



RESEARCH ARTICLE

Magnesium, Zinc, and Vitamin B6 Related Measures in Children with Tourette's Syndrome

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Abstract

Background and Objective: The functions of magnesium, zinc, and vitamin B6 have been hypothesized to work against the symptoms of Tourette Syndrome (TS). This study tested the hypothesis that children with TS would have low values for markers of status for magnesium, zinc, and vitamin B6.

Methods: Children with TS were compared to control children for blood measures related to nutritional status of the above mentioned nutrients.

Results: No differences were seen for any of the following measures: plasma magnesium, erythrocyte magnesium and potassium, plasma zinc, plasma activity of the zinc enzyme 5'-nucleotidase and plasma B6 as pyridoxal phosphate.

Discussion: These results suggest that children with TS do not show depletion of magnesium, zinc, or vitamin B6. However, this study does not rule out that TS creates conditions where normal nutrient levels do not provide adequate functional capacities.

Keywords: Tourette's syndrome; Magnesium; Zinc; Vitamin B6

Introduction

Tourette's syndrome (TS) is a chronic complex neurological movement disorder characterized by multiple vocal and motor tics [1]. Conventional treatments have intolerable side effects or are ineffective for many patients. This has spawned frequent use of nutritional supplements as alternative therapy [2]. However, as noted by Ludlow and Wilkins, the efficacy of supplements is not backed by well controlled studies [3].

One study, though based on anecdotal evidence and survey statistics, shows interesting results. The supplement contained magnesium, zinc and vitamin B6 (ts-PLUS CONTROL™ by Bontech® Supplements, Ltd.). In this study, 85% of the supplement consumers reported improved TS symptoms [4]. In addition, 75% called it their best treatment. Similarly, a non-controlled, open trial of magnesium + vitamin B6 showed improved symptoms [5].

The California Pharmacist's Association taught in their Feb. 2003 continuing education program that magnesium supplementation provides an alternative TS treatment [6]. Some TS symptoms overlap magnesium deficiency [3,6]. For example, magnesium deficiency can cause high activation of NMDA receptors [7]. NMDA receptors in the feline retrorubral nucleus can cause tic-like facial contractions. The retrorubral nucleus can project afferent fibers into the caudate nucleus [8]. The caudate nucleus in the basal ganglia could be the locus of TS pathology [9].

In another area, high values for kynurenine, a tryptophan

metabolite, can occur in TS [10, 11]. Such high values can result from decreased kynureninase activity, which can occur in magnesium deficiency [12, 13]. Kynurenine injections increases TS-like tics in laboratory animals [14].

A vitamin B6 coenzyme (PLP) is needed for kynureninase function. The coenzyme formation may be inhibited by magnesium deficiency [15]. Vitamin B6 deficits may also aggravate TS in other ways since both B6 deficiency and TS can produce hyperirritability, inattention, and abnormal head movements [16].

Zinc may also relate to TS symptoms since zinc touch so many processes [17]. A zinc-TS connection could involve the neurotransmitter gamma-aminobutyric acid (GABA). Increases in this molecule may help with TS [18]. Zinc deficient rats have diminished capacity to produce GABA [19]. Also, low serum zinc is seen in a group of TS children [20]. Although a zinc-TS connection remains inconclusive, the Internet notes frequent interest in this area.

This study compared TS children to controls for blood status markers for magnesium, vitamin B6, and zinc. The hypothesis was the TS children would show lower values.

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Study Population and Methods

The Ohio State University Biomedical Human Subjects Institutional Review Board approved this protocol. Permission was obtained from the National TS Association's Medical Advisory Board to recruit members. Informed consent was given by parents/guardians; subjects signed an assent form. Permission to view medical information for confirmation of TS diagnosis and symptomology description was obtained from the parent/guardian. Males and non-pregnant females aged 10-17 were recruited from the TS Association's Central Ohio support group and the Reynoldsburg United Methodist Church (11 TS and 11 controls). Each group had 8 males + 3 females (TS age: 12.8 + 2.3; control age: 13.2 + 1.9; mean + SD). Vitamin and mineral supplements were not taken 2 wk before blood draw. Participants were asked to fast 12 h before a morning blood draw into a heparinized tube (batch checked for magnesium and zinc contamination). Specimen identities were blinded to the person doing analysis.

Plasma magnesium was assessed colorimetrically (kit from Sigma Chemical Co, St. Louis, MO). Atomic absorbance spectrometry was used for erythrocyte magnesium and potassium and plasma zinc. Plasma 5'-nucleotidase activity was measured by a kinetic spectrophotometric assay [21]. Plasma vitamin B6 was quantitated as PLP by HPLC.

Results for each group were compared using unpaired t-test (significance at $p < 0.05$). Results for different assays were compared by Pearson correlation coefficient analysis. Statistical analysis used the Statistical Package for the Social Sciences (SPSS) program. Outliers were identified by boxplot graphs using a Minitab program.

Results

No significant differences were found for TS vs controls by unpaired 2-tailed t-tests (Table 1). Measure were: plasma magnesium ($p = 0.545$); erythrocyte magnesium ($p = 0.376$); erythrocyte potassium ($p = 0.596$); plasma zinc ($p = 0.834$); plasma 5'-nucleotidase ($p = .873$). Similarly, no significant differences were seen for plasma PLP (Figure 1).

