Could Your Child’s Behavior be PANS/PANDAS?

National Autism Association Conference
May 2019

Lindsey E. Wells, ND
www.lindseywellsND.com

What is PANS/PANDAS

- **PANDAS** = Pediatric Autoimmune Neuropsychiatric Disorder Associated with Strep
- **PANS** = Pediatric Acute-Onset Neuropsychiatric Syndromes
- **PITANDS** = Pediatric Infection-Triggered Autoimmune Neuropsychiatric Disorders
- Post-streptococcal Autoimmune Encephalitis (of the basal ganglia)
- Sydenham Chorea
  - Post-Streptococcal Striatal Autoimmune Encephalitis
  - 95% with emotional lability, 50-75% with OCD at initial presentation and 100% with recurrence (Russel Dale & colleagues)
PANS/PANDAS

- 1 in 150-200 children diagnosed with PANS
- Subgroup of those children with OCD (which represents 2% of population)
- At least 25-30% of OCD and Tic disorders are acute onset
- More prevalent in males than females (2.6:1)
- Increased occurrence with family history of autoimmune disease
  - 64% have 1st degree relative with inflammatory disease

Swedo et al, Ped Ther, 2012
DIAGNOSTIC CRITERIA

• ACUTE ONSET of DRAMATIC OCD (or anorexia and/or severe, restrictive eating disorder) in addition to TWO of the following neuropsychiatric symptoms (with severe and acute onset):
  • Separation Anxiety
  • Emotional lability
  • Behavioral/developmental regression
  • Sensory/motor abnormalities – handwriting deterioration
  • Deterioration of school performance
  • Urinary symptoms (urgency, frequency, enuresis)
  • Sleep disturbance (difficulty falling asleep, REM disinhibition/restless sleep)
  • Symptoms not better explained by another disorder


CLINICAL OBSERVATIONS

• Aggression 60%
• Sleep Disorders 80%
• Insomnia, night terrors, inability to sleep alone
• Behavioral Regression
• Separation anxiety 98%
• Learning Difficulties 60%
• Hyperactivity; Inattentiveness 70%
• Inability to concentrate 90%
• Eating Disorder 20%
• Hallucinations 10%
• Terror Stricken look or Hyper-alert appearance 80%
• Urinary Frequency, urgency, urinary accidents 90%
• Handwriting deterioration 90%
• Tics 70%
• Short-term memory loss 60%
• Sensory -hypersensitive or insensitive 40%
• History of repeated UTIs or sinusitis

Toufexis et al., JACP, 2015
ADDITIONAL OBSERVATIONS

- Margin Drift (left sided neglect)
- Shortened attention span
- Difficulty with memory
- Loss of math visuospatial skills
- Dysgraphia/clumsiness
- Patterns of executive function deficit different than those children with Tourette’s
- EEG – 17% show spikes (4/42) or diffuse slowing (3/42) consistent with autoimmune encephalitis
- Sleep study – 85% show nonspecific REM motor disinhibition

Buckley et al, NIH, J Clin Sleep Med, 2016

ADDITIONAL OBSERVATIONS

- Studies reveal that 80% of patients diagnosed with PANS have post-infectious autoimmunity and/or neuroinflammation (Swedo et al, 2015)
- Neuroinflammation seen in the caudate/putamen (Kirvan et al, 2003)

DIFFERENTIAL DIAGNOSIS

- Sydenham chorea (acute rheumatic fever)
- Other forms of encephalitis, cerebral vasculitis
- Child abuse, sexual abuse, psychological trauma
- Toxins, medications, illicit drugs
- Tumors, strokes
- Tourette’s, OCD – not ACUTE

PATHOGENESIS

Group A Strep
- Genetic Susceptibility
- HLA-B alleles

Mis-directed Immune Response
- Molecular Mimicry
- AntiGAS Abs Recognize Host

SC/PANDAS
- Rheumatic Fever
- Carditis, Polyarthritis Erythema Marginatum
MOLECULAR MIMICRY

• Process that occurs when our immune system mistakenly attacks normal body tissues because of the structural similarities between a particular molecule on an infectious agent and the molecules in our own body tissues.

