history of abdominal pain, associated distension and vomiting was asked for so as to exclude intestinal obstruction. The patients were not on any drugs which could affect their renal or intestinal functions. They underwent a detailed physical examination and height and weight measurement for calculation of the body surface area according to Dubois' chart.

Twenty five normal individuals (6 males, 19 females; aged 18-54 years, mean 24.4) served as controls. These individuals had no history of diarrhea in the past 2 years and had at least two tests of malabsorption, ie 72 hr fecal fat and 5 hr urinary d-xylose excretion, within normal limits. They had normal renal functions as assessed by blood urea and or serum creatinine levels and were not on any drugs which could interfere with their intestinal or renal functions.

Investigations included three stool examinations by concentration method, complete hemogram, chest X-ray, blood urea and or serum creatinine estimation. Specific tests included 72 hr fecal fat estimation, d-xylose urinary excretion using 25 g d-xylose orally, and vitamin B12 absorption test. Jejunal biopsy was done in only 12 patients. Pancreatic function tests were not done. The blood xylose estimation was done in blood samples at 0, 0.5, 1, 1.5, 2, 3 and 5 hr after the oral dose of 25 g d-xylose. Fasting (0 hour) blood values were deducted from each subsequent blood value so as to exclude non-xylose reducing component. Measured blood xylose (mg/dl) was corrected to a constant surface area of 1.73 m² according to the following formula:

\[ \text{Corrected blood xylose value} = \frac{\text{Measured blood value} \times \text{Actual surface area}}{\text{Constant ideal surface area}} \]

For comparison correction to a constant body weight of 45 kg in females and 55 kg in males was also made, based on ICMR standard for Indians.

Results

The final diagnosis in the patient group included tropical sprue (9), giardiasis (5), megaloblastic anaemia with malabsorption (5), abdominal tuberculosis (5), and diffuse primary intestinal lymphoma, contaminated small bowel syndrome and malabsorption with hypercosyphilic syndrome of undefined cause (1 each).
Stool Fat
The faecal fat values ranged between 1.8 and 5.8 g/day (mean 4.2 ± 1.1) in the control group whereas in the patient group it ranged from 7.5 to 82.9 g/day (mean 19.4 ± 16.1; p < 0.001).

D-xylene Tests
Urinary xylene: The 5 hour urinary excretion of d-xylene varied from 4.7 to 88.9 g/25 g dose (mean 633 ± 92) in the control group whereas in the patient group it ranged from 0.5 to 4.0 g/25 g dose (mean 2.9 ± 0.9; p < 0.001). The patients had significantly lower excretion.

Blood xylene: Full absorption curves over a period of three hours were obtained in all the subjects. Ninety percent of the 25 normal subjects reached their peak blood xylene values at 1 hr. Two subjects had insignificantly higher peak blood xylene at 1 1/4 hours. The mean blood xylene value in the control group (42 ± 4.2 mg/dl) at 1 hr was higher than the values at all the other times and this was statistically significant as compared to those at 1/2 hour (P < 0.0001) and at 1 hr (P < 0.001).

In contrast, a wide scatter in the time of peak of blood xylene was noted in the patient group. Only 6 (24%) patients had peaked at 1 hour; the rest reached peak values between 1 and 3 hours (44% at 1 hr, 28% at 2 hr and 4% at 3 hr). Further, in the patient group the peak was well defined (Fig 1). The mean blood xylene value at 1 hr (27.5 ± 9.7 mg/dl) was higher than that at 1 hour (27.3 ± 7.9 mg/dl) and at 2 hr (22.5 ± 11.7 mg/dl; both P < 0.05). However, after correcting all these values to a constant surface area, the differences between the mean blood xylene value at 1 hr (23.9 ± 9.2 mg/dl) at that at 1 hr (19.5 ± 7.9 mg/dl) and at 2 hr (19.3 ± 9.9 mg/dl) were not significant (P > 0.05).

Validation of correction for body size
Correlation analysis: The correlation between the measured blood xylene at 1 hr and the inverse of surface area (t = 3.08) and inverse of body weight (t = 5.69) were significant (P < 0.01). After correction for surface area, there was no significant correlation between the resultant xylene values and inverse of surface area (t = 0.26; P > 0.7).

Narrowing of distribution ranges for normals after correction for body size: The distribution ranges could be narrowed down maximally at 1 hr (F = 2.61) for surface area correction and at this time were greater for the surface area than for weight correction (F = 1.25) (Table 1).

Discrimination between normal and abnormal subjects: The maximal discrimination between the normal and abnormal group of subjects was at 1 hr (Table 2). Further the separation between the mean values for the two groups after surface area correction was also greater at 1 hr (t = 12.09). An excellent correlation was seen (Fig 2) between the 5 hour urinary excretion of D-xylene and the 1 hr surface area corrected blood xylene in controls (r = 0.92; P < 0.001) and in the patient group (r = 0.90; P < 0.001). Applying the regression analysis, the equation derived was Y = 0.18 + X 13-15 where Y is the 1 hr surface area corrected blood xylene value and X the percentage of 25 g d-xylene excreted in 5 hr urine.

