

MITIGATING NEURODEVELOPMENTAL SYMPTOMS IN CHILDREN THROUGH DETOXIFICATION

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ABSTRACT

Recent studies show neurodevelopmental symptoms are strongly associated with the concentration of circulating or stored heavy metals and chemicals. They suggest enhancing the excretion of heavy metal and chemicals decreases neurodevelopmental symptoms. This study investigates the effects of dietary supplements, NDF and NDF Plus, on heavy metal and chemical detoxification and behavioral symptoms of children with neurodevelopmental disorders. Thirty four children with neurodevelopmental symptoms were separated into four groups, tested for concentrations of heavy metals and chemicals utilizing urinary porphyrins and measuring severity of symptoms based on autism treatment evaluation checklist (ATEC). Improvements in sociability, sensory/cognitive awareness, health/physical behavior, and speech/communication were observed in different groups following intake of dietary supplements. A significant reduction in levels of urinary porphyrins was found in group B utilizing NDF and group C utilizing both NDF and NDF Plus. The performance of Group C was found most notable, where the concentration of total precoproporphyrins was significantly lower after treatment (-45% change) with a p-value of 0.004, followed by coproporphyrin III (-43% change) with a p-value of 0.018, and total porphyrins (-42% change) with a p-value of 0.029. This study shows the benefits combined supplement therapy may have on heavy metal and chemical detoxification and overall improvement in symptoms of children with neurodevelopmental disorders, as well as, the correlation between the decrease in porphyrin levels and improvement in ATEC scores.

KEY WORDS

heavy metals, chemicals, detoxification, dietary supplement, NDF, NDF Plus, ATEC, porphyrin, environmental toxicity, pollution, natural detoxification, autism, behavior, brain function, development, children

INTRODUCTION

Environmental pollution has become a public health emergency that has planetary¹ implications for governments,²

families, nutrition levels, ecology,³ and evolution of all living matter. Environmental pollution includes heavy metals such as mercury, lead, cadmium, arsenic, tin, etc., toxic nanoparticles, multiple chemicals like dioxin, also known as persistent organic pollutants (POPs), and pesticides, a general term for substances which are used to poison pests, weeds, insects, molds, rodents, etc.

Elemental metals, in low concentrations, are essential to support and maintain various biochemical and physiological functions in living organisms. In high concentrations, these same elements can become toxic, contributing to imbalances throughout the body and cell death. Similar cell destruction occurs with chemical and pesticide exposure. Once environmental toxins enter the body, they are absorbed into the adipose tissue where they can be stored for long periods of time due to their chemical stability.

The level of pollution and toxicity in this century is detrimental to maintaining homeostasis in the human body; negatively impacting the brain, nervous system, lungs, liver, kidney and other vital organs.⁴ Pollution often exceeds WHO (World Health Organization) limits by 5-10 times.⁵ These groups of heavy metals and chemicals are found in mining, industrial drainage, urban runoff, sewage discharge, insect or disease control agents applied to crops, and many others.⁶ They are tasteless, odorless and enter the body through hands, eyes, mouths, and lungs from the air, water, and food we ingest. Pollution, heavy metals, and multiple chemicals have been found worldwide to negatively impact neurological development.^{7,8} Today, 1 in 4 children has unhealthy levels of mercury in their body. Approximately 1 in 6 children in the United States has a neurodevelopmental disability.^{9,10}

In a recent study, higher mercury concentrations were found in the urine of children with neurodevelopmental disorders compared with the control group.¹¹ Moreover, it was concluded that the association between increased mercury concentrations and the neurodevelopmental symptoms is significant.¹² It has been suggested the use of dietary supplements in the management of neurodevelopmental issues is an integrative approach that can successfully decrease symptoms. Indeed, dietary supplements have a strong potential to reduce body burden of toxins, reduce excitotoxicity, minimize stress and environmental contamination.¹³ In this study we evaluate the effects of dietary supplement therapy on detoxification of environmental pollutants and behavioral