• Example of molecular mimicry = Rheumatic fever
  • Immune system is triggered to attack heart valves after a strep infection

• Similar process occurs in PANS and PANDAS, where antibodies are triggered to attack the Basal Ganglia causing movement and behavioral manifestations

Group A Streptococcus intranasal infection promotes CNS infiltration by streptococcal-specific Th17 cells.


Abstract

Group A streptococcal (GAS) infection induces the production of Abs that cross-react with host neuronal proteins, and these anti-GAS mAbs Aβ are associated with autoimmune diseases of the CNS. However, the mechanisms that allow these Aβs to cross the blood-brain barrier (BBB) and induce neuropathology remain unresolved. We have previously shown that GAS infection in mouse models induces a robust Th17 response in nasal-associated lymphoid tissue (NALT). Here, we identified GAS-specific Th17 cells in tonsils of humans naturally exposed to GAS, prompting us to explore whether GAS-specific CD4+ T cells home to mouse brains following i.n. infection. Intranasal challenge of repeatedly GAS-inoculated mice promoted migration of GAS-specific Th17 cells from NALT into the brain, BBB breakdown, serum IgG deposition, microglial activation, and loss of excitatory synaptic proteins under conditions in which no viable bacteria were detected in CNS tissue. CD4+ T cells were predominantly located in the olfactory bulb (OB) and in other brain regions that receive direct input from the OB. Together, these findings provide insight into the immunopathology of neuropsychiatric complications that are associated with GAS infections and suggest that crosstalk between the CNS and cellular immunity may be a general mechanism by which infectious agents exacerbate symptoms associated with other CNS autoimmune disorders.
TH17


HLA SUSCEPTIBILITY

• Increase incidence of PANS in subjects which had the following HLA-B alleles:
  • HLA-B 55
  • HLA-B 38
  • HLA-B 52
    • Associated with vasculitis (i.e Behcets)
• Shows genetic predisposition to vulnerability

Frankovich, 2016
CAM KINASE II

- Calcium-dependent Calmodulin Protein Kinase II
- Cam Kinase II is an enzyme that is involved in the upregulation of many neurotransmitters (i.e. dopamine)
- Known to increase the sensitivity and responsiveness of neurologic receptors to neurotransmitters
- This marker is elevated in PANDAS

DIAGNOSIS

- PANS/PANDAS is a CLINICAL DIAGNOSIS
- Based on History and Physical Exam
- Clinical Diagnosis of ACUTE onset symptoms
- Evidence of infection/inflammation
HISTORY

• Recent illness before the onset of symptoms
• History of family members being ill around the onset of symptoms
• IMPORTANT TO NOTE: Our kids will not always present with the typical acute illness symptoms and may just present with behavioral issues

HISTORY

• Strep:
  • Sore throat
  • Fever
  • Food refusal – due to pain on swallowing
  • Nausea or vomiting
  • Headache
  • Scarlatina Rash
HISTORY

- **Mycoplasma:**
  - Fever (usually low grade)
  - Respiratory symptoms (cough)
  - Fatigue
  - Headache
  - Ear infections
  - Croup
  - Anxiety/ depression

- **Viral**
  - Fever
  - GI symptoms
  - Vomiting
  - Viral Rash
  - Fatigue/ lethargy
  - Nasal discharge
  - Respiratory Symptoms

- **Parasites**
  - Worsening around the full moon
  - Grinding of teeth
  - Itching of buttocks
PHYSICAL EXAM

• Choreiform Movements ("piano playing fingers")
• Strep (PANDAS)
  • Red anal ring
  • Peeling fingers
  • Tongue
  • Palate petechiae
  • Damaged nail bed vasculature

PHYSICAL EXAM

• Other:
  • Erythema Migrans – BORRELIA
  • Striae that blanches – BARTONELLA
  • Swollen/tender glands
  • Tenderness to palpation of sinuses
  • Whiteness on tongue – YEAST OVERGROWTH
DIAGNOSIS

