Current Literature in Pediatric Psychosomatics (CLiPPs)

CLiPPs: Inflammation in Children and Adolescents With Neuropsychiatric Disorders

Mitchell, RH, MD, Goldstein, BI. Inflammation in children and adolescents with neuropsychiatric disorders: a systematic review. *J Am Acad Child Adolesc Psychiatry.* 2014; 53(3):274-296.

Reviewed by: Nicole A. Mavrides, MD, University of Miami/Jackson Memorial Medical Center, Miami, FL

Background: Inflammation is well established as a factor in the pathogenesis of chronic medical diseases that are highly co-morbid with psychiatric disorders. There is great evidence supporting the link between inflammation and major depressive disorder in adults, and more research is also linking inflammation and MDD and other psychiatric disorders in children. The purpose of the review was to summarize the evidence regarding inflammation and psychiatric disorders in children and adolescents.

Methods: A systematic review of the literature on inflammation, neuropsychiatric disorders in children and adolescents was performed via MEDLINE looking at all studies from 1946 to August 2013. Studies were included if the pro-inflammatory markers (PIMs) in children and or adolescents with neuropsychiatric disorders were measured.

Results: 67 studies, involving 3,952 youth, were included in the final analysis and review, but the MEDLINE search yielded 667 citations. Evidence for the pro-inflammatory state was found to be strongest in autism spectrum disorders (ASD). IFN-γ was elevated or showed a trend toward elevation in many of the studies compared to controls. Some of the other pro-inflammatory markers were inconsistent with some studies show increases and others showing no difference between controls. The data also demonstrated increases in PIMs in children and adolescents with MDD, Bipolar Disorder, PTSD, OCD, Tourette's Disorder, ADHD, and Schizophrenia. The data was inconsistent across the many studies. The findings in youth with MDD, Bipolar Disorder, and PTSD seem to be similar and equivocal to the adult literature in this area. Specifically, IL-6, IFN-γ, IL-2, CRP, and TNF-α were seen to be elevated in both children and adolescents with the above disorders, but also in first degree relatives of those with the above disorders.

Conclusion/Commentary: There is preliminary evidence for elevated markers of inflammation in children and adolescents with neuropsychiatric disorders, specifically ASD, MDD, Psychotic Disorder, Bipolar Disorder, and PTSD. Pro-inflammatory markers are unlikely to serve as diagnostic biomarkers because of the non-specific nature, but they may serve as essential markers of illness activity and potential treatment response. One other recent study did find that IL-8 was increased in ASD patients, which may demonstrate immune dysfunction in ASD.[1] More research needs to be completed with larger, prospective studies to appreciate the goal of inflammatory markers apprising clinical practice.

Take Away

Inflammation and neuropsychiatric disorders in children and adolescents appear to have a relationship similar to that in adults, with elevated PIMs, but more research needs to be done to truly understand the implication.

This article review originally appeared in the CLiPPs Spring 2016 Edition.

References

1. Tonhajzerova I, Ondrejka I, Mestanik M. *et al.* Inflammatory activity in autism spectrum disorders. *Advances in Experimental Medicine and Biology*. 2015; 861:93-98.

CLiPPs: Seropositive vs. Seronegative Autoimmune Panencephalitis

Hacohen Y, Wright S, Waters P, *et al.* Paediatric autoimmune encephalopathies: clinical features, laboratory investigations and outcomes in patients with or without antibodies to known central nervous system antigens. *J Neurol Neurosurg Psychiatry* 2013;84:748-755.

Reviewed by: Emily Katz, MD, Brown University School of Medicine; Hasbro Children's Hospital, Providence, RI.

Background: There is a growing recognition of autoimmune encephalitis such as anti-NMDA receptor encephalitis as a cause of psychiatric symptoms and altered mental status in children. Some patients may present with signs and symptoms suggestive of an autoimmune process but do not test positive for known autoantibodies. The objective of this study was to describe the clinical features of children with suspected autoimmune encephalitis and compare findings and outcomes of patients with and without identified CNS autoantibodies. Some authors refer to this latter entity as SNAPE (seronegative autoimmune encephalitis).

Methods: Serum samples of 111 children presenting with encephalopathy plus neuropsychiatric symptoms, seizures, movement disorders and/or cognitive dysfunction seen at 5 tertiary referral centers in the UK with encephalopathy were sent to the Oxford lab for CNS autoantibody testing. A blinded clinical review panel identified 48 probable cases of autoimmune encephalitis. Clinical data including demographic information, features of presentation, imaging and other laboratory testing results, response to immunotherapy and other outcomes were compiled, with reviewers blinded to autoantibody testing results.

Results: Serum antibodies were detected in 44% of the patients with probable autoimmune encephalitis. Patients ranged between just under 2 to 18 years of age. Antibody negative patients were clinically similar to those with identified auto-antibodies and had similar response to immunotherapy. Seizures (86%) and behavioral changes (63%) were the most common associated clinical findings. EEGs were abnormal in 70% of patients. 52% of patients receiving immunotherapy experienced a complete recovery, as opposed to 28% of untreated patients.

Conclusion/Commentary: Patients with probable autoimmune encephalitis share clinical features regardless of presence of detected autoantibodies. Treatment response to immunotherapy was generally positive, with 94% of treated patients classified having some response and 58% experiencing a full recovery. These data suggest that an autoimmune work-up should be strongly considered for patients who present with encephalopathy and at least one of the following features: neuropsychiatric symptoms, seizures, movement disorders, or cognitive dysfunction.

