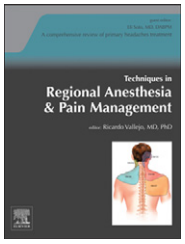
Techniques in Regional Anesthesia and Pain Management 16 (2012) 25–29

Available online at www.sciencedirect.com

SciVerse ScienceDirect

www.elsevier.com/locate/trap



Intravenous treatment of migraine

Sait Ashina[a,b,*], *Russell K. Portenoy*[a,b]

[a]*Department of Pain Medicine and Palliative Care, Beth Israel Medical Center, New York, New York*
[b]*Albert Einstein College of Medicine, Bronx, New York*

ARTICLE INFO

Keywords:
Headache
Infusion
Intravenous
Migraine
Treatment

ABSTRACT

Migraine is a common primary headache disorder. A subset of patients may become disabled by frequent, severe, or treatment-refractory headache. Most patients respond adequately to drugs administered by the oral, intramuscular, or subcutaneous route. Intravenous therapy is an option for the treatment of severe headache in a monitored setting. The most common scenario is the treatment of acute refractory headache in the emergency department. Intravenous treatment may be undertaken with common analgesics, such as acetaminophen, ibuprofen, and ketorolac, or an opioid, or with a drug used specifically for migraine. Among the latter drugs are antiemetic dopamine antagonists, dihydroergotamine, magnesium, valproate sodium, and glucocorticoids. Some of the latter agents have been studied in controlled trials but data are too limited to inform clinical guidelines. Larger placebo-controlled trials of these and other agents will be needed to better position the intravenous drugs in the treatment strategies for acute refractory headache, refractory chronic migraine, and withdrawal headache during the management of medication overuse headache.

Introduction

Migraine is a common primary headache disorder associated with substantial disability and burden.[1] The standard acute treatment for patients at home relies on triptans delivered by the oral, intranasal, or subcutaneous (SC) routes, and on acetaminophen or nonsteroidal antiinflammatory drugs (NSAIDs) administered orally.[2] Few patients benefit from access to a short-acting opioid. When headache is refractory to treatment, care may be sought in the emergency department (ED) or related settings. Although this is a rare occurrence from the perspective of a very large population with migraine, it is observed commonly by the health professionals. Indeed, headache accounts for 2% of all ED visits.[3]

In the ED setting, and other settings with adequate monitoring, acute treatment may be more effectively undertaken using drugs administered via the intravenous (IV) route. The IV route eliminates the need for absorption and yields drug effects that have an onset more quickly than other routes of drug delivery. The IV access established for drug delivery can be used concurrently for hydration, which can be particularly important if vomiting has occurred. If multiple treatments are needed, repeated skin punctures are avoided, often lessening distress in patient. The major pharmacodynamic risk associated with the IV drug delivery—peak concentration toxicity—can be mitigated by using brief infusions, typically 20-30 minutes.

Understanding the options for IV therapy of migraine provides a potential option for a variety of challenging scenarios (Table 1).[4-7] Safe and effective IV treatment requires specific policies and procedures, trained nursing staff, and a setting that includes a comfortable room with a reclining chair or bed.[5] The most common setting for IV therapy is the ED,[6] but other settings, including office-based practices, that meet the requirement for policies, trained staff, and environment of care would be able to offer these treatments.[5,7]

*Corresponding author at: Headache Program, Department of Pain Medicine and Palliative Care, Beth Israel Medical Center, 10 Union Square East, Suite 2Q-R, New York, NY 10003.
E-mail address: sashina@chpnet.org (S. Ashina).

1084-208X/$ - see front matter © 2013 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1053/j.trap.2012.11.004

Table 1 – Possible indications for the treatment of migraine with intravenous medications.

1. Status migrainous
2. Intractable headache with nausea/vomiting
3. Refractory migraine/intractable chronic daily headache
4. Medication overuse headache/withdrawal headache
5. Migraine flare-ups

The empirical data related to the IV treatment of migraine derives mostly from small observational surveys and a few randomized trials. The indications for this approach, therefore, are not evidence-based . Rather, they reflect clinical judgments about severity and refractoriness of headache, combined with the capability to provide IV treatments safely. The most common scenario for a trial of IV therapy is treatment in the ED of patients with prolonged severe headache that have not responded to usual therapy, including patients who meet criteria for a diagnosis of status migrainosus, and patients who develop severe headache associated with repeated vomiting. Less commonly, the IV therapy is offered by some headache and pain management outpatient practices for intractable chronic daily headache and migraine flare-ups .[5] The latter settings also may be the places that can offer supplemental treatment with the IV therapy during management of medication overuse headache with detoxification or withdrawal of short-acting abortive therapies.[4,7]

