Saudi Pharmaceutical Journal (2013) **21**, 233–243

King Saud University

Saudi Pharmaceutical Journal

www.ksu.edu.sa
www.sciencedirect.com

REVIEW

The role of nutraceuticals in the management of autism

Abdulrahman S. Alanazi *

Consultant Clinical Pharmacist, P.O. Box 1627, Hail 81441, Saudi Arabia

Received 4 July 2012; accepted 11 October 2012
Available online 23 October 2012

KEYWORDS

Autism;
Autistic spectrum disorders;
Nutraceuticals;
Vitamins;
Diet;
Probiotics

Abstract Autism and related disorders are increasingly prevalent behavioral syndromes of impaired verbal and nonverbal communication and socialization owing to neurodevelopmental abnormalities. The most recent estimate for the prevalence of autistic disorders is about 1% on a global scale. Etiology of autism is multifactorial and multidimensional that makes therapeutic intervention even harder. Heterogeneity of genetic factors, oxidative stress, autoimmune mechanism, and epigenetic mechanisms complicate the nature of pathogenesis of the disease. Nutraceutical approach to treat this disease is a promising strategy, especially in some areas, it is more attractive than others. This review critically analyzes the roles of vitamins and cofactors, dietary modifications and gut abnormalities, probiotics and prebiotics, phytochemicals, and environmental factors in order to determine the state of evidence in nutraceutical-based autism management practices. This article presents a systematic review of randomized- and placebocontrolled trials to examine the evidence supports the use of autism nutraceuticals. The results will be discussed in the light of all relevant evidence generated from other clinical and exploratory studies.

Contents

1. Introduction . . . 233
1.1. Nutraceuticals and autism . . . 234
2. Method . . . 234
3. Results . . . 235
4. Discussion . . . 235
5. Conclusion . . . 241
References . . . 242

* Mobile: +966 501744888.
E-mail address: Alanazi_abdulrahman@yahoo.com
Peer review under responsibility of King Saud University.

Production and hosting by Elsevier

1. Introduction

Autistic spectrum disorders (ASDs) are increasingly prevalent neurodevelopmental behavioral syndromes of impaired verbal and nonverbal communication and socialization skills among

1319-0164
http://dx.doi.org/10.1016/j.jsps.2012.10.001

children. Individuals with ASDs suffer from impairments in social interactions; in language, communication and imagination; and in the range of interests and activities. In the last few decades, refinements of diagnostic techniques have led to the differentiation and variation in traditional use of the term autistic disorder to include autism, Asperger's syndrome, Rett's syndrome, and childhood disintegrative disorder. The ASD onset occurs during the first three years of life and has a gender bias with a ratio of 5 males to 1 female (World Health Organization, 1992; Fombonne, 2002; Rapin, 2002; Tonge and Brereton, 2011; Center for Disease Control). Common comorbidities associated with ASDs include gastrointestinal disease and dysbiosis, autoimmunity and mental retardation (Bolte and Poustka, 2002; Sweeten et al., 2003; Buie et al., 2010).

One of 88 children in USA develops any form of ASD, and global prevalence is about 1% (Muhle et al., 2004). In Saudi Arabia, there were 42,500 confirmed cases of autism in the year 2002 (Al-Yafee et al., 2011). In reality, many cases remain undiagnosed in the Arabian Peninsula as suggested by Mostafa et al and other authors as well, who indicate autism prevalence of 1.4 cases per 10,000 children in Oman and 2.9/10,000 in United Arab Emirates (Mostafa, 2011). About 22–30% of children suffering from ASDs also develop seizures without exhibiting underlying pathology. Moreover, about 25% children with ASDs show hypersensitivity-like symptomatology (Theoharides and Zhang, 2011).

Among the ASDs, autism is particularly a severe syndrome characterized by the impairment of reciprocal social interactions and communication development along with extremely restricted and repetitive stereotyped behaviors and corresponding motivational profiles (American Psychiatric Association, 2000). Among the autistics, about 85% suffer from idiopathic autism or primary autism where the exact cause of the disease remains unknown. On the other hand, symptomatic or secondary autism where the causative factor can be determined exists only in 15% of the cases (Sakai et al., 2011).

