



오 경 미

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## 편두통 급성기 치료 목표

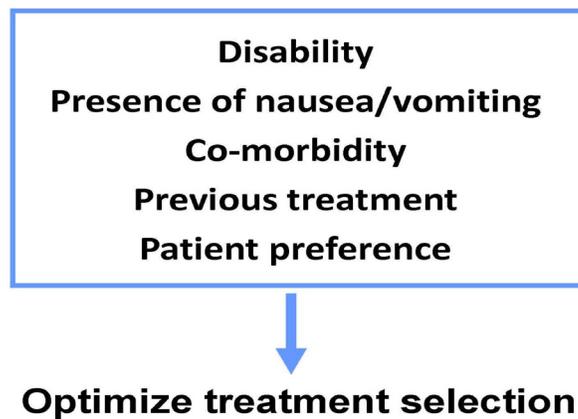
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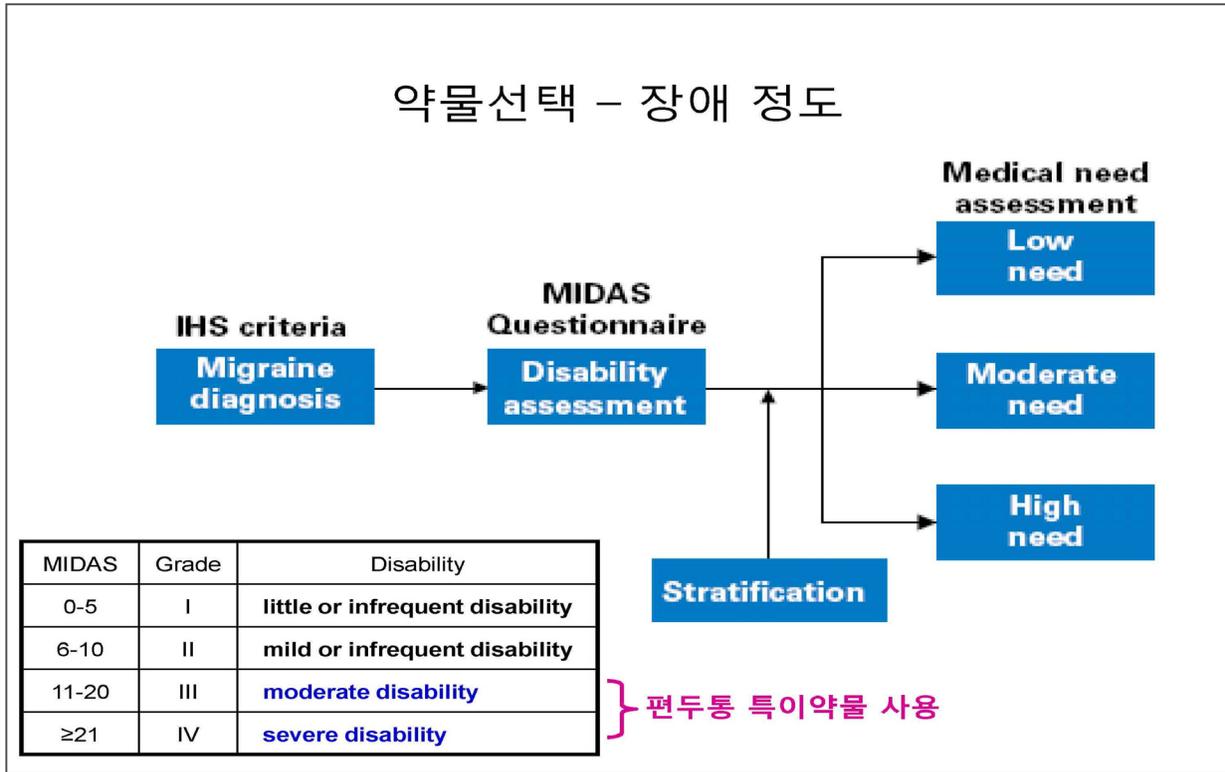
빠른 통증 완화 및 해소 → 일상생활 유지

## 편두통 급성기 약물

<b>비특이 약물</b>
Aspirin, acetaminophne, NSAIDs, 복합진통제
Antiemetics – metocloprime, prochlorperazine, chlorpromazine
Opioids
<b>편두통 특이약물</b>
Triptans
Ergotamine
CGRP inhibitor
기타약물

## 급성기 치료 약물 선택





- ### 약물선택 - 구역, 구토
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- 경구 항구토제를 같이 보조제로 사용한다.  
ergotamine, NSAIDs, triptans + metoclopramide
  - IV 항구토제를 치료제로 사용한다.  
IV metoclopramine, prochlorperazin, chlorperazine
  - SC, nasal spray, IV/IM 제제를 선택한다.  
traptans, NSAIDs

## 약물선택 - 동반이환

- 심혈관질환 – 난치성 고혈압, 협심증, 심근경색  
triptan과 ergotamine 주의  $\leftrightarrow$  CGRP inhibitor
- Allergy
- MAO inhibitor를 복용중인 환자  
triptan과 ergotamine 주의
- 임산부  
aspirin, ergotamine, triptan 주의  $\leftrightarrow$  steroid, acetaminophen