¹ World Federation of Scientists. "The continuing environmental pollution of Earth and the degradation of its ecosystems both constitute one of the most significant planetary emergencies today." ² Shock Figures to Reveal Deadly Toll of Global Air Pollution. Web access June 12, 2016 <https://www.theguardian.com/environment/2016/jan/16/world-health-organisation-figures-deadly-pollution-levels-world-biggest-cities> ³ Nagajyoti PC, Lee KD, Sreekanth TVM. Heavy metals, occurrence and toxicity for plants: a review. *Environ Chem Lett.* 2010;8(3):199–216. [Ref list] ⁴ Stephan Bose-O'Reilly, MD, MPH, Kathleen M. McCarty, ScD, MPH, Nadine Steckling, BSc, Beate Lettmeier, PhD. Mercury Exposure and Children's Health. As published in *National Institute of Health, Curr Probl Pediatr Adolesc Health Care.* 2010 Sep; 40(8): 186–215. ⁵ WHO's Eastern Mediterranean and South-East Asia Regions, with annual mean levels often exceeding 5-10 times WHO limits, followed by low-income cities in the Western Pacific Region. Web access June 12, 2016. <http://www.who.int/mediacentre/news/releases/2016/air-pollution-rising/en/> ⁶ Morais S, Costa FG, Pereira ML. Heavy metals and human health. In: Oosthuizen J, editor. *Environmental health – emerging issues and practice.* 2012. pp. 227–246. [InTech] [Ref list] ⁷ Herbert L. Needleman, M.D., Charles Gunnoe, ED.D., Alan Leviton, M.D., Robert Reed, Ph.D., Henry Peresie, Ph.D., Cornelius Maher, Ph.D., and Peter Barrett, B.S. Deficits in Psychologic and Classroom Performance of Children with Elevated Dentine Lead Levels. *N Engl J Med* 1979; 300:689-695 March 29, 1979 ⁸ Heather E. Volk, PhD, MPH; Fred Lurmann; Bryan Penfold; Irva Hertz-Picciotto, PhD; Rob McConnell, MD. Traffic-Related Air Pollution, Particulate Matter, and Autism. *JAMA Psychiatry.* 2013;70(1):71-77. doi:10.1001/jamapsychiatry.2013.266. ⁹ Data & Statistics. Centers for Disease Control. USA. Web access June 12, 2016: <http://www.cdc.gov/ncbddd/autism/data.html> ¹⁰ Neurodevelopmental Disorder. Copyright American Psychiatric Association <http://dx.doi.org/10.1176/appi.books.9780890425596.dsm01> ¹¹ Jeff Bradstreet, David A. Geier, B.A. Jerold J. Kartzinel, James B. Adams, Mark R. Geier, M.D. A Case-Control Study of Mercury Burden in Children with Autistic Spectrum Disorders. *Journal of American Physicians and Surgeons.* Vol 8, 2003 ¹² Robert Nataf, Corinne Skorupka, Lorene Amer, Alain Lam, Anthea Springbet, Richard Lath. Porphyrinuria in childhood autistic disorder: Implications for environmental toxicity. *Toxicology and Applied Pharmacology,* Volume 214, Issue 2, 15 July 2006, Pages 99–108. ¹³ Abdulrahman S. Alanazi. The role of nutraceuticals in the management of autism. *Saudi Pharmaceutical Journal* (2013) 21, 233–243.

symptoms of children with neurodevelopmental disorders. The relationship between the severity of neurodevelopmental issues and the concentration of environmental pollutants was evaluated and potential detoxifying effects of dietary supplements NDF and NDF Plus are discussed. Herbs to support the liver detox pathways and adrenal function were given to participants concurrently with detoxification supplementation. Each participant provided baseline and 6-week ATEC, as well as urinary porphyrin tests.

MATERIALS AND METHODS

Participants

40 children, between the age of 2 - 14 years old, with neurodevelopmental issues of varying degrees were originally accepted as participants in this study. Symptomatology included: lack of eye contact, cognitive impairment, brain fog, lack of appetite, food aversions, deficit in social skills, inability to follow directions, low energy, unaware of environment, nonverbal, dark circles under eyes, sluggish bowels, underweight, absence of imaginary play, sensory issues and self stimulatory behaviors. A majority of the participants were referred from Generation Rescue.¹⁴ Each participant had a signed consent waiver provided by their legal guardian.

