DIET AND NUTRITION IN AUTISTIC SPECTRUM DISORDERS

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ABSTRACT

Introduction: *The Autistic spectrum disorders (ASD) is a group of neurodevelopmental disorders that are characterized by poor social skills with difficulties in communication, stereotyped and repetitive behaviours, and restricted interests. Researches have shown that quite a number of children with ASD often present with gastrointestinal (GI) problems which have been thought to be one of the aetiological factors for the disorder and a reason for the increase in severity of the behavioural symptoms of autism. This led to the advent and use of biomedical treatments (non-drugs, special diets) by parents for the treatment of the disorder.*

Objective: *This article elucidates the relationship between diet and the severity of ASDs, and the use of special diets in the management of autism.*

Method: *A review of literature was done to examine gastrointestinal pathology associated with ASD and how dietary control can be used in managing them. A thorough search through medical databases including PubMed, Google Scholar and MEDLINE was carried out.*

Results: *It was shown that there is a significant prevalence of intestinal abnormalities in children with ASD which include chronic constipation, diarrhoea, abdominal pain and so on. In addition, there is alteration in serotonine signaling which may be responsible for some of the symptoms. Children with ASD tend to be selective in what they eat and as such some of them may present with some vitamin and mineral deficiency. Parents of these children have reported improvement in symptoms as a result of use of gluten free, casein free (GFCF) diets. However, research has not backed this up as the use of diet as a treatment option and an indication of severity may be due to unique gastrointestinal properties in each child.*

Conclusion: *More studies should be carried out to show the effects of dietary control in the alleviation of behavioural and gastrointestinal symptoms associated with ASD.*

INTRODUCTION

The Autistic spectrum disorders (ASD), more commonly referred to as Autism is not a single disorder but a syndrome of disorders. It is a group of neurodevelopmental disorders that are characterized by poor social skills with difficulties in communication, stereotyped and repetitive behaviours, and restricted interests. The symptoms vary at different ages depending on the child and the influences of the environment but are commonly first noticed in the first 3 years of life which is usually the age at which the child starts school[1]. According to the Centre for Disease Control and Prevention(CDC) 2012 as cited by Kral *et al.*,[2] the symptoms could come as a failure to develop certain skills, or a regression after normal development has already started or a complete stop in development. Children with Autism are found to stay on their own most times, with difficulties in forming relationships, no interaction with their peers and never showing interests in group plays. The parents of these children realize that they are poor at using words, not communicating like others and have developed repetitive skills like spinning objects[3].

The autistic spectrum consists of disorders such as childhood autism, early infantile autism, Aspergers disorder, Kanners autism, high functioning autism, atypical autism, pervasive developmental disorder not otherwise specified and childhood disintegrative behaviour[1]. Due tothis, the onset, manifestations, presentations and the severity of the disorder vary and are dependent on the autistic condition, developmental level and chronological age of the children[1]. The prevalence of the autistic spectrum disorders as reported by the Centre for Disease control and Prevention in 2012 through the 14 Autism and Developmental Disabilities Monitoring (ADDM) Network sites in 2008 was that 1 out of 88 children had ASD and that it was commoner (about four times more) in male children (1 in 54) than in female children (1 in 252). This prevalence has been increasing over the years mostly because there is an increasing awareness of the condition and there are better diagnostic methods and guidelines for the disorder[2].

The primary cause of ASD is not fully known but it has been found to be associated with a lot of comorbidities such as other neurodevelopmental disorders, mental and behavioural conditions which include but are not restricted to conduct disorders, attention deficit hyperactivity disorder, intellectual disability, mood

disorders, feeding and elimination disorders, language impairment, epilepsy and motor disorders. The presence of these comorbidities and their severity determine the prognosis of the disorder[1]. The risk factors for ASD have been found to be both environmental, genetic and physiological. The environmental risk factors include advanced paternal and maternal age at the time of pregnancy, in-utero exposure to sodium valproate and low birth weight. Currently, the autistic spectrum disorders found to be due to genetic factors account for about 15% of cases and are thought to be due to genetic mutations although they are not fully penetrant and not expected to be transferred from one person to the other in the family[1]. Although this genetic risk has been linked to mutations, no specific mutation has yet to be identified. Some investigations regarding endogenous biomarkers for autism has been done and they may help with the identification of the defective genes.