No outliers were found for most measures. However, a low outlier occurred for one control for plasma zinc (0.69), and a high outlier occurred for 5'-nucleotidase activity in a TS child (7.5). These were not excluded from Table 1 data calculations. One outlier for PLP occurred in the controls (Figure 1). This

value was about 3 times the mean calculated with the outlier value. The controls did not differ significantly from the TS group with or without the outlier ($p = 0.45$ without exclusion; $p = 0.900$ with exclusion).

Erythrocyte magnesium levels significantly correlated with erythrocyte potassium levels (Pearson correlation coefficient $r = .853$) ($p = 0.002$, 2-tailed).

Discussion

The TS children showed no signs of depletion for magnesium, zinc, or vitamin B6. Thus, the project hypothesis of poor status with TS was not supported. Subject number was not large. However, three reasonings suggest the results would apply to larger subject numbers. One, standard deviations were low. Two, where normal ranges were available, TS vales fell in those ranges (Table 1) (Figure 1). Third, only 3 outliers were seen for all measures in both groups combined (different subjects for each outlier).

This study did not consider all status indicators for magnesium, zinc, and B6, but the ones chosen had rationale. Plasma PLP is recognized for evaluating B6 status [22]. Plasma magnesium is the standard clinical assessment even though values don't always reflect moderate deficiencies [17]. Even so, the very similar results between groups suggest that big differences in magnesium status were unlikely. Moreover, erythrocyte magnesium also showed no difference. Low values can be seen in intracellular

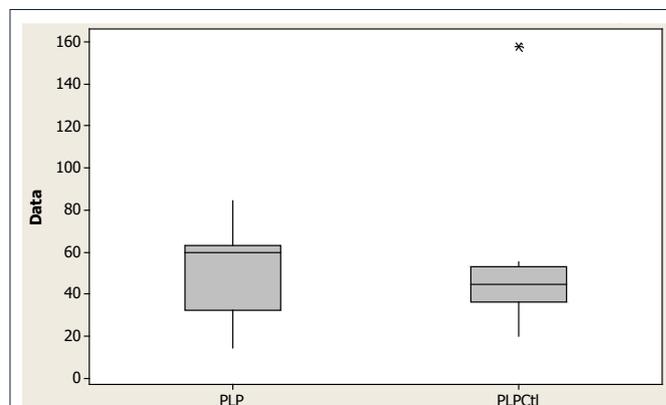


Figure 1: Boxplots of pyridoxal 5'-phosphate (PLP) values (nmol/L). No significant difference was found between Control (PLPct) and TS (PLP) values (unpaired t-test, $p > 0.05$). No accepted normal mean, though 35 and 41 nmol/L have been cited as normal.

Table 1: Blood test results in children with and without Tourette Syndrome.

Measure	Tourette Syndrome	Control	Normal Range
Plasma magnesium (mEq/L)	1.76 ± 0.20	1.82 ± 0.27	1.5-3.0*
Erythrocyte magnesium (mg/L)	44.9 ± 9.7	41.4 ± 6.6	40-64**
Erythrocyte potassium (mmole/L)	74 ± 14	70 ± 13	***
Plasma zinc (µg/dL)	115 ± 19	114 ± 18	64-124 (Lin et al. 2012)
Plasma 5'nucleotidase (U/L)	4.8 ± 1.2	4.9 ± 1.0	***

Values are means ± SD; $p > 0.05$ for all measures Tourette's Syndrome vs Control, unpaired t-test

*<https://www.fda.gov/downloads/ICECI/Inspections/IOM/UCM135835.pdf>

** <http://www.questdiagnostics.com/testcenter/BUOrderInfo.action?tc=10551&labCode=AMD>

*** None established for this age group

magnesium deficiency, and this measure is a validated test for assessing chronic marginal magnesium deficiency [23]. Erythrocyte potassium also showed no difference. Although this measure is not solely determined by magnesium status, magnesium function helps transport potassium into cells [24]. Recently, magnesium supplementation raised erythrocyte potassium concentrations in active young adults [25]. Also, in the present study, erythrocyte magnesium correlated positively with erythrocyte potassium.

Plasma zinc was examined because it provides the standard way of evaluating zinc status. Values can be affected by other factors, but these generally produce low readings, which were not seen here. Plasma zinc may not always decrease rapidly in mild zinc deficiencies, but plasma activities for the zinc enzyme 5'-nucleotidase can respond more in these cases [26]. In the present study, the two groups showed no difference for these activities either [27].

Conclusion

The subjects with TS showed no significant differences versus controls with both groups showing means in normal ranges when known. The current results, even if reproduced in larger studies, do not rule out that increasing intake of magnesium, zinc and B6 could reduce TS symptoms in some people. Even if these people are not depleted in these nutrients, normal function may not keep pace with high functional needs in TS. For example, if kynurenine is being produced at a high rate, higher than normal magnesium intake may be needed to counteract this process. Further research should examine the possibility that functional deficiencies can occur in TS despite the lack of nutrient accumulation deficits.

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Conflicts of Interest and Source of Funding

This project received no outside funding. At the time of the research, BG owned Bontech Supplements, which sold product to people with TS. This company no longer operates. RAD has no conflicts of interest.

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