Three participants were excluded from the study for failing to follow dosing instructions, complete follow up porphyrin testing and/or ATEC. One participant was excluded from the ATEC analysis due to failure to submit follow up survey. Two participants were removed from study prior to beginning detoxification products as mother reported 'bad timing'. One participant was removed due to antibiotic therapy, which was confirmed by Doctor's Data laboratory to interfere with porphyrin results. 34 participants were included in the porphyrin analysis and 33 participants were included in the ATEC analysis.

34 participants, 30 boys and 4 girls, were sorted into the following groups:

- **Group A:** 9 participants
- **Group B:** 8 participants
- **Group C:** 6 participants
- **Group D:** 11 participants

ATEC (Autism Treatment Evaluation Checklist)

All children were evaluated using the ATEC (Autism Treatment Evaluation Checklist) which measures four areas or subtests: I. Speech/Language Communication; II. Sociability; III. Sensory/Cognitive Awareness; and IV. Health/Physical/Behavior. The Autism Treatment Evaluation Checklist (ATEC) was developed in 1999 as a measurement tool to assist researchers in evaluating the effectiveness of various interventions for children and adults with neurodevelopmental issues.

Porphyrins Test; Urine

Concentration of urinary porphyrins was determined using Urinary Porphyrins tests from Doctors Data laboratory. Each participant submitted a baseline test established from their current healthcare practitioner and a follow up test at the end of the 6 week intervention period.

"Urinary porphyrins...will inhibit different enzymes of the heme porphyrin pathway and will thus cause different and specific porphyrin patterns (or "profiles") in the urine, the analysis of which can help determine which metal is involved, and to what degree."¹⁵

High levels of urinary porphyrins are associated with metabolic disturbances, oxidative stress, and exposure to toxic chemicals or heavy metals.

Each marker represents:^{16,17}

- **Uroporphyrins:** Aluminum, Arsenic, Hexachlorobenzene, Dioxin, PBB
- **Heptacarboxylporphyrins:** Arsenic, Dioxin, PBB, Hexachlorobenzene
- **Hexacarboxylporphyrins:** Arsenic, Dioxin, Hexachlorobenzene, PBB
- **Pentacarboxylporphyrins:** Mercury, Arsenic
- **Coproporphyrin I:** Arsenic, Methylchloride, PVC, PBB
- **Coproporphyrin III:** Mercury, Arsenic, Lead, Methylchloride, PVC, PBB
- **Total Porphyrins:** Arsenic, Dioxin, Lead, Mercury, Hexachlorobenzene, Methylchloride, PVC, PBB
- **Total Precoproporphyrin:** Mercury
- **Precoproporphyrin/Uroporphyrins:** Ratio detects abnormalities in individuals with low heme biosynthesis as may occur in kids with nutritional deficiencies and autism.

Porphyrin Pattern Recognition Guide:

- **Mercury:** Pentacarboxylporphyrins, Coproporphyrin III, Precoproporphyrin, and Precoproporphyrin/Uroporphyrin
- **Arsenic:** Uroporphyrin, Coproporphyrin I, and Coproporphyrin III
- **Lead:** Coproporphyrin III
- **Hexachlorobenzene, Dioxin:** Uroporphyrins
- **Methylchloride, PVC, PBB:** Coproporphyrin I and Coproporphyrin III

Considerations: Various drugs and other substances can suppress enzymes involved in porphyrin metabolism and affect the levels of urinary porphyrins. Such compounds include alcohol, sedatives, analgesics, antibiotics, estrogens, and oral contraceptives. Anemia, pregnancy, and liver disease can also affect porphyrin metabolism.¹⁸

¹⁴ Generation Rescue is the leading national organization that provides hope, information and immediate treatment assistance to families affected by autism spectrum disorders. <http://generationrescue.org/>.

¹⁵ D. Rossignol. The Use of Urinary Porphyrins Analysis in Autism. D. Rossignol/Medical Veritas (4) 1-6. 2007. ¹⁶ Genova Diagnostics <https://www.gdx.net/core/interpretive-guides/Porphyrins-IG.pdf>

¹⁷ Doctor's Data Inc. <https://www.doctorsdata.com/urine-porphyrins> ¹⁸ Doctor's Data Inc. <https://www.doctorsdata.com/urine-porphyrins>

Concomitant Therapy

All four groups, A, B, C and D were given a natural herbal liver support formula,¹⁹ Liver Life for the duration of this study. In addition, children in Groups A, B and C, were given adrenal support formula, Loving Energy.