ASD has also been found to be related to genetic conditions such as Fragile X Syndrome, Rett syndrome with which it shares a lot of features such as sensory impairment and language and social interaction problems. Making a diagnosis of these conditions would require clear and accurate differentiation between them as only minor differences separate them[4].

THE GASTROINTESTINAL SYSTEM OF THE AUTISTIC CHILD

Of the many medical problems frequently complained about by parents of autistic children, gastrointestinal symptoms are the commonest. These GI symptoms have been reported by parents to be involved with increased severity of the symptoms of autism[5]. The symptoms vary and include but are not limited to chronic constipation, diarrhoea, abdominal pain, vomiting, gastroesophageal reflux, lymphoid nodular hyperplasia and enterocolitis. Review and investigation of gastrointestinal disorders in children with ASD who are symptomatic is not done routinely in practice and could be due to lack or poor description of the GI symptoms experienced by the children. This may have resulted in a reduced attention to gastrointestinal symptoms relative to other comorbidities they have. Behavioural challenges and limited communication skills contribute largely to the poor identification of GI disorders in children with Autism[6]. The total prevalence of GI disorders in children with Autism is about 9% to 91%[7]. Leo Kenner as cited by Hsiao[5] reported that 7 out of 11 children diagnosed with infantile autism have feeding and dietary problems and helps to prove the point that the gastrointestinal symptoms are associated with ASD early in its development although it is not well understood how the fundamental nature of gastrointestinal dysfuction is related to the aetiology of ASD and its symptoms as research on this subject matter as been limited[7].

White[8], also reported that in a study conducted by *Wakefield et al*[9] 12 children who were diagnosed with autism presented with a variety of GI symptoms and when endoscopy was done, 10 out of the 12 children displayed ileal lymphoid hyperplasia. Eight of 12 children were also found to have abnormalities of the intestinal mucosa including the absorption epithelium, the connective tissue and the muscle layer with features of non-specific colitis (referred to as leaky gut). An extension of the study was done with more children in 2000 with children that had various developmental disorders including the 12 children in the earlier stated study. The subject group included 60 children diagnosed with autism (including the 12 children from the original study) as well as five with Asperger's syndrome (autism without retardation) and two children with disintegrative disorder. Of all the 60 children, only one did not have any GI symptoms. Others had symptoms such as abdominal pain, constipation, diarrhoea, and bloating[9].

The findings from the study were compared with another study in which a group of thirty-seven developmentally normal (non-autistic) children with similar GI symptoms were used as a control group. It was noticed that Ileal Lymphoid Nodular Hyperplasia deceloped in 93% of the children with ASD and 14.3% of control children. Colonic Lymphoid Nodular hyperplasia was seen in 30% of the children with ASD and 5.4% of control children. Intestinal lymph nodes enlarge was found in 88.5% of autistic chidren when biopsies were taken. Active inflammation of the ileum (ileitis) and chronic inflammation of the colon(colitis) were also observed in 8% and 88% of austistic children respectively. These inflammatory processes were described by the authors as a new type of inflammatory bowel disease that could not be specifically classified as either ulcerative colitis or Crohn's disease[9].

