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Vitamin, blood lead, and urine pyrrole levels in Down Syndrome

NUMEROUS STUDIES have been conducted regarding the use of vitamins, minerals, and other nutritional supplements and their effects on the cognitive intelligence of individuals with Down Syndrome.[1-7] These studies were very exact in their protocols for measuring intelligence quotients and in the amount and type of supplements given to the patients. However, only three studies[1,5,8] measured blood or urine levels resulting from the supplements given to the Down Syndrome (DS) individuals.

The purpose of this study was to measure the blood levels of vitamins A, C, E, B1, B2, B3, B6, B12, folate, and urine vitamin C in DS subjects. Because it is perceived to be a widespread pollutant in the environment, and DS subjects are said to have high levels of toxic metals,[1] blood lead was also measured in these individuals. Pyrrole ("mauve factor," kryptopyrrole) which may appear in the urine of schizophrenics and in patients under physical and mental stress was also measured.[9]

Methods

Individuals with Down Syndrome were recruited from the Wichita, Kansas area. All included in the study were previously diagnosed by karyotyping and exhibited the physical characteristics of Down Syndrome. Eleven females and 18 males were included in the study. Ages ranged from 2 yr to 38 yr. Urine samples were collected and blood samples were drawn after an overnight fast. Lead was measured from whole blood in an atomic absorption graphite furnace spectrophotometer (Perkin-Elmer Corp., Norwalk, Connecticut) following the instructions of the manufacturer. Vitamins A and E were measured in serum by the spectrofluorometry method described by Hansen and Warwick.[10]

Vitamin B2 was measured by the erythrocyte Flavin Adenine Dinucleotide (FAD) level method with a VP® analyzer (Abbott Laboratories, North Chicago, Illinois) involving the enzyme glutathione reductase. The enzyme is saturated in vitro by incubating a hemolysate in FAD solution and the activity of the saturated enzyme is compared with the activity of the enzyme in the absence of added FAD.[11] Vitamin B3 was measured using a fluorometric modification of previous methods.[12,13] Vitamin B6 was measured in heparinized whole blood by determination of aspartate aminotransferase activity with the analyzer. The difference in enzyme activity between the samples with and without coenzyme addition is known as the pyridoxal phosphate effect (PPE) and is expressed as percent saturation, which is an indication of an individual's vitamin B6 status.[14] Plasma vitamin C was measured by the dichlorophenol indophenol method.[15] Urine vitamin C was measured using the same method. Urine pyrroles was measured according to the method described by Sohler and others.[16]

Vitamin B1 was performed by the method described by Bayoumi and Rosalki[14] but modified to be run on the instrument.

Results were compared to accepted reference ranges for the age and sex for the specific metabolite studied.

Results

In all 29 subjects, vitamins B2, B3, and B6 were normal. The various other changes are shown in *Table 1*. Eleven out of 29 (37.9%) had one vitamin deficiency, and 2 out of 29 (6.8%) had two deficiencies, none had more than two deficiencies (*Table 2*).

All 29 subjects had normal blood lead levels and 20 out of 28 (71.4%) had elevated urine pyrroles (*Table 3*). Two male subjects, both 24 years of age, had very high levels of urinary pyrroles, 165 and 434 mg/dL respectively (normal is less than 20 mg/dL).

Discussion

Reading[1] found that patients with Down Syndrome are likely to have low levels of certain vitamins, minerals, and trace elements despite supplementation. His study with 27 male and female patients showed that 23 out of 27 (85.2%) had one vitamin deficiency, 13 out of 27 (48%) had two vitamin deficiencies, and 6 out of 27 (22.2%) had three deficiencies. The results from our study of 28 male and female DS patients did not show as high of a vitamin deficiency rate; 11 out of 29 (37.9%) had one deficiency, 2 out of 29 (6.8%) had two deficiencies, and none had three vitamin deficiencies. In a group of 18 DS subjects, Matin and others[5] reported a deficiency in vitamin C, thiamine, and nicotinic acid in two-thirds of the subjects. One-third were reported as having a deficiency of vitamins A and E. In another study, Justice, et al.[8] measured plasma Zn, Cu, folate, vitamin A, B6, retinol binding protein and RBC transketolase, and glutathione reductase in 50 DS subjects. Except for a low plasma zinc, there was no evidence of gross malnutrition.

