Author’s response to reviews

Title: Prenatal Exposure to Herbal Remedy in a Girl with Autism Spectrum Disorder: A Case Report

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Author’s response to reviews: see over
November 16, 2010

Dear Dr. Khalid Munir,

RE: Manuscript ID JMCR entitled "Prenatal Exposure to Herbal Remedy in a Girl with Autism Spectrum Disorder: A Case Report"

Thank you for the thoughtful and useful comments and suggestions sent by the reviewers. We believe we have now satisfactorily addressed all of the issues raised. We highlight in yellow the changes introduced in the text. Additionally, we have now made language changes and corrected any grammatical errors that needed correcting. We have included 3 new references and we have eliminated 2 references (numbers 11 and 12).

References eliminated:

References incorporated: we have highlighted in yellow in the text.

1) Case presentation (Paragraph 5), please elaborate the drug history a bit more. The reader may be more interested in knowing the duration of the use of the drug, especially when it was stopped before pregnancy. Moreover, in maternal history exclusion of the other conditions which could cause weight loss during pregnancy must be mentioned to nullify the confounding factors.

In Paragraph 5, we have now included the duration of drug use (i.e. maternal drug intake begun one year prior to conception up to 3 years postnatal life). In addition, we have indicated that the patient had a non-restrictive diet with a high caloric intake. Paragraph 5 now reads as follows:

From a year prior to conception the mother began a weight loss diet and ingested approximately 1,200 mg per day of “horsetail” (equinosetum arvense) herbal remedies up to 3 years after birth. At conception maternal body mass index (BMI) was 31.6 kg/m² that decreased to 30.1 kg/m² at the end of gestation, a net loss of almost 4 kg. Throughout pregnancy, despite adequate caloric intake, the mother reported a daily food intake of folate (199 µg), vitamin of B1 (1.18 mg), vitamin B6 (1.31 mg) and vitamin B12 (30.8 µg). Vitamin B12 and folate intake supplements began approximately on day 42-48 of gestation.

2) As per history, she started B12 and Folate supplementation on day 42-48, this fact needs to be acknowledged in discussion, because the relationship of folate deficiency with autism is something well established and is a confounding factor.
Other research studies have speculated that folic acid deficiency may be associated with autism. We have included one reference in this work, and made the following changes in the text:

In the patient’s mother, the ingestion of B-complex vitamins did not reach the Recommended Daily Allowance levels for pregnant women (thiamine 1.4 mg/day, folic acid 600 mcg/day) and lactating women (thiamine 1.4 mg/day, folic acid 500 mcg/day). Additionally, this possible neurotoxicity caused by thiamine and folic acid deficiency could have been potentiated by the horsetail’s anti-thiamine activity and ethanol exposure during early pregnancy [11,18-20].


3) If possible, just mention the half-life of the thiaminase. This will give us a rough idea about the duration during which thiaminase related effects of the herbal medication can occur.

Horsetail remedies are not recommended for use during pregnancy or breastfeeding, since little information is available on their safety. Horsetail remedies have been known to cause neurodevelopmental toxicity, and have a high potential to cause thiamine depletion and nicotine-like effects [9,10,11]. Thiamine is water soluble and has a short half-life. Thiamine status can be altered due to: dietary thiamine deficiency, breakdown by thiaminase and the administration of thiamine analogues [12]. Recent phytochemical analyses have detected the presence of tannins, saponins, sterols and flavonoids in horsetail residues [13-15]. In addition, horsetail contains thiaminase, an enzyme that destroys thiamine (vitamin B1) and, with long-term use, could lead to vitamin deficiency [11]. Thiaminase-induced deficiency of thiamine has been implicated to thiamine degradation by thermolabile thiaminases present in raw fish and shellfish [16].

Plant thiamine antagonists are heat-stable and occur as both the ortho- and para-hydroxyphenols. Some examples of these antagonists are caffeic acid, chlorogenic acid, and tannic acid. These compounds interact with the thiamine to oxidize the thiazole ring, thus rendering it unable to be absorbed resulting in thiamine deficiency. Two flavonoids, quercetin and rutin, have also been implicated as thiamine antagonists [17]. Several spontaneous central nervous system disorders due to thiaminase effects have occurred in experimental animal studies [18].

4) Please rewrite the reference number 16 as names of the two of the authors are Missing.

Reference number 16 is number 11 in this revised version of the manuscript. We have fixed the reference. It now reads as follows:

Thank you
I await your news,
Kindly,
Ortega Garcia JA, MD, PhD