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Letters to the Editor: Published Article

Reply to Letter to the Editor: "A Complex Phenomenon: Medication Overuse Headache and Childhood Experiences"

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We thank the authors for their letter to the editor[1] regarding our study on adverse childhood experiences (ACEs) and medication overuse headache (MOH).[2] We were pleasantly surprised to receive a letter after such a length of time since our paper was first published in November 2022. We will respond to the several interesting points raised in the letter.

With respect to the literature review performed by the authors, we observe with surprise the inclusion of two papers by the authors themselves, neither of which relate in any clear way to the subject matter claimed. For example, the authors cite their own study using a scale assessing headache-related disability in pediatric cluster headache in support of their suggestions about smoking, working status and alcohol use contributing to migraine-related disability (reference 6 in the submitted letter). We would like to suggest that migraine and cluster headache are distinct disorders, as defined by ICHD-3,[3] and a study assessing disability using a cluster headache scale in a pediatric population cannot be suggested to apply to migraine-related disability in adults. The authors would have been better served to cite original literature to support their point.

The authors also cite their own study about telehealth in pediatric migraine when making a statement about the best method for withdrawing some medications such as non-opioid analgesics (reference 4 in the submitted letter). We are again unsure of the relevance of their pediatric telehealth satisfaction study to this point, and in our detailed reading of their paper, neither medication overuse nor medication withdrawal appear to be mentioned at any point. We would also like to highlight that neither of the two large published randomized controlled trials on the subject of the best strategy for managing MOH suggest that abrupt withdrawal is required, and we argue that a more patient-centred approach would allow for tailoring of treatment plans to the individual patient.[4,5] We clearly outlined that our patients received multimodal treatment, which commonly included bridge therapy with a long-acting nonsteroidal anti-inflammatory (NSAID). This was an outpatient retrospective study and no specific withdrawal methodology was employed; in particular we do not perform opioid withdrawal therapy and no patients were encouraged to abruptly stop opioids, due to concerns for opioid withdrawal.

Regarding types of overused medications, unfortunately our sample size was small and we did not note any significant differences in triptan and NSAID use between those with and without ACE (data not submitted with original paper due to space constraints), but we agree that this would be interesting to explore. However, such differences could also reflect other baseline differences, since triptans are prescription-only in Canada while many NSAIDs and some versions of codeine are over the counter, thus only those who had previously received medical care for migraine could have accessed triptans before our first visit.

The authors suggest that "the authors need to reevaluate some of the *p*-values in Table 1" but do not mention which *p*-values nor share their own calculations to this effect. We are therefore unsure which values exactly are asked to be commented on and unsure why the authors did not contact us directly with this question. Table 1 represents baseline demographic data, and we did not identify any statistically significant differences between groups at baseline although we agree that the sample was heterogeneous and we agree that the sample was not normally distributed. The CJNS kindly obtained an independent statistical review of our article following submission of this letter, as per which many of these concerns appear to be unfounded plus major revisions were suggested to this letter before publishing given this uncertainty. As such, we are unable to reliably comment on this aspect of the letter.

With respect to anxiety and depression, we submit that the absence of a previous formal diagnosis of depression or anxiety does not conclusively identify whether a patient does or does not have depression or anxiety. Given healthcare limitations and patient factors, many patients are unfortunately not formally diagnosed with mental health comorbidities. The PHQ-4 explores symptoms related to depression and anxiety but does not necessarily imply a formal diagnosis. Given small patient numbers, we were unfortunately not able to perform any analysis as to the impact of anxiety versus depression symptomatology on our results, which we agree would have been a helpful addition to our study.

With respect to the concerns raised around methods of questioning about ACE, as noted in our article, since this was a retrospective study of data that were obtained during routine clinical encounters, our institution felt that detailed ACE questioning could

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be viewed as overly intrusive on the first visit to a headache neurologist. As we note, we typically ask an open-ended question and explore different types of ACE in more detail if patients are comfortable doing so. We clearly acknowledged this as a limitation of the study, and agree that further work delineating the relationship between types of ACE and MOH is very important. We would like to note that the list of types of ACE proposed by the authors of the letter and drawn from the study of Anto et al. includes several of the types of ACE we mention, such as emotional abuse and parental substance abuse, so we are unsure where they drew the conclusion that we did not consider the numerous types they mention. Both our small study size and paper space constraints limited detailing all the types of ACE that patients did describe when they volunteered to do so. We also note that the Anto et al.[6] study from 2021 the authors cite (which is also in a pediatric rather than adult population), does not at any point address MOH and no conclusions are drawn regarding ACE and MOH in that paper, nor does the paper assess treatment response relative to ACE, contrary to the suggestions of the current letter authors. We suggest that a strength of our study is that it is one of the first to examine the link between ACE, MOH and treatment response.

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