British Journal of Medicine & Medical Research
4(20): 3800-3813, 2014

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Emergency and Inpatient Treatment of Migraine: An American Headache Society Survey

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Authors' contributions

This work was carried in collaboration between all authors. Authors COD and MJM designed and distributed this survey and performed statistical analysis. Author COD wrote the first draft of the manuscript. All authors reviewed the literature, read and approved the final manuscript.

Original Research Article

Received 20th January 2014
Accepted 14th April 2014
Published 5th May 2014

ABSTRACT

Objective: To determine the medication and management preferences of headache specialists in treating migraine in the ED and during inpatient hospitalization.
Background: Despite the frequency of migraine as a presenting complaint and the cost of acute treatment, there is no clear consensus on the standard of care for acute migraine management in the ED or during hospitalization.
Methods: The American Headache Society (AHS) Special Interest Group for Inpatient and Emergency Care developed an online survey that was distributed to AHS members.
Results: There were 106 survey respondents, 87 of whom completed all 13 questions. The most frequent choices for first-line ED migraine treatment in an otherwise healthy adult were dopamine antagonists (58.7%), non-steroidal anti-inflammatory drugs (NSAID) (49.0%), and IV hydration (48.1%). The most frequently selected second-line treatments were valproic acid, dihydroergotamine (DHE), and NSAIDs. Opioids were

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chosen by 1% for first line and 4.8% for second line. No respondents selected barbiturate containing medications for either treatment. The most frequently selected medications for initial treatment during inpatient hospitalization for migraine were DHE (64.5%), dopamine antagonists (61.3), and NSAID (37.6%). The most frequent adjunctive treatments were valproic acid and corticosteroids. Vomiting, medication overuse with opioids or barbiturates, and ED recidivism were the most frequently selected indications for inpatient treatment. The majority of respondents (71%) indicated they would taper or stop opioid medication as a part of migraine treatment in patients admitted for intractable migraine who were taking opioids for an unrelated indication such as low back pain. Commonly selected ancillary services included psychology (80.6%), physical therapy (64.5%), nutrition (50.5%), and psychiatry (46.2%). The majority of respondents (79.3%) indicated that outpatient follow-up should occur within 4 weeks of discharge from the hospital.

Conclusions: Headache specialists indicated neuroleptics, NSAID and migraine-specific agents should be considered before opioids or barbiturates for both adults and children with migraine. There was consensus that worsening or refractory migraine treatment should not include the escalation of chronic opioids. Opinion suggested that opioid or barbiturate overuse is more likely to warrant inpatient treatment than triptan or NSAID overuse. Multidisciplinary care and close follow-up are important components of inpatient migraine treatment.

Keywords: Migraine; emergency; inpatient; pediatric; chronic daily headache.

1. INTRODUCTION

Migraineurs often seek acute headache treatment in the emergency department (ED). A recent evaluation of ED visits in the US lists headache as the fourth most common chief complaint [1]. In one study, 7% of migraine patients had sought ED treatment for severe headache in the previous year, with many patients reporting multiple visits [2]. The economic burden of treating migraine in the ED is significant. In the US in 2010, the estimated annual cost of these visits was $700 million US dollars [3]. Migraine is defined by the International Classification of Headache Disorders as headache attacks lasting 4-72 hours without treatment with at least two of the following–unilateral location, pulsating quality, moderate-severe intensity and aggravation by physical activity–and one of either nausea or vomiting or both photophobia and phonophobia which is not accounted for by another diagnosis [4]. As such, migraine attacks are frequently disabling and have a major impact on quality of life.

Despite the frequency of migraine as a presenting complaint and the cost of acute treatment, there is no clear consensus on the standard of care for acute migraine management, and there is considerable variability in prescribing practices [5]. A variety of parenteral medications are available for migraine treatment including triptans, dopamine receptor antagonists, ergots, lidocaine, ketamine, non-steroidal anti-inflammatory drugs (NSAID), and opioids. A recent meta-analysis of 71 randomized controlled trials found that neuroleptic monotherapy or dihydroergotamine (DHE) combined with a neuroleptic or metoclopramide were the most effective acute abortive medications [6]. Opioids, metoclopramide monotherapy and NSAID were moderately effective. Triptans and DHE monotherapy were the least effective, reducing pain on a visual analog scale by only 12-16mm. Evaluating the evidence is complicated by the lack of placebo controlled trials and inclusion of combination regimens in many of the comparative trials.

