The risks of adding orthostatic intolerance to the list of the differential diagnoses of somatic symptom disorder

To the Editor:

Tarbell et al reported extraintestinal comorbidities in children with functional nausea; we agree with their call for a holistic approach.[1]

Although warning against the risks and costs of unnecessary diagnostic procedures, the authors support the performance of autonomic testing addressing orthostatic intolerance. In view of the lack of a clear clinical significance of these tests, the Editorial by Santucci mitigates this conclusion.[2] We suggest that the search for orthostatic intolerance in this context may not be useful.

According to the *Diagnostic and Statistical Manual of Mental Disorders Fifth Edition*, school, sport, and social withdrawal, together with excessive related worries and thoughts, support the diagnosis of somatic symptom disorder (SSD).[3] In the study population, a high frequency of school absence and mood disorders is reported, suggesting the psychosomatic nature of the children's complaints.

The diagnosis of SSD should be made on the ground of the specific *Diagnostic and Statistical Manual of Mental Disorders* criteria, and does not rely on the exclusion of underlying organic conditions, often being reported in association with chronic diseases as well. Tests addressing orthostatic intolerance may simply add another diagnostic procedure to the endless list of poorly substantiated possible alternative diagnoses.[4] Children with long-lasting nonspecific symptoms are prone to receive alternative diagnoses before the recognition of SSD,[5] including chronic Lyme disease,[6] fibromyalgia, chronic fatigue syndrome, and postural orthostatic tachycardia. These diagnoses may expose patients to the risks related to the missing recognition of SSD, including the perpetuation of disability, and the delayed identification of underlying psychiatric conditions.

Rather than orthostatic intolerance, physicians should address markers for missed functioning and associated risk factors (eg, familial and academic pressure, abuse, bullying, gender dysphoria), to inform a positive diagnosis of SSD, avoiding a "Munchausen by physician" mechanism.

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Reply

To the Editor:

We thank Wiel et al for their thoughtful comments on our report. To clarify, our study aimed to identify comorbidities in pediatric patients with functional nausea and evaluate the diagnostic yield of the gastrointestinal tests they underwent. Our cohort was not a group of patients diagnosed with a somatic symptom disorder. We found these youth are often subjected to invasive diagnostic or surgical procedures performed based on "soft" indications putting them at risk for iatrogenic problems. Coexisting psychiatric symptoms were common in these patients. It is reasonable to add somatic symptom disorder to the differential. We appreciate the authors bringing attention to this entity as part of a biopsychosocial approach to these complex patients. However, just as vague gastrointestinal complaints do not prove a gastrointestinal origin, similarly, the presence of psychiatric symptoms, even with somatic symptoms, does not necessarily indicate an somatic symptom disorder. The presence of psychiatric comorbidity in youth with unexplained nausea can be dismissed as only a psychiatric condition. This practice may result in missing a potentially treatable health condition. Therefore, we still recommend testing for orthostatic intolerance (OI) when symptoms of orthostatic dizziness, lightheadedness, or syncope are present. The identification

of conditions such as postural orthostatic tachycardia syndrome based on OI and nausea has resulted in a treatable problem in many of these youth.[1] In fact, we have seen the nausea resolve when the OI is treated.[2] Screening for OI can be easily done in the physician's office without the need to expose the child to unnecessary procedures. If there is evidence of OI, the child and family can be advised to follow recommendations for management of OI, the first choice of which is lifestyle modifications, such as increased fluid intake and physical activity.[3]

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A phase II randomized clinical trial of the safety and efficacy of intravenous umbilical cord blood infusion for treatment of children with autism spectrum disorder

To the Editor:

Dawson et al have drawn attention to the outcomes of umbilical cord blood (UCB) administration for the treatment of 180 children with autism spectrum disorder (ASD).[1] Because there is a substantial interest in stem cell therapy as a potential candidate or therapeutic approach for ASD, these outcomes are noteworthy. The authors provide findings from a large sample size, randomized process with a control group, and processing paradigms, although the results did not support the efficacy of UCB administration. However, several points may influence interpretation of the findings.

First, we note that the authors administrated a relatively low dose of UCB-derived mononuclear cells and CD34+ cells compared with previous studies.[2,3] Other investigators have suggested that the minimum cell dose at which the CD34+ could show influence in nonmalignant diseases is 1.7×10^5 CD34+ cells per kilogram of patient's body weight (PBW).[4] The CD34+ cells in the current studyare 0.3×10^5 cells/kg PBW and 0.7×10^5 cells/kg PBW for autologous UCB and allogeneic UCB, respectively. In addition, intravenous infusion of cells limits delivery, as cells might be trapped in organs such as the lung, heart, liver, or kidney, which in turn reduces therapeutic effects on the brain.[5] Hence, the dosage of UCB may be a reason for the lack of evidence of efficacy. Second, the authors reported the results of a 6-month follow-up; this is a relatively short period to observe the progressive improvement of children with ASD. Previous studies demonstrated improvements observed after 12-month and 18-month follow-up, especially on the Childhood Autism Rating Scale score[3] and the Clinical Global Impression Scale.[6,7]

In summary, the authors' conclusion may be limited within the trial's scope and suggest no significant difference between 2 groups when CD34+ cells were administrated intravenously at the lower dose with a 6-month follow-up. Future research using UCB (high CD34+ cells and multiple doses) via other administration routes should be considered.

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