Liver Life:

- **40 lbs and under:** 166 mg (15 drops or 0.4 ml), 2x per day
- **41 - 75 lbs:** 576 mg (2 droppers or 1.6 ml), 2x per day
- **Over 75 lbs:** 864 mg (3 droppers or 2.4 ml), 2x per day

Loving Energy:

- **40 lbs and under:** 360 mg (1 dropper or 0.8 ml), 2x per day
- **41 - 75 lbs:** 720 mg (2 droppers or 1.6 ml), 2x per day
- **Over 75 lbs:** 1080 mg (3 droppers or 2.4 ml), 2x per day

Interventions Used

After baseline ATEC and Urinary Porphyrins test were completed on all children, the following interventions were given:

Group A: NDF Plus

Group B: NDF

Group C: NDF and NDF Plus

Group D: Placebo group, chlorella tincture

Intake was given according to weight for 6-weeks:

NDF Plus:

- **40 lbs and under:** 34 mg (1 dropper or 0.8 ml), 2x per day
- **41 lbs and over:** 67 mg (2 droppers or 1.6 ml), 2x per day

NDF:

- **40 lbs and under:** 48 mg (1 dropper or 0.8 ml), 2x per day
- **41 lbs and over:** 96 mg (2 droppers or 1.6 ml), 2x per day

Chlorella tincture:

- **40 lbs and under:** 11 mg (1 dropper or 0.8 ml), 2x per day
- **41 lbs and over:** 22 mg (2 droppers or 1.6 ml), 2x per day

Parents were instructed to make no changes to their child's diet or other interventions throughout study. The only detoxification agents taken were of those in the designated protocol groups.

RESULTS

Urinary Porphyrins: Before and After

In Group A, the reduction of urinary pentacarboxylporphyrins and total precoproporphyrins was observed after intake of NDF plus, where the percentage of change was from -10% to -13%. In the same group, an increase in uroporphyrins (28% of change), total porphyrins (5% of change), and coproporphyrin III (4% of change) values was observed.

Table 1: Porphyrin Results by Group

Environmental Toxin/ Urinary Porphyrins	Group A				Group B				Group C				Group D			
	Pre	Normal	Post	% of Change	Pre	Normal	Post	% of Change	Pre	Normal	Post	% of Change	Pre	Normal	Post	% of Change
Mercury/Arsenic/ Hexachlorobenzene/Dioxin (Uroporphyrins)	12.6	< 28	16.1	28%	16.7	< 30	13.3	-20%	14.6	< 29	10.1	-31%	15.3	< 30	15.3	0.3%
Arsenic/Organotoxins (Heptacarboxylporphyrins)	1.7	< 5	2.3	37%	1.7	< 6	2.5	45%	6.3	< 6	2.2	-65%	2.9	< 6	3.1	7%
Arsenic/Organotoxins (Hexacarboxylporphyrins)	0.85	< 5.2	1.61	89%	1.53	< 5.2	1.05	-31%	2.49	< 5.2	1.10	-56%	1.19	< 5.2	0.90	-24%
Mercury/Arsenic (Pentacarboxylporphyrins)	1.26	< 4.5	1.14	-9.5%	1.24	< 4.5	1.09	-12%	1.69	< 4.5	1.17	-31%	1.21	< 4.5	1.25	3.3%
Arsenic/Organotoxins (Coproporphyrin I)	25.5	< 36	24.8	-2.9%	30.6	< 36	29.9	-2.4%	39.3	< 36	22.3	-43%	39.1	< 36	41.2	5.4%
Mercury/Arsenic/Lead/ Methylchloride/PVC/PBB (Coproporphyrin III)	125.5	< 97	131.1	4%	154.1	< 105	148.2	-4%	221.7	< 101	126.2	-43%	149.1	< 103	153.6	3%
Mercury/Arsenic/Lead/PVC/ PBB/Methylchloride/ Dioxin/Hexachlorobenzene/ Organotoxins (Total Porphyrins)	168.4	< 147	176.4	5%	205.0	< 160	197.9	-3%	286.7	< 154	165.0	-42%	197.9	< 157	207.3	5%
Mercury (Total Precoproporphyrins)	1.6	< 4	1.4	-13%	1.9	< 4	1.5	-23%	2.0	< 4	1.1	-45%	1.8	< 4	1.8	2%
Heme Biosynthesis (Precoproporphyrins/ Uroporphyrins)	0.15	< 0.10	0.10	-14%	0.13	< 0.10	0.13	22%	0.18	< 0.10	0.13	-23%	0.12	< 0.10	0.11	-8%

