

Treatment of acute migraine in the emergency department

Saurabh Gupta MD CCFP Richard Oosthuizen MD CCFP Simon Pulfrey MD CCFP(EM)

Case description

Erica, a healthy 24-year-old medical student, presents to your emergency department (ED) during your evening shift with a severe headache that she has had for the past 6 hours. She has had similar headaches once a term that keep her from her clinical duties for 1 or 2 days if untreated. After a careful history and physical examination you decide she has a migraine.

What is the best treatment for her in the ED?

Migraine is a common presentation in the ED. Migraines are characterized by recurrent, unilateral, throbbing headache associated with photophobia and nausea. Diagnosis is made clinically using tools such as the POUND (pulsatile, one-day duration, unilateral, nausea or vomiting, and disabling) mnemonic.¹ While our understanding of the pathophysiology of migraine continues to evolve, it is hypothesized that the pain of migraine results from a cyclic propagation of neural dysfunction and vasospasm in the brain.² Purported therapies for the ED treatment of acute migraine are legion and of mixed efficacy. Some ED therapeutic strategies might even increase ED recidivism.³ This article aims to provide an evidence-based and effective strategy for treating acute migraine in the ED.

Discussion

Nonsteroidal anti-inflammatory drugs. Multiple, different nonsteroidal anti-inflammatory drugs (NSAIDs) have been shown in randomized, placebo-controlled trials to be effective for acute migraine.⁴⁻⁹ Given its parenteral formulation, ketorolac is a reasonable option in the ED. The recommended ketorolac dosage is a 60-mg intramuscular dose or 30-mg intramuscular or intravenous (IV) doses every 6 hours (maximum daily dose of 120 mg).¹⁰ The incremental benefit of NSAIDs combined with other therapies remains unclear, but it is reasonable to prescribe NSAIDs alone given their consistent efficacy when studied as monotherapy.

Acetaminophen. Acetaminophen is frequently taken by patients before ED presentation. A Cochrane

meta-analysis estimated the number needed to treat to be 12 for acetaminophen in acute migraine.¹¹ Given the low cost, wide availability, and safe side effect profile of acetaminophen, it is a useful first-choice drug for acute migraine. No studies have been undertaken to see whether the addition of acetaminophen to the standard abortive migraine therapy provides substantial incremental benefit.

Acetaminophen alone in the ED is a reasonable option only for patients who have not taken acetaminophen in the preceding 4 hours and have only a very minor migraine.

Triptans. Abortive therapy using serotonin 1B or 1D agonists (triptans) for migraine is now a well-accepted strategy for acute migraine in the outpatient setting.¹² Several medications have been developed that can be delivered by oral, nasal, or subcutaneous routes. Evidence suggests that subcutaneous delivery is fastest and most effective, although there is no clear superiority of one triptan over another.¹³ Common side effects include injection site reactions, dizziness, and paresthesias. Triptans are contraindicated in cardiovascular disease, pregnancy, basilar migraines, Prinzmetal angina, and ischemic stroke, and with the use of ergotamines within the previous 24 hours.¹⁴ Studies have also suggested that triptan therapy is less effective in patients with prolonged and severe migraine.¹⁴ Given the side effect profile, lack of efficacy in severe migraine, and relative contraindications, triptan use in the ED is of limited value.

Ergotamines. Traditionally, dihydroergotamine (DHE) has been used for abortive therapy in migraine, as it acts on serotonin 1B and 1D receptors, similar to triptans. There is some evidence that DHE combined with an antiemetic medication is as effective as meperidine, valproate, or ketorolac in relieving migraine and preventing relapse.¹⁵ However, studies comparing the efficacy of DHE monotherapy with antiemetic therapy are small and favour non-DHE therapies.¹⁶⁻¹⁸ Contraindications to DHE use are similar to those of triptans. Given the potential side effect profile and lack of superiority compared with common treatment modalities, ergotamine use is not a preferred strategy for ED patients.

