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A need for an expert consensus guideline on performing peripheral nerve blocks in headache patients

Dear Editor,

We read the recent article published in Cephalalgia with great interest (1). The authors assessed the preventive effect of greater occipital nerve (GON) block on patients with episodic migraine. In this study, the authors concluded that, regardless of the type of injection medication, the GON block significantly reduced the severity and duration of headaches for at least two weeks, and the use of corticosteroids for GON was not recommended. We think that these conclusions are not justified due to the trial design, methodological considerations and not agreeing with that previously reported. Recently, a guideline to optimize the design of controlled trials of preventive pharmacological treatment of episodic migraine in adults has been published by The International Headache Society (IHS) (2). Here, we aim to address several specific points regarding this study: First, episodic migraine has a fluctuating course regarding attack severity, duration, frequency and associated symptoms. A 4–8 week screening phase, adherence to preventive and acute attack treatment and headache diary is recommended before randomization (2). However, the authors stated that they included the migraine patients with a frequency of at least 4 attacks/month, without assessing a screening phase. Second, the authors reported that the most significant changes were noted at the first 2 weeks in all groups, including the placebo (saline) group. However, the follow-up visits in this study were conducted after very short intervals: at week 1, week 2 and week 4, which might have increased the rate of placebo response. Actually, during the treatment phase, a headache diary to overcome recall bias and patient-reported outcome measures provides additional benefit and site visits are recommended for every 4–8 weeks (2). The placebo effects in episodic migraine studies are also variable (2). Higher rates of placebo response are observed by the parenteral or interventional treatments, than when the medication is orally administered (2). Since the attack frequency, duration, and severity can vary weekly and monthly in migraineurs, data from the 4-week follow-up conducted in this study is clearly not sufficient to make these conclusions. A long-term ($\geq$3 months) follow-up may be used in evaluating cumulative benefit, persistence of efficacy and for further analyzing safety and tolerability (2). Third, the authors did not report the sign of GON tenderness in their participants, which might indicate the difference of outcome measures across the groups. The presence of tenderness over the GON palpation was reported to be a good predictor for the effectiveness of the procedure, although hypoesthesia or local anesthesia after the injection was not (3). Fourth, since the desired sample size was not met in each group the authors should have also specified the post-hoc power analysis of the study. The controlled studies must be adequately powered to facilitate the detection of clinically-relevant benefit versus placebo (2). This study also has limitations on randomization of the groups. If such imbalances are observed for key variables of interest, then analysis needs to be performed using regression methods (2). Here, the study groups were not uniform, Group 1 included only 10 patients and 50% of these patients were already on preventive therapy. The authors stopped recruiting patients both due to COVID-19 pandemic and cutaneous atrophy linked to local corticosteroids (1). The blinding of the trial was also violated as the authors stopped recruiting patients to Group 1 and Group 3. The question arises as to why the authors designed this study by using triamcinolone. In GON block procedures, the local cutaneous atrophy due to triamcinolone (especially in the superficial injected sites) was previously reported (4) and therefore, alternative steroid preparations (higher water solubility formulations) with adequate dose ranges were recommended (5). Fifth, the normality test should be performed to determine if a data set is well-modeled by a normal distribution. The authors used parametric tests. However, based on data provided by the authors with very high standard

deviations, and such imbalances were observed, then analysis needed to be performed by using non-parametric tests.

To the best of our current knowledge, we still do not have an updated consensus on peripheral nerve blocks in headache patients. In the absence of higher quality data, there is an urgent need to proceed with multicenter and well-designed studies using the IHS recommendations. This expert consensus may guide headache specialists in selecting the correct candidate patient, the standardized interventional technique, the type, the dosage, and the volume of the pharmacological agents to be used, and defining the optimum intervals for repeat procedures. We hope these efforts in near future may improve the quality of headache management worldwide.

Declaration of conflicting interests

The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article:
IUC: Reports no conflict of interest.
DU: Has served as a lecturer for Novartis and Lilly, is a board member of the European Headache Federation and vice-president of the Global Migraine and Pain Society.
AO: Has served as a lecturer for Novartis, Lilly and Allergan, is an executive board member of The International Headache Society and president of the Global Migraine and Pain Society.

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