Opioids remain one of the most commonly prescribed migraine abortive in EDs in North America [7]. Colman et al. [8] reported nearly 60 percent of patients presenting to one of five linked EDs in one Canadian center received opioids as first line treatment. The efficacy of opioids as a class is based on evaluations of meperidine, nalbuphine and tramadol among others [9]. Frequentopioid use can be concerning in light of data that demonstrates that opioids are associated with migraine progression, ED recidivism and a high rate of headache recurrence [7,10,11]. In addition, patients who received opioids had significantly longer ED stays and those patients given multiple doses of opioids had longer stays than those who received one dose in one study [12].

Refractory or complicated migraine patients may require hospitalization. In 2008, an estimated 51,116 patients were hospitalized for migraine in the US [3] which accounts for 63% of all admissions for headache. The mean length of inpatient stay for headache was 2.7 days, with an aggregate cost of over 407 million US dollars [13]. As with ED management, there is a lack of consensus on the optimal strategy for treating these patients. Many of the available parenteral medication are administered sequentially or in combination. In addition, because the great majority of persons with migraine are managed as outpatients and do not require diagnostic testing, there is no universal consensus on when to admit persons with migraine.

The objective of this study was to determine the practice preferences of AHS members for acute migraine treatment in the ED and inpatient setting. Expert opinion on the treatment of migraine, especially in circumstances where there is a lack of evidence-based treatment protocols, should help guide the development of a better paradigm for treating patients.

2. METHODS

The AHS Special Interest Section for Inpatient and Emergency Care developed these survey questions during and after section meetings. The goals of this survey included: (1) to determine pharmacologic preferences for emergency and inpatient treatment; (2) to identify indications for inpatient, as opposed to outpatient, treatment; (3) to assess differences in adult and pediatric acute migraine emergency and inpatient treatment. AHS distributed the survey via Survey Monkey, an internet based survey site, to the AHS membership on April 23, 2011, with a response deadline set for one week after distribution.

Survey questions are listed in Appendix A. Questions 7, 9, 13 were single choice, the remaining questions allowed selection of multiple answers. Respondents also had the option of submitting demographic data.

3. RESULT

The survey was distributed to 807 AHS members. There were 106 survey respondents with 87 respondents completing all 13 questions. 104 members responded to questions 1-3 and 93 responded to questions 1-9.

The most frequent choice for first line ED migraine treatment in an otherwise healthy adult was a dopamine antagonist Table 1. The most frequent second line treatments were valproic acid (31.7%), dihydroergotamine (DHE) (28.8%), and NSAIDs (26%). Opioids were chosen by 1% for first line and 4.8% for second line. No respondents selected barbiturate containing medications for either treatment Table 1. Oral triptans (55.8%), injectable sumatriptan (30.8%), and NSAID (30.8%) were the most common choices for outpatient use after ED discharge.

Table 1. Treatment recommendations for acute migraine in the ED in adults

Treatment option	First-line treatment (% response)	Second-line treatment (%response)
Dopamine antagonist	58.7	21.2
NSAIDs	49.0	26.0
IV hydration	48.1	16.3
DHE	33.7	28.8
SC sumatriptan	21.2	5.8
Corticosteroids	15.4	22.1
IV magnesium	15.4	14.4
IV valproic acid	7.7	31.7
Ondansetron	7.7	2.9
Oral triptan	5.8	3.8
Triptan NS	3.8	1.0
Peripheral nerve block	1.9	8.7
Opioids	1.0	4.8
IV levetiracetam	0	4.8
Barbiturate-containing combination medications	0	0

The top three responses for each category are indicated in bold. NSAIDs=non-steroidal anti-inflammatory drugs; IV=intravenous, DHE=dihydroergotamine; SC=subcutaneous; NS=nasal spray

The most frequent medications for initial treatment during inpatient hospitalization for migraine were DHE (64.5%), dopamine antagonists (61.3%), and NSAID (37.6%). As a back-up if the initial treatment were not successful, the most frequent adjunctive treatments were valproic acid (35.5%) and corticosteroids (34.4%) Table 2.