Summary of Results for Group A: This group shows the overall need for more detoxification. Multiple environmental pollutants were still being excreted. **Summary of Results for Group B:** This group shows the overall need for more detoxification. Multiple environmental pollutants were still being excreted. **Summary of Results for Group C:** Using both NDF and NDF Plus increased removal of environmental toxins far more quickly as seen in porphyrin tests while improving neurological and behavioral issues at the same time. **Summary of Results for Group D:** Some movement, however, very mild shifts. Nothing outstanding in any urinary porphyrin profile.

¹⁹ S.Ray, T.Wilken, USA. Impact of Liver Support Therapy on 11 Children with Neurodevelopmental Issues. 2013 Generation Rescue/Bioray ATEC Results.

According to the results of the Group B, the highest reduction in concentration was observed in the levels of total precoproporphyrins (-23% of change) and uroporphyrins (-20% of change), followed by pentacarboxylporphyrins (-12% of change), coproporphyrin (-4% of change), and total porphyrins (-3% of change).

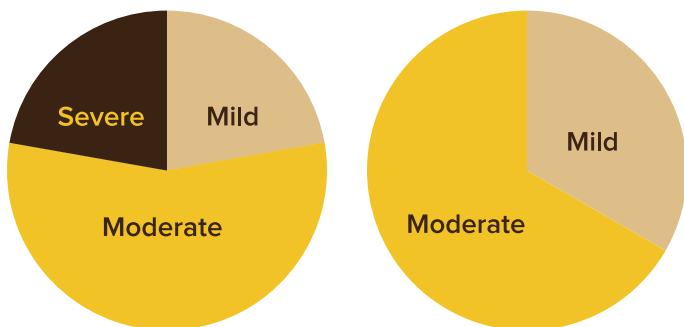
In Group C, total precoproporphyrins significantly decreased after intake of NDF and NDF Plus (-45% of change) with a p-value of 0.004, followed by coproporphyrin (-43% of change) with a p-value of 0.018, and total porphyrins (-42% of change) with a p-value of 0.029. Similar results are obtained for two other subsets: uroporphyrins and pentacarboxylporphyrins where the reduction level was -31%, however the p-values were only 0.256 and 0.214 respectively.

No significant differences were found in Group D, control group, where chlorella tincture was used for the intervention.

Autism Treatment Evaluation Checklist (ATEC): Before and After

The ATEC scores were evaluated in 33 out of 34 study participants before and after detoxification. The average improvement for all participants after the use of dietary supplements was 20% with a p-value of 0.048. The overall improvement in Group A was 25%. The most improvement was observed in sociability domain at 42%, followed by sensory/cognitive awareness at 27%, health/physical behavior at 25%, and speech at 5%. In Group B, overall improvement was 18%. The most notable improvement was seen in health/physical behavior at 26%, followed by sociability at 17%, sensory/cognitive awareness at 14%, and speech improved by 12%. Similar results with Group A was observed in the Group C where the overall improvement was 23%. The most notable improvement in this group was seen in sociability at 35%, followed by health/physical behavior at 32%, sensory and cognitive awareness at 17%, and speech at 6%. In all three groups; A, B and C, improvements were more significant than the placebo in 4 out of 5 areas tested including overall symptoms, sociability sensory/cognitive awareness, and health/physical behavior. All groups experienced mild improvements in speech with Group B showing the greatest at 12%.

