

Droperidol and Other Neuroleptics/Antiemetics for the Management of Migraine

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Key words: migraine, droperidol, neuroleptics

(*Headache* 2003;43:811-813)

CLINICAL HISTORY

A 30-year-old woman with a history of migraine without aura since her teenaged years presented to the emergency department with an 8-hour history of a severe, left-sided, throbbing headache with nausea, vomiting, and light and noise sensitivity. Her headache was similar to previous migraines. She had tried oral rizatriptan 10 mg at home, without benefit.

Questions.—Would droperidol be indicated? What route of administration and dosage would you recommend? What are the possible side effects, and how are they treated? What are the contraindications? How would you compare the use of droperidol for acute migraine and migraine status with other agents such as prochlorperazine, intravenous dihydroergotamine, divalproex sodium, and others? Could droperidol be used if the patient did not respond to intravenous dihydroergotamine and metoclopramide, phenergan, or compazine? What are your personal preferences for the use of these drugs for acute migraine and migraine status (ie, do you have a first, second, and third choice, and, if so, why)?

EXPERT COMMENTARY

Droperidol has been shown in 2 double-blind, controlled trials and 3 case series to be effective for

the management of acute migraine.¹⁻⁵ Recently, however, the Food and Drug Administration imposed a “black box” warning about the potential for droperidol to cause QT prolongation, and many patients with headache consequently are now being deprived of the medicine most likely to benefit them.

Neuroleptics, in general, are effective abortive agents, but the route of administration matters. The US Headache Consortium’s acute treatment group reviewed the results of the double-blind, placebo-controlled trials involving neuroleptics used for acute migraine.⁶ (At that time, no such trials involving droperidol had been published.) Intravenous metoclopramide, chlorpromazine, and prochlorperazine had demonstrated efficacy, and weaker efficacy was demonstrated for intramuscular and rectal (but not for oral) prochlorperazine and for intramuscular metoclopramide. Intramuscular droperidol subsequently was found to be effective in a placebo-controlled trial, and an emergency department comparison trial demonstrated it to be superior to prochlorperazine in effectiveness. The original case series involving droperidol used 2.5-mg intravenous doses repeated hourly up to 10 mg or relief of headache. The placebo-controlled, double-blind study found little difference in efficacy between doses of 2.75, 5.5, and 8.25 mg, but side effects were greater for the 2 higher doses.^{2,7}

Extrapyramidal side effects and sedation are the 2 most common side effects of droperidol when administered for acute migraine. In our experience, akathisia is much more common than dystonia and generally responds promptly to diphenhydramine or benztropine.

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Accepted for publication March 20, 2003.

If those agents fail, we generally give low-dose intravenous lorazepam. Hypotension is listed as a side effect of intravenous delivery, but this complication was not seen even at the relatively high doses used in the intramuscular dose-ranging study.

Recently, the Food and Drug Administration imposed upon droperidol a black box warning as to the potential for QTc prolongation, with possible torsades de pointes resulting in fatal arrhythmia. A review of the literature reveals, at most, a handful of cases of arrhythmia in operating room settings that involved

approximately the dose of droperidol advocated for headache and did not involve administration of other potentially cardiotoxic drugs or medically unstable patients. The Food and Drug Administration warning recommends cardiac monitoring for patients receiving droperidol. There probably have been at least 20 million intravenous doses of droperidol administered in the United States in the last 20 years, and few cases of torsades de pointes or sudden death potentially attributable to this drug and occurring in patients without acute medical illness have been reported. It is

Neuroleptic Agents for Acute Migraine Therapy

Efficacy for head pain		Maximum 24-hour dose
More effective	→ IV chlorpromazine (12.5 to 50 mg q6-8h)	150 mg
	→ IV droperidol (0.625 to 2.5 mg q6-8h)	10 mg
	→ IV prochlorperazine (5-10 mg q6-8h)	40 mg
	→ IV drip chlorpromazine (12.5 to 50 mg q6-8h)	100 mg
	→ PO olanzapine (5-10 mg prn, max 20 mg in 24h)	20 mg
	→ PO chlorpromazine (25 to 50 mg)	200 mg
	→ IV metoclopramide (10 mg)	30-60 mg
Less effective	→ IV promethazine (12.5-50 mg)	100 mg
Side effects		
Sedation		
More sedating	→ IV chlorpromazine	
	→ IV droperidol	
	→ IV promethazine	
	→ PO chlorpromazine	
	→ IV prochlorperazine	
	→ PO olanzapine	
Less sedating	→ IV/PO metoclopramide	
Dystonia/Akathisia		
More symptoms	→ droperidol	
	→ prochlorperazine	
	→ metoclopramide	
	→ chlorpromazine	
	→ promethazine	
Less symptoms	→ olanzapine	
Anticholinergic		
More symptoms	→ chlorpromazine	
	→ promethazine	
	→ prochlorperazine	
	→ droperidol	
	→ metoclopramide	
Less symptoms	→ olanzapine	
Increasing or unmasking of restless leg syndrome		
Special considerations	→ cholestatic jaundice: chlorpromazine	
	→ prolonged QT: droperidol > chlorpromazine + prochlorperazine > others; olanzapine doubtful	
	→ risk of tardive akathisia: theoretically droperidol > prochlorperazine > metoclopramide > chlorpromazine > promethazine > olanzapine	

not at all clear that droperidol for acute migraine conveys a greater overall risk than intravenous ketorolac, intravenous steroids, or the vasoconstrictors we regularly use to treat migraine. The black box warning threatens to deprive many patients of an excellent treatment.

In the above case, droperidol is a good treatment option. I would check an electrocardiogram to assure that the QTc is less than 450 msec before administering the drug. If there is any reason to suspect a low potassium or magnesium level, this should be checked. Either intravenous or intramuscular administration is acceptable and effective. If the patient is receiving intravenous fluids, the intravenous route is perhaps a little more effective. Other neuroleptics could be used. Intramuscular or intravenous prochlorperazine are not currently available due to a manufacturing problem. Intravenous chlorpromazine is very effective, but appears to have a greater risk of causing hypotension or excess sedation than does droperidol. If the patient would benefit from the sedation of chlorpromazine, then it may be an excellent choice; the patient's vital signs should be checked before and after administration. Derived mostly from clinical experience, the Table may be helpful in assisting one to select a neuroleptic agent for acute migraine therapy.

Except for the concern about mixing vasoconstrictors (in this case, rizatriptan), dihydroergotamine is a good choice for this patient. My criterion is that the patient must wait 12 hours to receive dihydroergotamine after use of a short half-life triptan. Intravenous dival-

proex sodium is probably effective for acute migraine and has few side effects, yet it does not appear to be as effective as the neuroleptics and dihydroergotamine. Intravenous steroids or opioids are other less satisfactory last choices.

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