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doi: 10.3122/jabfm.2009.05.090083

The above letter was referred to the author of the article in question, who offers the following reply.

Response: Re: Effectiveness of Vitamin B₁₂ in Treating Recurrent Aphthous Stomatitis: A Randomized, Double-Blind, Placebo-Controlled Trial

To the Editor: We are satisfied to see that not only our last study, but recent research (including your own),^{1,2} support the conclusions of our previous observations^{3,4} as well. I have some commentaries on your remarks.

In my opinion, your adhering discs as well as sublingual tablets, injections, swallowed tablets, and intranasal sprays could be effective for many conditions (including recurrent aphthous stomatitis [RAS]) in regard to the effect of vitamin (Vit) B₁₂ itself. Undoubtedly, the time of response depends on the chosen form of cobalamin (cyanocobalamin, methylcobalamin, or hydroxycobalamin), the mode of use, and individual dosage. For example, according to my own 6 years experience you can receive an adequate response to injections of Vit B₁₂ (cyanocobalmin!) in first 2 or 3 wk. Nevertheless, some patients dislike injections and prefer tablets. The largest drawback our study was the issue of participant compliance. RAS is not a life-threatening disease, and therefore some patients even refused sublingual tablets.

The Mechanism of Successful Treatment Is Still Unclear

I disagree with the claim that the positive effect of Vit B₁₂ on RAS is related to its local action on the buccal mucosa. How can you explain the response to parenteral treatment? I presume there is a generalized effect of Vit B₁₂, and we hold a “working hypothesis” which, in our opinion, could explain this phenomenon. Vit B₁₂ has unique yet obscure and unrecognized function. We assume that there are universal, interchangeable (as required) biologically active substances that regulate different systems of our body and provide homeostasis. We propose that one of these substances is Vit B₁₂. Perhaps Vit B₁₂ can correct defects caused by other biological substances. We call this phenomenon the “Master Key effect.”⁵ In summary, this fascinating and unelucidated topic definitely demands further research to disclose the underlying secrets nature set in this field.

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doi: 10.3122/jabfm.2009.05.090161

Re: Postepidural Headache: How Late Can It Occur?

To the Editor: I applaud the author’s enthusiasm to contribute to the medical literature; however, a number of issues detract from the validity of the published data and any conclusions that may be drawn from it.¹ Although Dr. Reamy suggests that this is the first case to demonstrate the onset of postdural puncture headache (PDPH) beyond the well-accepted normal range of 1 to 7 days after epidural puncture, a range of 1 to 12 days has previously been reported in at least one case series as well as in editorials and review articles.^{2–4}

According to the cited meta-analysis, the incidence of PDPH in an obstetric population is roughly 0.75% and occurs when there is an accidental entry into the intrathecal space while attempting epidural placement.⁵ In this case, epidural placement was uneventful—ie, without dural puncture—and thus a mechanism for entry into the intrathecal space is unclear. Furthermore, it is impossible to place an epidural catheter through a 25-gauge needle; this is the instrument most often used to provide intrathecal analgesia.³ It is unlikely that the patient received analgesia through this route because the duration of action (>4 hours) is beyond the abilities of intrathecal medications at conventional doses. Epidural catheters are typically placed through 16- to 18-gauge Tuohy needles.

Another major issue that is not adequately addressed in this report is the fact that the patient underwent a diagnostic lumbar puncture in the emergency department. Most emergency department lumbar puncture kits include a 20-gauge spinal needle, which carries a 40% risk of PDPH in the obstetric population.³ Moreover, in the setting of an existing symptomatic dural puncture, further drainage of cerebrospinal fluid exacerbates symptoms. The patient’s symptoms were apparently improved with intravenous analgesics, antiemetics, and fluid to the point that she was discharged from the hospital after the diagnostic procedure. Interestingly, the patient’s symptoms worsened significantly the day after intervention in

the emergency department. This may suggest that the epidural blood patch served as an effective therapeutic modality because of a PDPH from the lumbar puncture in the emergency department.

In addition to these issues, some of the technical jargon is used in a very confusing manner. For example, “high or spinal anesthesia” is listed as a potential complication of epidural placement. This is very ambiguous because the terms “high” and “spinal” are not synonymous. It is possible to have a high epidural level, but only accidental or unrecognized dural puncture can lead to a “spinal” (which may progress to a high spinal). Patient management in each of these situations may be markedly different. Nonetheless, it is crucial to note that Dr. Reamy’s central message of not allowing patient care to be negatively influenced by the findings of a single, non-authoritative, pooled analysis remains extremely important.

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doi: 10.3122/jabfm.2009.05.090098

The above letter was referred to the author of the article in question, who offers the following reply.

Response: Re: Post-Epidural Headache: How Late Can It Occur?

To the Editor: I want to thank Dr. Quraishi for his comments, insights, and 3 additional literature citations on post-dural puncture headaches (PDPH) by Greene, Quraishi, and Lybecker.^{1–3} After careful review of these articles, I strongly disagree with his contention that the onset of a PDPH has previously been reported outside the widely accepted range of 1 to 7 days and maintain that the case I described is the first reported instance of

a markedly delayed presentation at 12 days post-procedure.⁴

The fascinating 1961 article by Greene on the neurological sequelae of spinal anesthesia specifically states that, “postspinal headaches will not be considered . . .” and does not discuss the onset of PDPH in his otherwise thorough review.¹ The 2005 commentary by Quraishi cites this same Greene article as the source for the statement that onset of PDPH can be as late as 12 days after dural puncture.² Finally, the 1995 case series by Lybecker et al specifically reviewed the onset of PDPH in its case series of 873 consecutive patients undergoing 1021 spinal anesthetics that led to 75 episodes of PDPH.³ While he states that the *duration* of headache was from 1 to 12 days, he reports that, “PDPH occurred within 2 days in 96% of the 75 cases included in this study. In all cases the symptoms disappeared spontaneously or because of AEBP within 5 days regardless of the severity of the PDPH.”³ Therefore, in this series *no cases* had *onset* outside a 5-day window, which is well within the traditional 1- to 7-day window reported in the literature.

Dr. Quraishi also raises concerns that the patient’s headache could have been worsened by the lumbar puncture done in the Emergency Department (ED). This is certainly a valid point, but it does not mitigate the fact that the onset of the severe headache had already occurred before the ED evaluation. I agree with his feeling that the terms “high” and “spinal” are used in a confusing fashion throughout the literature on PDPH. I applaud Dr. Quraishi’s re-emphasis of the key point that individual patient care should not be negatively influenced by the findings of a single pooled analysis.

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Disclaimer: The views expressed in this reply represent the views of the author and not necessarily those of the United States Air Force, the Uniformed Services University, or the Department of Defense.

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doi: 10.3122/jabfm.2009.05.090109