Intravenous drugs used in the treatment of migraine

Migraine is a pain syndrome and it may be addressed with medications used specifically for migraine, common analgesic drugs, or a combination of these therapies. Medications that are used specifically for migraine and have been evaluated as the IV therapy include dopamine antagonists: dihydroergotamine (DHE), magnesium, valproate sodium, and corticosteroids. The common analgesics available in the IV formulations include acetaminophen, ibuprofen, and a large number of opioid drugs such as morphine, hydromorphone, and fentanyl. Although some of these drugs have been studied in controlled trials, the data are inadequate to judge comparative efficacy and safety. The clinical approach to the management of migraine using IV drugs is therefore empirical, based on knowledge of the options and an assessment of risk and benefit in the individual patient.

Anti-emetic dopamine antagonists

Intravenous anti-emetic dopamine antagonists have long been used in the treatment of migraine. These medications have been suggested to be a first-line treatment of acute migraine in the ED.[6] They also can be used in inpatient settings and in outpatient infusion clinics. The drugs include metoclopramide, droperidol, and phenothiazines such as chlorpromazine and prochlorperazine.

The mechanism of action of the anti-emetic dopamine antagonist in migraine is unknown. Central dopaminergic pathways may be involved in the migraine attack,[8,9] and this suggests that the effects of these drugs on central dopamine receptors mediate benefits for headache. For the patient with severe nausea and vomiting, a prompt antinauseant effect also may speed recovery from the attack.

Several dopamine antagonists have been studied in controlled trials for the treatment of acute migraine. The major limitation of these studies is the small sample size. IV metoclopramide 10 mg was demonstrated to be efficacious in placebo-controlled trials,[10,11] and a randomized, double-blind, comparative trial showed that IV metoclopramide 20 mg was superior to 6 mg of SC sumatriptan in overall efficacy.[12] A controlled trial of IV prochlorperazine found that this drug was efficacious compared with both metoclopramide and placebo.[13] In contrast to the studies noted previously, metoclopramide and placebo did not differ from each other in the latter trial.

Chlorpromazine at a dose of 0.1 mg/kg IV was studied in the ED setting in 128 migraineurs and was shown to significantly reduce pain scores compared with placebo.[14] In a randomized, single-blinded comparative study, IV chlorpromazine 12.5-37.5 mg was significantly superior to IV DHE 1-2 mg in reducing mean headache intensity.[15] Compared with placebo, intramuscular (IM) droperidol at doses of 2.75, 5.5, and 8.25 mg was efficacious,[16] and a pilot study of IV droperidol 2.5 mg administered every 30 minutes for up to 3 doses showed efficacy (>80% relief at 2 hours) in status migrainosus.[17]

These trials support the potential for prompt benefit in acute migraine following the IV administration of antiemetic dopamine antagonists. The data are too limited to confirm efficacy and do not illuminate key clinical questions, including comparative safety and efficacy across drugs and comparative therapeutic index of this group compared with other IV treatments. The positioning of these drugs relative to other treatments, when patients present for acute therapy in a setting capable of providing IV therapy safely, must be based on a careful individualized assessment of risk and potential benefit. This assessment, in turn, should be informed by an understanding of the side effects and toxicities that characterize these medications (Table 2).

The most common side effect of the antiemetic dopamine antagonists is drowsiness.[18] Anticholinergic effects, such as dry mouth, also occur often but are rarely a problem in the acute treatment setting. A more serious concern is the potential for extrapyramidal side effects, including acute dystonic reactions and akathisia. The risk of these extrapyramidal effects can be minimized by the administration of IV or IM benztropine 1 mg, or IV or IM diphenhydramine 25 mg, prior to infusion of the dopamine antagonist.[19,20] Chlorpromazine has been reported to cause postural hypotension, which can possibly be prevented by a bolus of 250-500 mL of normal saline before treatment.[6,14,18]

The antiemetic dopamine antagonists, droperidol in particular, can prolong the QTc interval, a potentially serious effect.[18] An electrocardiogram (ECG) prior to administration of prochlorperazine, chlorpromazine, and droperidol is recommended.[6,18]

Dihydroergotamine

DHE, a semisynthetic formulation of an ergot alkaloid, has been a well-established treatment for migraine for the past