Rescue Therapy
Parenteral Headache Treatments

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Following the administration of oral sumatriptan which of the following is contraindicated for parenteral administration for the next 24 hours?

A. DHE
B. Dexamethasone
C. Chlorpromazine
D. Droperidol
E. Valproic Acid

Which of the following agents given parenterally for headache has a black box warning that it may cause QT prolongation?

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Objectives

- To understand the role and goals of parenteral headache treatments.
- To define a rationale parenteral treatment regiment based on treatment mechanism of action.
- To understand contraindications and safety concerns with some commonly used parenteral headache treatments.
- To define a follow-up treatment approach to limit headache recurrence.

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Scenarios

- 34 F followed in pain clinic for chronic LBP and common migraine
  - Presents with 2 days severe typical migraine refractory to typical abortive regiment; prior ONB ineffective
  - Presents with 1 week severe HA which began with typical migrainous features - status migrainosus
  - Chronic migraine but twice per month presents to ED for severe HA
    - Neurologists request help with non-ED infusion rescue plan to be administered in pain clinic where sedation/infusion nursing support available

Background

- HA 4th most common reason for ED care in adults
  - 1.4-3.3 million ED visits/yr
  - 1-3% of all ED visits
  - Majority of these ED visits for primary HA disorders

- Reasons for visit
  - Symptoms more severe and/or prolonged than normal
  - Usual abortive regiment fails
  - Symptoms not typical of usual HA
    - Consider secondary HA causes

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Goals of Parenteral Rescue Plan

- Outpatient treatment
  - Avoid ED visit or hospitalization
- Effective
- Limited SE profile
- Low recurrence rate
- Hydration

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Opioids

- Most common Rx of HA in US/Canadian EDs (two-thirds)
- Meperidine most commonly studied (50-100 mg IM)
  - Often with hydroxyzine
  - We do NOT recommend
- More commonly used opioids poorly studied
- LOS increased if opioids administered
- Increased likelihood of ED recidivism in next 7 days if opioids used

Triptans

- Sumatriptan 6mg SQ, May repeat x1, 1 hr later
  - 67-85% response rate
  - Cannot use – pregnancy; CAD, PAD, other triptan/DHE < 24 hours; migraine with neurologic deficits

- SEs
  - Chest pressure
  - Neck tightness
  - Limb heaviness
  - Tingling
  - Dizziness
  - Flushing

- Head to head trials – as efficacious as
  - Droperidol
  - Prochlorperazine
  - DHE

DHE

- 1 mg IV or SQ, may repeat x1; nasal DHE 2mg
  - Very efficacious
  - Sumatriptan pain relief faster than DHE, but similar at 4 hrs
  - 75--90%
- Similar contraindications to triptans
  - But with risk of 5HT syndrome
- SEs
  - N/V
  - Diarrhea
  - Abdominal cramping

  - vasoconstriction
  - leg pain
- Must treat with anti-emetic

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DHE protocols for Status Migrainosus

Raskin Protocol Raskin NH. Headache 1990; 2: 550-

- Pretreat
  - Metoclopramide (10mg IV) +/- benztropine (1mg IV, PO, IM)
- DHE 0.5mg IV (over 2-3 minutes)
  - HA persists and was tolerated
    - May repeat at 1 hr x1 (without metoclopramide)
- Ongoing HA – repeat DHE (0.5-1mg IV) w/ metoclopramide q 8 hrs prn x 2-5 days
  - Lower DHE dose if nausea limiting despite metoclopramide

Ford protocol Ford RG. Headache 1997; 37: 129-

- IV DHE infusion (beginning with DHE 3mg in 1000 mL NS IV @ 42 ml/hr) - up to 7 days
  - Intermittent metoclopramide 10mg IV q 8hrs

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Dopamine Antagonists (Anti-emetics)

- Highly effective
- Metoclopramide
  - 10m IV
  - Single dose less effective than other DA antagonists
  - Common in combination treatment algorithms with DHE
- Prochlorperazine (Compazine)
  - 10mg IV (4 trials)
  - But 3.5 mg IV nearly as effective as 10mg IV (89 vs. 95%)
    - Sedation ½ of that with higher dose (38 vs 73%)
    - Less akathisia (3 vs. 25%)
    - Hypotension risk does not appear to be significant

