ABSTRACT

This study was aimed to screen the patients for phenylketonuria among chronic psychiatric inpatients. A total of 577 cases were studied which included mentally retarded patients, schizophrenics and those suffering from depressive disorders. During the extensive screening not a single positive case could be identified. The findings of this screening support the previous studies. Looking at low incidence of PKU we do not recommend extensive screening for PKU.

Key words : Phenylketonuria, screening, mental retardation, schizophrenia

Phenylketonuria (PKU) designate a group of inborn error of metabolism of phenylalanine that share the common feature of impaired phenylalanine oxidation, which results in elevated tissue and serum phenylalanine.

Phenylketonuria is a disorder of amino acid metabolism that leads to hyperphenylalaninemia, mental retardation and several psychiatric symptoms that resemble autism or schizophrenia (Jervis, 1963).

Phenylalanine is an essential amino acid for protein synthesis in mammalian tissues. The proportion of dietary phenylalanine that is utilized for protein synthesis varies with age. It is about 50% of the daily intake during early growth and decreases as the growth rate declines.

Physiologically, the most significant pathway of phenylalanine metabolism is through hydroxylation to tyrosine. The reverse reaction i.e. tyrosine to phenylalanine, does not take place even in phenylalanine deficient state. This hydroxylation is limited to the liver, kidney and pancreas in mammalian tissues. Tyrosine, the product of hydroxylation is an essential amino acid and a precursor of such biogenic amines as dopamine and norepinephrine.

Membrane transport of amino acids and synthesis of protein require critical minimum and maximum phenylalanine concentrations in tissues and in brain. Liver phenylalanine hydroxylase regulates the levels of phenylalanine and tyrosine.

The breakdown of concentration boundaries and the consequent devastating effects on brain development are well documented in classic PKU, in which liver phenylalanine hydroxylase is nonfunctional because of mutation.

| Clinical aspect                  | Mental Retardation & associated symptoms if untreated |
|----------------------------------|--------------------------------------------------------|
| Defect                           | Phenylalanine hydroxylase absent/deficient             |
| Blood phenylalanine             | >20 mg/100 ml on regular diet                         |
| Blood Tyrosine                   | Normal to low                                          |
| Urine                            | Elevated phenylalanine metabolites                    |
| Treatment                        | Low phenylalanine diet                                 |

Table showing major features of phenylketonuria:

L-Phenylalanine $\xrightarrow{\text{Hydroxylase}}$ L-Tyrosine
SCREENING FOR PHENYLKETONURIA

The metabolic flow of phenylalanine and tyrosine

MATERIAL AND METHOD

The sample size for screening consisted of 577 patients out of which 351 were suffering from mental retardation, 112 from schizophrenia and 114 from depression, of those which visited to Government Medical College, Nagpur and Mental Hospital, Nagpur.

Ferric chloride test was carried out to screen phenylketonuria.

Ferric Chloride Test (Gowenlock, 1968): A few drops of 10% ferric chloride solution were added to 5 ml of the urine in a test tube. Phenylpyruvic acid gives a green or blue colour for one to two minutes; it then gradually fades. Phenylpyruvic acid may disappear quite rapidly in alkaline urine by oxidation. So the test was carried out on fresh urine. p-Hydroxyphenyl pyruvic acid which is present in more than one percent of the urines of young infants gives a similar colour.

In our study, we have not come across, even a single patient of phenylketonuria.

DISCUSSION

There have been several case reports of unrecognized PKU in adult psychiatric patients, some of whom were not retarded (Perry et al., 1973; Fisch et al., 1979). Such findings, even
A.K. TADAS et al.

if rare, are extremely important, since even PKU that has not been recognized until adulthood may be partially treatable with a low phenylalanine diet (Marholin et al., 1978). The case reports also raise the issue of whether adult psychiatric inpatient populations should be screened for PKU.

At least three screening programs from adult psychiatric inpatients have been reported. Cares (1956), screened 4,246 inpatients of a state mental hospital using the ferric chloride test on urine and more recently Willett et al. (1980) screened 635 consecutive admissions to state mental hospital by testing urine with the dry reagent ferric ammonium sulfate. Neither survey detected any patients with PKU. Reveley and Reveley (1982), who also used a urine test relying on ferric salts, found no cases of PKU among 586 inpatients.

The prevalence of PKU is known to vary directly with the severity of mental retardation. Its prevalence in the educable mentally retarded is between 1/750 and 1/2,363 (Williamson et al., 1968). In contrast, the prevalence of PKU among the severely retarded is about 1/72 (Henderson et al., 1961).

All these surveys are conducted in foreign states and not a single survey has been conducted so far in India, to best of our knowledge. This led us to conduct this study.

However, use of any ferric salt as the screening test might not have detected all patients with PKU, because antipsychotics excreted in the urine can interfere with the colour change produce by a positive ferric salt test (Allen et al., 1964).

Because of the low prevalence of PKU in this psychiatric population, extensive screening programs are probably not necessary. However, even though descriptive data are not available for the patients, we believe, that there are specific clinical indications for carrying out the test on psychiatric patients, including mental retardation, a family history of PKU, or a DSM-III diagnosis of any of the pervasive developmental disorders (Szymanski et al., 1984).

Patients with pervasive developmental disorders may be particularly important to test, given the findings of Lowe et al. (1980), that three of 65 such children had unrecognized PKU, patients with schizophrenia or an unexplained seizure disorder who also have eczema or light hair colour (where both parents are dark haired) should also be considered for testing. Patients who have any of the above characteristics are particularly at risk for unrecognized PKU. We therefore, do not plead for extensive screening for PKU further more.

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SCREENING FOR PHENYLKETONURIA

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