

Migraine & Epilepsy

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Disclosures

- Consultant: Atkins Nutritionals, NeuroPace, Nutricia, Bloom Science
- Grant Support: Vitaflo
- Royalties: UpToDate, Demos Medical Publishing

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- *I am a pediatric epileptologist who enjoys seeing children with migraine*

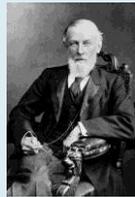


Dr. Don Lewis

"Some surprise may be felt that migraine is given a place in the borderland of epilepsy, but the position is justified ... the two maladies are sometimes mistaken, and more often their distinction is difficult."



"Some surprise may be felt that migraine is given a place in the borderland of epilepsy, but the position is justified ... the two maladies are sometimes mistaken, and more often their distinction is difficult."



Sir William Richard Gowers, London (1907)



Migraine and Epilepsy: Similar (Common) Conditions!

- Cortical events, at times with subcortical onset zones
 - Brainstem for migraine; thalamus for epilepsy
- Paroxysmal, short-lived, stereotyped events
 - High disability despite normal neurologic examinations
 - Treatments help but do not typically cure
- Patients often report triggers such as stress, sleep deprivation, menses
 - Attempts made by both societies to predict and prevent, but incomplete success





ANNUAL MEETING

Migraine and Epilepsy

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- Overview of the shared pathology
 - An epileptologist's approach...
- Expanding role of Genetics today
 - What are the key genes to be aware of?
- Treatment strategies
 - Options beyond valproate and topiramate...

ANNUAL MEETING

Epilepsy Syndromes (rare) with Increased Migraine Frequency

- Occipital epilepsies
 - Gastaut syndrome
 - Panayiotopoulos syndrome
- Metabolic/mitochondrial conditions
 - MELAS
 - Alexander Disease
- Neurocutaneous syndromes
 - Tuberos sclerosis complex
 - Sturge-Weber syndrome
- Alternating hemiplegia of childhood

ANNUAL MEETING

Comorbidity of migraine in children presenting with epilepsy to a tertiary care center

Seah A. Kufic, MD
Adam L. Hinton, MD
Eva H. Kowalek, MD

ABSTRACT
Objective: Migraine and epilepsy are 2 of the most common neurologic disorders in children. In this cross-sectional study we investigated a population of children with epilepsy to determine if children with a greater seizure burden or certain epilepsy syndromes had a higher risk of migraine. We also examined how often migraine is addressed and treated in a pediatric epilepsy cohort.
Methods: Between January 2010 and March 2011, we distributed questionnaires regarding headache symptoms and treatment to consecutive children with epilepsy seen in clinic at Johns Hopkins Hospital (JHO) children were studied. Records were subsequently reviewed for seizure type, age at onset, and treatment.
Results: The prevalence of migraine in our pediatric epilepsy population was 25%, which is greater than reported for children without epilepsy (9%-25%). Migraine was more prevalent in children <10 years ($p = 0.0005$), children with benign epilepsy with centrotemporal spikes (BECTS) ($p = 0.003$), and children with juvenile myoclonic epilepsy (JME) ($p = 0.008$). Migraine onset was more likely to have occurred after epilepsy was diagnosed ($p = 0.0002$), but was not more prevalent in those with intractable epilepsy. Only 50% of patients with weekly or greater migraines had documented discussions regarding headaches with their neurologist.
Conclusion: Migraine was comorbid in one-quarter of children with epilepsy in a tertiary care center. Children who were older or who had BECTS or JME were more likely to have migraines. Migraines were infrequently addressed within the neurology clinic. It is imperative to address comorbid migraines in treating children with epilepsy. [See www.pediatrics.com](#)

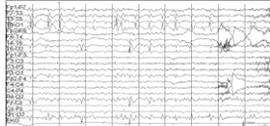
Table 2. Compared prevalence of demographic groups

| Category | No. (%) | % Migraine | p-Value (L ²) |
|-----------------|----------|------------|---------------------------|
| Epilepsy clinic | 312 (78) | 24 | 1 |
| Resident clinic | 88 | 25 | |
| Male | 209 (51) | 24 | 0.6 |
| Female | 197 | 26 | |
| <10 y | 195 (49) | 21 | 0.0009* |
| ≥10 y | 205 (51) | 32 | 0.047* |
| Syndromes | 160 (40) | 30 | 0.047* |
| No syndromes | 240 | 23 | |
| BECTS | 64 | 39 | 0.0029* |
| No BECTS | 22 | 22 | |
| JME | 23 | 48 | 0.0082* |
| No JME | 23 | 23 | |
| Intractable | 68 (17) | 26 | 0.73 |
| Not intractable | 332 | 24 | |
| Generalized | 159 (40) | 23 | 0.56 |
| Partial | 241 | 26 | |

Abbreviations: BECTS = benign epilepsy with centrotemporal spikes; JME = juvenile myoclonic epilepsy.
 * Significant.

