Paediatrica Indonesiana

VOLUME 46 January - February • 2006 NUMBER 1-2

Original Article

Intestinal permeability of autistic and healthy children as measured by D-xylose test

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ABSTRACT

Background The etiopathogenesis of autistic disorder is unknown. Some authors suggest that food peptides may reach the central nervous system through a defect of intestinal permeability and produce toxic effects resulting in behavior impairment.

Objectives To investigate the prevalence of increased intestinal permeability in children with autistic disorder using oral D-xylose test.

Method A cross-sectional study was conducted on 27 children with autistic disorder and 54 healthy children (27 siblings and 27 unrelated children matching with those of the autistic group). The subjects underwent oral D-xylose test. Subjects were free from fever, drugs, and diarrhea. Student t-test and chi-square were used for statistical analysis.

Results Prevalence of increased intestinal permeability in the autistic group was 63%, which proved to be significant (P=0.007, 95%CI: -0.931; -0.987) compared to controls.

Conclusion The intestinal permeability significantly increased in autistic children **[Pediatr Indones 2006;46:37-40].**

Keywords: Autistic disorder, intestinal permeability, oral d-xylose test, gastrointestinal disorders.

Autistic disorder is a spectrum of developmental disorder characterized by impairment of social interaction and communication. The prevalence and incidence of autism have risen steeply over the past decade; however, the etiopathogenesis is still unknown. Recently, some authors have suggested that food peptides may reach the central nervous system through a defect of the intestinal permeability and produce toxic effects fowards the central nervous system.[1]

It has been reported that 43% of autistic patients showed increased intestinal permeability. A study on 36 autistic children who experienced gastrointestinal symptoms, by using endoscopy with biopsy, found that gastrointestinal abnormalities may contribute to behavioral problems.[3] Intestinal permeability can be indirectly measured by oral D-xylose test. It has been used to compare intestinal function between healthy infants and infants with mucosal abnormalities of the small intestines.[4] In subjects with normal intestinal permeability, orally administered D-xylose is absorbed which results in high blood concentrations and therefore can be measured, where the maximum level is reached at 1 hour.[6] In conditions of increased intestinal permeability, due to mucosal abnormalities, D-xylose can not be absorbed therefore only little xylose concentration can be detected in blood.[4,5]

The aim of this study was to investigate the prevalence of increased intestinal permeability using oral D-xylose test in children with autistic disorder compared to normal children. The results obtained from this study may contribute to the management of autistic patients.

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Methods

This was a cross-sectional study conducted at Klinik Anakku, a private clinic in Jakarta, during July-September 2004. Twenty seven children aged 2-18 years, who met inclusion criteria for the autistic group [based on Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV)] were enrolled in this study. Fifty-four healthy children, consisting of 27 siblings and 27 unrelated children (recruited from a foster home in Jakarta) who matched with those of the autistic group in age, sex, and nutritional status, were also enrolled as comparison. All subjects were free from fever or drugs, such as acetyl salycilic acid, ibuprofen, and neomycin, and free from diarrhea for at least 1 week before the test. Parents of subjects signed the informed consent and allowed their children to participate in this study. The study was approved by the Committee of Medical Research Ethics, Medical School, University of Indonesia.

A five percent solution of D-xylose was administered orally after the subjects underwent fasting for at least 4 hours. Sixty minutes after administration, venous blood was taken and blood xylose concentration level was determined using a modified micro-method determination.[6] Normal blood xylose concentration was obtained from healthy children, since there was no study on D-xylose concentration in Indonesian children.

Anthropometric data including weight and height were obtained from all subjects using standard anthropometrics procedures. Nutritional status was determined by calculating percentage of weight for height.

Data were processed by SPSS version 11.5 for Windows and analyzed using student t-test and chi-square. $P<0.05$ was considered as a statistically significant difference.

Results

Eighty one subjects were included in this study. **Table 1** shows that there were no statistical differences among three groups.