• Culture of possible sites of infection:
  • Throat (rapid test – high false negative rate)
  • Tonsils and Adenoids (surface/core)
  • Urinary Tract
  • GI Tract/Perianal (Toufexis et al, JCAP, 2013)
  • Sinuses - cryptic, recalcitrant (Mahoney et al, J Ped Otorhinolar, 2017)

• Laboratory evidence
  • Strep markers– ASO, antiDNaseB Ab
    • 6-8 weeks for rise in titers post infection
    • These antibodies only mean that the child has had a previous strep infection. It does NOT mean the child has PANDAS
    • About 40% of children with documented GAS infections do not show a rise in titers – leading to false negatives.
  • Other infectious markers :
    • Mycoplasma IgG/IgM
    • Lyme and Coinfections (Babesia, Bartonella, Ehrlichia)
    • Viral markers – influenza, EBV, CMV, etc.
  • Inflammatory markers – CRP, ESR, ANA
    • ANA is positive in > 56 % (Cox et al, JACP, 2015)
  • CaM Kinase – Moleculara labs
    • Testing may be helpful when child in a flare or not classical clinical picture
DIAGNOSIS

- MOLD – mycotoxin profile
- Chemical exposures
- Immunizations

Environmental Exposures:

- Food Allergies
- Celiac screen
- Thyroid abs
- Cerebral Folate Deficiency
- Metabolic markers
- Endocrine markers

Additional Markers:

TREATMENT

- Treating the symptoms with supportive interventions (CBT, supplements, psychoactive medications)
- Removing the source of the infection – treating with antimicrobials (natural and pharmaceutical)
- Treating immune disturbances with immunomodulatory and/or anti-inflammatory interventions

Swedo et al, J Child Adol Psychopharm, 2017
PRINCIPLES OF TREATMENT

Establish the correct diagnosis

Provide symptomatic relief – comprehensively treat symptoms causing the most distress (Thienemann et al, J Child Adol Psychopharm, 2017)

Treat infections – therapeutic and prophylactically (Cooperstock et al, J Child Adol Psychopharm, 2017)

Treat neuroinflammation and post-infectious autoimmunity with anti-inflammatory and immunomodulatory interventions (Frankovich, J Child Adol Psychopharm, 2017)

Evaluate effectiveness of treatment, modifying as warranted by relapsing and remitting symptoms (Swedo et al, J Child Adol Psyhopharm, 2017)

TREATMENT FOR SYMPTOMS

OCD
Tics
Anxiety
Aggression/Irritability
Sleep Disturbances
ADHD
Eating Disorders/Restrictions
NATURAL INTERVENTIONS

- N-Acetyl Cysteine (NAC)
  - 18 grams/day found to decrease OCD (Palatnik et al, J Clin Psychopharm, 2001)
- CBD (Hemp Oil) – Cannabidiol
  - Reverses mCPP-induced marble burying in mice (Nardo et al, 2013; Delana et al, Psychopharm, 2012)
- Inositol
  - 18 grams/day found to decrease OCD (Palatnik et al, J Clin Psychopharm, 2001)
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- 18 grams/day found to decrease OCD (Palatnik et al, J Clin Psychopharm, 2001)
- Passionflower – helps to calm mind of repetitive thoughts
- Ashwagandha
  - Comparable efficacy in mice models to fluoxetine (Asian Pac J Trop Med, 2012)
- GABA
  - Modulates glutamate that has been found to be significantly higher in CSF of subjects with OCD compared to controls (Pittenger et al, 2011)
- Mindfulness (Hansteded et al, J Nerv Ment Dis, 2008)
- Exercise (Otto et al Oxford Univ Press, 2011)
OCD