In another study done by Horvath *et al*(10), the upper gastrointestinal tract of 36 children diagnosed with autism was viewed using endoscopy plus biopsy. These children were found to have been experiencing chronic abdominal, diarrhoea, loss of sleep and excessive irritability. The endoscopy showed abnormal findings which were reflux oesophagitis in 25 of the children, chronic gastritis in I5, and chronic duodenitis in 24. Low activity of intestinal carbohydrate digestive enzymes was observed in 21 children, whereas 27 exhibited increased exocrine secretion of pancreatic-biliary fluid

after intravenous administration of the GI hormone secretin[10]. Furthermore, food allergies, metabolic disruptions and altered dietary intake are associated with ASD[11]. Altered intestinal microbiota especially with elevated levels of Clostridium *sp.* were also found in children with autism[12]. These intestinal problems have been reported to be due to antigens in diet, the Measles, Mumps and Rubella vaccine(MMR), impaired gut development, increased acid in the gut due to reduced secretion of Secretin, reduced absorption of vitamin B12 which causes impaired nervous system function[13,14]. The implicated antigen Gliadin is a peptide derivative of gluten which has been found to increase intestinal permeability similar to what is seen in Celiac disease[14]. Parents reported that the symptoms of autism were noticed to have started after taking the trivalent vaccine MMR. Studies done to confirm this showed that the measles virus was found in the intestinal tissues of the children examined[15]. The impaired gut development has been thought to be due to abnormal levels of neuropeptides and neutrophins. No significant evidence was found to support these claims as the studies done to confirm these theories yielded only a small amount of positives compared to the total number of children used[13].

Altogether, the gastrointestinal symptoms, food allergies and immune abnormalities of the GI combined with the studies done by on the upper GI and the lower GI point to the fact that there's a widespread gastrointestinal system pathophysiology that may be found in children with autism and this may be a core feature in the aetiology of the disorder or may be a consequence of the disorder itself. Either way, the GI is implicated in the symptomatology of autism[5,16]. More studies need to be done to integrate these factors and findings in order to form a unifying theory on the mechanisms of GI dysfunction in ASD. The limitations encountered must also be taken into consideration for future research. Most of the limitations encountered include lack of control groups, bias, reliance on only parent reports for information, variability of the control groups and inclusion of children with heterogeneous ASD in the studies[17].

THE GUT AND THE BRAIN

The digestive system has its own nervous innervation that controls its reflexes and functions in addition to a pathway that the gut uses to signal to the brain to influence satiety and anxiety[7]. The relationship between the brain and the gastrointestinal tract is bidirectional. In light of this, several mechanisms mediate how functioning of the GI system affects brain growth and development. Serotonin, a neurotransmitter produced in the brain is one of the most significant signaling molecules in the gut important for proper functioning. It has been implicated in the GI symptoms found in ASD in the sense that it is pro–inflammatory and alteration in its signaling causes ulcerative colitis, chronic constipation and inflammatory bowel disease and reduced bone density[18]. Studies which used germ-free mice that were infused with selective bacteria have further explained that gut microbiota can influence brain activity and behaviour[19].

Antibiotic treatment is also reported to improve autism symptoms. In a study of 11 children with regressive-onset autism, oral vancomycin treatment reduced autism associated behavioural abnormalities supporting a role for dysbiosis of the gut microbiota in the development or persistence of autism symptoms. Interestingly, vancomycin treatment provided only short-term improvement of autism-related behavioural abnormalities; the beneficial effects of vancomycin were lost after stopping antibiotic treatment, suggesting an active and persistent interaction between microbial colonization and behavioural outcomes[20].

Collins[21], talked about the fact that alterations in the microenvironment of the GI system affects the vagal nerve afferents lining the intestinal epithelium. These afferent nerves extend up to the brain stem innervating the nucleus tract solitarus and are also involved with the complex modulation of behaviours including emotions, anxiety, stress and cognition[22]. GI dysfunction were also found to be associated with sleep disorders and food intolerance and effects on the immune system can also influence brain and behaviour[6].

