

Migraine - to be or not to be - that is the Headache!

Roy G Beran^{1,2,3*}

¹Department of Clinical School, University of New South Wales, Australia

²Department of Medical School, Griffith University, Australia

³Department of Medical Law, Moscow First State University, Russia

Correspondence should be addressed to Roy G Beran, roy@royberan.com

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ABSTRACT

INTRODUCTION

This paper presents an alternative hypothesis for the classification of primary headaches, especially migraine headaches (MHs) and tension type headaches (TTHs).

BACKGROUND

There is a dichotomy of opinions regarding the most prevalent primary headache type with US neurologists claiming this to be MHs while most of the rest of the world favours TTHs as most prolific.

ARGUMENTS FAVOURING THE HYPOTHESIS

This paper presents the hypothesis that primary headaches, be they TTHs or MHs, reside on a continuum with the capacity to morph from one to another and to move up and down the continuum. This creates an ever changing backdrop for which treatment is determined by the most prominent headache type at the time of attending the doctor and the argument is that TTHs are the most prominent, making use of tricyclic antidepressants the most efficacious headache remedy.

MORE RECENTLY

There is a new kid on the block with calcitonin gene related peptide antibodies being hailed by some as the first specific migraine prophylactic, ignoring the contribution of pizotifen which is not available in the USA.

EFFICACY

It is argued that 50% reduction in headache frequency represents successful treatment, but this paper argues the only truly successful treatment is headache eradication which should be the aim of all headache treatment.

CONCLUSION

Primary headaches rest on a continuum making separation into arbitrary classifications of TTHs and MHs somewhat distorting of the true picture and headache types can morph from one into another, thereby suggesting that the most appropriate treatment reflects the headache type at the time of presentation.

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KEYWORDS

Migraine; Tension type headache; Diagnosis; Critical appraisal; Continuum; Hypothesis

INTRODUCTION

The motivation behind the development of the current paper was an invitation to referee a submission which reviewed the current status of migraine headaches. The authors diligently, and without question, reported the material which was cited from within the world literature, without questioning the proffered nomenclature nor the philosophy behind same. The issue that arose was that the paper read like the manifesto of a devotee who blindly accepted that, if it was published, it must be correct, especially if published by well accepted experts in the field. This would be akin to the executive of the flat earth society which, in its day, was the accepted dogma of the scientific community, requiring many years and evolution of knowledge to undo the wrong.

Having reviewed the paper, the response to the journal was that the paper should be accepted as the author(s) had fulfilled their objective of providing the currently accepted material, in good faith and with proper referencing. It was felt that the authors should not be penalised because of their lack of questioning of the widely accepted views when preparing a review article. Having acknowledged that the authors were in concert with the majority opinion, it would be a shame if an alternative perspective were not canvassed, to provide food for thought. What follows is an alternative perspective which rests on the concept that: Not all bad headaches are migraines; that headaches exist on a continuum, with tension type headaches (TTHs) at one end of that spectrum and migraine headaches (MHs) at the other and a combination of features of both in between; and the type and nature of the headache can change between headache types along that continuum; and that the absolute classification

of headaches, into the main primary headaches, namely TTHs and MHs (not ignoring the less common forms of primary headaches) is an artificial differentiation designed to facilitate research collaboration, rather than reflect the true nature of the headache as they exist within the community.

BACKGROUND

MHs are divided into episodic and chronic migraines [1-3] with set diagnostic criteria, accepted by the headache industry as obligatory to diagnose this form of headache [1]. These criteria are set out in the International classification of headache disorders [1-3]. Chronic migraine is defined as headaches occurring on at least 15 days per month (on at least half the days of the month) of which at least 8 are considered MHs (namely headaches, occurring on at least 8 days of half of the days per month are considered MHs) for the period of the previous 3 months. It follows that, should a patient have headaches on 20 days per month, of which 8 are MHs and 12 are unequivocally TTHs, the dogma dictates that the patient has chronic migraine, even though the more prevalent headache type is that of TTHs.