Take Away

SNAPE happens. If autoimmune encephalitis is strongly suspected, clinicians should consider immunotherapy even in cases where tests for known autoantibodies are negative.

This article review originally appeared in the CLiPPs Summer 2016 Edition.

Additional resources related to this CLiPP:

- Leypoldt F, Armangue T, Dalmau J. Autoimmune encephalopathies. *Ann NY Acad Sci.* 2015;1338:94-114.
- Najjar S, Pearlman DM, Devinsky O. Neuropsychiatric autoimmune encephalitis without vgkc-complex, nmdar, and gad autoantibodies: case reports and literature review. *Cogn Behav Neurol.* 2013;26(1):36-49.
- Lancaster E, Dalmau J. Neuronal autoantigens—pathogenesis, associated disorders and antibody testing. *Nat Rev Neurol.* 2012;8(7):380-90.
- Najjar S, Pearlman DM, Alper K, *et al.* Neuroinflammation and psychiatric illness. *J Neuroinflammation.* 2013;10:43.
- Bale JF. Virus and immune-mediated encephalitides: epidemiology, diagnoses, treatment, and prevention. *Pediatr Neurol.* 2015;53:3-12.

CLiPPs: Psychiatric Boarding in the Pediatric Inpatient Medical Setting: A Retrospective Analysis

Gallagher KA, Bujoreanu IS, Cheung P, *et al.* Psychiatric boarding in the pediatric inpatient medical setting: a retrospective analysis. *Hospital Pediatrics*. 2017;7(8):444-450.

Reviewed by: Yasas Tanguturi, MD, MPH, Vanderbilt University Medical Center

Background: The number of pediatric patients presenting to emergency rooms for acute psychiatric concerns has increased, but the number of available inpatient psychiatric beds has decreased. This has led to the problem of 'Psychiatric Boarding', where patients are admitted either to an emergency room or to an inpatient pediatric service awaiting psychiatric placement.[1] The Joint Commission recommends that boarding not exceed 4 hours. There are various problems associated with boarding including delayed care, negative outcomes for patients, families and the hospital system, along with financial losses.[2] The literature has identified that patients who are more psychiatrically acute or clinically severe tend to have longer wait times before placement (a so called 'reverse triage' effect).[3,4] This paper explores the increase in volume of psychiatric boarders in a pediatric inpatient unit from 2011 to 2013 and describes the characteristics of those boarding in 2013 along with outcomes and interventions delivered.

Methods: This is a retrospective chart review of boarders admitted to the pediatric unit at Boston Children's Hospital in the year 2013. All boarders on the unit were followed by the psychiatry consult service. Patients were assessed using the CGAS (Clinical Global Assessment Scale) upon admission; they were also assessed daily using the CGI-S and CGI-I (Clinical Global Impression Scale - Severity and Improvement).

Results: There was an almost 50% increase in boarders from 2011 (n=241) to 2013 (n=437). Out of 437 charts reviewed for the year 2013, the most common presenting complaint was suicidal attempt, followed by aggressive behavior and suicidal ideation. Mean CGAS scores indicated a high clinical severity for the population (risk of self-harm/impaired functioning). More than 70% had 2 or more psychiatric diagnoses, 66% had previous psychotropic medication treatment and nearly 40% had previous psychiatric admissions. Average length of boarding was 3.11 days. CGI scores demonstrated a significant improvement from admission to discharge. This was even more pronounced in the small percentage of kids who boarded for longer than 5 days. Around 23% of boarders were discharged to lower levels of care (partial hospitalization programs or outpatient treatment). A majority of the boarders received interventions such as psycho education (91%) and individual psychotherapy (87%).

Conclusion/Commentary: Findings highlight the clinical severity of boarding patients, consistent with previous literature on the subject. This paper demonstrates a role for the delivery of interventions associated with improvement during the boarding period. In contrast to previous studies,3 the team was able to spend one hour per day on average with the boarders and deliver psychosocial supports including psychotherapy. This led to the development of a new service model which included addition of new social workers, psychiatric nurses for behavioral interventions and new standardized protocol. This study also demonstrates a useful way of clinical monitoring of kids while boarding that need to be further validated.

Take Away

There has been an increase in psychiatric boarding in pediatric inpatient units. The time period of boarding allows for the delivery of interventions to help with stabilization and treatment. Enhanced program interventions could help with faster stabilization and discharge to lower levels of care.

This article review originally appeared in the CLiPPs Spring 2019 Edition.

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1. Hazen EP, Prager LM. A quiet crisis: pediatric patients waiting for inpatient psychiatric care. *J Am Child Adolesc Psychiatry*. 2017;56(8):631-3.
2. Wharff EA, Ginnis KB, Ross AM, Blood EA. Predictors of psychiatric boarding in the pediatric emergency department: implications for emergency care. *Pediatric Emergency Care*. 2011;27(6):483-9.
3. Mansbach JM, Wharff E, Austin SB, Ginnis K, Woods ER. Which psychiatric patients board on the medical service? *Pediatrics.* 2003;111(6):e693-8.
4. Claudius I, Donofrio JJ, Lam CN, Santillanes G. Impact of boarding pediatric psychiatric patients on a medical ward. *Hospital Pediatrics.* 2014;4(3):125-32.

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