## 약물선택 – 이전약물, 선호도

### Per oral

ergotamine  
triptans  
NSAIDs  
analgesics  
opioid  
isometheptene  
steroid  
domperidone

### Intravenous

DHE  
Immunosuppressant (steroid)  
magnesium sulphate  
valproate sodium  
propofol  
metoclopramide  
prochlorperazine  
opioid  
CGRP R antagonist  
barbiturate  
lidocaine

### Intramuscular

droperidol  
prochlorperazine  
DHE

### Nasal spray

sumatriptan  
zolmitriptan  
DHE  
civamide  
opioid (butophanol)  
lidocaine

### Subcutaneous

sumatriptan  
almotriptan  
DHE

### Per rectal

ergotamine

## 교육 : 급성기 약물의 부작용

NSAIDs	GI trouble, renal toxicity
Metoclopramine	akathisia, dystonia
Prochlorperazin, chlorpromazine	sedation, BP drop
Opioid	dependency
Triptans	chest tightness, flushing, dizziness, paresthesia
Ergotamine	nausea, vomiting, peripheral vasoconstriction

## 교육 : 약물남용 방지

**RR = 13.3                      6.2                      2.4                      2.3**

*Table 2 Risk ratio (RR) with 95% CI of chronic pain ( $\geq 15$  d/mo), i.e., migraine, nonmigrainous headache, and neck and low-back pain, for men and women at HUNT-2 (1995–1997) related to use of analgesics at HUNT-1 (1984–1986), i.e., 11 y earlier*

Analgesic consumption at baseline (HUNT-1, 1984–1986)	Chronic migraine		Chronic nonmigrainous headache		Chronic neck pain		Chronic low-back pain	
	No.	RR (95% CI)	No.	RR (95% CI)	No.	RR (95% CI)	No.	RR (95% CI)
<b>Men</b>								
Never, n = 12,012	28	1.0	134	1.0	541	1.0	484	1.0
Less than weekly, n = 2,366	14	2.5 (1.3–4.8)	47	1.7 (1.2–2.4)	174	1.6 (1.4–2.0)	162	1.8 (1.5–2.1)
Daily or weekly, n = 751	17	11.2 (6.0–20.8)	45	5.1 (3.6–7.3)	67	2.1 (1.6–2.7)	46	1.7 (1.2–2.3)
<b>Women</b>								
Never, n = 10,708	31	1.0	109	1.0	438	1.0	351	1.0
Less than weekly, n = 4,491	51	3.7 (2.4–5.9)	84	1.9 (1.4–2.5)	279	1.5 (1.3–1.8)	237	1.6 (1.4–1.9)
Daily or weekly, n = 1,739	59	14.9 (9.5–23.4)	119	7.0 (5.3–9.1)	153	2.6 (2.1–3.2)	138	2.7 (2.2–3.3)

The analyses were adjusted for age and education calculated in multiple logistic regression.

HUNT = Nord-Trøndelag Health Study; No. = total no. of subjects in different diagnostic groups.

Zwart JA. *Neurology* 2003;61:160-164

## 교육 : 급성기 약물의 복용 제한

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- Ergotamine-overuse HA :  $\geq 10$  days/M  
Triptan-overuse HA :  $\geq 10$  days/M
- Analgesic-overuse HA :  $\geq 15$  days/M

## 편두통 급성기 약물 치료 Evidence-based Medicine

### 편두통 비특이약물

NSAIDs, 비아편진통제, 복합진통제  
항구토제  
아편제  
기타

NSAIDs, 비아편진통제, 복합진통제

EBM

- 편두통으로 인해 일상생활에 장애가 초래되지 않는 경우  
: aspirin, naproxen sodium, ibuprofen, diclofenac-K (A 등급)  
acetaminophen (B 등급)
- Isometheptene + dichloralpherazone + acetaminophen 복합제 (A 등급)  
Acetaminophen + aspirin + caffeine 복합제 (A 등급)
- 심한 구역/구토가 있는 경우  
: Ketololac IV or IM (B 등급)

항구토제

EBM

- 구역/구토가 있는 경우에는 통증강도가 약하더라도 항구토제 병용요법을 고려해야 한다(B 등급).
- Metoclopramide  
: PO - 단독요법은 불가(A 등급), 보조약물로 사용(B 등급)  
IV - 구역/구토가 있는 경우(B 등급)
- Chlorpromazine IV - 구역/구토가 있는 경우 (A 등급)
- Droperidol IV - 중등도-심도 편두통 환자에서 선택적 사용(B 등급)
- Ondansetron /granisetron은 급성기 치료제로 사용 불가(B 등급)

## 아편제

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- 아편제 PO와 butorphanol NS (A 등급)  
임신/수유, 트립탄제나 NSAID가 금기인 경우에만 사용  
환자의 임의 사용 제한(U 등급)
- 아편제는 과용과 의존 위험성이 크므로 가급적 사용하지 않는다.