The US headache fraternity have gone so far as to suggest that TTH is uncommon, something not echoed by neurologists in other parts of the globe [4,5]. Diagnosis is the foundation of proper management and selection of appropriate medications, so why is there this dichotomy of diagnoses, between US neurologists and those from the rest of the non-US, non-headache industry. One of the reasons may well be that of financial return based on health insurance criteria. In the US, insurance paid for management of TTHs may be either much lower than that for MHs or possibly even no remuneration at all for treating patients with

TTHs [6]. This creates obvious potential for bias that may result in under-representation of the true extent of TTHs, which many believe to be the most prevalent type of headache to present to treating neurologists [7]. The potential bias also could result from an over diagnosis of MHs, which includes the more significant headaches that fall between TTHs and MHs, on that continuum spectrum, but would be more akin to TTHs were it not for the prevalent bias.

ARGUMENTS FAVOURING THE HYPOTHESIS

The Hypothesis, presented within this paper, is that primary headaches reside on a continuum in which TTHs sits at one end of the primary headaches' spectrum and MHs reside at the other end thereof, with a conglomerate of symptoms and signs for those headaches which do not adequately satisfy the diagnostic requirements for either classification as pure TTHs or MHs. These 'mixed' headache types used to be called "tension vascular headaches", a term no longer in vogue in the international classification [1-3,5,8].

It follows that the medication of choice, to aim to prophylactically prevent MHs, should be specifically one of the anti-migrainous agents, such as pizotifen malate (Sandomigran®) but, review of the literature suggests that, in America, antiseizure medicines, such as valproate and topiramate, or beta blockers, such as metoprolol, propranolol or timolol, are more commonly used as the first line prophylactic medications [9]. The medication classification that is next most commonly advocated was amitriptyline which is a tricyclic antidepressant [9] which is a first line medication for treatment and prophylaxis of TTHs but often found to be less efficacious when treating classical MHs.

Pizotifen (Sandomigran®) is not even available in the US, despite many years of usage elsewhere in the

world. There are problems with both amitriptyline and pizotifen, such as weight gain and somnolence, but neither of these are insurmountable, although the patient needs to be warned of their potential, as well as the potential for anti-cholinergic properties, such as dryness which attached to the tricyclic antidepressants.

In a recent study of chronic daily headache, in which patients experienced headaches on an almost daily basis, it was shown that the initial headaches, experienced by the cohort more than 20 years earlier, were most prominently episodic MHs which later morphed into chronic daily TTHs, based on strict patient interview and application of diagnostic criteria [10]. This is perhaps the best example of primary headaches being on a continuum and possibly moving up, and down, that continuum spectrum and offers unequivocal evidence in support of the hypothesis that headaches are not a static diagnostic phenomenon but a more fluid experience which can fluctuate [10].

If one is to accept the continuum hypothesis, for the diagnosis and treatment of primary headaches, ensuring that secondary headaches have been excluded, on the basis of history, examination and, where applicable, investigation, including magnetic resonance imaging and possible angiography, one would choose the medication most suitable to the presenting headache type at the time. Primary headache type is more likely to be a TTH, rather than MH, once satisfied that the headaches are not secondary in nature. TTHs respond best to tricyclic antidepressants, namely amitriptyline (Endep®) (assuming the patient also has problems with insomnia) or either nortriptyline (Allegron®) or imipramine (Tofranil®), if there is little or no sleep disturbance reported. In general, these agents have little benefit for true MHs and yet they are widely advocated for use in MHs [11], the argument being

that the continuum, spectrum of headaches applies, even though it is not officially recognised. The dosage of tricyclic antidepressant, used to treat TTHs may start with as little as 5 mg per night, in the most susceptible individuals, and can be incrementally increased up to 250 milligrams, as required to alleviate the headaches [5].

For those headaches, previously identified as tension-vascular headaches, namely those headaches which neither fit properly into either classification of TTHs or MHs, beta blockers, such as propranolol (Inderal®) are efficacious [5]. Propranolol appears to have some benefit in the treatment of MHs [12], hence their use in patients with mixed symptoms involving features of both TTHs and MHs, as per the continuum spectrum hypothesis.

In all cases, the maxim of ‘start low and go slow’, starting with a minimum dosage, based on clinical impression, and increasing that dosage, in an incremental fashion appears to produce the best outcomes [4,5]. This may result in giving patients larger dosages than do many colleagues, with approximate maximal dosages of up to 250 mg nocte for tricyclics to treat TTHs; up to 9 pizotifen tablets daily (given as III tds, 500 µg tables, namely 4.5 mg daily) for MH prophylaxis or 640 mg of propranolol daily, maintaining close patient supervision and working in close conjunction with the referring family physicians.

