Integrative Medicine Approach to Caring Autism Spectrum Disorder (ASD) with Gastrointestinal Symptoms: An Uncontrolled Pilot Study

Yu-Lan Chiang, ND, RD, DrPH[1], Yan Wang, MD[2], Qianqian Wang, MS[4], Zhixian Cheng, MS[4], Li Zou, B.S.[5], Jianzhong Shao, MD[3]
Red House Children's Hospital, Longyou, China

Abstract

No two children with ASD are alike and no single care plan is one-size-fits-all. In this respect, studies have shown that a majority of ASD children display gastrointestinal symptoms, which impacts neurodevelopment during early childhood in susceptible subjects by way of gut-brain axis. Thus, we performed an uncontrolled pilot study to assess the efficacy of Integrative Medicine (IM) approach, based on specific carbohydrate diet-diary free diet, biomedical, lifestyle, behavioral, music and sand art intervention, to caring five children, ages 4-6, diagnosed with an ASD with gastrointestinal symptoms for 12 weeks. All completed a 3-day washout period with Dietary Guideline for Chinese resident. All Parents were signed informed consent forms. Childhood Autism Rating Scale (CARS), Sensory Integration (SI) functional Checklist, and SI clinical observation were implemented to gather baseline, 4, 8 and 12 weeks data. Diet and stool diary were daily recorded for 12 weeks. Fecal, urine and blood sample were collected by 0, 8, and 12 weeks for analysis. There was a significant decrease CARS score and increase in SI functional score ($p<0.05$) from baseline to week12. Also, it was found a statistically significant increase in intestinal microbial diversity from baseline to week 8. Blood lead and mercury level were found a significant decrease compared baseline to week12 ($p<0.05$). However, applied IM approach to caring ASD improves in constipation, bloating, social behavior, eye contact, communication, and decreases in anxiety, stereotyped behavior, and aggressiveness. Further research is needed, including a suitable control group, to promote the IM approach to caring ASD.

Keywords: ASD, Integrative Medicine, Specific Carbohydrate Diet-Diary free, Childhood Autism Rating Scale, Sensory Integration

What is Integrative Medicine?

Integrative Medicine does not replace any therapies or medicines, but it is the **intelligent combination of conventional Medicine and other therapies and treatments** from Naturopathic Medicine, Traditional Chinese Medicine, Nutritional Medicine, Lifestyle Medicine, Environmental Medicine, Sleep Medicine, Mind and Body Medicine and so on to ensure the best results for patients.

It is a **holistic approach** based on

- **Science-Based Medicine,**
- **Patient-Centered/ Whole-Person Care**
- **Addressed the root causes**
- **Non /less -invasive therapies to healing mind, body, and spirit.**



What is Autism Spectrum Disorder?



DSM-5, Diagnostic and Statistical Manual-5th Edit

Children or Adults with ASD might:

(Social Communication)
- Not point at objects to show interest
- Not look at objects when another person points at them
- Have trouble relating to others or not have an interest in other people at all
- Appear to be "in their own world"
- Avoid eye contact and want to be alone
- Have trouble understanding other people's feelings or talking about their own feelings

(Restricted & Repetitive Interests)
- Repeat actions over and over again
- Play with toys or objects non-functionally
- Have trouble adapting when a routine changes
- Have unusual reactions to the way things smell, taste, look, feel, or sound
- Have unusual motor movements

CDC Learn the Signs. Act Early. www.cdc.gov/actearly

What causes ASD?

- **"No two autistic children are alike…**
- **Unknown** - No one cause of autism has been identified
- Most cases involve a complex and variable combination of **genetic risk and environmental factors** that influence early brain development

Autismspeaks.org

Systematically observe and find the specific pattern of response each child exhibits Gastrointestinal disorders

- ASD is the **GI-allergic-immunological-toxicant-nutritional-environmental disorder**.
- ASD is **a systemic inflammatory disorder** that involves not only the brain, but also the the gastrointestinal (GI) tract (Gut-Brain Axis)
- There is no one autistic child that is the same as another. ASD is a multisystem condition disorder. **There is no one therapy work for ASD.**

Microbiota-gut-brain axis vs. ASD

The origins of neural crest cells that colonize the developing GI tract

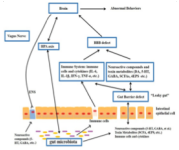


Potential relationships between the microbiota and ASD (the gut-brain axis).

