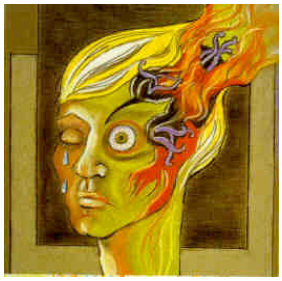
Drugs for headaches



Drugs that cause headaches

Amitriptyline, imipramine
ASA, acetaminophen (frequent use)
Benzodiazepines
Nitroglycerine
MAOIs
Metoclopramide
Estrogen
Sulphonamides
Theophylline
NSAIDS
Fluoxetine

Withdrawal of:
Benzodiazepines
Caffeine Ergotamine
Methysergide
ASA, APAP (±codeine)
some antihypertensives

Aspirin for migraine

Migraine headache pain will be reduced from moderate or severe to no pain by 2 hours in approximately 25% of people taking a single dose of 1000 mg of aspirin, compared with about 10% taking placebo. CD008041

Migraine headache pain will be reduced from moderate or severe to no worse than mild pain by 2 hours in roughly 50% of people taking a single dose of 1000 mg of aspirin compared with approximately 33% taking placebo. CD008041

ASA vs sumatriptan vs ibuprofen vs placebo for acute migraine

Patients

312 patients - cross-over DB RCT - mean age 38, 81% women, severe headaches (45%)

Treatment

effervescent ASA (1000 mg), sumatriptan (50 mg), ibuprofen (400 mg), or placebo

Cephalalgia 2004;24: 947–54

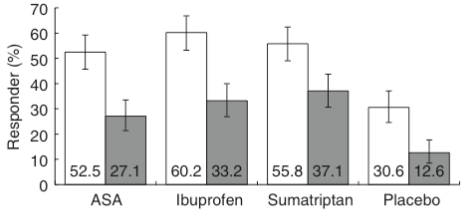


Figure 1 Pecentage of ITT patients (responders, mean and 95% confidence intervals) with reduction in headache severity from severe or moderate to mild or no pain at 2h (□) and percentage of patients (responders) pain-free at 2h (■). All active drugs are superior to placebo.

Cephalalgia 2004;24: 947–54

Adverse events

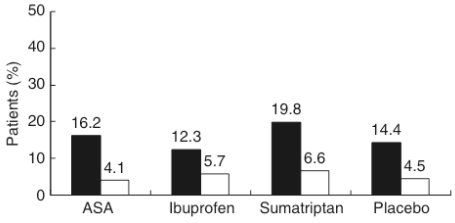


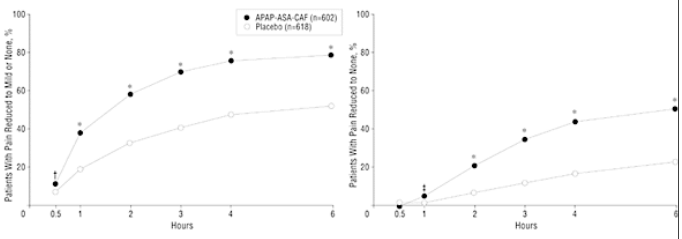
Figure 5 Adverse events (safety population, $n = 313$). Total adverse events (■); drug-related averse events (□) were investigstor attributed.

Stats and type of AE not reported

Cephalalgia 2004;24: 947–54

500 mg aspirin/500 mg acetaminophen/130mg caffeine or placebo

1220 patients with moderate "migraine"



Percentage of patients with pain intensity reduced to mild or none (left) or to none (right)

Arch Neur 1998;55:210-7

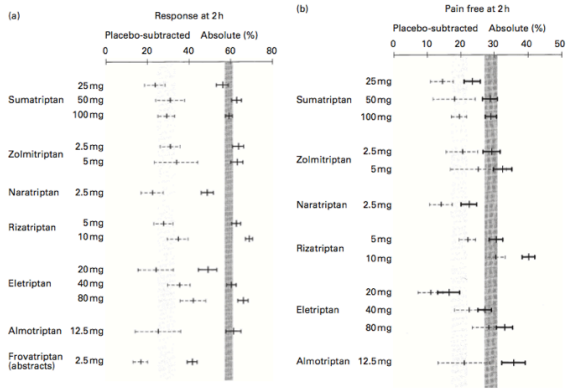


Figure 2 Data (mean and 95% confidence intervals) for headache response at 2 h (a) and pain free at 2 h (b) are shown for each triptan. Absolute and placebo subtracted outcomes are presented with the hatched region being the 95% confidence interval envelope for sumatriptan 100 mg.