MORE RECENTLY

Of late, there has been much excitement regarding the ‘new kid on the block’. Namely the calcitonin gene related peptide (CGRP) antibody [3,13-15], be it to the cell receptor or the blockage on the peptide, with many indicating that, up until now, there has not been an effective prophylaxis for migraines despite the presence of pizotifen which is not

available in the USA. The adherence to the continuum spectrum theory argues strongly against this posture as with proper patient selection and proper medication selection, most headaches are manageable and of those which are refractory, the CGRP antagonists are still only an effective medication in approximately half of the patients but, in those, in which it is effective, it is very effective. The same could be said for pizotifen which when it works it provides miraculous relief.

EFFICACY

The accepted dogma is that 50% reduction in headache frequency equates to effective treatment. While this is impressive, the patient with debilitating episodic MHs, occurring on 4 days per month, who, following treatment, reduces the frequency to 2 debilitating headaches per month is still incapacitated by migraines. Such a person remains difficult to employ and quality of life is still driven by frequency of MHs. The aim of headache treatment should be headache eradication, rather than halving the headache frequency. It is a positive move to have ‘a new kid on the block’ but the new class of medications have not been tested in tension type headache in which they also may show sufficient efficacy if accepting the continuum hypothesis. It follows that headache management remains on a moving platform and one needs to read each new development with both caution and excitement while always questioning the information being proffers.

CONCLUSION

This paper was motivated by refereeing a paper examining MHs and providing the party line which is at odds with the views relating to the continuum spectrum hypothesis. While many accept that TTHs and MHs are separated by what amounts to an arbitrary distinction leading to the perception that the most headaches are MHs, the hypothesis,

presented in this review, argues in favour of a continuum of primary headaches with the capacity to morph from one into the other and the optimal treatment depends on the type of headache which is present at the time of evaluation.

CONFLICT OF INTEREST

There are no conflicts of interest to declare.

REFERENCES

1. (2018) Headache classification committee of the International headache society the International classification of headache disorders 3rd (Edn.). Cephalalgia 38: 1-211.
2. Olesen J (2018) International classification of headache disorders. The Lancet Neurology 17(5): 396-397.
3. Ray JC, Kapoor M, Stark RJ, et al. (2021) Calcitonin gene related peptide in migraine: Current therapeutics, future implications and potential off-target effects. Journal of Neurology, Neurosurgery & Psychiatry.
4. Beran RG (2011) Primary headache management in military medicine. ADF Health 12(1): 23-28.
5. Beran R (2014) Management of chronic headache. Australian Journal of General Practice 43(3): 106-110.
6. Levin M (2008) Making a headache practice work: The elements of diagnosis and coding headache medicine. Headache 48(3): 491-496.
7. Therapeutic guidelines (2011) Headache. In: Neurology, Version 4: 73-99.
8. Beran RG (2012) Headache. In: Neurology for general practitioners. Sydney: Elsevier: 45-55.
9. Ha H, Gonzalez A (2019) Migraine headache prophylaxis. American Family Physician 99(1): 17-24.
10. Beran RG, Spira PJ (2011) Levetiracetam in chronic daily headache: A double-blind, randomised placebo-controlled study: (The Australian KEPPRA Headache Trial [AUS-KHT]). Cephalalgia 31(5): 530-536.
11. Xu XM, Liu Y, Dong MX, et al. (2017) Tricyclic antidepressants for preventing migraine in adults. Medicine 96(22): e6989.
12. Jackson JL, Kuriyama A, Kuwatsuka Y, et al. (2019) Beta-blockers for the prevention of headache in adults, a systematic review and meta-analysis. PloS One 14(3): e0212785.
13. Deen M, Correnti E, Kamm K, et al. (2017) Blocking CGRP in migraine patients-a review of pros and cons. The Journal of Headache and Pain 18(1): 1-9.
14. Rivera-Mancilla E, Villalón CM, Maassen Van Den Brink A (2020) CGRP inhibitors for migraine prophylaxis: A safety review. Expert Opinion on Drug Safety 19(10): 1237-1250.
15. Edvinsson L, Haanes KA, Warfvinge K, et al. (2018) CGRP as the target of new migraine therapies-successful translation from bench to clinic. Nature Reviews Neurology 14(6): 338-350.