The production of metabolites, such as SCFAs and toxin metabolites, by certain microbiota (e.g., *Lactobacillus*) can cross the "leaky gut" to affect brain function.

Some microbiota can produce neuroactive compounds (e.g., 5-HT and GABA) that cross the "leaky gut" and influence brain function and induce abnormal behaviors.

These neuroactive compounds can directly influence the HPA axis and increase circulating levels of cortisol. Metabolites, certain microbiota and neuroactive compounds can activate enteric neurons and affect brain function through the vagus nerve. Some microbiota and metabolites can activate gut immune cells, which can release cytokines into circulation. 4-EPS, 4-ethylphenyl sulfate; 5-HT, serotonin; HPA, hypothalamic–pituitary–adrenal; SCFAs, short-chain fatty acids; BBB, blood-brain barrier; 5-HT, 5-hydroxytryptamine; ENS, enteric nervous system; GABA, γ-aminobutyric acid; DA, dopamine. J Pediatr Gastroenterol Nutr. 2010 Oct; 51(4):418-24



Hsiao EY, et al. Cell. 2013. Slattery J. et al. Clin Med Insights Pediatric, 2016.

Hypothesis

The Integrative Medicine approach will be effective improvement in reducing GI problems, the symptoms of ASD and increasing overall functioning level.

Key Research Objectives

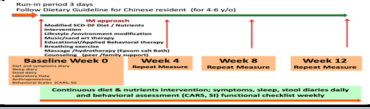
- To identify Integrative Medicine approach the difference between before / after interventions on Autistic children with GI symptoms
- To characterize meconial community composition and structure
- To identify biomarkers for assessing the status of these conditions and guide identification and treatment.
- To identify biomarkers of nutritional status that will not only guide monitoring of response to treatment but help identify those requiring intervention
- To identify behavioral phenotypes related to GI symptoms and poor nutritional status in order to better identify and treat this population

Study Design- An Uncontrolled Pilot Study

Participant- five children, ages 4-6, diagnosed with an ASD with gastrointestinal symptoms

Sexes eligible for study: all; **Study Duration:** 12 weeks

To assess the efficacy of Integrative Medicine (IM) approach, based on subjects provided all food (3 meals and 3 snacks per day) for 12 weeks prepared for them by trained chefs specializing in preparing for the foods that are approved **for Modified Specific carbohydrate diet-Diary free diet and other interventions**



Modified SCD-DF diet composition

	Protein /g	Fat /g	Carb /g	Fiber /g	VA /ug	VB1 /mg	VB2 /mg	Niacin /mg	VE /mg	Ca /mg	P /mg	K /mg	Na /mg	Mg /mg	Fe /mg	Zn/ mg	Se /ug	Cu/ mg	Mn /mg	Calorie Kcal
Intro	42.08	39.89	136.42	12.04	6437.44	0.51	0.58	27.28	6.51	319.51	526.36	2582.06	769.96	258.14	13.14	4.18	26.98	1.12	3.34	800-900
Stage I	62.53	27.36	135.88	13.61	1060.70	1.01	0.92	16.17	5.15	256.54	793.70	2861.15	280.96	369.17	8.13	6.66	41.92	1.28	3.12	900-1050
Stage II	78.10	32.85	140.85	16.07	555.60	1.16	0.91	19.58	6.38	358.60	972.90	2942.10	390.06	442.40	11.09	7.92	50.12	1.50	3.08	1100-1200
Stage III	112.73	55.87	84.53	15.45	2237.00	2.02	1.39	26.98	8.80	540.35	1368.95	3254.70	728.60	426.05	17.22	13.16	65.62	1.64	2.25	1200-1350

Food Quality/safety Management

Test food including drinking/cooking water for Heavy mental, pesticide residue analysis by Enzyme inhibitor, Spectrophotometry, Immune colloidal gold technique

Supplements & other intervention

Milk thistle, essential Fatty acid, Omeg-3 fatty acid, MCT, Vitamin C, VA, VD3, VB1, VB2, VB6, VB12, folate, Niacin, Biotin, Choline, Calcium, Mg, Zn, Se, CoQ10, L-carnitine, curcumin, NAC, Lipoic acid, Probiotic, Saccharomyces boulardii, Digestive enzymes, L-Glutamine etc., Melatonin VB12 im injection twice a week