Cephalalgia 2002;22:633–58

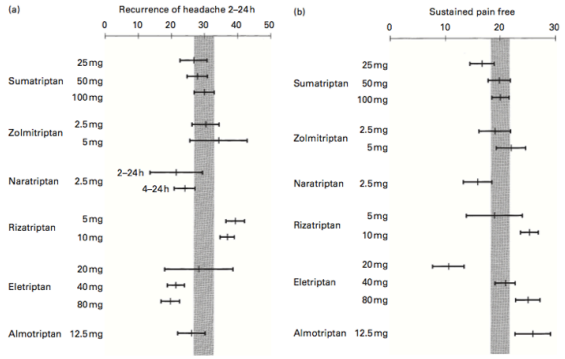


Figure 3 Data (mean and 95% confidence intervals) for headache recurrence from 2 h to 24 h (a) and sustained pain free (b) are presented with the hatched region being the 95% confidence interval envelope for sumatriptan 100 mg. For naratriptan the recurrence rate is given for the time period 4–24 h post-dose (as presented in the original publications) and for 2–24 h post-dose (after recalculating the data).

Cephalalgia 2002;22:633–58

Triptan AEs

"tingling, paraesthesias, and warm sensations in the head, neck, chest, and limbs; less frequent are dizziness, flushing, and neck pain or stiffness"

Much rarer 'central nervous system (CNS) AEs "asthenia, abnormal dreams, agitation, aphasia, ataxia, confusion, dizziness, somnolence, speech disorder, thinking abnormal, tremor, vertigo, and other focal neurological symptoms) and notably the 'chest- related AEs' (chest pressure, chest pain, radiating pain in arm, other chest feelings, heavy arms, shortness of breath, palpitations, and anxiety)"

Cephalalgia 2002;22:633–58

Triptan dosage forms

Oral
sumatriptan, zolmitriptan, naratriptan, rizatriptan, almotriptan, eletriptan, frovatriptan
Nasal spray
sumatriptan, zolmitriptan
Subcutaneous inj
sumatriptan

Dihydroergotamine

Can be used SC, IM, IV

more nausea but less chest pain than the triptans

An approach for migraines

Mild - NSAID/acetaminophen/caffeine +/- metoclopramide

If no effect in an hour - triptan

If no effect in a couple of hours - narcotic

Who is a candidate for prophylaxis?

- Recurring migraines which significantly interfere with daily routines, despite acute treatment
- Frequent headaches
- Contraindication to, failure of, or overuse of acute treatments
- Adverse effects with acute treatments
- Patient preference

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Effects of starting prophylactic therapy

During 6-12 mos following initiation of prophylaxis:

- Office visits ↓ 51%
- ED visits ↓ 82%
- CT scans ↓ 75%, MRIs ↓ 88%
- 21% ↓ triptan utilization
- Triptan cost/month ↓ $48 - $132

Headache 2003;43:171-8

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Principles of Prevention

Loneliness, Pain, Tears. Denise Auger

- Avoid trigger factors
  - Oral contraceptives
- Use lowest effective doses
- May take 2-4 months for effect
- Educate (mechanism, goals, likely adverse effects)
- Discuss expectations
  - frequency vs. severity
- Design formal management plan (including rescue plan)
- Headache diaries (frequency, severity, duration, disability, treatment response, adverse effects)

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All agents below have demonstrated efficacy superior to placebo in randomized trials of appropriate duration:

- Propranolol 80-240mg/d, Nadolol 80-240mg/d, Atenolol 100mg/d, Timolol 20-30mg/d, Metoprolol 200mg/d, Bisoprolol 5mg/d
- Flunarizine 10mg/d, Verapamil 240mg/d
- Methysergide 6mg/d, Pizotifen 1.5-6 mg/d
- Naproxen 500 mg/d, Flurbiprofen 200 mg/d, Fenoprofen 1800 mg/d, Mefenamic acid 1500 mg/d, Ketoprofen 150 mg/d, ASA 500-650mg/d
- Amitriptyline 30-150mg/d, Fluoxetine 20 qOd – 40mg/d
- Valproic Acid / Divalproex 500-1500 mg/d, Topiramate 25-325 mg/d, Gabapentin 900-2400 mg/d
- Riboflavin (B2) 400 mg/d,Magnesium 400-600 mg (16-24mmol)/d,Feverfew 50-82 mg/d, Histamine 1ng SC 2x weekly
- Lisinopril 20mg daily, Bromocriptine 2.5 mg tid (menstrual), Naratriptan 1 mg bid (menstrual), Estradiol 1.5 mg/d via gel x 7 days (menstrual), Botulinum toxin A?

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The Bottom Line on Prevention

RESPONSE = ≥50% reduction in headache severity, frequency, or duration (usually assessed at 3 mos)

Across all high-quality trials, **24%** will have response to placebo, **45%** respond to drug

each patient's chance of response with drug:

either **"50/50"** or

"1 in 5" depending on whether you are comparing to doing "nothing" or giving placebo.

Van der Kuy & Lohman. Cephalalgia 2002;22:265-70

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