Epilepsy Currents
2023, Vol. 23(5) 294-295

DOI: 10.1177/15357597231182484
journals.sagepub.com/home/epi
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The ACTH Quandary: Balancing Efficacy and Affordability for Infantile Spasms Treatment

Temporal Trends in the Cost and Use of First-Line Treatments for Infantile Epileptic Spasms Syndrome

Sanchez Fernandez I, Amengual-Gual M, Aguilar CB, Romeu A, Sheikh T, Torres A, Chao J, Jonas R, Gaínza-Lein M, Harini C, Douglass L. *Epilepsia.* 2023;64(3):630-640. doi:10.1111/epi.17498

Objective: To describe the temporal trends in the cost and use of adrenocorticotropic hormone (ACTH), oral prednisolone, and vigabatrin, the first-line treatments for infantile epileptic spasms syndrome (IESS). Methods: Retrospective observational study using the MarketScan Commercial database from 2006 to 2020. We identified patients with IESS diagnosed between birth and 18 months of age who received at least one of the first-line treatments within 60 days of diagnosis. Costs were adjusted for inflation using the Gross Domestic Product Implicit Price Deflator. Results: A total of 1131 patients received at least one first-line treatment (median [p25-p75] age: 6.3 [4.5-8.3] months, 55% male), of whom 592 patients received ACTH, 363 patients received oral prednisolone, and 355 patients received vigabatrin. After adjusting for inflation, the median average wholesale price of a 14-day course of treatment increased for ACTH from $3718 in 2006 to $100 457 in 2020, ~2700% (by a factor of 27), whereas it decreased for oral prednisolone from $169 in 2006 to $89 in 2020, ~50% (by a factor of 0.5), and increased for vigabatrin from $1206 in 2009 (first year with data on vigabatrin used for IESS) to $4102 in 2020, ~340% (by a factor of 3.4). During the first 60 days after diagnosis, inpatient admission days and costs were higher for ACTH than for oral prednisolone and vigabatrin-5.0 (3.0-8.3) days vs 2.0 (0.0-5.0) days vs 2.0 (0.0-6.0) days, $p < .0001$; and $32 828 ($14 711-$67 216) vs $16 227 ($0-$35 829) vs $17 844 ($0-$47 642), $p < .0001$. ACTH use decreased from representing 78% of first-line treatments in 2006 to 18% in 2020 ($p < .0001$). Sensitivity analyses confirmed the robustness of the results. Significance: The gap between the cost of ACTH and the cost of oral prednisolone or vigabatrin has widened markedly from 2006 to 2020, whereas the relative proportion of ACTH use has decreased.

Commentary

Infantile spasms treatment can be expensive, and unfortunately, adrenocorticotropic hormone (ACTH), one of the most effective treatments, is also the priciest. The cost of ACTH has increased dramatically over the last 2 decades. What was once a $40 vial became $39,000 in 2018. To put this into perspective, it's like buying a $3 gallon of milk that costs almost $3000 in about 2 decades. Unlike milk, which has numerous options, ACTH treatment has limited alternatives, leaving doctors and parents grappling with balancing effectiveness and affordability.

The American Academy of Neurology has recommended low-dose ACTH as the preferred first-line treatment for infantile spasms based on scientific evidence focusing on spasms resolution. Additionally, hormonal therapy has been found to be more effective than vigabatrin in cryptogenic infantile spasms. However, a recent study compared the cost-effectiveness of ACTH and oral steroids as first-line treatments and found no compelling evidence to support the superiority of ACTH over oral prednisolone in short-term effectiveness (2 weeks).[1] Moreover, oral prednisolone was also more cost-effective than ACTH.[1] Unfortunately, the study did not report on the long-term outcomes.

Infantile spasms treatment with ACTH is expensive due to several reasons. Firstly, there is limited competition in the United States market for animal-derived ACTH (Acthar® Gel), the only FDA-approved option for this condition. Despite the expiration of Acthar® Gel's patent, generic versions' development is hindered by complex manufacturing processes and regulatory hurdles. Furthermore, its distribution is limited as a specialty medicine that requires special handling and storage.

Synthetic ACTH is a potentially more affordable option for infantile spasms treatment. However, the depot formulation typically used for this purpose is not available in the United States. Despite the lack of direct comparison between synthetic and animal-derived ACTH, the synthetic version has proven efficacy and is widely used for infantile spasms treatment in many countries.[2-4] Barriers were created to block synthetic ACTH production in the United States, leading to a lawsuit

in 2017 between the Federal Trade Commission and the company regarding the alleged illegal monopoly.[5] Then, the case was settled, and the price issue remained.

Are you confident in the efficacy of the more affordable alternative treatments? Iván Sánchez Fernández reported a significant increase in the use of prednisone and vigabatrin as the first-line treatment for infantile spasms over the past decade. Their median costs were about 10% and 60% of the cost of ACTH, respectively.[6] While some studies suggest no significant difference in short-term outcomes between ACTH and oral steroids,[7,8] there is insufficient evidence to determine their long-term comparative outcomes, causing hesitancy for many providers.

In conclusion, balancing the efficacy and affordability of infantile spasms treatment is challenging because of the high cost of ACTH. One way to address this issue is by promoting market competition to help control its price. Furthermore, it is crucial to have strong evidence that supports the comparable long-term effectiveness of the more affordable options in controlling spasms and improving developmental outcomes. We need robust evidence to justify changes in recommendations and to create meaningful practice changes in the United States.

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Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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