Table 2. Treatment recommendations for hospitalized migraine patients

Treatment option	First-line treatment (% response)	Second-line treatment (% response)
DHE	64.5	21.5
Dopamine antagonist	61.3	14.0
NSAIDs	37.6	18.3
Corticosteroids	22.6	34.4
IV valproic acid	21.5	35.5
IV magnesium	16.1	19.4
SC sumatriptan	11.8	2.2
Peripheral nerve block	6.5	21.5
IV lidocaine	4.3	6.5
Oral triptan	4.3	2.2
Triptan NS	3.2	2.2
Acetaminophen	2.2	0
Opioids	1.1	4.3
IV ketamine	1.1	4.3
IV levetiracetam	0	6.5
Barbiturate-containing combination medications	0	0

The top three responses for each category are indicated in bold. DHE=dihydroergotamine; NSAIDs=non-steroidal anti-inflammatory drugs; IV=intravenous; SC=subcutaneous; NS=nasal spray

Nausea and vomiting was the most popular factor favoring inpatient admission (63.4%). The majority of respondents suggested medication-overuse headache with opioids (68.3%) or barbiturates (58.1%) would be a factor in deciding on inpatient treatment for migraine. The majority of respondents, however, did not consider overuse of triptans (28.0%) or NSAIDs (15.1%) to warrant admission. Indications for inpatient treatment are listed in Fig. 1.The majority of respondents (71%) indicated they would taper or stop opioid medication as a part of migraine treatment in patients admitted for intractable migraine who were taking opioids for an unrelated indication such as low back pain. The majority of respondents considered ancillary services such as psychology (80.4%), physical therapy (65.2%), nutrition (51.1%), and psychiatry (46.7%) to be useful. Only 13% of respondents chose healing touch or Reiki therapy. The majority of respondents (60.9%) indicated they would discharge a patient who had improved but continued to have mild headache, while the remainder (39.1%) would continue treatment with the goal of becoming headache free. Recommended follow-up was within 4 weeks of discharge for 79.3% of respondents, and 1 month or longer for 20.7%.

For the treatment of a pediatric patient, age 14 in the survey question, the most frequent choice for first line ED migraine treatment was NSAIDs (55.2%), followed by dopamine antagonists (37.9%), and intravenous hydration (35.6%). The most frequent second line treatments were NSAIDs (28.7%), intravenous valproic acid (27.6%), DHE (21.8%) and dopamine antagonists (21.8%) Table 3. Opioids were not chosen by any respondents for first line and by only 1.1% for second line. Barbiturate containing medications were no selected for either treatment. Oral triptans(67.8%), NSAIDs (44.8%) and triptan nasal spray (14.9%) were the most common choices for outpatient use after ED discharge.

Table 3. Treatment recommendations for pediatric patients with acute migraine in the ED

Treatment option	First-line treatment (% response)	Second-line treatment (%response)
NSAIDs	55.2	28.7
Dopamine antagonist	37.9	21.8
IV hydration	35.6	11.5
IV magnesium	14.9	12.6
SC sumatriptan	13.8	10.3
Oral triptan	13.8	9.2
Ondansetron	12.6	3.4
Triptan NS	9.2	3.4
DHE	8.0	21.8
Corticosteroids	8.0	18.4
IV valproic acid	6.9	27.6
Peripheral nerve block	2.3	5.7
Acetaminophen	2.3	1.1
IV levetiracetam	1.1	1.1
Opioids	0	1.1
Barbiturate-containing combination medications	0	0