Dopamine Antagonists (Anti-emetics)

- Chlorpromazine (Thorazine)
  - Very Effective 81-94%
  - 0.1mg/kg IV q 15 minutes up to 3 x (max 37.5mg)
  - OR 12.5 mg IV q 20 minutes up to 3 x (max 37.5mg)

- Limitations DA antagonists
  - Orthostatic hypotension (pre-hydrate and monitor) – up to 50%
  - Sedation (70%)
  - Dysphoria

  - Risk of extrapyramidal effects (akathisia, dystonia)
    - Rx – benztropine 1mg IV (PO, IM)
    - Some pre-medicate with diphenhydramine or benztropine

Droperidol

- 2.5mg IV
  - Repeat q 30 minutes x 2 additional dosages if HA persists (max 7.5mg)
- Risk –
  - **QT prolongation (Black Box Warning)**
    - Must check QTc prior to usage (assure <450ms) as well as K and Mg levels
    - Recheck after infusion
  - Extrapyramidal SE
    - Pretreat benztropine 1mg IV/IM/PO
    - Continue to treat benztropine 1mg PO BID x 3 days (akathisia)
  - Hypotension
    - Hydrate
  - Sedation, akathisia common
- Higher risk than other options

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Antihistamines

- Diphenhydramine (12.5-25 mg IV)
- Hydroxyzine (50mg IM)

- Used commonly to prevent akathisia and extrapyramidal effects with DA antagonists

- Usually combined with other agents
  - Commonly felt to improve HA relief
  - Little evidence stand as alone agents (some negative studies)

Valproic Acid

- 500mg IV infusion (@ 20mg/min)
  - Efficacy ~ 2/3 pts
    - As efficacious as DHE 1mg + metoclopramide 10mg IV
    - Prochlorperazine 10mg IV was slightly more efficacious
  - May repeat q 8 hrs

  - Well-tolerated
  - No interactions w/ triptans / DHE
  - No cardiovascular SE
  - Avoid in pregnancy (Category D) or hepatic dysfunction

Magnesium

- 1 – 2 grams IV
- Response rates variable 30 – 85%
  - More effective if migraine HA with aura
    - In common migraine – most effective for photo/ phonosensitivity
- Does NOT need to be low for Mg infusion to be effective
  - But more effective if it is low
- Safe in pregnancy
- SEs
  - Flushing common
  - Diarrhea

NSAIDS

- Ketorolac 15-30mg IV/ 30-60 mg IM
  - Trial efficacy variable IM formulation
  - IV formulation (64-77% response)
    - More effective than nasal or SQ sumatriptan (2 trials)
    - Was less effective than DHE + metoclopramide

- Diclofenac 75mg IM
  - Similar to tramadol 100mg IM

Steroids

- Dexamethasone
  - Effective in uncontrolled trials -- 10(-20mg)IV/ 8-10mg IM
    - Similar efficacy to DHE/metoclopramide
  - Commonly used
    - Severe HA
    - Status migraine HA
    - To decrease rate of HA recurrence after dismissal
- 10mg IV dexamethasone vs. Placebo
  - Lower HA recurrence @48-72 hours post-ED discharge (13% vs 58%)
  - Other studies results mixed

Follow-up Expectations and Treatments

- Migraine persists or recurs in up to 73% after ED dismissal @ 24-72 hrs
  - Dexamethasone 10mg IV with original infusion
    - decreases HA recurrence rate
  - Discharge medications important to prevent recidivism
    - Sumatriptan 100mg po
    - Naproxen 500mg po
    - Highly effective when HA recurs

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Summary

- When possible use migraine specific meds
  - Sumatriptan / DHE
- Parenteral ketorolac also reasonable 1st line
- Combine with anti-emetic
  - Prochlorperazine IV – best ratio efficacy/SE
- Could consider addition
  - Steroid (abortive Rx and HA recurrence prevention)
  - Mg
  - Antihistamine (least evidence)
    - Pretreat if using any DA antagonist other than prochlorperazine

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Thank you

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Good Reviews

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- Friedman BW. Treating headache recurrence after emergency department discharge: A randomized controlled trial of naproxen vs. sumatriptan. Ann Emerg Med 2010; 56: 7-17.