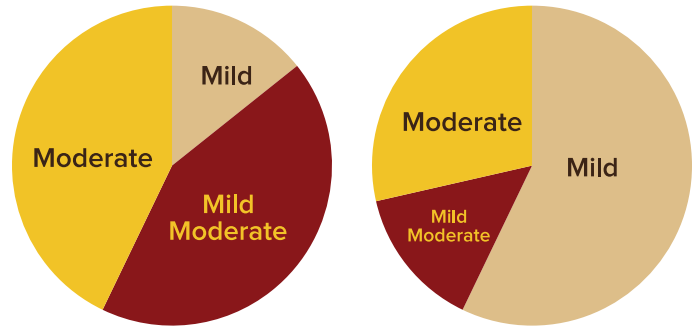
Graph 1: Group A - ATEC Pre and Post



Overall Results for Group A (pre-left; post-right): Eight out of nine participants improved. Total improvement overall was 25%. The group initially had two participants that were classified as mild (22%), five classified as moderate (56%), and two classified as severe (22%). After six weeks of intervention, the group was comprised of three participants

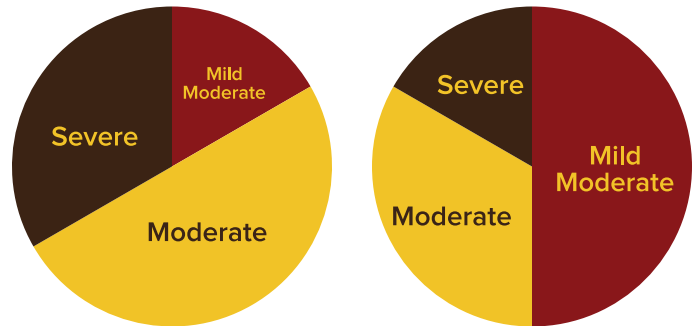
classified as mild (33%), six classified as moderate (67%), and zero classified as severe (0%).

Graph 2: Group B - ATEC Pre and Post



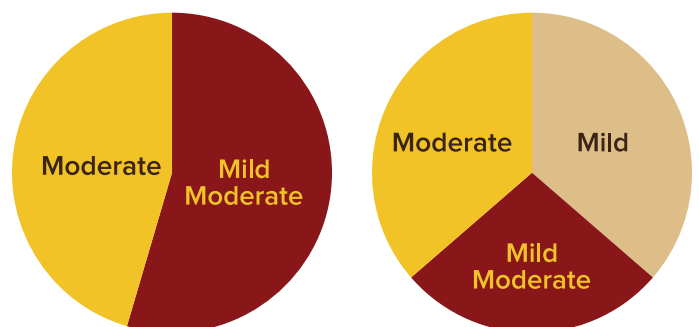
Overall Results for Group B (pre-left; post-right): Five out of seven participants improved. Total improvement overall was 18%. The group initially had one participant that was classified as mild (14%), three classified as mild-moderate (43%), and three classified as moderate (43%). After six weeks of intervention, the group was comprised of four participants classified as mild (57%), one classified as mild-moderate (14%), and two classified as moderate (29%).

Graph 3: Group C - ATEC Pre and Post



Overall Results for Group C (pre-left; post-right): Five out of six participants improved. Total improvement overall was 23%. The group initially had one participant that was classified as mild-moderate (17%), three classified as moderate (50%), and two classified as severe (33%). After six weeks of intervention, the group was comprised of three participants classified as mild-moderate (50%), two classified as moderate (33%), and one classified as severe (17%).

Graph 4: Group D - ATEC Pre and Post



Overall Results for Group D (pre-left; post-right): Nine out of eleven participants improved. Total improvement overall was 11%.

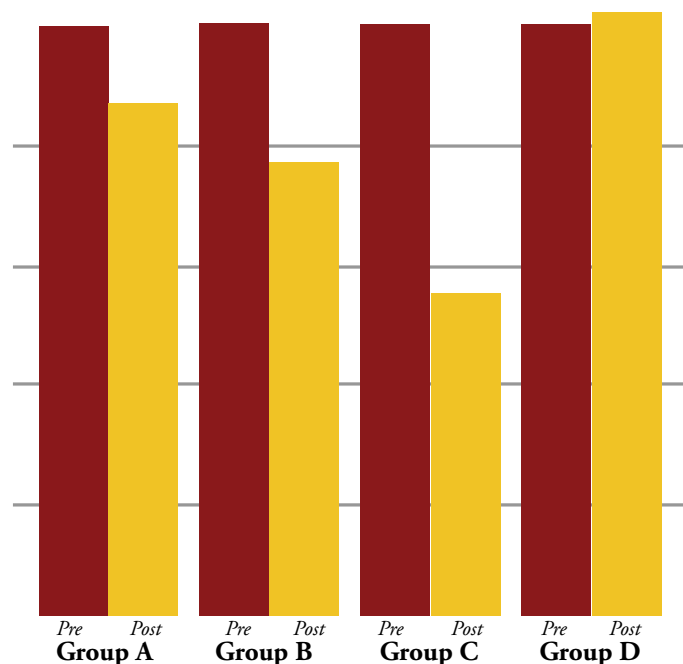
The group initially had six participants that were classified as mild-moderate (55%) and five classified as moderate (45%). After six weeks of intervention, the group was comprised of four participants classified as mild (36%), three classified as mild-moderate (27%), and four classified as moderate (36%).