The mean level of oral D-xylose in control subjects was 18.5 (SE 1.45) mg/dl and it was not statistically different in sibling and non-sibling group ($P=0.270$), but it was significantly different in autistic and control groups (**Table 2**).

As illustrated in **Figure 1**, the results and median level of blood xylose concentration in autistic and control groups were different. The prevalence of increased intestinal permeability in autistic group was 17 of 27 children while in the control group only 17 of 54 children, while in the control group it was only 17 of 54 children ($P=0.026$, 95% CI: 0.345; 0.918).

Discussion

There was no significant difference between levels of D-xylose concentration in the sibling and non-sibling

Table 1. Characteristics of children with autistic disorder and matched controls

Subject characteristics	Autistic group n=27	Control group	
		Sibling n=27	Non sibling n=27
Sex			
Male	21	21	21
Female	6	6	6
Age, mean (SD) (years)	4.3 (1.2)	4.0 (1.5)	4.2 (1.3)
Weight for height, mean (SD) (%)	103 (14.9)	101 (7.3)	97 (9.5)

Table 2. D-xylose test results in autistic and control group

Group	Total sample	Mean	SD	SE Mean	P value	95%CI
Autistic	27	14.9	5.17	0.99		- 0.931;
Control	54	18.5	5.34	0.73	0.007	- 0.987

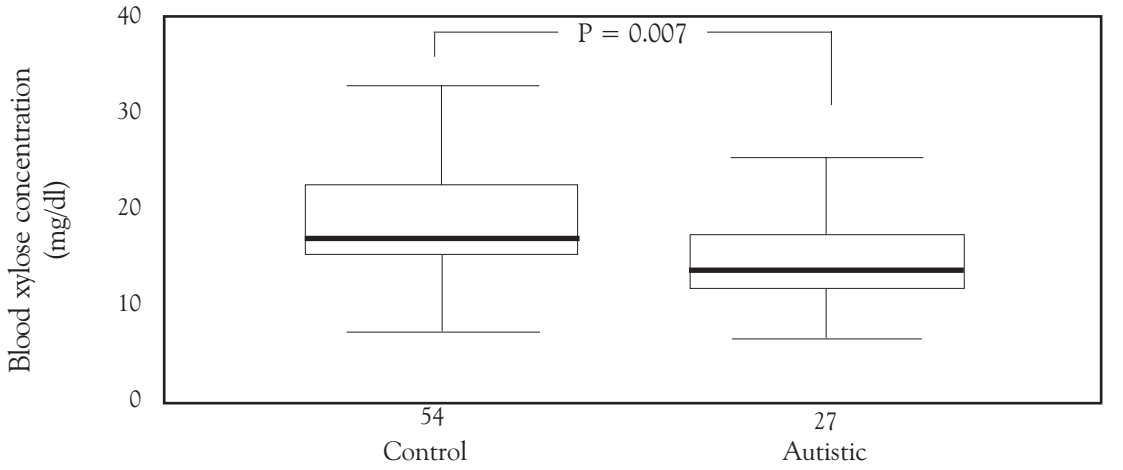

FIGURE 1. ORAL D-XYLOSE TEST RESULTS IN AUTISTIC GROUP DISORDER AND CONTROL SUBJECTS

subjects (P=0.270). It was previously reported that one-hour blood D-xylose test for healthy children showed levels over 20 mg/dl and a mean level of 35 mg/dl. In this study, the lower limit in healthy children was 17 mg/dl and the mean level was 18.5 mg/dl. The prevalence of increased intestinal permeability in autistic group was 17 of 27 (63%). This result is higher than the prevalence reported by D'Eufemia *et al*[2], who measured intestinal permeability with lactulose-manitol and found increased intestinal permeability in 9 of 21 (43% subjects). There are several possible explanations for such different results.[2,4,7] Tropical enteropathy in developing countries were often diagnosed on the basis of morphological abnormalities of duodenal and jejunal mucosa as well as depressed xylose absorption. Oral D-xylose test might also be difficult to interpret since the day-to-day variation of absorption. Nevertheless, these factors presumably affect the interpretation of the D-xylose test, both in developed and developing countries.[8,9] The clinical significance of the increase in intestinal permeability for sugar probes is still a subject of investigation. Although the assumption has been made that alterations in gut barrier function, as assessed by changes in intestinal permeability, predispose to bacterial translocation, there is yet no evidence in humans to support this view.[10]