It is not known the degree to which gastrointestinal abnormalities contribute to the development and persistence of the main autistic symptoms. It is however plausible that behavioural problems such as self-injury, repetitive and stereotypic behaviors may result from discomfort from gastrointestinal issues. In case of an abdominal pain, it may manifest as abnormal posturing, injury to the abdomen and other parts of the body in other to distract themselves from the pain or from screaming[23]. This is corroborated by the fact that a lot of mental illnesses such as depression and anxiety disorders are associated with GI problems. About 60% of patients who were found to have functional GI disorders were also seen to have comorbid major affective disorders such as depression and anxiety[24].
It is however unclear whether GI complications in autism arise as a result of primary neural dysfunction or through an independent pathway. However, the degree of particular GI abnormalities has been reported to correlate with the severity of core autism behavioural symptoms, which suggests that GI problems can

contribute to the manifestation of ASD-related behaviours[25,26]. Children with ASD who have comorbid GI symptoms show more behavioural problems such as extreme irritability and this supports the theory of brain- gut connection in ASD. In addition, many reports provide convincing evidence that limited diet or antibiotic treatment can effectively improve autism-related behavioural problems[27,28].

PECULIARITIES OF THEIR NUTRITION

A lot of factors are associated with the diet and nutrition of children with Autistic Spectrum Disorders but most can be grouped into medical/nutritional factors and behavioural factors. The nutritional factors are the GI problems, food allergies and metabolic dysfunction already mentioned above and the behavioural factors are the unusual eating behaviours, impaired sensory processing and family factors[29]. Over the years, it has been found that children with autism are picky with food and prefer limited types and quantity of food whether it be because of the texture of the food or because of its colour and they sometimes refuse food[2].

In a study conducted by Lockner, Crowe, & Skipper[30], parent of children with autism reported that their children were picky with foods, were less likely to eat a variety of foods and resisted trying new foods. This is In contrast to parent of children with typically developing children who had none of these peculiarities. In another study by Bandini et al.[31], parents of children between 3-11 years old with or without ASD were asked to complete questionnaires on a 3day record of eating and to describe the food intake of their children. The children with ASD were found to consume significantly small amounts of different types of food compared with their mates who were typically developing. They were also found to show reduced interest in a lot of food variety per month when the questionnaire on dietary intake was increased to a 12months period in a study by Zimmer et al[32]. In yet another study done with only male children, it was reported that boys with ASD ate less variety of foods to a greater extent than typical devloping boys. They also based their food choices on texture[33]. Nonetheless, no literature curently states that there should be a differing or similar nutritional intake in children with ASD and those typically developing[29]. The problem that results from these eating behaviours however, is the fact that their diet quality will be altered and they will not get all the required nutrients or balanced diet and may be at a risk of long term nutritional challenges[2].

Concerning the specific types of macronutrients, it was seen that despite the food selectivity shown by children with ASD, there was quite a good consumption of carbohydrates, fats and protein when compared with their typically developing mates. Some of the children were even found to consume more proteins. Overall, there is no significant difference in their daily energy intakes when compared with other children[34]. When their micronutrient intake was accessed, Johnson et al., 2008[35], found that there was no significant difference in mineral and vitamin consumption when compared with other children except for vitamin K which was found to be low in children with ASD. Some other studies also showed that children with ASD had some vitamin A, calcium and iron deficiency. Children with ASD were also found to be taking nutritional supplements and this was attributed to the fear of their parents who thought that their children were deficient in some nutrients based on their selectivity and picky nature with food[36]. Herndon et al.[37], attributed some of the dietary differences between children with ASD and those typically developing to be due to the implementation of a special diet (e.g., gluten-free, casein- free) by caregivers of children with ASD who believe that these special diets may help improve their children's ASD symptoms.

Overall, nutritional adequacy in children with ASD is mixed. Children with ASD, appear to have a higher risk for inadequate nutrient intakes and nutrient deficiencies. It is often difficult to compare findings on the topic from already existing literature because varying assessment methods were used for dietary intakes and their recommendations. For example, different food frequency questionnaires are used, such as the habitual intake over the past 612 months which asseses dietary intake for a longer period of time and 3-day food records or 24-hour dietary recalls which asssess intake over a much shorter period of time such as days[2].

