

A NEW ARTICLE ABOUT Methodology of a Natural History Study of Alternating Hemiplegia of Childhood as a Prototype Disease (OBSERV-AHC Study) HAS BEEN PUBLISHED IN THE JOURNAL OF CHILD NEUROLOGY

Synopsis from the first author of the article Dr. Shital Patel (Duke University, Durham, NC USA)

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Methodology of a Natural History Study of a Rare Neurodevelopmental Disorder: Alternating Hemiplegia of Childhood as a Prototype Disease

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This article is about how to study a rare disease such as Alternating Hemiplegia of Childhood (AHC). It uses our international multicenter OBSERV-AHC study methods as a prototype model for studying rare diseases. This article reviews the steps taken to study a rare disease. This included identification of relevant questions about AHC natural history and expected challenges. Based on review of the literature, we identified solutions to determine appropriate methods to address these questions.

In this article, we reviewed these solutions which included how we developed and standardized an AHC-specific spell video-library and spell calendars. We then reviewed how we used specific methods of study for ongoing measurements of developmental and behavioral (non-paroxysmal) and seizures, movement disorders and AHC spells (paroxysmal manifestations) using unified data collection protocols and centralized data platform. We reviewed how we were then able to use specialized analysis methods which included, but was not limited to Cohen's kappa, interclass correlation coefficient, linear mixed effects models, principal component, propensity score, and ambidirectional analyses.

This article is able to break down the ways in which not only AHC can be studied, but also benefit in the study of other rare pediatric neurodevelopmental disorders.

Shital Patel and all the OBSERV-AHC workgroup
29 September 2023

RESEARCH ARTICLE | ARTICLES IN PRESS
Development and testing of methods to record and follow up spells in patients with alternating hemiplegia of childhood

- A video-library of AHC type spells was developed along with specific training for caregivers who were trained on recognition of the different types of spells.**
- An Event Calendar was developed and provided to 3 caregivers with weekly video-conferences with providers for 8 weeks.**
- An Electronic Diary (e-Diary) was developed with smart phone and computer access and shared to 23 patients. Providers reviewed entries for up to 2 years.**

Result: Training led to improved identification of spells by caregivers (p<0.001) and to a high degree of agreement between caregivers' and experts' identification (Cohen's Kappa >0.8).

Result: 78% of all entries had complete information (see diagram above), and this high percentage did not change during follow up (> 0.95).

Result: 52% of caregivers used e-Diary for 13-24 months, 66.2% used it in future studies. Those who used it for 13 months, were very likely continue to use it during the rest of that year.



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Abstract

Here we describe the process of development of the methodology for an international multi-center natural history study of alternating hemiplegia of childhood as a prototype disease for rare neurodevelopmental disorders. We describe a systematic multi-step approach to which we first identified relevant questions about alternating hemiplegia of childhood natural history and expected challenges. Then, based on our experience with alternating hemiplegia of childhood and a separate natural history study, we identified solutions to determine appropriate methods to address these questions. Specifically, these included: video-library, spell calendars, unified data collection protocols, centralized data platform, adoption of standardized analysis methods (kappa, interclass correlation coefficient, linear mixed effects models, principal component, propensity score, and ambidirectional analyses). These methods and approaches may be applicable to the study of other rare pediatric neurodevelopmental disorders.

See also the article published on the European Journal of Pediatric Neurology, 2023 Aug 4, “**Development and testing of methods to record and follow up spells in patients with alternating hemiplegia of childhood**”.

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The multicentre **OBSERV-AHC Study**, on natural history and therapy for AHC, is led by Prof. Mohamad Mikati (Duke University, Durham, NC USA) and is being carried out within the collaborative framework of the IAHCRC Consortium, according to the rules on collaboration and on data sharing provided for by the IAHCRC Charter.