- **Pharmaceuticals**
  - SSRI’s (Selective Serotonin Reuptake Inhibitors) prescribed for OCD
    - Low dose with slow titration (Coffey, 2007)
    - Study found that 30% of patients have treatment-refractory (Goddard et al., 2008)
    - Reason to implement natural interventions!
    - Possible benefit from additional treatment that addresses other neurochemical pathways (i.e dopamine and glutamate)
  - Memantine (Namenda)
    - NMDA receptor antagonist and regulates glutamate (excitatory neurotransmitter)
    - Study showed improvement in OCD and impulsivity (Ghaleiha et al, 2013)
    - Animal models show anti-inflammatory benefits
  - Amantadine
    - NMDA receptor antagonist that decreases glutamate to help with OCD (Hosenbocus and Chahal, 2013)

ANXIETY

- 5-HTP
- GABA
- L-Theanine
- B6
- B complex
- Magnesium
- Probiotics
- Multi-mineral
- EFA
- L-MTHF (if MTHFR mutation OR CFD)
- Ashwagandha
- Lemon Balm
- Motherwort
- Passionflower
- Mimosa Bark
- Hemp oil
- EXERCISE
- Meditation
- Classical Homeopathy
**ANXIETY**

- Dosages based on TD children
- Start at low dosage and slowly titrate up
- SSRIs most successful treatment for TD youth with anxiety
- SSRIs used in ASD population but lack of double-blind placebo controlled trials
- Data from SSRI trials report behavioral activation (increased activity, impulsivity, insomnia, etc.) in children with ASD (Walkup and Labellarte, 2001).

### TABLE 1: Summary of Medications for the Treatment of Anxiety in Youth With ASD

<table>
<thead>
<tr>
<th>Symptom <em>a</em></th>
<th>Medication</th>
<th>Dose Range</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute anxiety symptom</td>
<td>Sertraline</td>
<td>10-50 mg daily</td>
<td>Review in typically developing youth, Meltzoff et al (2010)</td>
</tr>
<tr>
<td>Acute anxiety symptom</td>
<td>Flupentixol</td>
<td>2.5-6 mg daily</td>
<td>No data available</td>
</tr>
<tr>
<td>Acute anxiety symptom</td>
<td>Lorazepam</td>
<td>0.1 mg PO, 0.5 mg IM</td>
<td>No data available</td>
</tr>
<tr>
<td>Behavioral dysregulation</td>
<td>Divalproex</td>
<td>2-6 mg/lb body weight daily</td>
<td>Review by Mahajan et al (2012), and Hadingh (2014)</td>
</tr>
<tr>
<td>Behavioral dysregulation</td>
<td>Zolpidem</td>
<td>0.25-5 mg PO</td>
<td>No data available</td>
</tr>
<tr>
<td>Thought</td>
<td>Propranolol</td>
<td>5-10 mg PO</td>
<td>No data available</td>
</tr>
</tbody>
</table>

**ANXIETY**

- Modified CBT (MCBT) is an effective treatment of children and adolescents with high-functioning ASD and anxiety disorders
- Can be administered individually or in a group and often includes parental involvement
- This therapy includes affective education, cognitive restructuring, reducing avoidance behaviors, relaxation, modeling, and exposure to the feared stimuli (with response prevention)
SLEEP DISTURBANCES

- **Herbals:**
  - Passionflower
  - Skullcap
  - Oat
  - Chamomile
  - Valerian
  - Chinese Skullcap
  - Kava
  - Lavender
  - Ashwagandha

- **Nutrients:**
  - Melatonin
  - GABA
  - Magnesium
  - 5-HTP
  - L-theanine

- **Homeopathy:**
  - Constitutional Remedy
  - Coffea Cruda 30c

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TICS

- Oral or IV Magnesium (Garica-Lopez et al, 2009)
- GABA
- L-Theanine
- B6 (Garica-Lopez et al, 2009)
- Essential fatty acids (Gabbay et al, 2012)
- CBD (Seif Kanaan et al, 2017)
- Homeopathy
  - Constitutional Homeopathy
  - Agaricus Muscaris
- Exercise
- Acupuncture (Ma et al, 2006)
FOOD RESTRICTIONS

• ZINC
• Increasing protein in diet (i.e. protein powders)
• MCT OIL
• Digestive bitters
  • Ginger
  • Gentian
  • Anise

ANTIMICROBIAL TREATMENT

• Subjects with new onset of PANDAS and positive rapid strep test/throat cultures treated with appropriate antibiotics – their OCD resolved.