Intravenous fluids. Dehydration is a known trigger of migraine.^{19,20} Persistent nausea and vomiting further



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exacerbates the migraine. Although there is a relative paucity of strong evidence for the administration of IV fluids, adequate hydration might improve patient malaise and could prevent some of the adverse cardiovascular effects seen with many migraine therapies.^{19,20}

Antiemetic medications. Parenteral metoclopramide, chlorpromazine, and prochlorperazine all have demonstrated efficacy in randomized trials as monotherapy for acute migraine.²¹⁻²³ While metoclopramide has been the most studied, there is some evidence that chlorpromazine and prochlorperazine might be more effective in reducing pain and nausea.^{23,24}

The most common adverse reactions are sedation and postural hypotension. True and clinically relevant akathisia and acute dystonic reactions have been difficult to interpret from the literature but appear rare.²⁵ Akathisia was more commonly associated with prochlorperazine than metoclopramide, and adjuvant diphenhydramine reduced the relative risk of akathisia induced by prochlorperazine by 61%.²⁶

Antiemetic medications are efficacious and are recommended for acute migraine in the ED. To reduce the risk of akathisia, diphenhydramine should be included.

Butyrophenones (haloperidol and droperidol). Randomized controlled trials have demonstrated efficacy of haloperidol and droperidol monotherapy compared with placebo for acute migraine.²⁷⁻²⁹ However, these drugs have been associated with frequent side effects (somnolence, akathisia, anxiety) and have a black-box warning for QT prolongation. As a result, these medications are generally reserved for rescue therapy in refractory migraine.

Opioids. When compared with NSAIDs, DHE, and antiemetic medications, opioids are less effective for migraine.^{30,31} Unfortunately, most of the literature about the use of opioids for migraine was published when meperidine was commonly used.

Use of opioids for migraine control has also been associated with higher recurrence rates, greater functional disability, and an increased likelihood of ED recidivism.³²

While these data cannot demonstrate causation, they indicate that opioids are not an effective first-line strategy for patients with severe migraines.³ However, there are circumstances in which using opioids in the ED as a second-line treatment for an individual patient with an acute migraine is entirely appropriate, and it would be cruel to do otherwise.

Dexamethasone. The role of dexamethasone in treating the inflammatory processes of acute migraine has been investigated.³³ Adjunctive parenteral dexamethasone (10 to 25 mg intravenously or intramuscularly) did not

reduce acute pain scores in the ED, but did reduce the likelihood of migraine recurrence within 72 hours when added to standard abortive therapy.³³ Dexamethasone was shown to have a number needed to treat of 9 and an adverse event profile equal to placebo. Oral administration of dexamethasone was not studied.

Sequence and combination of therapies. *Stepped care within attacks* is a treatment plan in which medications are added depending on patient response. *Stratified care based on severity* is a treatment plan in which all of the anticipated medications are given up front. Patients have improved outcomes with stratified care.³⁴

Until we have further evidence to guide our medication combinations, treating the patient with multiple medications that have independently been found to be efficacious at the onset of his or her ED visit is recommended over stepped care (**Box 1**).

Box 1. Suggested prescription for severe migraine

1-L bolus of IV normal saline solution
10 mg of IV prochlorperazine
25 mg of IV diphenhydramine
30 mg of IV ketorolac
10 mg of IV dexamethasone

IV—intravenous.

Case resolution

Erica's severe migraine was treated with parenteral prochlorperazine, diphenhydramine, and ketorolac after a bolus of normal saline solution. She also received a dose of parenteral dexamethasone. Her discharge instructions included a handout on migraines (widely available online), a family physician referral, and a prescription for triptan therapy to be used early for future migraines. The next time you see her, she is doing her emergency medicine rotation during residency. 