The top three responses for each category are indicated in bold. NSAIDs=non-steroidal anti-inflammatory drugs; IV=intravenous; SC=subcutaneous; NS=nasal spray; DHE=dihydroergotamine

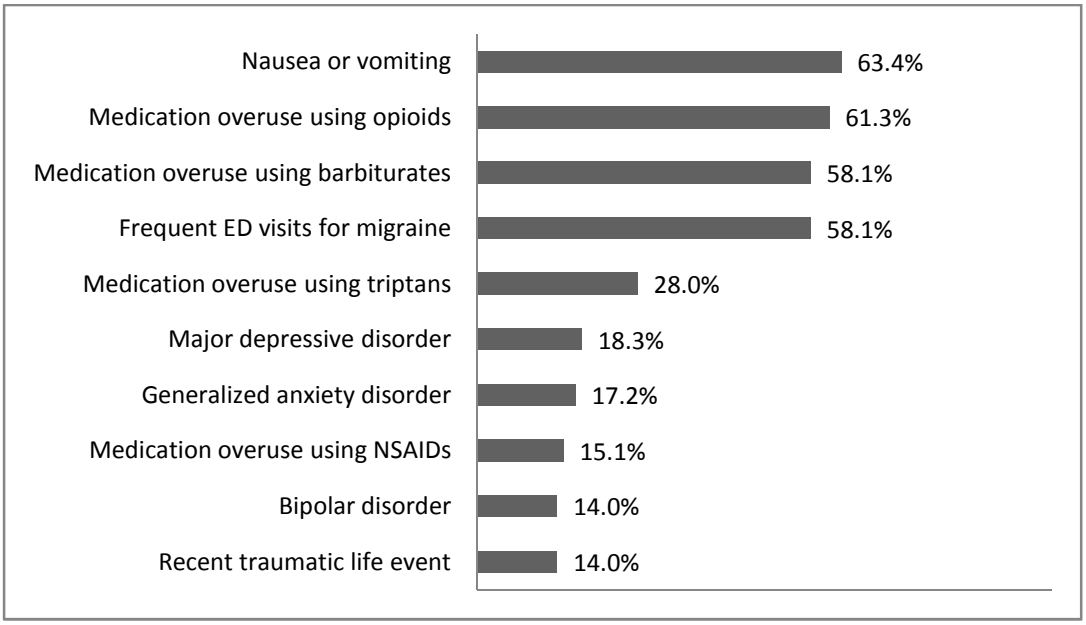

Fig. 1. Indications for hospitalization for migraine treatment by survey response
ED=emergency department; NSAIDs= non-steroidal anti-inflammatory drugs

4. CONCLUSION

This survey attempts to describe what clinicians treating headache consider the best practices in the treatment of migraine. As would be expected given the lack of clear guidelines for emergency treatment, respondents selected multiple different types of medications as first- or second-line treatment. Most selected multiple treatments for use as first-line and second-line therapy, suggesting that many AHS members consider migraine as seen the ED or in the inpatient setting to be challenging, and less likely to respond to a single agent. Data collected after ED discharge suggests that migraine commonly recurs within 24 hours [14]. Given the prevalence of migraine, only a small minority of persons with migraine are ever admitted for inpatient care, which implies that those who are admitted tend to be refractory.

The responses of AHS members indicate reference for dopamine antagonists, IV hydration and NSAIDs for acute migraine treatment in the ED, with the addition of DHE and/or valproic acid for adjunctive treatment. Opioids were rarely selected as first-line treatment. The responses for initial treatment of migraine in the inpatient setting indicated more frequent use of DHE than in the ED. These preferences are in agreement with recent evaluations of efficacy of parental migraine medications [9,15-16]. DHE may be less favorable amongst providers in the ED because of its side effect profile including nausea and vomiting, diarrhea, abdominal cramping, vasoconstriction and the risk of adverse events such as hypertension and chest pain. DHE may also require multiple doses to achieve best results in pediatric and adult patients [17]. In one study, 100% of patients receiving DHE monotherapy reported side effects [18]. The current survey allowed respondents to select multiple interventions but did not specifically address preferences for combination versus monotherapy of listed medications. The second -most used second-line treatment in an inpatient setting, as represented by percentage of respondents, was corticosteroids (34.4%). This may reflect

previous data on corticosteroids in the management of headache and with the recent findings that although there were no differences seen at 10 minutes, intravenous dexamethasone significantly reduces the severity of acute migraine headache attacks more effectively than intravenous morphine at time points one hour and 24 hours after administration [19].