Reading[1] suggested that some of the DS patients in his study could have a celiac-like disease with impaired pancreatic and hepatic function which could interfere with normal digestion.

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Table 1

Summary of vitamin deficiencies in 18 male Down Syndrome subjects

	Vit. A	Vit. C	Vit. E	Folate	Vit. B12	Vit. B1	Vit. B2	Vit. B3	Vit. B6	Urine vit. C
Number assayed	18	18	18	18	18	18	18	18	18	18
High (%)	0(0%)	5(28%)	1(5.5%)	5(28%)	3(17%)	0(0%)	0(0%)	0(0%)	0(0%)	5(28%)
Low (%)	1(5.5%)	2(11%)	0(0%)	0(0%)	0(0%)	2(11%)	0(0%)	0(0%)	0(0%)	4(14%)

Summary of vitamin deficiencies in 11 female Down Syndrome patients

	Vit. A	Vit. C	Vit. E	Folate	Vit. B12	Vit. B1	Vit. B2	Vit. B3	Vit. B6	Urine vit. C
Number assayed	11	10	11	11	11	11	11	11	11	10
High (%)	0(0%)	2(20%)	0(0%)	1(9%)	2(18%)	0(0%)	0(0%)	0(0%)	0(0%)	1(10%)
Low (%)	1(9%)	4(40%)	0(0%)	0(0%)	0(0%)	3(27%)	0(0%)	0(0%)	0(0%)	5(50%)

Summary of total vitamin deficiencies in 29 Down Syndrome patients

	Vit. A	Vit. C	Vit. E	Folate	Vit. B12	Vit. B1	Vit. B2	Vit. B3	Vit. B6	Urine vit. C
Number assayed	29	28	29	29	29	29	29	29	29	28
High (%)	0(0%)	7(25%)	1(2.4%)	6(20.5%)	5(24%)	0(0%)	0(0%)	0(0%)	0(0%)	6(21.4%)
Low (%)	2(6.8%)	6(21.4%)	0(0%)	0(0%)	0(0%)	5(24%)	0(0%)	0(0%)	0(0%)	9(32.2%)

Table 2

Total number of subjects with vitamin deficiencies

	Male	%	Female	%	Total	%
One deficiency	5/18	27.7	6/11	54.5	11/29	37.9
Two deficiencies	0/18	0	2/11	18.1	2/29	18.1
Three deficiencies	0/18	0	0/18	0	0	0

Table 3

Blood lead and urine pyrroles in 29 male and female Down Syndrome subjects

	Blood lead	Urine pyrroles
Number Assayed	29	28
High (%)	0(0%)	20(71.4%)

Blood lead levels were determined on the 29 DS subjects in this study due to the evidence that DS subjects are likely to have high levels of toxic metals.[1] All subjects in this study had normal blood lead levels.

The finding of high levels of urine pyrrole in 20 out of 28 (71.4%) of the DS subjects was interesting. According to one theory, pyrrole (kryptopyrrole) combines chemically with B6 to remove B6 from the body.[9] However, in all the 20 subjects in this study who had elevated urine pyrroles (one with levels 20 times the normal range), none had a deficiency in vitamin B6 as measured in their blood. Sohler[16] reported that urine pyrroles (the "mauve factor") was found in over 60% of schizophrenics. Others since have corroborated the findings while others have not. Further studies need to be done to confirm the finding of high levels of urine pyrroles in Down Syndrome individuals and if confirmed, exactly what the increase of this urine metabolite means.

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