Propofol for Abortive Treatment of Migraine in the Pediatric Emergency Department

December 2021

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Headaches affect individuals across all age groups, races, genders, and socioeconomic statuses, however when severe or recurrent, they can lead to loss of time in school activities, social participation, and more. Headaches are the third leading complaint in pediatric ED visits and of all headache presentations, 40-65% were for primary headache disorder with the majority being migraines.

The pathophysiology of migraine headaches while not fully understood, is thought to be a primary neuronal process associated with an underlying genetically determined hyperexcitable cerebral cortex. This inherent disturbance of the neuronal calcium channels leads to a lowered threshold by which numerous internal and external factors can trigger episodes of cortical spreading depression (CSD). CSD is a process by which slowly propagating waves of neuronal hyperpolarization are followed by depolarization causing vascular dilation and extravasation of plasma proteins from the dural vessels. This leads to a sterile neurogenic inflammation which stimulates nociceptive afferents causing migraine aura and pain along with allodynia in the form of photo or tactile sensitivity among others.

The standard therapy (ST) for the treatment of migraine in the pediatric emergency department includes IV/PO Metoclopramide, Ketorolac or Ibuprofen, and IV Fluid/PO Hydration. These abortive medications commonly used in the emergency department have several potential adverse effects including drowsiness, the potential for prolonged emergency department length of stay, and dystonic reactions for which diphenhydramine is generally added to prevent the response. While these medications, now considered standardized therapy for the abortive treatment of migraine do have a reasonable efficacy and safety profile, there have been no significant developments in abortive treatment for pediatric migraine in the recent years.

A study by Krusz et al was the first to publish incidental findings that adults with migraine headache treated with propofol in preparation for nerve blocks experienced significant relief from their migraine pain, prior to the administration of the nerve block. Based on these observations, the researchers performed a randomized control trial to review the efficacy of propofol for the use of abortive treatment of migraines. The study recruited patients with a history of refractory migraine and treated them with subanesthetic doses of propofol and demonstrated the average reduction in the visual analog pain scale was 95.4% after an average of 20 minutes. Most importantly for the application of treatment to the pediatric population, there were no reported adverse effects or outcomes related to the propofol administration. Propofol, when used in subanesthetic doses, generally 0.5 mg/kg/dose, does not produce respiratory depression or hypotension as seen in its use as general anesthesia, generally administered at 3.3-3.5 mg/kg/dose. It has a high safety profile, rapid onset and resolution of effects, and also has antiemetic properties. The promising studies surrounding the use of propofol in the adult population for treatment of migraine headaches led me to pose the question if low dose propofol provided the same abortive effects and carried similar safety profile for the treatment of migraines in the pediatric population as compared to the standardized therapy in use today.

A literature search was conducted through PubMed using the MeSH terms Migraine Disorders, Pediatrics, Ti terms Migraine\*, Pediatric\* Child\*, Emergenc\*, and Keyword Propofol. Two studies were found surrounding the efficacy and safety profiles of low dose propofol as compared to standard migraine therapy in the pediatric population and one study was found reviewing the safety and efficacy of standard migraine therapy as compared to non-standard treatment in the pediatric emergency department.

The first study by Sheridan et al (2018) published in the Journal of Emergency Medicine was a prospective randomized controlled trial (RCT) conducted in the Emergency Department with patients between 7-19 yo who presented with a diagnosis of migraine. The patients were randomly assigned to two groups, low dose propofol therapy or the standard IV migraine therapy, and the primary outcome measured was reduction in pain using the visual analog pain scale. The data did not show a significant difference between the reduction in pain scale of the two groups, however it did result in a statistically significant decrease in the number of rebound headaches reported at 24 hours and a clinically, although not statistically, significant decease in emergency department length of stay. The study was limited by the presentation of data in aggregate making further statistical analysis difficult to obtain. Additionally, the study, while conducted as an RCT, was blinded to the patients but not the healthcare staff which could certainly cause bias when obtaining pain scale results.