The exact etiology of autism is unclear, and because of the fact that its pathogenesis starts quite early during embryonic development preventive measures are hard to take. Multifactorial and multidimensional causation of autism include genetic basis and heterogeneity, gastrointestinal pathology, autoimmune complications, inflammation, high level of oxidative stress, decreased ability of the body to detoxify toxins, decreased function of mitochondria, and iatrogenic causes such as vaccinations and food additives. Thus, a number of factors contribute to the pathogenicity of ASDs, of which many are interactive. Autoimmunity to central nervous system exists in many autistic patients (Al-Yadhi and Mostafa, 2011). Oxidative stress from reactive oxygen species is a substantial causative factor for the development and severity of ASDs (Al-Ayadhi et al., 2012).

Genetic studies involving twins, families and genetic associations have revealed a strong genetic correlation in the etiology of autism (Muhle et al., 2004; Folstein and Piven, 1991; Campbell et al., 2006). Heritability in autism exists in as high as 90% of cases. Moreover, twin studies have revealed monozygotic concordance rate of 36–96% as against 0–27% in dizygotic twins (Bakare et al., 2011). Furthermore, genetic heterogeneity behind ASDs is a crucial aspect of their etiology. Also, the potential role of X-linked inheritance has also been demonstrated (Liu et al., 2001; Glessner et al., 2009). Environmental factors also have potentials to contribute significantly to autistic pathogenesis, which besides others, also involve epigenetic mechanisms (Folstein and Piven, 1991; Kinney et al., 2008; Kubota et al., 2012) and even there are some theories from an evolutionary perspective as well (Ploeger and Galis, 2011). Recent studies in animals as well as in humans have identified a vital aspect of gene-environment interaction. An individual with a particular genetic makeup is far more vulnerable to any behavioral disorder such as autism if exposed during the perinatal period to an environmental pathogen or stress (Meaney and Szyf, 2005; Caspi and Moffitt, 2006; Rutter et al., 2006).

1.1. Nutraceuticals and autism

Food is no longer valued from a nutritional point of view only rather it is equally valuable from a health perspective. The use of food or food products in disease prevention or health promotion is an emerging trend that has given rise to the concept of 'nutraceuticals'. Nutraceuticals is a term first coined in 1989 by the US Foundation for Innovation in Medicine (FIS). FIS defined nutraceuticals as "any substance that is food or a part of food and provides medical or health benefits, including the prevention and treatment of disease" (Brower, 1998; Alissa and Ferns, 2012). General forms of nutraceuticals consist of dietary supplementation (products that supplement the diet such as vitamins, minerals, amino acids, and herbal substances in any composition). Moreover, the term nutraceuticals go a level up in the sense that it also helps in the prevention or treatment of disease by modifying conventional foods like sole meal as against dose based dietary supplements (Kalra, 2003; Pandey et al., 2010).

The use of nutraceuticals in autism management can create a successful integrative model with current treatment to achieve desired results. Nutraceuticals offer several promising benefits that may include promoting healthy gut and lowering body burdens of toxins, reducing excitotoxicity, improving antioxidant capacity, enhancing immunomodulatory systems and minimizing stress and environmental contamination/hazards (Defeat Autism Now (DAN) Project, 2002). Indeed, in 1995, a campaign (Defeat Autism Now) was started by a collaborative network including scientists and physicians with support from parents of autistic children and community. Besides boosting passion for research and practice, to its favor, go a number of scientific publications specifically intervention protocols that guide physicians to manage autistic patients (Levy and Hyman, 2008). Nutraceuticals can significantly advance autism management in a situation where etiological complexity and limitations in earlier interventions hinder therapeutic regimens. Because of their potential benefits, a number of companies have produced several compositions of nutraceuticals available in the market, and there is anecdotal evidence for their efficacies in autistic as well as patients with similar neurological complications. This paper reviews research-based findings about various factors of nutraceuticals in relation to their potentials in autism treatment by consulting the most relevant literature available on this subject.

2. Method

In this systematic analysis, literature was gathered from Pubmed (US National Library of Medicine) /PsycINFO/CINAHL databases using search keywords with restriction to articles