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Propofol for Migraine – Just Because We Can, Should We?

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Migraine headache can be disabling. It accounts for approximately 24% of headaches presenting to EDs (unpublished data, HEAD study). Most patients have already tried their usual remedies before attending ED, so we are treating refractory rather than typical migraine.

The search for an effective treatment for refractory migraine has been a long and complicated one. Studies specific to the ED migraine population are few and small, the selection criteria are variable and treatment protocols complicated by the use of drug combinations where more than one drug has some efficacy for migraine. There have also been few direct agent-to-agent comparisons.

Available data suggest that the phenothiazines (e.g. prochlorperazine and chlorpromazine) and triptans are the most effective treatments in ED migraine patients. These drugs have achieved greater than 70% effective pain relief in a number of studies [1-4]. That said, we also know that there is individual variation in response and a significant placebo effect. Recently, interest in agents such as ketamine and propofol has increased.

This issue of *Emergency Medicine Australia* reports the results of a pilot study comparing propofol at procedural sedation doses with standard intravenous therapy for migraine.[5] Although this pilot study has some methodological flaws, let me commend the researchers for undertaking research in this area. From personal experience, I know that research like

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this is hard to design well and has significant ethical and operational challenges. This study is one of only a few prospective, comparative trials of propofol for the treatment of migraine. The debatable points in the study are that the so-called standard arm was not standardized (either in drug administered or dose) and the choice of primary endpoint (time from first intravenous drug administration to discharge), especially as lack of availability of a resuscitation cubicle was an exclusion criterion. I don't think this is an appropriate patient-centred outcome, as patients presenting with migraine want sustained, effective pain relief (including absence of significant rebound headache) and prompt return to normal function. Although not powered to do so, this study does not appear to have demonstrated a pain relief benefit and it did not collect data on rebound headache, return to function or patient satisfaction with treatment. Forty percent of patients treated with propofol required additional analgesia for their headache; two-thirds of these were given intravenous chlorpromazine. This is a high rate of rescue analgesia when compared to other commonly used agents. For example, in metanalysis, prochlorperazine had a rescue analgesia rate of 16%.[6] To date, there is no convincing evidence that propofol provides better sustained headache relief when compared to recognized abortive agents for migraine.[7]

Setting aside these concerns, there are three broad issues related to propofol administration for migraine – feasibility and resource allocation, consent and off label use, and the risk of addiction.

Procedural sedation in EDs is safe when administered in an appropriate environment by trained staff with critical care skills.[8] ED resuscitation spaces and teams are scarce resources. The fact that the study ED, with an annual ED census of approximately 70,000 patients, was only able to enroll 30 patients over 29 months, due mainly to lack of resuscitation space availability, challenges the feasibility of propofol treatment of migraine

and the appropriateness of resource utilization for this purpose. This is particularly true if there is no patient-centred outcome advantage from treatment with propofol.

Obtaining valid consent for treatment of migraine with propofol outside a clinical trial will not be straightforward. First, sufferers are in pain which, it could be argued, limits their ability to give free and informed consent. Second, the provision of detailed information about risks and alternative treatments would be the minimum legal requirement. Australian case law is clear that this applies even if the risk of harm is remote if potential consequences would be of significance to the patient.[9] Third, this would be 'off-label' prescription of propofol, as migraine is not a recognized indication for its use. There is no legal impediment to off-label prescription, but the onus is on the prescribing doctor to justify its use. Ideally, patients should be informed that the use is off label, the justification explained and specific acknowledgement of this documented as part of the consent process.

An unanswered question is the risk of addiction. Migraine is a chronic condition, so recurrence of migraine is expected. We know that propofol carries a risk of addiction. The available data on propofol use for migraine is too small to have reliable data about this risk. When there are alternative treatments with similar effectiveness and without the risk of addiction, is use of propofol justified?

I am not suggesting that we abandon investigation of propofol as a treatment for ED migraine patients completely. What is needed are well-designed trials with appropriate patient-centred outcomes. Propofol should be compared to agents that are recognized as being effective (e.g. phenothiazines, triptans) in standardized doses with a standardized rescue treatment pathway. Long term multi-site data collection is also needed to identify whether issues of addiction arise. For me, given the operational and consent issues and the

addiction risk, propofol will need to be clearly superior to the alternatives for me to change my practice. Just because I can, does not mean I should.

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