Clinical Effectiveness and Notations

The clinical effectiveness and notations by parental guardians included the following improvements; overall cognition, following directions, social skills, eye contact, sensory issues (especially auditory, less issues with food textures) ABA (Applied Behavioral Analysis) trials, words/speech, weight gain for underweight children, imaginary play, attention, energy, potty training, moods, independence, complex thoughts, appropriate play, toe walking, histamine/allergies, sleep, facial tics & headaches, anxiety, running away, being helpful and growth hormone normalized.

While these observations given by parents and teachers of the participants are subjective, they are a notable contribution to this paper. They illustrate the quality of life patterns that can occur when supporting the body to remove environmental toxins.

Graph 5: Mercury Comparison according to Total Precoproporphyrins



Group A (NDF Plus): Mercury levels were decreased in children by 13% in 6 weeks. **Group B (NDF):** Mercury levels were decreased in children by 23% in 6 weeks. **Group C (NDF & NDF Plus):** Mercury levels were decreased in children by 45% in 6 weeks. **Group D (Chlorella tincture - Placebo Group):** Mercury excretion increased by 2%.

Adverse Events

There were no serious adverse events in this study. Some participants experienced mild detox reactions which included feeling irritable, skin irritations, sluggish or loose bowel movements which were mitigated with an increase in adrenal and/or bowel support.

DISCUSSION

Urinary Porphyrins

These results confirm that the concentration of urinary porphyrins associated with heavy metal toxicity is strongly correlated with the neurobehavioral deficits assessed using ATEC scores. The levels of improvement are more significant in all three groups, A, B and C, compared to the control group, D. These results provide new evidence that the combination of two natural detoxifying dietary supplements NDF and NDF Plus have a significant effect in reducing the concentration of urinary porphyrins and thus removing toxic heavy metals and chemicals from cells and support the natural detoxification pathways without reported side effects.²⁰

The severity of neurodevelopmental issues is reported to have strong correlation with mercury concentration levels which is associated with elevated levels of coproporphyrin (cP), pentacarboxyporphyrin (5cxP), and precoproporphyrin (prcP).²¹ The higher concentration levels of such porphyrin groups appear due to inhibition effects of mercury on specific enzymes, coproporphyrin oxidase CPOX, in the heme biosynthesis pathway. Inhibition of heme biosynthesis have several implications in other biochemical processes due to the fact that heme is a component of several essential proteins such as: hemoglobin, the cytochrome p450 family for detoxification, mitochondrial cytochromes for ATP synthesis, and nitric oxide synthase for nitric oxide-mediated membrane signal transduction.²²

The detoxification efficacy of NDF and NDF Plus was observed particularly in the case of total precoproporphyrin and coproporphyrin as specific indicators of mercury exposure and might enhance the integration of porphyrins in the heme molecule, which carries oxygen in the body.²³ This is very beneficial in reducing the incidence of the neurodevelopmental disorders since these individuals are characterized with hypoperfusion and poor oxygenation to several areas of the brain.²⁴

Supporting the heme biosynthesis by removing heavy metals and inhibitory chemicals with NDF and NDF Plus supplements can help compensate for decreased blood flow by increasing the oxygen content on the affected regions and thus helping these individuals improve their neurological function. Moreover, through this mechanism, NDF and NDF Plus enhance the natural detoxification processes because heme is a cofactor of several enzymes including cytochromes of the P(450) class which are fundamental in the detox of the body from many organic toxicants including pesticides and PCBs.²⁵ Indeed, continuous application of NDF and NDF Plus can be very beneficial because decreased blood flow and oxygen to areas associated with communication has been