AHS members rarely recommend opioids and do not recommend barbiturates in persons the emergency treatment or inpatient setting. This survey did not focus on patients with secondary headache or contraindications to specific agents such as known cardiovascular disease – situations in which opioid use might be more acceptable. This reflects a difference in the treatment preferences of AHS members as compared to reports of ED prescribing practices [7]. Many AHS members also indicated that they would taper or discontinue chronic opioids. This likely reflects prior studies that have demonstrated that the use of daily opioids for non-headache indications, such as arthritis and low back pain, can lead to progression of chronic daily headache and chronic migraine [20-21]. Obviously, patients receiving very high doses of long-acting opioids for conditions such as cancer pain or failed back syndrome may not be able to discontinue opioid therapy. For patients with worsening migraine on daily opioids, clinicians need to consider the indication for opioids, the daily dose, any ongoing opioid-related adverse effects, and if there is clear relationship between opioid use and worsening migraine or not.

The majority of respondents selected oral triptans, a migraine-specific medication, for home use after discharge from the ED. Friedman et al noted infrequent triptan use by patients presenting to the ED for treatment of acute migraine [22]. In fact, one study reported that up to 50% of migraine patients have not taken any abortive medication prior to seeking care in the ED [23]. This may represent a lack of access to outpatient migraine treatment, lack of education on the use of prescribed medication or other factors. Prescribing sumatriptan for migraine patients is associated with improved quality of life and patient satisfaction as well as reduction in healthcare use including ED visits [24].

The goals of inpatient treatment may vary, depending on the indication for admission. Studies of tertiary headache centers have identified several conditions necessitating hospitalization, including medication overuse, failure of outpatient therapy, functional disability, or severe psychiatric comorbidity [3.25]. Respondents considered the presence of vomiting, multiple ED visits and overuse or either opioids or barbiturates more problematic for outpatient treatment compared with the presence of a mood disorder or overuse of either triptans or NSAIDs. AHS member responses also reflected the published utility of ancillary services to address comorbid conditions such as anxiety and depression [25-26]. Although one tertiary headache center has reported positive three-month outcomes when migraine treatment was directed with the goal of becoming headache free prior to discharge, there are no specific studies addressing the endpoint of inpatient headache treatment [3]. Responses in this survey indicated most providers would discharge an improved patient rather than aim for complete headache resolution. This may reflect pressure on providers to reduce patient's length of stay, which currently averages less than 3 days for those with migraine [13]. Lake et al. describe outcomes after comprehensive admissions with an 8.5 day mean length of stay which demonstrated significant benefit after weeks and months in terms of functioning, mood and ability to work [26]. For those suffering from long-standing migraine and severe disability, perhaps longer admissions should be considered.

Guidelines for the treatment of acute migraine in the pediatric population are limited by a lack of data and most recommendations are based on expert opinion and extrapolated from

studies in adults. A recent evaluation of the treatment of pediatric migraine in the ED established the effectiveness of a standardized combination therapy including normal saline, ketorolac, prochlorperazine and diphenhydramine [27]. Survey respondents indicated similar choices with the addition of valproic acid and/or DHE for second line treatment.

This survey mirrors previous surveys of inpatient management [28]. The most common reason for admission then and now is for medication-overuse including opioids or barbiturate containing medications [29]. Other criteria for admission such as dehydration, nausea and/or vomiting and failed emergency room visits are in line with previous published criteria [30-31]. This survey did not address issues of secondary headache other than medication-overuse or the treatment of migraine in patients with contraindications to various acute medications.