Prospective identification and treatment of children with pediatric autoimmune neuropsychiatric disorder associated with group A streptococcal infection (PANDAS).

Harris ML, Friedman ML
© Author Information

Abstract

BACKGROUND: The current diagnostic criteria for pediatric autoimmune neuropsychiatric disorder associated with group A streptococcal infection (PANDAS) are pediatric onset, neuropsychiatric disorder ( obsessive-compulsive disorder [OCD]), and/or disorder, abrupt onset and/or exacerbation of symptoms, association with group A betahemolytic streptococcal infection, and association with neurological abnormalities (e.g., hypereflexia or ataxia). Ineffective treatment was often required.

OBJECTIVES: To assess new-onset PANDAS cases in relation to strep sore throat.

SUBJECTS: Prospective PANDAS case identification and follow-up.

METHOD: Over a 3-year period (1998-2002), we identified 12 school-aged children with new-onset PANDAS. Each patient had the abrupt appearance of severe OCD behavior, accompanied by mild symptoms and signs of acute GAS pharyngitis. Throat swabs tested positive for GAS by rapid antigen detection and/or culture. The GAS was negative, when performed in n-13, showed a very high rate of GAS pharyngitis antibody titers. Mean age at presentation was 7 years (age range, 3-11 years). OCD symptoms were treated with antibiotics effective in eradicating GAS pharyngitis, including azithromycin, and other strategies, including the use of blood cultures and antibiotics. Follow-up throat cultures negative for GAS were obtained prospectively after the first PANDAS episode. Neurological OCD symptoms were seen in patients, and no one with a positive intranasal washout test was seen in acute GAS pharyngitis and responded to appropriate antibiotic therapy in the acute episode.

CONCLUSION: To our knowledge, this is the first prospective study to confirm that PANDAS is associated with acute GAS pharyngitis and responds to appropriate antibiotic therapy in the acute episode.
ANTIMICROBIAL TREATMENT

Antibiotics

• IM Bicillin
• Penicillin, Amoxicillin-Clavulanate, Azithromycin, Clarithromycin, Cephalexin, Cefadroxil, Clindamycin (Shulman et al, Clin Inf Dis, 2012)
• Cefdinir
  • Randomized Trial of CEFDINIR vs. Placebo found that the Cefdinir group with significant improvement in tics and OCD over placebo group (Murphy et al. J of Child & Adolesc Psychopharm, 2015)
• Azithromycin
  • For long term use must have EKG to rule out prolonged QT interval
  • Is effective against Mycoplasma and has immunomodulatory properties (Obregon et al, Neuropsych, 2012; Murphy et al, J Antimicrob Chemoth, 2008)
• Antibiotic Prophylaxis with Penicillin or Azithromycin

A Double-Blind Randomized Placebo-Controlled Pilot Study of Azithromycin in Youth with Acute-Onset Obsessive-Compulsive Disorder.

Murphy T1,2,3,4,5, Becker MA1,3,4,5, Parker-Abbott EC1, Storch EA1,2,3,4,5,6,7, Levin AB1,2,3,4,5,6,7

@ Author Information

Abstract

OBJECTIVES: Sudden and severe onset of obsessive-compulsive disorder (OCD) may present secondary to infectious and/or immune-mediated triggers. We assessed the preliminary efficacy, tolerability, and safety of azithromycin compared with placebo in the treatment of OCD and associated symptoms in children with pediatric acute-onset neuropsychiatric syndrome (PANS).

METHODS: Thirty-one youth aged 4–14 years (M = 8.26 ± 2.78 years, 62.5% male) were randomized to receive either placebo or azithromycin for 4 weeks (10 mg/kg up to 500 mg per day). Both groups were administered twice daily probiotics. The primary outcome, obsessive-compulsive symptom severity, was assessed using the OCDS Clinical Global Impressions Severity (CGI-S OCD) and Children’s Yale-Brown Obsessive Compulsive Scale (CY-BOCS).