²⁰ S. Ray, T. Wilken. How plant based detoxifiers benefit chemical detoxifiers. Explore. Volume 21, Number 2, 2012 ²¹ Kern JK, Geier DA, Adams JB, Mehta JA, Grannemann BD, Geier MR. Toxicity biomarkers in autism spectrum disorder: a blinded study of urinary porphyrins. *Pediatr Int.* 2011 Apr;53(2):147-53. ²² Beri R, Chandra., Chemistry and biology of heme. Effect of metal salts, organometals, and metalloporphyrins on heme synthesis and catabolism, with special reference to clinical implications and interactions with cytochrome P-450. *Drug Metab Rev.* 1993;25(1-2):49-152. ²³ Berg JM, Tymoczko JL, Stryer L. Hemoglobin Transports Oxygen Efficiently by Binding Oxygen Cooperatively. *Biochemistry.* 5th edition. New York. 2002. ²⁴ Daniel A. Rossignol, Lanier W. Rossignol. Hyperbaric oxygen therapy may improve symptoms in autistic children. *Medical Hypotheses* (2006). ²⁵ Heinemann IU1, Jahn M, Jahn D. The biochemistry of heme biosynthesis. *Arch BiochemBiophys.* 2008 Jun 15;474(2):238-51.

shown to worsen with increasing age.^{26,27}

Statistical analysis found multiple and significant correlations between the severity of the neurodevelopmental issues and concentration of porphyrins. The correlation between precoproporphyrin and ATEC performance was of particular interest due to the unusual elevation of this porphyrin in children with prolonged exposure to mercury.²⁸

Before the intervention, results show in Group A and C, the highest level of correlation between the precoproporphyrin (mercury) and the ATEC in the sociability domain ($r = 0.21, 0.70$), followed by health/physical/behavior domain ($r = 0.51, 0.31$), and then sensory/cognitive awareness domain ($r = 0.43, 0.26$). This positive association is attributed to elevation levels of heavy metals and environmental toxins that are known to increase the risk of neuro-developmental disorders.²⁹

Autism Treatment Evaluation Checklist

This data shows that by removing heavy metals and chemicals from cells using NDF and NDF Plus detoxifiers, ATEC performance improved more in all three groups compared to control. It was concluded that the ATEC performance was significantly improved after several days of heavy metal excretion.³⁰ Considering the fact that the majority of children with autism are characterized with porphyrinuria,^{31,32} and have a decreased detoxification capacity due to genetic polymorphism,³³ detoxification effects of NDF and NDF Plus will support the normal function of biochemical steps necessary for generating energy and healthy brain function.

Another effect of NDF and NDF Plus is attributed to improving the essential nutritional metabolites which are often out of balance in children with autism.^{34,35} NDF and NDF Plus are composed of herbs and medicinal mushrooms that include trace vitamins, minerals and amino acids.³⁶ In Group A, two participants provided additional baseline and follow up lab testing, Toxic & Essential Elements Hair Analysis from Doctor's Data. In one participant, six toxic elements decreased; antimony, arsenic, cadmium, lead, tin and titanium, while nine beneficial elements shifted towards balance; magnesium, copper, chromium, molybdenum, boron, iodine, lithium, sulfur and iron with improvement in zinc/copper and zinc/cadmium ratios. In the other participant, seven toxic metals decreased; aluminum, antimony, bismuth, cadmium, lead, silver and tin while eleven beneficial elements shifted towards balance; sodium, potassium, zinc, manganese, chromium, boron, iodine, selenium, sulfur, iron, rubidium and zirconium. This is important to note as toxic metals displace essential nutrients. As these toxins are removed, we see essential elements shift towards balance. This decreases the support remedies required throughout detoxification and speeds up the healing process.

It was also evident that the participants using NDF and/or

NDF Plus resulted in no significant adverse health effects. The addition of liver support to assist the children's ability to transport toxic metabolic waste was a consideration to prevent back up into the body during deep detoxification. Adrenal support was given to Groups A, B and C to test the hypothesis that addressing the body's stress response to detoxification could mitigate any and all herxheimer reaction(s), improving tolerance for deep detoxification. This was successful with 23 out of 23 participants. Further research into the synergy between NDF and NDF Plus is warranted to gain more understanding of the impact on both porphyrin concentrations and ATEC performance in children with symptoms of neurodevelopmental disorders.

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