The current study is limited by 18% non-completion rate. The drop in respondents at question 4, which addresses inpatient treatment, and question 10, which addresses a pediatric patient, may indicate that respondents did not answer questions that did not address their practice experience. Still this survey suggests some general principles for acute migraine management in the ED or inpatient setting. First of all, neuroleptics, NSAIDs and migraine-specific agents should be considered before opioids or barbiturates for both adults and children. In patients already on opioids, their dose should not be increased for migraine. The presence of opioid or barbiturate overuse is more concerning than triptan or NSAID overuse and may warrant inpatient treatment. Having ancillary services available such as psychology is helpful. Outpatient follow-up after discharge is essential and ideally should occur within 1 month of discharge.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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APPENDIX

Appendix A

The following is a series of questions developed by the inpatient and emergency section of AHS to gauge the opinions of our members and develop recommendations for best clinical practices. Unless otherwise specified, you may choose as many responses as you would like.

Questions 1-3: Emergency room treatment

1. An otherwise healthy adult with migraine presents to your emergency department with a prolonged attack of 3 days of their typical migraine. Usual attacks are responsive to medication and last less than 2 days with about 2-3 migraines/month. Exam is normal and there are no “red flags” to indicate secondary headache or need for further diagnostic testing. Assuming the patient has no allergies or contraindications to medication, what treatment(s) would you recommend as first line treatment?

2. The patient has mild improvement with the initial treatment. What treatment(s) would you recommend as a second line treatment if the initial treatment was inadequate?

Note 1: the potential answers for 1-2 are the same and can be placed side by side.
Note 2: can choose as many answers as you like

a) Oral triptan
b) Triptan nasal spray (sumatriptan or zolmitriptan)
c) Injectable sumatriptan
d) Dihydroergotamine (DHE) IV, IM or NS
e) Dopamine antagonist (i.e. prochroperazine, promethazine, metoclopramide) IV or IM or PO
f) Peripheral nerve block
g) Odansetron (zofran)
h) Opioids
i) Barbiturate-containing combination medications (i.e. Fioricet, Fiorinal)
j) Non-steroidal anti-inflammatory medication (i.e. ketorolac, ibuprofen)
k) Corticosteroids (i.e. dexamethasone, methylprednisoline)
l) Intravenous valproic acid (Depacon)
m) Intravenous levetiracetam (Keppra)
n) Intravenous magnesium
o) Intravenous hydration

3. The patient is significantly improved and would like to be discharged. What treatment(s) would you recommend for home use after discharge?

a) Oral triptan
b) Triptan nasal spray (sumatriptan or zolmitriptan)
c) Injectable sumatriptan
d) Dihydroergotamine (DHE)
e) Dopamine antagonist (i.e. prochroperazine, droperidol)
f) Opioids
g) Barbiturate-containing combination medications (i.e. Fioricet, Fiorinal)

h) Non-steroidal anti-inflammatory medication (i.e. ketorolac, ibuprofen)
i) Corticosteroids (i.e. dexamethasone, methylprednisoline)

Questions 4-7: Inpatient treatment

4. An adult patient with intractable migraine, disabled from work due to migraine, is admitted for migraine treatment. The patient is not currently on preventive therapy. Which of the following treatment(s) would you begin on admission?

5. The patient has not significantly improved after 1 day. Which of the following treatments would you add as a back-up treatment.

Note 1: the potential answers for 1-2 are the same and can be placed side by side.
Note 2: can choose as many answers as you like

a) Oral triptan
b) Triptan nasal spray (sumatriptan or zolmitriptan)
c) Injectable sumatriptan
d) Dihydroergotamine (DHE) IV, IM or NS
e) Dopamine antagonist (i.e. prochroperazine, promethazine, metoclopramide) IV or IM or PO
f) Peripheral nerve block
g) Opioids
h) Barbiturate-containing combination medications (i.e. Fioricet, Fiorinal)
i) Acetaminophen
j) Non-steroidal anti-inflammatory medication (i.e. ketorolac, ibuprofen)
k) Corticosteroids (i.e. dexamethasone, methylprednisoline)
l) Intravenous valproic acid (Depacon)
m) Intravenous levetiracetam (Keppra)
n) Intravenous magnesium
o) Intravenous lidocaine
p) Intravenous ketamine