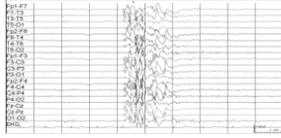
Benign Epilepsy with CentroTemporal Spikes (BECTS)

- 5-10 year old age of onset
- Brief seizure after falling asleep
 - Face and shoulder twitching with occasional preserved awareness
- Seizures sporadic and remit in puberty
- Most anticonvulsants work, but aren't always necessary to begin



Juvenile Myoclonic Epilepsy (JME)

- 12-15 year old with a convulsion upon awakening
- Reports early morning arm/body "jerks" which resolve by breakfast
- Nearly all will have seizures recur without anticonvulsants
- Easily treatable



Are migraines ignored in pediatric epilepsy clinics?

- Only 50% with > weekly migraines had a documented discussion (in the medical record)
- Only 28% were prescribed anticonvulsants with combined benefit vs. migraine
- No child was prescribed a triptan
 - *We can do better as epileptologists!*

Kelley et al. Neurology 2012;79:468-473



Migraine and Epilepsy

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Migraine and Epilepsy

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| |
|---|
| <p>Topiramate for the prophylaxis of episodic migraine in adults (Review)</p> <p><small>Linde M, Mulleners WM, Chronicle EP, McCrory DC</small></p> |
| <p>Valproate (valproic acid or sodium valproate or a combination of the two) for the prophylaxis of episodic migraine in adults (Review)</p> <p><small>Linde M, Mulleners WM, Chronicle EP, McCrory DC</small></p> |
| <p>Antiepileptics other than gabapentin, pregabalin, topiramate, and valproate for the prophylaxis of episodic migraine in adults (Review)</p> <p><small>Linde M, Mulleners WM, Chronicle EP, McCrory DC</small></p> |
| <p>Gabapentin or pregabalin for the prophylaxis of episodic migraine in adults (Review)</p> <p><small>Linde M, Mulleners WM, Chronicle EP, McCrory DC</small></p> |





- **Better than placebo**
 - Topiramate, valproate
- **No better than placebo**
 - Lamotrigine, clonazepam, oxcarbazepine
 - Gabapentin
 - "it is advocated that gabapentin should not be used in routine clinical practice"
- **Insufficient data to recommend**
 - Pregabalin (0), zonisamide (1), levetiracetam (1)
 - "considerable methodological limitations"



Vagus nerve stimulation

- Widely used for patients with refractory epilepsy
 - Devices becoming smaller with now a heart rate sensor/stimulator
- 6 patient series for migraine (Mauskop, *Cephalgia* 2005)
 - 4 responded
- 4 patients (Cecchini, *Neurol Sci* 2009)
 - 2 responded



Photo from epilepsy.com



nVNS (gammaCore)

- Portable, non-implanted device that delivers stimulation to the vagus nerve
- Demonstrated to reduce duration and pain intensity for migraine and episodic cluster headache
- Abortive (as VNS can be), but not designed currently as a preventative therapy (as VNS primarily is)



Photo from www.gammacore.com

Silverstein SD, et al. *Headache* 2016;56:1317-1332.
 Goswamy PJ et al. *Cephalalgia* 2014;28:959-969.



Ketogenic Dietary Therapies

- High fat, low carbohydrate diets
 - Continuous use since 1921
- Increasing popularity for pediatric, and now adult, epilepsy
- 50% reduction in seizures by 2-4 weeks
 - Typically used for 2 years in children when successful



www.chauffefoundation.org
 www.chauffefoundation.org



Can Ketosis Help Migraine Sufferers? A Case Report

The ketogenic diet has long been used in the treatment of severe epilepsy in children, adolescents, and adults and more recently in obese children and adults. In the Ketosis diet, there is a low carbohydrate intake and a high fat intake. The diet has been shown to be effective in the treatment of epilepsy and has been shown to have neuroprotective properties.¹

My wife began having severe headaches in elementary school. The headaches worsened during her teenage years and were officially diagnosed as migraines. The family history is significant for severe migraines in the maternal side.

The migraines were described as a "throbbing, burning, hot, sick" sensation in one temple. During her middle school years, the headaches progressed and were occurring more than 1 week. She tried multiple lifestyle changes without any change in the frequency of the headaches. Her diet, dieting, and two pregnancies did not alter the frequency.

Heretics medications were prescribed for approximately 10 years. Agents that helped the most included Ibuprofen, Aspirin, and Phenytoin. Phenytoin was discontinued in the fall of '05, the patient was being pregnant every 2 years for 10 years (1st, 2nd, 3rd, 4th, 5th, 6th, and 7th).

In an effort to lose the weight gained during pregnancy, she started on a diet program under medical supervision. Patients undergo a modified diet, taking 3 or 4 high protein, low carbohydrate snacks a day. Each snack is 200 calories, and the shakes are the only calorie source. Ketosis is

not and the modified diet for about 7 months and then was off diet and began to eat regular food. She has continued to be headache free. She has not gone from daily migraines to going 10 months without an attack and has gradually eaten unlimited sugar foods such as chocolate and chocolate without getting a headache.