After 3 months

Chelation

FBT (Fecal Microbiota Transplant)

Other intervention

Educational Interventions

- Montessori /Sensory Integration class
- Music & Sand art therapy
- Social class & Community activities (peer support)
- Crafting class
- Language class



- Tuina Massage & hydrotherapy (Epsom Salt Bath)
- Animal therapy (dog, Chicken)



Parents Training

- Family support
- Parents Counseling
- Parents education – stress management, family counseling, prepare to continue treatment at home
- Parents and ASD Joined community activities once in month (Social activities, peer support)

Assessments

Diagnostic Evaluation

The child was measured with Childhood Autism Rating Scale (CARS) & Sensory Integration (SI) functional Checklist

Additional Baseline information

- Anthropometric measurements
- Diet / Symptoms/sleep Dairy
- Stool Dairy (included photos) – Bristol Stool Scale

Laboratory assessment included

- CBC + CMP Panel
- Ferritin
- Serum Homocysteine
- hs C Reactive Protein
- 25 (OH)Ds
- Copper, Zinc and Ceruloplasmin
- Vitamin ADEK, Vitamin B1, B2, B3, B5, B9
- Oxidative Stress test
- 90 Food Allergy assessment (included blood IgG + IgE test)
- Stool analysis (Analysis of Intestinal Flora)
- Urine organic acid test (OAT panel)
- Urine/blood Heavy Mental Analysis

Results

Characteristics	Mean
N	5
Age	5 (4-6) y/o
boy/girls	4/1
Body Weight (kg)	19.8
Height (cm)	114.94
Body Mass Index (kg/m2)	15
Caesarean Section	3/5
Formula/ Breastfeeding	3/2
Diagnosis	ASD with gastrointestinal symptoms
Constipation, bloating	5/5
Sleep problems	5/5
Self-injury	1/5 (hit the head)
Asthma	1/5
Allergies (food allergy)	3/5
Heavy mental blood/urine test positive	5/5
Low blood Thiamine level	5/5
High blood Platelet level	5/5
Other Health issues	Anemia (1/5), ADHD (3/5)

Table Characteristics of participant at entry

Weight / Height change from baseline to the end of 3rd Month

Kids/T	Age (y)	Baseline	1 Mth	2nd Mth	3rd Mth
A	4	21.5	21	21	21.5
B	5	20	20	20.5	20.5
C	5	20	20.5	20	20
D	4	17	17	17	17
E	5	22.5	23.4	22	23

Table Weight Change from baseline to the end of 3rd month
S: Subject, T: time (kg), T here, P<0.05

Normal BMI for participants

Kids/T	Age (y)	Baseline/cm	1st Mth	2nd Mth	3rd Mth
A	4	101	101	101.5	101.5
B	5	102	102	102.5	103
C	5	103.5	104	103	103.5
D	4	100	100	100	100.5
E	5	108.1	107	107.5	107.5

Table Height Change from baseline to the end of 3rd month
S: Subject, T: time (kg), T here, P<0.05
Values within a row with different superscript asterisk are significantly different, p<0.05 (t-test)

Results

CARS score



SI score



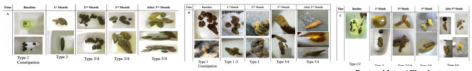
SI score



SI score



The differences in stool form according to Bristol Stool Scale from baseline to the end of 3rd month



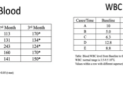
Bacteroidetes / Firmicutes



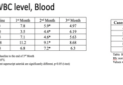
Platelet level, Blood



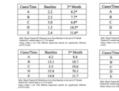
WBC level, Blood



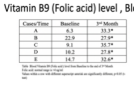
Hemoglobulin level, Blood



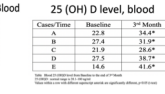
Vitamin B1,2,3,5 level, Blood



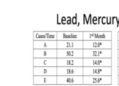
Vitamin B9 (Folic acid) level , Blood



25 (OH) D level, blood



Lead, Mercury level, blood







Conclusions

Applied IM approach to caring ASD improves in constipation, bloating, social behavior, eye contact, communication, and decreases in anxiety, stereotyped behavior, and aggressiveness. Further research is needed, including a suitable control group, to promote the IM approach to caring ASD.

