

Successful Opioid Monotherapy in Migralepsy: A Case Series

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Abstract

Background: There is a consensus that migraine and epilepsy are comorbid conditions. The novel concept explored and developed in this case series is that of the primacy of headaches in generating seizures in those patients suffering from migraine-triggered epilepsy (i.e., migralepsy). As demonstrated in the five cases described here, much like the effect of ketogenic-diet on migraine-triggered epilepsy, once the migraine headaches were completely suppressed after adopting daily scheduled opioid therapy the seizures stopped from occurring, but they returned with the recurrence of the migraines once the patients had stopped their daily opiate regimen for any reason.

Clinical implications: The above pharmacological scenario is reminiscent of a similar but naturalistic course of events as described in reports concerning the salutary effects of ketogenic diet, or restoration of sleep, in cases of migraine-triggered epilepsy. In all three instances it is the migraines that drive epilepsy, not the other way around, as it is commonly assumed.

Conclusion: Although epilepsy is the more impressive aspect of migraine-triggered convulsions, the cases described in this report point to the primacy of migraine in bring about the whole picture from the start. In every case, seizures were controlled by adopting a treatment plan for preventing the migraines from occurring in the first place, i.e., the daily scheduled opioid treatment for refractory chronic headache. Given the role of cortical spreading depression (CSD) in the genesis of migraine and epilepsy, it is suggested that opiates suppress the development of CSD, thereby prohibiting the progression of migraine to epilepsy.

Keywords: Opioid; Migraine; Seizures; Anticonvulsants

Introduction

The causal relationship between migraine and epilepsy is best displayed by the curative effect of pharmaceutical and non-pharmaceutical means of forestalling migraines and the ensuing epilepsy.

Thus, a ketogenic diet has been found effective in preventing the migraines and the ensuing epilepsy [1-3].

Pharmacological elimination of headaches by lamotrigine has also been shown to have a similar effect [4].

A similar phenomenon has been demonstrated by the salutary effects of sleep in forestalling migraine-triggered epilepsies [5,6]. This article reports the occurrence of the same phenomenon in five cases of intractable headaches associated with epilepsy. All patients had a combination of drug resistant epilepsy and migraine. In these cases, however, the contributions of migraines in triggering seizures were demonstrated by the total abolition of epilepsy once the migraines were fully under control following a regimen of daily scheduled opioid as reported earlier [7-11]. In the series described here seizures returned.

Whenever the subject abandoned the maintenance opiate therapy, causing the return of the migraines forthwith. This sequence of events is against the recently expressed concept that the headaches observed in migralepsy are simply part of an ictal epileptic headache [12,13].

Similarly, the fact that continued occurrence of migraines is associated with presence of antiepileptic drug resistance points to the independent role of headaches in perpetuating the seizures, making the case for opioid-monotherapy even stronger in those who suffer from migralepsy [5,14,15].

Case 1

BJL, a 50 year old woman, was first seen in 2013. She complained of seizures since 2002. Four of the eight headaches she endured in the month of October of 2013 ended with seizures, despite daily use of one or more of the following anticonvulsants: Depakote, Topamax, and Neurontin (taken in appropriate amounts). Neurological examination and the initial unenhanced CT of brain were normal. She was titrated on daily scheduled opioid for prevention of migraine, resulting in complete abatement of headaches and seizure once the dose of oxycodone reached 180 mg per day. She remained asymptomatic when last seen in January of 2016.

Case 2

DDH, born in 1957, was first seen in office in 2004. His main complaint was occurrences of debilitating headaches with features of migraine often associated with seizures. After initial evaluations (initial neurological examination and a CT of brain, both normal) he was put on different anticonvulsants for prevention of headaches and the attendant seizures with only partial effectiveness despite laboratory confirmed therapeutic levels of felbamate, zonisamide and lamotrigine

in different occasions. Daily scheduled opioid therapy for prevention of migraine and seizures were then started, with hydrocodone/acetaminophen 10/325 mg tablet, culminating at 2 tablets three times daily. This resulted in lessening of number of headaches and seizures but did not completely suppress them, despite the continuation of anticonvulsants. Later he was switched to oxycodone 30 mg tablets which were titrated to 2 tablets three times daily as the anticonvulsants were slowly withdrawn in toto. This resulted in complete suppression of seizures and headaches. He was last seen in December 2015.

Case 3

DHW, a 24 year old married man, was first seen in November of 2014 for frequent occurrences of severe headaches, often associated with loss of consciousness and convulsions witnessed by his wife. An abbreviated account of DHW has been accepted for publication elsewhere. His headaches began at age 9 while under the care of pediatric neurologist in Charleston, West Virginia. His condition worsened after a motor vehicle accident, particularly the headaches of which he had [3,4] bad ones per week. Neurontin, 400 mg, two tablets three times per day and 400 mg of felbamate daily did not reduce the headaches in number or in severity nor did the seizures change. After switching to daily scheduled opioid therapy, however, both the severity and number of headaches and seizures diminished when the opiate was titrated to 30 mg of oxycodone, 2 tablets three times daily; a dose that completely suppressed both the migraines and the seizures. After several months of the above-mentioned regimen pharmacists refused to supply him with the prescriptions given and his symptoms returned in earnest; these did not respond to the resumption of previously prescribed anticonvulsants. He was last seen in January of 2016.