Despite all the differences in eating habits and selectivity of food by children with ASD, no appreciable difference was seen in their growth and development when compared with typically developing children[34]. This was ascertained using a study done to access their nutritional status and adequacy of diet and basing it on anthropometric and clinical parameters. The result showed that both groups of children had the same height, weight and body mass index[38].

DIET AND NUTRITION TREATMENT OF AUTISM

Children with Autistic Spectrum Disorders are frequently being treated with nutritional supplements and special diets, generally referred to as biomedical treatment of autism. So far, there has been no curative treatment for ASD although some clinicians have used dietary methods successfully to treat the disorder specially to control behavioural symptoms and have seen some positive results. This is why Geraghty *et al.*[39], talked about how parents are more inclined to use biomedical methods (including non-drug, special diets) of treatment and that doctors should get more acquainted with these methods of treatment and the perception of the parents on the overall efficacy. The commonest nutritional method used is elimination of diet, which in this case is the elimination of gluten foods and casein foods (GFCF) from diets. Others include specific carbohydrate diets, probiotics, omega 3 supplementation and digestive enzyme supplementation[40].

Elimination of casein diet would mean the removal of foods such as dairy products including breast milk and removal of gluten containing foods such as those made with flours, pastries and pasta. The prevalence of GFCF use in the treatment of autism although poorly studied was found to be between 20% to 70% in the studies that have been done[41]. The exclusion of casein and gluten has been theorised to affect brain function by preventing the undigested peptides of these foods from crossing the blood-brain barrier and initiating neurologically toxic responses through binding to opioid receptors. It is also theorised to have beneficial effects on gastrointestinal lesions by preventing immune responses against casein and gluten in the GI mucosa. Notably, the use of casein and gluten free diet to manage the main symptoms of autism lacks empirical support from well-designed scientific studies[20]. Parents have reported that the GFCF affects significant change in gastrointestinal symptoms and even core features of autism such as language, socialization, and repetitive behaviours[39]. In addition, these diets involve significant changes to the normal routine of children with ASD and such changes can in themselves affect their eating behaviours. The introduction of gluten free and casein free diets by parents into the foods of their children can also contribute to their food behaviour as there is a significant change from what the children are used to and what their counterparts are exposed to. These special diets have also not been fully backed by evidence to actually improve autism or make the symptoms better unless special allergies to particular types of food have been identified[42].

The use of elimination diets works against all the efforts by clinicians to improve the social integration of such children, in that a personal diet is an isolating factor[41]. An important factor also noticed by Arnold et al.[43], was that there was a low level of the tryptophan amino acid in the children on GFCF diet. Children with ASD have also been thought to be at a long-term risk of cardiovascular disease because of the deficiency of folates and vitamin B6 found in them as a result of GFCG[44]. Slower bone development and lower bone densities were also noticed with those on casein free diets[45].

The use of specific carbohydrate as a dietary treatment of ASD involves eating only monosaccharide. Although, this diet was original created for people with inflammatory bowel disease, it has been found that its consumption reduces the gastrointestinal irritation that leads to chronic abdominal pain, constipation, and diarrhoea that results from eating disaccharides which are inadequately digested[39].

There's no doubt that biomedical treatments work to improve some of the symptoms of autism especially with the fact that there are no side effects the children with ASD would experience as with pharmacological treatments, but a recent systematic review of gluten-free and/or casein-free (GFCF) diets concluded that to date there is no conclusive evidence that the GFCG diet can help improve ASD symptoms, and many of these benefits have also not been reproducible by the clinicians that use them[46].

CONCLUSION

The use of biomedical treatment methods in improving the symptoms of autism and as a total cure would no doubt bring relief to parents of children with Austim, but no solid evidence exists yet to prove that these methods work. Doctors should work with the families of these children to discover which treatment methods work the best. It is also important that since parents are now more inclined to use biomedical methods (including non-drug, special diets) of treatment, doctors should get more acquainted with these methods, perception of the parents on the overall efficacy and also continue to stay aware of new developments on this subject matter as it is fast becoming an area of broad scientific inquiry.

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