Table 1: Narrowing of distribution ranges for 25 normal subjects after correction for body size (full absorption curves)

<table>
<thead>
<tr>
<th>Blood xylene (hours)</th>
<th>1/4</th>
<th>1</th>
<th>1 1/4</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface area corrected values n = 25 (F)</td>
<td>1.39</td>
<td>2.61</td>
<td>2.20</td>
<td>1.29</td>
<td>1.35</td>
</tr>
<tr>
<td>Body weight corrected values n = 25 (F)</td>
<td>1.20</td>
<td>1.25</td>
<td>1.67</td>
<td>1.16</td>
<td>1.12</td>
</tr>
<tr>
<td>F = ratio of measured variance to corrected variance</td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Table 2: Discrimination between normal and abnormal groups using blood xylene values (values in mean ± SD)

<table>
<thead>
<tr>
<th>Group</th>
<th>1/4 hr</th>
<th>1 hr</th>
<th>1 1/4 hr</th>
<th>2 hr</th>
<th>3 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normals (N = 25)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>21.8 ± 12.3</td>
<td>24.8 ± 12.4</td>
<td>33.1 ± 12.7</td>
<td>20.9 ± 12.6</td>
<td>11.9 ± 12.6</td>
</tr>
<tr>
<td>SA</td>
<td>19.4 ± 12.0</td>
<td>20.8 ± 11.9</td>
<td>22.8 ± 12.6</td>
<td>19.1 ± 12.0</td>
<td>10.6 ± 12.0</td>
</tr>
<tr>
<td>W</td>
<td>24.6 ± 12.0</td>
<td>28.6 ± 12.0</td>
<td>28.6 ± 12.0</td>
<td>23.6 ± 12.0</td>
<td>13.4 ± 12.0</td>
</tr>
<tr>
<td>Patients (N = 25)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>11.9 ± 5.3</td>
<td>22.3 ± 5.9</td>
<td>27.3 ± 5.7</td>
<td>22.5 ± 5.7</td>
<td>13.3 ± 5.7</td>
</tr>
<tr>
<td>SA</td>
<td>10.3 ± 4.8</td>
<td>19.3 ± 4.8</td>
<td>23.3 ± 4.8</td>
<td>19.3 ± 4.8</td>
<td>11.5 ± 4.8</td>
</tr>
<tr>
<td>W</td>
<td>11.5 ± 5.6</td>
<td>22.1 ± 5.6</td>
<td>26.4 ± 5.6</td>
<td>21.3 ± 5.6</td>
<td>12.4 ± 5.6</td>
</tr>
</tbody>
</table>

M = Measured blood xylene value
SA = Surface area corrected value
W = Weight corrected value
P < 0.05 ** < 0.01 *** < 0.001 as compared to normals.

Screening test of intestinal malabsorption—Gupta ET AL.

Fig 1: Mean blood xylene values (full absorption curve) in normals and in patients.
Reference range: The reference range of 1 hr surface area corrected blood xylose as calculated from the normal subjects was found to be 34.7 to 45.1 mg/dl (mean ±SD). The mean was 39.9 ± 2.8 mg/dl. Only one of 25 patients had the 1 hr surface area corrected blood xylose value of 35 mg/dl which was near the lower limit of the reference range for normals. All other values were much lower than this reference range.

Discussion

The present study confirms that the control population had the peak blood xylose concentration after 25 g dose at one hour whereas a widespread trend in the timing of appearance of the peak was found in the patient group. Over 75% of patients had a delayed peak which could itself be of diagnostic value. The peak values at 1 hr in them were significantly lower than in normal controls.

The correction of measured serum values to a constant surface area narrowed the range of values at all times and improved the discrimination between the normal and abnormal groups. The difference between the corrected blood xylose values at 1 hr in the abnormal group when compared with the normal group was of diagnostic significance. These findings suggest that the correction for varying circulating blood volumes enhances the discriminatory capacity. These observations are in agreement with those of previous studies from the UK, South India and Saudi Arabia.

Only 1 of 25 patients had a 1 hr surface area corrected blood xylose value near the lower limit of the reference range for normals, giving a false negativity of 4%. Sladen and Kumar criticized the blood xylose test as they used the 90 minute blood xylose value to correlate with jejunal biopsy findings and found that 10-17% of their patients had false negative results. Haemey et al. recommended the use of the 1 hr surface area corrected blood xylose estimation as the incidence of false negativity was reduced to 10-4%. Hill and co-workers observed 17-1% false negative results in their study on South Indian subjects using 1 hr surface area corrected blood xylose values but the author attributed this to inadequate urine collection and decreasing renal functions as the cause of falsely low urinary xylose excretion in these subjects.

A good correlation was found between the 5 hr urinary excretion of d-xylose and 1 hr surface area corrected blood xylose values in controls as well as in patients. Similar observations were made by other workers, thereby suggesting that the surface area corrected blood xylose can be used as a test of intestinal absorptive function. This test, if reproducible, will prove to be an easy outpatient procedure and could be employed as a screening test for intestinal malabsorption as it has a low incidence of false negativity. Further methodological studies should be undertaken to overcome the need for a basal sample and the requirement of an automated analyser system to achieve the required precision.

References

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