Drs Gupta and Oosthuizen are emergency medicine residents at the University of British Columbia in Vancouver. **Dr Pulfrey** is Clinical Associate Professor in the Department of Emergency Medicine at the University of British Columbia.

Competing interests

None declared

References

1. Wilson JF. In the clinic. Migraine. *Ann Intern Med* 2007;147(9):ITC11-1-ITC11-16. Erratum in: *Ann Intern Med* 2008;148(5):408.
2. Pietrobon D, Moskowitz MA. Pathophysiology of migraine. *Annu Rev Physiol* 2013;75:365-91. Epub 2012 Nov 26.
3. Buse DC, Pearlman SH, Reed ML, Serrano D, Ng-Mak DS, Lipton RB. Opioid use and dependence among persons with migraine: results of the AMPP study. *Headache* 2012;52(1):18-36.
4. Kirthi V, Derry S, Moore RA. Aspirin with or without an antiemetic for acute migraine headaches in adults. *Cochrane Database Syst Rev* 2013;(4):CD008041.
5. Rabbie R, Derry S, Moore RA. Ibuprofen with or without an antiemetic for acute migraine headaches in adults. *Cochrane Database Syst Rev* 2013;(4):CD008039.

6. Andersson PG, Hinge HH, Johansen O, Andersen CU, Lademann A, Götzsche PC. Double-blind study of naproxen vs placebo in the treatment of acute migraine attacks. *Cephalalgia* 1989;9(1):29-32.
7. Nestvold K, Kloster R, Partinen M, Sulkava R. Treatment of acute migraine attack: naproxen and placebo compared. *Cephalalgia* 1985;5(2):115-9.
8. Derry S, Rabiee R, Moore RA. Diclofenac with or without an antiemetic for acute migraine headaches in adults. *Cochrane Database Syst Rev* 2013;(4):CD008783.
9. Vécsei L, Gallacchi G, Sági I, Semjén J, Tajti J, Szok D, et al. Diclofenac epolamine is effective in the treatment of acute migraine attacks. A randomized, crossover, double blind, placebo-controlled, clinical study. *Cephalalgia* 2007;27(1):29-34.
10. Jakubowski M, Levy D, Goor-Aryeh I, Collins B, Bajwa Z, Burstein R. Terminating migraine with allodynia and ongoing central sensitization using parenteral administration of COX1/COX2 inhibitors. *Headache* 2005;45(7):850-61.
11. Derry S, Moore RA. Paracetamol (acetaminophen) with or without an antiemetic for acute migraine headaches in adults. *Cochrane Database Syst Rev* 2013;(4):CD008040.
12. McCrory DC, Gray RN. Oral sumatriptan for acute migraine. *Cochrane Database Syst Rev* 2003;(3):CD002915.
13. Tfelt-Hansen P. Efficacy and adverse events of subcutaneous, oral, and intranasal sumatriptan used for migraine treatment: a systematic review based on number needed to treat. *Cephalalgia* 1998;18(8):532-8.
14. Jamieson DG. The safety of triptans in the treatment of patients with migraine. *Am J Med* 2002;112(2):135-40.
15. Colman I, Brown MD, Innes GD, Grafstein E, Roberts TE, Rowe BH. Parenteral dihydroergotamine for acute migraine headache: a systematic review of the literature. *Ann Emerg Med* 2005;45(4):393-401.
16. Winner P, Ricalde O, Le Force B, Saper J, Margul B. A double-blind study of subcutaneous dihydroergotamine vs subcutaneous sumatriptan in the treatment of acute migraine. *Arch Neurol* 1996;53(2):180-4.
17. González-Espinosa LE, Gómez-Viera N, Olivera-Leal I, Reyes-Lorente R. Treatment of acute attack of migraine with sumatriptan [article in Spanish]. *Rev Neurol* 1997;25(147):1672-5.
18. Bell R, Montoya D, Shuaib A, Lee MA. A comparative trial of three agents in the treatment of acute migraine headache. *Ann Emerg Med* 1990;19(10):1079-82.
