Efficacy of IVIg in Patients with Paediatric Acute-Onset Neuropsychiatric Syndrome (PANS)

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Introduction

- Paediatric acute-onset neuropsychiatric syndrome (PANS) is triggered in children by infectious agents and presents as severe, acute neuropsychiatric symptoms, including obsessive-compulsive disorder (OCD) and tics[1]
- A clinical trial of 21 children with PANS showed that multiple, consecutive infusions of intravenous immunoglobulin (IVIg) were effective in treating psychiatric symptoms[2]
- This study aimed to explore immune dysregulation in PANS and its potential amelioration with IVIg therapy

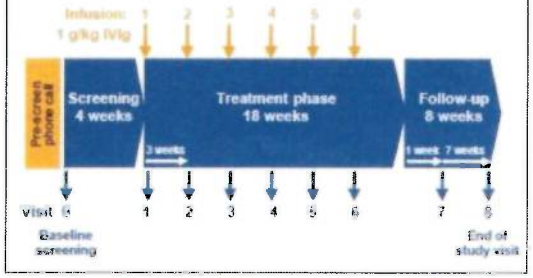
Objectives

- Objectives of this study were to assess the effect of IVIg therapy on monocyte activation and psychological evaluations in patients with PANS

Methods

- Open-label study included children aged 4–16 years old with moderate-to-severe PANS diagnosed according to accepted criteria[1]
- Study design is shown in Figure 1. Patients received 1 g/kg body weight IVIg (Octagam 5%, Octapharma AG) at Visits 1–6
- Primary endpoint was change in monocyte activation in children with PANS from baseline to post-infusion following six infusions of IVIg
- Blood samples were taken for laboratory analysis at Visits 1 (pre-treatment), 7 and 8, and monocyte activation was assessed via flow cytometry
- Psychiatric assessments were performed at Visits 1, 7 and 8, including the Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS), Yale Global Tic Severity Score (YGTSS), and Parent-Rated PANS Questionnaire

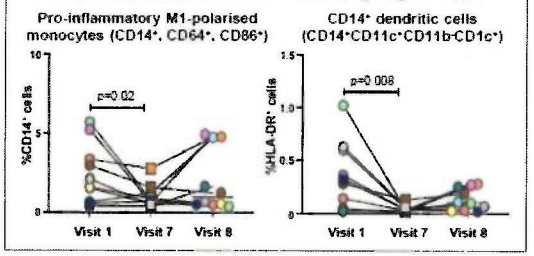
Figure 1. Study design



Results

- Ten patients were enrolled and completed the study. All participants were male and of White race, with a mean age of 12.4 years (6.4±3.92; range 6–16). Eight patients had been diagnosed with PANS >2 years prior to screening
- Overall levels of white blood cells and monocytes remained constant over the course of the study (data not shown)
- Levels of activated inflammatory monocytes decreased compared to pre-treatment values (Visit 1) in all patients by Visit 7 (Figure 2)
- In some patients, levels of inflammatory monocytes started to increase again by Visit 8 (i.e., after the 8-week follow-up period, when no further doses of IVIg were administered)

Figure 2. Frequency of pro-inflammatory monocytes and monocyte-derived dendritic cells following IVIg infusion



- OCD and tics (measured by CY-BOCS and YGTSS) improved significantly from Baseline to Visits 7 and 8 (Figure 3)
- PANS symptoms also improved significantly according to the parent-related PANS questionnaire (Figure 4) and the PANS Symptoms Scale, which decreased by 65.1% from baseline to Week 7 ($p<0.001$) and 44.8% to Week 8 ($p=0.006$)
- Reduced levels of inflammatory monocytes (M1-polarised cells) correlated significantly with reduced severity of tics (YGTSS). However, there was no significant correlation between M1 monocyte level and OCD (CY-BOCS) score (Figure 5)

Figure 3. Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS), Yale Global Tic Severity Score (YGTSS) following IVIg infusion

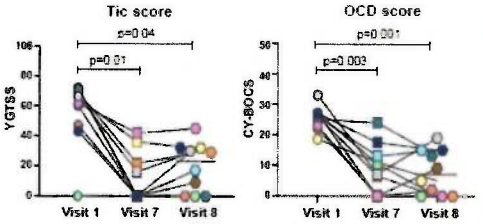


Figure 4. Parent-rated PANS questionnaire (N=10)

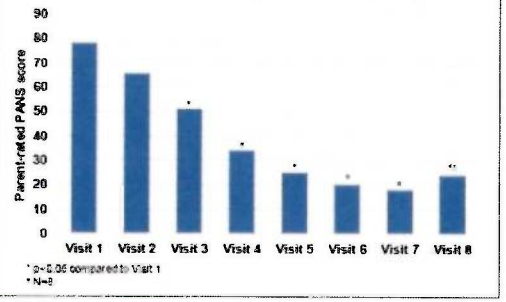
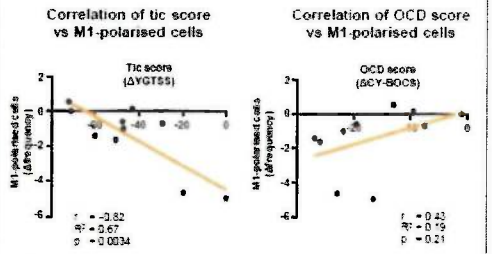


Figure 5. Correlation of pro-inflammatory M1-polarised cells with tic score (YGTSS) and OCD (CY-BOCS)



Conclusions

- Results from this study of 10 patients, together with our previous study in 21 patients,[2] indicate that PANS is an immune-mediated, inflammatory disease
- Both studies showed that treatment with IVIg significantly ameliorated the symptoms of PANS, including OCD and tics, as measured by psychological evaluations
- Here, we show treatment with IVIg also decreased levels of inflammatory monocytes; this correlated with the decrease in tic score
- Further analyses will help to clarify both the role of the immune system in this disease and the mechanism of IVIg in its regulation

References

1. Chang K, et al. *J Child Adolesc Psychopharmacol* 2015;25(1):3-13.
2. Melamed I, et al. *J Child Adolesc Psychopharmacol* 2021;31(2):118-128.

Disclosures

Isaac Melamed and Heather Pein are affiliated with the IMMUNOe Research Center, Centennial, CO, USA. Huub Kreuwel is an employee of Octapharma USA.