The second study conducted by Sheridan et al (2012) published in the Journal of Pediatric Emergency Care was a retrospective cohort study which sought to review the effectiveness of low dose propofol for the abortive treatment of migraine as compared to standard IV migraine therapy. In this hospital system, the use of low dose propofol therapy in the pediatric emergency department was approved due to success from published adult studies. This study reviewed charts of patients discharged from a pediatric emergency department with a diagnosis of migraine. The primary outcomes reviewed were reduction in pain and emergency department length of stay. The review concluded that there was a significantly greater reduction in pain score for low dose propofol vs standard IV migraine therapy groups. The decrease in mean length of stay was also noted to be clinically although not statistically significant. Of note, the results of this study are limited by the selection bias of retrospective design and small number of cases reviewed.

The third and final study by Leung et al (2013) published in the Journal of Head and Face Pain was a retrospective cohort study that reviewed the effectiveness of standardized IV combination therapy for the treatment of migraines in the pediatric population. The study reviewed charts of patients who presented to the pediatric ED with a primary migraine headache diagnosis and compared standardized IV migraine therapy to single medication or non-standardized medication therapy. It concluded that the utilization of standardized migraine treatment regimen in the pediatric ED significantly decreases headache pain scores, ED length of stay, and hospital admission rates. As in the previous study, the results of this study are limited by the selection bias of retrospective design and the inability to perform follow-up.

The available literature to date does not support transition to low dose propofol over standardized therapy at this time, however, the available studies demonstrated the potential for improved pain scores, decreased rebound headaches, and decreased emergency department length of stay. While the use of low dose propofol has demonstrated potential benefits, its use faces the potential for significant roadblocks including cost analysis as compared to the standard therapy regimen and the need for staffing during the duration of propofol use as required by many institutions. The direct patient supervision may be mitigated by studies evaluating adverse reactions including hypotension and respiratory depression when propofol is administered in low doses as compared to its known effects in anesthetic doses, however there is not currently sufficient evidence to support remote monitoring via cardiac monitor or infrequent vital sign checks. Low dose propofol for the treatment of migraines in the pediatric population requires further investigation however, given the promising results of adult studies, it may be a viable alternative, augmentation, or escalation to standardized therapy.

References

Kelly AM. Propofol for migraine: Just because we can, should we? Emerg Med Australas. 2020 Aug;32(4):540-541. doi: 10.1111/1742-6723.13555. PMID: 32705803.

Leung, S., Bulloch, B., Young, C., Yonker, M. and Hostetler, M. (2013), Effectiveness of Standardized Combination Therapy for Migraine Treatment in the Pediatric Emergency Department. Headache: The Journal of Head and Face Pain, 53: 491-197. <https://doi-org.proxy.library.stonybrook.edu/10.1111/head.12042>

Mitra, B., Roman, C., Mercier, E., Moloney, J., Yip, G., Khullar, K., Walsh, K., Smit, D.V. and Cameron, P.A. (2020), Propofol for migraine in the emergency department: A pilot randomised controlled trial. Emergency Medicine Australasia, 32: 542-547. <https://doi-org.proxy.library.stonybrook.edu/10.1111/1742-6723.13542>

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| Pediatr Neurol. 2012 October ; 47(4): 233–241. doi:10.1016/j.pediatrneurol.2012.06.001 |
| Piatka, Corissa, and Robert D. Beckett. "Propofol for treatment of acute migraine in the emergency department: a systematic review." *Academic Emergency Medicine* 27.2 (2020): 148-160. |
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Sheridan, David C. MD\*; Spiro, David M. MD, MPH\*†; Nguyen, Thuan MD, PhD‡; Koch, Thomas K. MD§∥; Meckler, Garth D. MD, MSHS\*† Low-Dose Propofol for the Abortive Treatment of Pediatric Migraine in the Emergency Department, Pediatric Emergency Care: December 2012 - Volume 28 - Issue 12 - p 1293-1296 doi: 10.1097/PEC.0b013e3182768a6b

Sheridan DC, Hansen ML, Lin AL, Fu R, Meckler GD. Low-Dose Propofol for Pediatric Migraine: A Prospective, Randomized Controlled Trial. J Emerg Med. 2018 May;54(5):600-606. doi: 10.1016/j.jemermed.2018.01.003. Epub 2018 Feb 15. PMID: 29456086.