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ORIGINAL ARTICLE

Improvement of autism spectrum disorder symptoms in three children by using gastrin-releasing peptide☆,☆☆

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KEYWORDS
Gastrin-releasing peptide receptor;
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Abstract
Objective: To evaluate the safety, tolerability and potential therapeutic effects of gastrin-releasing peptide in three children with autistic spectrum disorder.
Methods: Case series study with the intravenous administration of gastrin-releasing peptide in the dose of 160 pmol/kg for four consecutive days. To evaluate the results, parental impressions the Childhood Autism Rating Scale (CARS) and the Clinical Global Impression (CGI) Scale. Each child underwent a new peptide cycle after two weeks. The children were followed for four weeks after the end of the infusions.
Results: The gastrin-releasing peptide was well tolerated and no child had adverse effects. Two children had improved social interaction, with a slight improvement in joint attention and the interaction initiatives. Two showed reduction of stereotypes and improvement in verbal language. One child lost his compulsion to bathe, an effect that lasted two weeks after each infusion cycle. Average reduction in CARS score was 2.8 points. CGI was ''minimally better'' in two children and ''much better'' in one.

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☆☆ Study linked to the Hospital de Clínicas de Porto Alegre (HCPA), Porto Alegre, RS, Brazil.

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Conclusions: This study suggests that the gastrin-releasing peptide is safe and may be effective in improving key symptoms of autism spectrum disorder, but its results should be interpreted with caution. Controlled clinical trials–randomized, double-blinded, and with more children–are needed to better evaluate the possible therapeutic effects of gastrin-releasing peptide in autism.

PALAVRAS-CHAVE
Receptor do peptídeo liberador de gastrina;
Neuropeptídios;
Autismo;
Transtorno do espectro autista

Melhoria nos sistemas do transtorno do espectro autista em três crianças, utilizando peptídeo liberador de gastrina

Resumo

Objetivo: Avaliar a segurança, tolerabilidade e possíveis efeitos terapêuticos do peptídeo liberador de gastrina em três crianças com transtorno do espectro autista.
Métodos: Estudo de casuística com administração intravenosa de peptídeo liberador de gastrina na dose de 160 pmol/kg por quatro dias consecutivos. Para avaliar os resultados, foram utilizadas a impressão dos pais, a Escala de Classificação de Autismo na Infância (CARS) e a Escala de Impressão Clínica Global (CGI). Cada criança foi submetida a novo ciclo de peptídeo após duas semanas. As crianças foram acompanhadas por quatro semanas após o término das infusões.
Resultados: O peptídeo liberador de gastrina foi bem tolerado e nenhuma criança apresentou efeitos adversos. Duas crianças apresentaram melhora na interação social, com melhora na atenção compartilhada e nas iniciativas de interação. Duas mostraram redução dos estereotipias e melhora na linguagem verbal. Uma criança perdeu sua compulsão por banhos, efeito que durou duas semanas após cada ciclo de infusão. A redução média no escore da CARS foi 2,8 pontos. Quanto à CGI, os resultados foram ''minimamente melhor em duas crianças'' e ''muito melhor'' em uma.
Conclusões: Este estudo sugere que o peptídeo liberador de gastrina é seguro e pode ser efetivo na melhora dos principais sintomas do transtorno do espectro autista, porém seus resultados devem ser interpretados com cautela. Ensaios clínicos controlados, randomizados, duplo-cego e com maior número de crianças são necessários para melhor avaliar os possíveis efeitos terapêuticos do peptídeo liberador de gastrina sobre o autismo.

Introduction

Autism is a pervasive development disorder characterized by severe impairment in reciprocal socialization, qualitative problems in communication, and repetitive or unusual behavior.[1] The current estimated prevalence of autism is one in every 66 children.[2] Diagnosis is clinical and to date there is no specific treatment.[3] Neurochemical, neuropathological, neuroimaging, and genetic studies suggests disorganization of cortical neurons and cerebral disconnectivity, determined by both genetic and environmental factors.[4]

Over recent years the effects of endocrine peptides, including gastrin-releasing peptide (GRP), on the central nervous system (CNS) have been investigated.[5] GRP is released by glutamatergic neurons and acts as a neurotransmitter that regulates neuronal excitability.[6–8] In the brain, the gastrin-releasing peptide receptor(GRPR) is highly expressed in cerebral regions related to cognitive function and emotional processing, such as the dorsal hippocampus and basolateral amygdala.[6–9] Experimental studies have shown that pharmacological blockade of GRPR in neonatal rats leads to reduced preference for maternal odor and the development of late and permanent deficits in social interaction, a behavior consistent with animal models of autism.[10–12]

In this experimental study, GRP was given intravenously to three children with autism to test its safety, tolerability, and possible therapeutic effects on autism spectrum disorder (ASD) symptoms. To the best of the authors' knowledge, this is the first report of GRP use in humans with autism.

Methods

Children with autism diagnosed according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR),[13] aged from 3 to 18 years, were considered suitable for selection. Exclusion criteria were serious clinical disorders, psychiatric diseases, increased acid production in gastrointestinal system, secondary autism, and changes in medication or other treatments during the previous four weeks. Parents signed an informed consent and committed themselves to maintaining the current treatment unchanged during the study period.

The sample was selected by convenience from children seen at the ASD Clinic at the Hospital de Clínicas de Porto