6. Which of the following factors would make you likely to recommend inpatient treatment for migraine, as opposed to outpatient treatment or infusion?

a) Generalized anxiety disorder
b) Major depressive disorder
c) Bipolar disorder
d) Recent traumatic life event
e) Medication overuse using non-steroidal anti-inflammatory medication
f) Medication overuse using triptans
g) Medication overuse using opioids
h) Medication overuse using barbiturate-containing combination medications
i) Frequent ER visits for migraine
j) Nausea or vomiting/inability to take oral medications

7. A patient with intractable migraine reports taking oxycodone/APAP 5/325 mg 1-2 tablets at least twice daily for lower back pain for 6 months. The patient reports it has been mildly helpful for back pain. How would you manage this patient on opioid therapy when admitted for migraine?

a) Chronic opioids may worsen migraine – taper or stop in the hospital if possible
b) Maintain the opioids for back pain or change to another formulation which is longer-acting but do not increase dose for migraine
c) Increase the opioid dose to help both migraine and back pain

8. What ancillary services are useful when patients are admitted for intractable migraine?

a) Psychology consult
b) Psychiatry consult
c) Physical therapy
d) Nutrition
e) Healing touch or Reikki therapy

9. After 3 days of treatment, the patient is steadily improving but continues to have mild headache rated as 3/10 on an 11-point scale or "mild." You recommend (choose one):

a) Discharge with an updated acute and preventive plan
b) Continue treatment, with the goal of becoming headache free by discharge

Questions 10-11: Pediatric migraine

10. A 14 year-old patient prevents for migraine to the emergency room. Although more prolonged and severe than usual, none of the symptoms are unusual for the patient's typical migraine. Exam is normal and there are no "red flags" to indicate secondary headache or need for further diagnostic testing. Assuming the patient has no allergies or contraindications to medication, what treatment(s) would you recommend as first line treatment?

11. The patient has mild improvement with the initial treatment. What treatment(s) would you recommend as a second line treatment if the initial treatment was inadequate?

Note 1: the potential answers for 1-2 are the same and can be placed side by side.
Note 2: can choose as many answers as you like

a) Oral triptan
b) Triptan nasal spray (sumatriptan or zolmitriptan)
c) Injectable sumatriptan
d) Dihydroergotamine (DHE)
e) Dopamine antagonist (i.e. prochroperazine, promethazine, metoclopromide)
f) Odansetron (zofran)
g) Peripheral nerve block
h) Opioids
i) Barbiturate-containing combination medications (i.e. Fioricet, Fiorinal)
j) Acetaminophen
k) Non-steroidal anti-inflammatory medication (i.e. ketorolac, ibuprofen)
l) Corticosteroids (i.e. dexamethasone, methylprednisoline)
m) Intravenous valproic acid (Depacon)
n) Intravenous levetiracetam (Keppra)
o) Intravenous magnesium
p) Intravenous hydration

12. The patient is significantly improved and would like to be discharged. What treatment(s) would you recommend for home use after discharge?

a) Oral triptan
b) Triptan nasal spray (sumatriptan or zolmitriptan)
c) Injectable sumatriptan
d) Dihydroergotamine (DHE)
e) Dopamine antagonist (i.e. prochroperazine, droperidol)
f) Opioids
g) Barbiturate-containing combination medications (i.e. Fioricet, Fiorinal)
h) Acetaminophen
i) Non-steroidal anti-inflammatory medication (i.e. ketorolac, ibuprofen)
j) Corticosteroids (i.e. dexamethasone, methylprednisoline)

13. After discharge, when do you typically recommend follow-up in the office?

a) Within 2 weeks
b) Within 2-4 weeks
c) 1 month
d) 2 months or longer

Peer-review history:
The peer review history for this paper can be accessed here:
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