Case 4

LME, 35 years old woman; first seen in 2008 for the chief complaints of migraine and severe backache radiating into her legs. The headaches

had been present since her early childhood. Neurological examination was unremarkable. She was prescribed Keppra, Tofrani PM and Maxalt for symptom relief in addition to hydrocodone/acetaminophen (10/350 mg, 1-2 tablets twice daily) on as needed basis. Although she improved somewhat in the ensuing months, she required trials of other medication in a quest for better relief. These included Topamax, Zonegran, Amerge and various sedatives. Because of continued occurrences of debilitating headaches on a biweekly basis, all prophylactic medication were stopped in August of 2014 in favor of daily scheduled opioid treatment of migraine, using oxycodone 30 mg 2 tablets twice daily. Rare headaches followed, resulting in an increase of the oxycodone to 180 mg per day, following which the headaches stopped completely. Unfortunately, due to her inability to obtain opioid medication in December 2015, the headache resumed their appearance but this time associated with generalized seizures requiring hospitalization (due to loss of consciousness, associated with incontinence). She last contacted me in June 2016.

Case 5

PJH, 42 years of age, was first seen in 2002. She complained of headaches all her life, becoming worse in severity in the years prior to her visit. Diabetes runs in her family but not headache. Neurological findings in the examination were limited to those of carpal tunnel syndrome and peripheral neuropathy. Grand mal seizures were added to the picture soon thereafter and remained so until daily scheduled opioid therapy for chronic daily headache was started in 2005, having exhausted non-opioid analgesic options among several anticonvulsants. She remained symptom free so long that she could continue with her regimen of oxycodone, 30 mg 2 tablets three times per day. She was last seen in January 2016 (Table 1).

Patient initials	Clinical duration features,	Opioid treatment (final dosage)	Laboratory studies	Previous medications	Outcome
BJL, 50 y, w	14 years of headache and epilepsy	Oxycodone, 180 mg daily	CT of brain, WNL	Depakote, Topamax, Neurontin	Total Abatement of headaches and seizures
DDH, 59 y, m	Recalcitrant seizures for most of his life	Hydrocodone first, then switched to Oxycodone	CT of brain, WNL	Felbamate, Zonegran, Lamotrigine	As above
DHW, 24 y, m	Thunderclap headaches associated with seizures	Oxycodone, 180 mg daily	CT of brain, WNL	Neurontin and Felbamate	As above
LME, 35 y, w	Migraine, epilepsy, backache	Norco 10/325 mg, 2 x 3 then switched to Oxycodone, 180 mg daily	Normal EEG	Keppra, Tofranil PM	As above
PJH, 42 y, w	Headache, all her life, diabetes, peripheral neuropathy	Oxycodone, 180 mg daily	Normal MRI	Several anticonvulsants, all ineffective	As above

WNL, Within Normal Limits

Table 1: Clinical features, duration opioid treatment (final dosage) laboratory studies.

Discussion

Although daily scheduled opioid therapy has been a recognized method for preventing headaches [7-9,11] there have been no precedents for its use in preventing epilepsy, particularly those

associated with migraine. In fact, in recent decades, opiates have been unjustifiably maligned for causing the so-called 'medication overuse headache' [16,17] However, in a recent large scale study involving statistical analysis of data from thousands of patients with epilepsy, Wilner et al. found that a large majority of the population under

scrutiny had suffered from an ensemble of headache, migraine and cervicalgia (i.e., a surrogate for migraine) [18,19].

Clearly, despite Wilner et al. puzzlement by their own findings, what seems to have been driving the request for pain relief medication by these epileptic patients was the fact that a vast majority of them had migraine-triggered epilepsy for which they had empirically found opioid (s) an effective prophylactic agent, similar to the findings described in this article.

As a clinical neurologist with interest in headaches, I share the sentiment of those neurologists for whom opioids are irreplaceable, safe and effective medications for treating acute and chronic headaches [7-11]. However, the import of the present series is in their striking similarity to the result seen in patients with migralepsy after using ketogenic diet or with restoring the sleeping pattern, indicating a decrease of epileptogenicity within the brain once the migraines are fully controlled [18-20].

A similar phenomenon (amelioration of epilepsy after suppression of migraine) has been reported by Sadler et al. in a well-documented case of migralepsy. Their patient required placement of a vagus nerve stimulator to control his seizures. He reported a significant concomitant reduction of his migraines and seizures as these symptoms were being catalogued on a daily basis in a similar vein.

Wolf has documented the role of nonpharmacological interventions in prevention of migraine-triggered epilepsy [20].

Mechanisms by which opioids prevents migraine has been discussed in another occasion elsewhere.

To sum: In managing migralepsy it is the migraine that must receive therapeutic priority despite the more impressive scene presented by epilepsy, since it is the headache that brings about the seizure.

Acknowledgement

This article is dedicated to the memories of my sister Farkhondeh Derakhshan.

Clinical Implications

- In migralepsy, there a tight physiological connectivity between headache and seizure.
- To prevent the seizure preventing headache takes priority as the migraine is the driving factor.
- Maintenance opioid treatment is the safest and most effective method for preventing migraines.

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