RESULTS: Participants in the azithromycin group (n = 17) showed significantly greater reductions in OCD severity on the CGI-S OCD than the placebo group (n = 14) posttreatment (p = 0.003), although there were no significant differences on the CY-BOCS. Significantly more participants in the azithromycin condition met treatment responder criteria on the CGI-I OCD at the end of week 4 (41.2%, n = 7) in comparison to the placebo group (7.1%, n = 1; p = 0.045). Tic severity moderated treatment response, with greater tic severity being associated with enhanced treatment response on the CGI-I OCD. Azithromycin was well tolerated with minimal adverse effects and no study dropouts due to side effects. However, the azithromycin group showed a trend toward significantly greater electrocardiography QTc (p = 0.000) at the end of week 4, and significantly more reports of loose or abnormal stools (p = 0.009).

CONCLUSION: This double-blind pilot study suggests that azithromycin may be helpful in treating youth meeting the PANS diagnosis, especially those with elevated levels of both OCD and tic symptoms. Azithromycin was well tolerated, but the potential for cardiac risks suggests that additional monitoring may be needed to ensure safety.
ANTIMICROBIAL HERBS FOR STREP

- **Usnea**
  - Activity against strep species (Abachi et al., 2016)

- **Taiga** – Pine needle extract
  - Antimicrobial/antifungal activity (Lee et al., 2005)

- **Berberine (Goldenseal)**
  - Berberine sulfate blocks adherence of Streptococcus pyogenes to epithelial cells, fibronectin, hexadecane (Sun D et al., 1988)

- **Neem**
  - Neem extract effective against four Streptococcus species responsible for causing dental caries (Chava et al., 2012).

- **Oregano Oil**

ANTIMICROBIAL HERBS FOR STREP

- **Cordyceps**
  - Medicinal mushroom containing mycelium which showed to protect against strep in animal models (Kou et al., 2005)

- **Allium sativum**
  - Effective against multi-drug resistant bacteria including strep species (Iwalokun et al., 2004)

- **Coptis**
  - Antimicrobial properties against strep mutans (Choi et al., 2007)

- **Capsicum** (Cichewicz and Thorpe, 1996)

- **Achillea** (Candan et al., 2003)

- **Ligusticum** (Xiao et al., 2004)

- **Strep Throat Formula - Hydrastis, Echinacea, Myrrha, and Phytolacca**
# Antimicrobial Interventions for Mycoplasma

- Silvercillin
- Goldenseal
- Houttuynia
- Isatis
- Resihi
- Pomegranate juice
- Brazil Nuts
- Homeopathic Mycoplasma Nosode

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# Antimicrobial Interventions for Viruses

- Vitamin A
- Vitamin D
- Vitamin C
- L-Lysine
  - amino acid that decreases viral load
- Monolaurin
  - Interferes with virus assembly and viral maturation
  - Do not use if coconut allergy
- Zinc
- Elderberry
  - Hemagglutinin protein has been shown to stop a virus’ capability to replicate by inhibiting its ability to penetrate the cell wall (Serkedjiev J and Manolova N, 1999)
  - Do not consume raw elderberries - contain cyanogenic glycosides and must be cooked sufficiently to avoid risk of cyanide toxicity
ANTIMICROBIAL INTERVENTIONS FOR VIRUSES

- **Glycyrrhiza (Licorice)**
  - Glycyrrhizic acid present in the plant inhibits virus growth and inactivates virus particles (Arora R. et al, 2011)

- **Ginger**
  - Increase levels of antioxidant enzymes, including superoxide dismutase and glutathione peroxidase and TNF-alpha

- **Olive Leaf**
  - Prevents virus shedding, budding, and assembly of cell membranes

- **Lemon Balm**
  - Inhibits virus replication (Pourghanbari et al, 2016)

- **Echinacea**
  - To increase antibody production, increase and stimulate the activity of white blood cells (Brinkeborn et al, 1998)
  - Implement acute viral protocols at onset of viral illnesses (i.e. vitamin A, D, Zinc, L-lysine, enzyme defense, etc)