Histological examinations of small intestine in 36 children with autistic disorder, who had frequent gastrointestinal complaint, revealed grade I or II reflux esophagitis in 25 (69.4%), chronic gastritis in 15, and chronic duodenitis in 24. It was hypothesised that chronic intestinal disease and malabsorption may be causal factors in the development of autistic disorder.[3] The result obtained from this study may contribute to the management of autistic patients. Low levels of D-xylose concentration indicate upper small intestinal enteropathy while positive results can also occur in other conditions such as Celiac diseases, cow's milk protein enteropathy (CMPSE), protein loosing enteropathy, intractable diarrhea, etc.[11-15]

In conclusion, this study reveals that intestinal permeability in children with autistic disorder is significantly different compared to that of healthy children and the prevalence of increased intestinal permeability is 63% in the autistic group. Thus, we recommend to evaluate intestinal function, such as with oral D-xylose test in children with autistic disorder. It is presumed that increased intestinal permeability might play a role in the development of autistic disorder.

References

1. Reichelt KL, Hole K, Hamberger A, Saelid G, Edminson PD, Braestrup CB, *et al*. Biologically active peptide-containing fractions in schizophrenia and childhood autism. Adv Biochem Psychopharmacol 1981;28;627-43.

2. D'Eufemia P, Celli M, Finocchiaro R. Abnormal intestinal permeability in children with autism. Acta Pediatr 1996;85:1076-9.
3. Horvath K, Papadimitriou JC, Rabsztyn A, Dranchenberg C, Tildon JT. Gastrointestinal abnormalities in children with autistic disorder. J Pediatr 1999;135:559-63.
4. Lanzkowsky P, Lloyd EA, Lahey ME. The oral D-xylose test in healthy infants and children. JAMA 1963; 186:163-5.
5. Craig RM, Atkinson AJ. D-xylose testing: A review. Gastroenterology 1988;95:223-31.
6. Roe JH, Rice EW. A method for the determination of free pentoses in animal tissues. J Biol Chem 1948;173: 507-12.
7. Burke V, Charlotte MA, Dodge JA, Gracey M, Grove DI, Hadorn HB. Investigations and methodology. In: Gracey M, Burke V, editors. Pediatric gastroenterology and hepatology. 3rd ed. Boston: Blackwell Scientific Publications; 1993. p. 1080 – 92.
8. Brown KH, Khatun M, Ahmad G. Relationship of the xylose absorption status of children in Bangladesh to their absorption of macronutrients from local diets. Am J Clin Nutr 1981;34:1540-7.
9. Baker SJ. Subclinical intestinal malabsorption in developing countries. WHO Bull 1976;54:485-94.
10. O'Boyle CJ, Mac Fie J, Dave K, Sagar PS, Poon P, Mictchell CJ. Alterations in intestinal barrier function do not predispose to translocation of enteral bacteria in gastroenterological patients. Nutrition 1998;14:358-62.
11. Rolles CJ, Kendall MJ Nutter S, Anderson CM. One-hour blood-xylose screening-test for celiac disease. Lancet 1973;10:1043-5.
12. Morin CL, Buts JP, Weber A. One-hour blood-xylose test in diagnosis of cows milk protein intolerance. Lancet 1979;1(8126):1102-4.
13. Schaad U, Gaze H, Hadorn B. Value of 1-hour blood-xylose test in diagnosis of childhood coeliac disease. Arch Dis Child 1978;53:420-2.
14. Christie DL. Use of the one-hour blood xylose test as an indicator of small bowel mucosal disease. Pediatrics 1978;92:725-8.
15. Levine JJ, Seidman E, Walker WA. Screening tests for enteropathy in children. AJDC 1985;14:435-8.