19. Bhatia MS, Gupta R, Srivastava S. Migraine associated with water deprivation and progressive myopia. *Cephalalgia* 2006;26(6):758-60.
20. Blau JN. Water deprivation: a new migraine precipitant. *Headache* 2005;45(6):757-9.
21. Colman I, Brown MD, Innes GD, Grafstein E, Roberts TE, Rowe BH. Parenteral metoclopramide for acute migraine: meta-analysis of randomised controlled trials. *BMJ* 2004;329(7479):1369-73. Epub 2004 Nov 18.
22. Bigal ME, Bordini CA, Speciali JG. Intravenous chlorpromazine in the emergency department treatment of migraines: a randomized controlled trial. *J Emerg Med* 2002;23(2):141-8.
23. Coppola M, Yealy DM, Leibold RA. Randomized, placebo-controlled evaluation of prochlorperazine versus metoclopramide for emergency department treatment of migraine headache. *Ann Emerg Med* 1995;26(5):541-6.
24. Kelly AM, Walcynski T, Gunn B. The relative efficacy of phenothiazines for the treatment of acute migraine: a meta-analysis. *Headache* 2009;49(9):1324-32. Epub 2009 Jun 2.
25. Drotts DL, Vinson DR. Prochlorperazine induces akathisia in emergency patients. *Ann Emerg Med* 1999;34(4 Pt 1):469-75.
26. Vinson DR, Drotts DL. Diphenhydramine for the prevention of akathisia induced by prochlorperazine: a randomized, controlled trial. *Ann Emerg Med* 2001;37(2):125-31.
27. Miner JR, Fish SJ, Smith SW, Biros MH. Droperidol vs. prochlorperazine for benign headaches in the emergency department. *Acad Emerg Med* 2001;8(9):873-9.
28. Weaver CS, Jones JB, Chisholm CD, Foley MJ, Giles BK, Somerville GG, et al. Droperidol vs prochlorperazine for the treatment of acute headache. *J Emerg Med* 2004;26(2):145-50.
29. Honkaniemi J, Liimatainen S, Rainesalo S, Sulavuori S. Haloperidol in the acute treatment of migraine: a randomized, double-blind, placebo-controlled study. *Headache* 2006;46(5):781-7.
30. Rozen TD. Acute therapy for migraine headaches. *Semin Neurol* 2006;26(2):181-7.
31. Lane PL, McLellan BA, Baggoley CJ. Comparative efficacy of chlorpromazine and meperidine with dimenhydrinate in migraine headache. *Ann Emerg Med* 1989;18(4):360-5.
32. Colman I, Rothney A, Wright SC, Zilkalns B, Rowe BH. Use of narcotic analgesics in the emergency department treatment of migraine headache. *Neurology* 2004;62(10):1695-700.
33. Colman I, Friedman BW, Brown MD, Innes GD, Grafstein E, Roberts TE, et al. Parenteral dexamethasone for acute severe migraine headache: meta-analysis of randomised controlled trials for preventing recurrence. *BMJ* 2008;336:1359-61. Epub 2008 Jun 9.
34. Lipton RB, Stewart WF, Stone AM, Láinez MJ, Sawyer JP; Disability in Strategies of Care Study group. Stratified care vs step care strategies for migraine: the Disability in Strategies of Care (DISC) study: a randomized trial. *JAMA* 2000;284(20):2599-605.

BOTTOM LINE

- Acute migraine is a common presentation in the emergency department (ED).
- Opioids are, at best, a second-line treatment for acute migraine in the ED.
- Nonsteroidal anti-inflammatory drugs, antiemetic medications, diphenhydramine, dexamethasone, and intravenous fluids all have shown benefit for treating acute migraine in the ED. Their effect is greater when they are all administered up front as opposed to being delivered in a stepwise pattern throughout the ED stay.

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