OTHER INTERVENTIONS

- **Vitamin D**
  - Deficiency associated with increased frequency infections (Thornton et al, 2013)
  - Downregulate autoimmune processes (Rolf et al, 2014)

- **Ibuprofen/NSAIDS** (Spartz et al, 2017)

- **Xylitol**
  - Inhibits growth of strep mutans and Streptococcus pneumoniae (Tapianien et al, 2001)

- **Probiotics**

- **BLIS K12**

- **Essential Oils**
Vitamin D Deficiency in Obsessive-Compulsive Disorder Patients with Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections: A Case Control Study.

Celik G1, Tazi D2, Tahiroglu A1, Avci A1, Yıldız B2, Çam D2.

Abstract

INTRODUCTION: Previous studies have indicated that vitamin D deficiency is common in psychiatric patients, particularly in those with neuropsychiatric disorders such as autism and schizophrenia. Vitamin D is an important neurosteroid hormone and immunomodulatory agent that also has bone metabolic effects. There has been an increasing interest in immune-related neuropsychiatric symptoms that are triggered by group A beta-hemolytic streptococcal infections. In this study, we aimed to compare the serum levels of vitamin D between obsessive-compulsive disorder (OCD) patients with pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) and control subjects.

METHODS: Thirty-three OCD patients with PANDAS and 20 healthy controls were enrolled in the study. Serum 25-hydroxyvitamin D (25-(OH)D), calcium, phosphorus, alkaline phosphatase, and parathormone levels of the two groups were compared. Serum 25-(OH)D levels of <15 ng/mL were classified as vitamin D deficiency. The children’s Yale-Brown Obsessive Compulsive Scale (YBOCS) and Clinical Global Impression (CGI) were used to assess the severity of OCD symptoms.

RESULTS: There was no significant difference in serum 25-(OH)D levels between the patient and control groups. However, vitamin D deficiency was significantly more frequent in the patient group than in the control group (48.5% vs. 20.0%, p=0.038). Moreover, OCD patients with vitamin D deficiency had higher rates of comorbid ADHD than those without vitamin D deficiency (87.5% vs. 52.6%; p=0.027). While serum phosphorus levels were negatively correlated with age as well as alkaline phosphatase and ABO levels, they were positively correlated with the YBOCS total score and global severity score. Serum parathormone levels were positively correlated with the YBOCS total score, compulsive score, obsession score, and global severity score.

CONCLUSION: This study supports the hypothesis that an association between vitamin D metabolism and PANDAS-related OCD exists. We suggest that biochemical parameters predicting metabolic bone diseases are more common in PANDAS patients. There is a need for prospective studies to show a clear association between PANDAS and bone metabolic turnover based on autoimmune mechanisms.

Use of Streptococcus salivarius K12 in the prevention of streptococcal and viral pharyngotonsillitis in children.

Di Pietro E1, Colombo A2, Zanoli A2, Basso P1, Rotella AS1.

Abstract

BACKGROUND: Streptococcus salivarius K12 is an oral probiotic strain releasing two lantibiotics (salivaricin A2 and salivaricin B) that antagonize the growth of S. pyogenes, the most important bacterial cause of pharyngeal infections in humans also affected by episodes of acute otitis media. S. salivarius K12 successfully colonizes the oral cavity, and is endowed with an excellent safety profile. We tested its preventive role in reducing the incidence of both streptococcal and viral pharyngitis and/or tonsillitis in children.

MATERIALS AND METHODS: We enrolled 61 children with a diagnosis of recurrent oral streptococcal disorders. Thirty-one of them were enrolled to be treated daily for 90 days with a slow-release tablet for oral use, containing no less than 1 billion colony-forming units/tablet of S. salivarius K12 (Bactobis®), and the remaining 30 served as the untreated control group. During treatment, they were all examined for streptococcal infection. Twenty children (ten per group) were also assessed in terms of viral infection. Secondary end points in both groups were the number of days under antibiotic and antipyretic therapy and the number of days off school (children) and off work (parents).