In conclusion, ketosis appears to have cured my wife's migraines. Other cases of migraines suffered by the wife have been reported in a clinical trial of the diet.²

This letter is submitted with the hope of stimulating further research to confirm the benefits of a ketogenic diet in adolescents.

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2. Maly, MA, et al. The ketogenic diet substantially can do it, low. *Epilepsia*. 2004;45:1411-1413.
3. Swin, R, et al. The ketogenic diet for intractable epilepsy in adults. *Childs Nerv Syst*. 2003;19:171-176.
4. Kozloff EA, Swin DR, McDermott DL, Friesman DR. High protein of the Atkins diet as therapy for intractable epilepsy. *Neurology*. 2004;62:1281-1283.
5. Murphy F, Lakshmi S, Nelson K, Hesterman WM. The scientific progress of the ketogenic diet. *Child Psychiatry*. 2004;43:105.

Strahman R, *Headache* 2006



An Experience with a Ketogenic Dietary in Migraine*

By THOMAS G. SCHMAREL, M.D., Philadelphia, Pa.

December 1926.

MIGRAINE

RESULTS OF TREATMENT BY KETOGENIC DIET IN FIFTY CASES *

CLIFFORD J. BARBORKA, M.D., ROCHESTER, MINN.

December 1930



Use of the modified Atkins diet for adolescents with chronic daily headache

Table 1. Demographics and results of modified Atkins dietary intervention in the eight subjects

| Subject | Age (years) | Gender | Number of migraine preventative used | Body mass index (kg/m ²) (percentile) | Pre-ADHD ¹ Headache ² Baseline | Post-ADHD ¹ Headache ² 3 months* | Reasons for early discontinuation* | Weight loss (kg) | Diet duration (months) | Reason for early discontinuation* |
|---------|-------------|--------|--------------------------------------|---|--|--|------------------------------------|------------------|------------------------|-----------------------------------|
| 1 | 13 | Male | 2 | 20.8 (95%) | 68 | 33 | Small | 3.6 | 7.0 | |
| 2 | 13 | Male | 4 | 23.0 (99%) | 130 | 33 | Large | 1.4 | 4.0 | |
| 3 | 15 | Female | 2 | 20.0 (95%) | 47 | 10 | Small | 0.0 | 1.2 | Ineffective |
| 4 | 15 | Female | 2 | 21.2 (96%) | 240 | 190 | Large | 0.2 | 3.0 | |
| 5 | 15 | Male | 4 | 43.3 (99%) | 100 | 100 | Home | 2.3 | 1.2 | Recurrentness |
| 6 | 16 | Female | 3 | 37.0 (97%) | 65 | 65 | Phonotone | 0.1 | 1.2 | Recurrentness |
| 7 | 16 | Female | 10 | 19.0 (84%) | 240 | 240 | Large | 0.0 | 0.7 | Ineffective |
| 8 | 16 | Female | 7 | 20.8 (95%) | 17 | 17 | Home | 0.0 | 0.1 | Recurrentness |

*2 weeks/3 months.
¹Pre-ADHD¹, post-ADHD², post-diet migraine disability assessment scale.

Kossoff EH, et al. *Cephalalgia* 2010

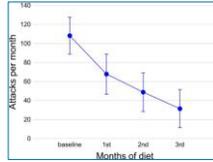


Efficacy of Modified Atkins Ketogenic Diet in Chronic Cluster Headache: An Open-Label, Single-Arm, Clinical Trial

Chenardon D, et al. *Cephalalgia*. 2016;36(12):1111-1117.

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- 18 CCH patients
 - 15 were responders (11 complete)
- Mean monthly attacks reduced from 108 to 31
- Suggests perhaps dietary therapy may be helpful for paroxysmal headache events (compared to chronic daily headache)



Di Lorenzo C, et al. *Front Neurol* 2016; 9:64.



Cannabidiol for Epilepsy?

- Grassroots effort after a child with Dravet syndrome in Colorado (Charlotte) responded well to home-made CBD and THC oil
- Two randomized-controlled trials published in NEJM 2017 and 2018
- Epidiolex® (100% CBD oil) likely to be approved by the FDA for seizures due to Dravet and Lennox Gastaut syndrome this Fall



Devinsky D et al. *N Engl J Med* 2017; 376:2011-2020.
Devinsky D et al. *N Engl J Med* 2018; 378:1888-1897.



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Cannabidiol for Migraines?

- UColorado 2016: 40% of 121 patients reported 50% migraine reduction
- Germany 2018: 10.2% patients using cannabis for self-medication used it for migraines
- Unknown if Epidiolex® would be beneficial at this time



Rhyne DN, et al. *Pharmacotherapy* 2016;36:505-510.
Kordemey R, et al. *Eur J Pharmacol*. 2018;618:371-377.



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Conclusions

- Epilepsy and migraine are two of the most common neurologic disorders afflicting children and adults
- Explosions in genetic diagnosis and understanding may lead to targeted therapies
- Great opportunities to share both our societies' treatment knowledge
 - Anticonvulsant drugs such as topiramate and valproate
 - Nonpharmacologic treatments such as diet and neuro-stimulation
 - Cannabidiol in the next few years



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