

Two Case Reports on the Treatment of Acute Migraine with Niacin: Its Hypothetical Mechanism of Action Upon Calcitonin-Gene Related Peptide and Platelets

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Abstract

Migraine headaches (MH) impose a tremendous economic drain upon our health care system. Some 50 percent of MH sufferers discontinue conventional treatment, in part, due to dissatisfaction with the conventional therapy they receive. Niacin (nicotinic acid) might be an alternative treatment for acute MH among individuals seeking a novel approach. Two case reports demonstrate that 500mg of oral niacin can abort acute MH. The therapeutic effectiveness of niacin appears to be related to the cutaneous flushing that occurs shortly after oral administration. The vasodilation causing the flush is due to the release of prostaglandin D₂ (PGD₂) in the skin and the subsequent increase of its metabolite in the plasma. The therapeutic benefits of niacin might also be related to the positive interactions between PGD₂ and the calcitonin-gene related peptide (CGRP) found in trigeminal neurons and in platelets.

Introduction

Migraine headaches can lead to tremendous debilitation among those suffering from them. In a review article, Aukerman, Knutson & Miser describe some of the unfortunate statistical consequences of MH.¹ In the United States MH affect 25 percent of women and 9 percent of men; in total, MH affect about 28 million people. Economically, MH lead to an annual loss

of 64 to 150 million work days in the United States and the estimated direct and indirect costs of MH amount to 17 billion dollars. Another concern is that MH sufferers discontinue medical care in 50 percent of cases, in part, due to dissatisfaction with the therapy they have received. Given the economic consequences and the fact that half of MH sufferers discontinue the conventional approach, perhaps it is time to consider the use of an alternative approach like niacin for the treatment of acute MH.

A review of the medical literature found only three reports on the use of niacin for acute MH. In the first report, Hendler mentioned that niacin was able to abort the onset of MH, but he did not elaborate on the dose required or on the possible mechanism of action.² In the second report, Hall described the use of niacin to treat his own MH.³ At the first sign of aura, he orally ingested 300 to 500mg of niacin, slightly chewing the niacin pills to allow them to dissolve slowly in his mouth. Hall found that the benefits of niacin were most pronounced when taken on an empty stomach, although it was noted that there was still a MH relieving effect when taken after meals. Additionally, he remarked that the migraines were resolved when intense flushing occurred. In the final report, Gedye investigated whether a combination of various medicines would benefit acute MH in 12 patients.⁴ At the onset of migraine symptoms, patients were instructed to take a combination 100mg of niacin, 500mg L-tryptophan, 500mg calcium carbonate, 64mg caffeine and 650mg of acetylsalicylic acid. They were further instructed to avoid

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a high-potassium food intake and magnesium supplementation during the MH. Of the 12 patients, 9 had significant benefits from this combination approach.

The following two case reports demonstrate the successful treatment of acute migraine with 500mg of oral niacin.

Case Report #1

A 32-year-old male, suffering from MH approximately once a week for the past 12 years, presents with a constant stabbing pain that lasts all day. He ingested 500mg of niacin and experienced a full body flush after 30 minutes. He reported partial relief after 30 to 40 minutes, followed by complete relief after 60 minutes. He had found niacin to completely resolve his acute MH on 3 prior occasions, and will continue to use it when necessary.

Case Report #2

A 27-year-old male, suffering from MH for the last 3 years, took niacin at a 500mg dose to relieve his migraine. He experienced a flush approximately 30 minutes after ingestion, after which he felt complete relief from his MH pain. Niacin, however, has only been used once as an acute treatment for his MH and was successful.

Discussion

In Hall's report, he mentioned that niacin was most effective when intense flushing occurred. In the two case reports, the therapeutic benefits of niacin were also associated with flushing. According to Hall, the possible reasons for niacin's efficacy are the result of niacin's ability to release serotonin and histamine from the stomach. However, according to one investigator, Hall's explanation for niacin's effect seems unlikely based on the following facts: Serotonin is not a peripheral vasodilator; and serotonin and histamine would be metabolically inactivated by the liver prior to reaching the peripheral circulation.³

According to Gedye, niacin helps

acute MH by facilitating the conversion of tryptophan to serotonin via its negative feedback upon the kynurenine pathway.⁴ This is further supported by a rat study in which the administration of 20mg of niacin resulted in increased levels of a serotonin metabolite (5-HIAA) and decreased levels of xanthurenic acid via the kynurenine pathway.⁵ Therefore, with an adequate intake of niacin there should be some feedback inhibition upon the kynurenine pathway, diverting more tryptophan to serotonin. For this reason, niacin might favourably influence the serotonergic system in a manner comparable to other agents. Studies have demonstrated that supplementation with 5-hydroxytryptophan (5-HTP)⁶ or L-tryptophan,⁷ both being precursors to serotonin, can result in both the reduction and intensity of MH. However, in these studies 3-4 months were necessary to demonstrate benefits. Therefore, it is unlikely that influencing the serotonergic system by the administration of niacin would be the mechanism responsible for aborting acute MH.

On the other hand, the possible pharmacological reasons for niacin's effectiveness in treating acute MH might be related to the induction of prostaglandin D2 (PGD2) in the skin and the production of its metabolite in the plasma. When niacin is administered orally in amounts of 500mg or topically via a 6-inch patch of 10-1 M aqueous methylnicotinate on the forearm, PGD2 is markedly released in the skin and its metabolite appears in high amounts in the plasma.^{8,9} However, neither the levels of histamine nor its metabolite are increased with the increased release of PGD2, evidence that the niacin flush is not mediated by the release of histamine from mast cells or other storage sites.⁸

It is interesting to note that PGD2 and calcitonin-gene related peptide (CGRP) both play a role in the pathogenesis of MH. For example, in cultures of adult rat trigeminal neurons CGRP can be induced by PGD2.¹⁰ In light of this evidence, it would

appear that the niacin-induced production of PGD₂ would have an adverse effect upon MH. However, the significant amounts of PGD₂ induced by niacin, might down-regulate the trigeminal output of CGRP, halt neurogenic inflammation, and, therefore, be therapeutic. Although this mechanism of action has yet to be adequately investigated, the increased production of PGD₂ by niacin might favourably modulate CGRP, and contribute to the rapid resolution of MH.

Alternatively, the therapeutic benefits of niacin might have to do with its interaction upon platelets. In one study, the synthesis of the platelet-derived PDG₂, which is anti-aggregatory, was studied and compared between female MH sufferers and healthy female volunteers matched for age and blood-groups.¹¹ It was found that levels of platelet-derived PDG₂ was significantly decreased in untreated female MH sufferers during their headache-free periods compared to the healthy group. From this, these investigators concluded that the lower amounts of specific platelet-derived prostaglandins among MH patients might contribute to the development of cellular, vascular and neurological events that trigger MH. When administered acutely, niacin might normalize the morphological and functional capacities of platelets by increasing the synthesis of platelet PGD₂ levels. Thus, this interaction might help to abort acute MH by preventing further platelet aggregation and the subsequent release of vasoactive chemicals.

Conclusion

In the two case reports, a single dose of 500mg of oral niacin was effective in aborting acute migraine. Its mechanism of action might be related to the production of PGD₂ in the skin and the subsequent increase of its metabolite in the plasma. Furthermore, the therapeutic benefits of niacin might be the result of its possible interactions upon CGRP in trigeminal neurons and among platelets. These findings justify further in-

vestigations into the use of niacin in treating MH. More case reports, research and rigorous controlled trials are needed to properly evaluate its therapeutic effectiveness, safety and mechanisms of action for the treatment of acute migraine headaches.

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