RESULTS: The 30 children who completed the 90-day trial with Bactobis® showed a significant reduction in their episodes of streptococcal pharyngeal infection (>90%), as calculated by comparing the infection rates of the previous year. No difference was observed in the control group. The treated group showed a significant decrease in the incidence (80%) of oral viral infections. Again, there was no difference in the control group. With regard to secondary end points, the number of days under antibiotic treatment of the treated and control groups were 30 and 300 respectively, days under antipyretic treatment 16 and 228, days of absence from school 16 and 228, and days of absence from work 16 and 228. The product was well tolerated by the subjects, with no side effects, and only one individual reported bad product palatability and dropped out.

CONCLUSION: Prophylactic administration of S. salivarius K12 to children with a history of recurrent oral streptococcal disease resulted in a considerable reduction of episodes of both streptococcal and viral infections and reduced the number of days under antibiotic and/or antipyretic therapy and days of absence from school or work.
IMMUNOMODULATORY TREATMENT

- Steroids (oral vs IV; length of course depends on symptom severity)
  - Short burst – used therapeutically and diagnostically
  - Temporary fix in some; need to do for 30 days with taper +/- pulses
  - Transient worsening typical
- Helminth Therapy – immunotherapy with the use of HDCs
  - www.biomerestoration.com
  - helminthictherapywiki.org
- Plasmaphoresis – process that filters the blood and removes harmful antibodies
  - severe-extreme disease (Dalmau et al, 2011)
- Rituximab – works by turning off a part of the immune system that is not working properly in autoimmune disease
  - Deteriorating, moderate-extreme disease & previous responsiveness & autoimmunity (Chang et al, 2015)
IMMUNOMODULATORY TREATMENT

IVIG – use of intravenous immunoglobulins to support immune system

- No improvements in control group; significant decrease in OCD severity in IVIG and plasmaphoresis groups after 1 month (Perlmutter et al., 1999)
- One to six month course in moderate/severe (Frankovich et al., 2017)
- > 60% reduction in symptoms in children with prophylactic antibiotics followed by open label IVIG (sustained > 6 mths)
- High ANA and Cam Kinase activation predictive of symptoms improvement → Antibiotics therapeutic when these elevated
**IMMUNOMODULATORY TREATMENT**

- **Probiotics and Prebiotics**
  - Lactobacillus, Bifidobacterium, Bacillus
  - Saccharomyces Boulardii
- **Essential Fatty Acids**—Omega 3 (EPA/DHA) & 6 (GLA)
  - Eat Sardines!
  - Modulation of inflammatory reactions, lowering triglycerides, nerve transmission
    - (Belluzzi et al, 1996)
- **Aloe**
  - Anti-oxidant properties to decrease ROS (Landmead et al, 2004)
- **Curcumin**
  - Efficacy of curcumin, and a saffron/curcumin combination for the treatment of major depression: A randomized, double-blind, placebo-controlled study.
    - (Lopresti et al, 2017)
- **CBD Oil**
  - Suppression of cytokines and chemokines at inflammatory sites and upregulation of FoxP3+ regulatory T cells (Nagarkatti et al, 2009)
- **Flavonoids**—Quercetin, Luteolin, Rutin
  - Potent mast cell stabilizer inhibits release of histamine & inflammatory mediators
  - Prevents excessive release of histamine (Chuenkityanaon et al, 2010)

**CLOSING REMARKS**

PANS/PANDAS is a CLINICAL DIAGNOSIS

Think PANS/PANDAS with ACUTE onset of symptoms (tics, OCD, anxiety, regression, etc.)

Not every child will present with all of these symptoms

Treatment plan should include antimicrobial interventions, immunomodulatory interventions, and therapy

Relapsing and remitting course of symptoms

Best to combine conventional and natural interventions

**TAKE CARE OF YOURSELF – YOUR CHILD’S HEALTH DEPENDS ON IT!**
THANK YOU!

www.lindseywellsnd.com

Instagram: @lindseywellsnd
Facebook: Lindsey Wells ND, LLC