## 편두통 급성기 약물 치료 Evidence-based Medicine

편두통 특이약물  
Triptans  
Ergot

## 트립탄제 (5-HT<sub>1</sub> 수용체 작용제)

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- 모든 트립탄제가 모든 강도의 편두통 급성기 치료에 효과적이다(A등급).  
: 국내 발매 - **sumatriptan, zolmitriptan, naratriptan**  
국내 미발매 - almotriptan, frovatriptan, rizatriptan, eletriptan
- 편두통으로 인해 일상생활에 장애를 느끼는 성인에서 사용 권고(A등급)
- 트립탄제 + naproxen sodium 병용요법(A등급)  
- 단독요법보다 임상적으로 효과가 더 좋다

## Triptans

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- 장점  
: 편두통 특이 작용  
다양한 제형  
확실한 임상근거 - 많은 수의 무작위대조시험 증거
- 단점  
: 비싸다.  
부작용과 재발이 흔하다.  
경구제는 bioavailability가 낮다 - 3번 이상 시도해 본다.
- 주의점  
주 2회 이하로 복용을 제한한다.  
Aura나 prodromal period에는 복용하지 않는다.  
Basilar migraine, hemiplegic migraine에서는 사용을 제한한다.

## Triptans

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	$T_{max}$	$T_{1/2}$
Almotriptan	2.1	3.1
Eletriptan	1.8	5
Frovatriptan	-2.5	-26
Naratriptan	3-5	6
Rizatriptan	2-3	5
Sumatriptan	2	2
Zolmitriptan	2.5	3

} Prophylaxis for menstrual migraine

— High recurrence rate

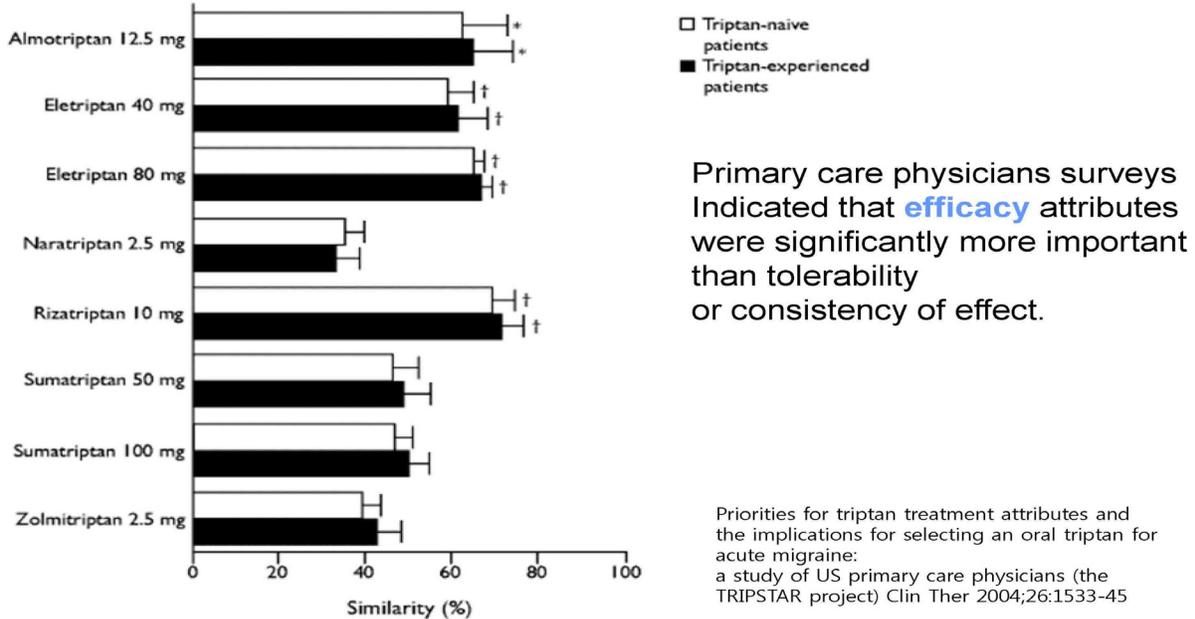
## Triptans: A meta-analysis

Cameron C, Headache 2015 Jul

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- 133 RCTs
- **2 hr pain relief: 42-76%**, 2 hr pain free: 18-50%
- Better than ergots (38%)
- Equal or better than NSAIDs, ASA, acetaminophen (46-52%)
- Equal or slightly worse than combination therapy (62-80%)
- The most favorable outcomes
  - Suma SC, Riza ODT, Zolmi ODT, Ele PO

## Priorities for triptans - efficacy



## 에르고트제

- ergotamine (caffeine 복합제) PO
  - 중등도의 효과, 선택적 사용(B등급)
- Ergotamine/caffeine 복합제
  - 트립탄제 복용시 재발이 흔한 경우 사용(B등급)
  - 초기에 복용하면 NSAIDs와 비슷한 효능이나 구토가 더 많다(B등급).
- Ergotamine제제
  - : 자궁 수축, 혈관 수축 작용 - 임신/수유 중 사용 금지

## 에르고트제

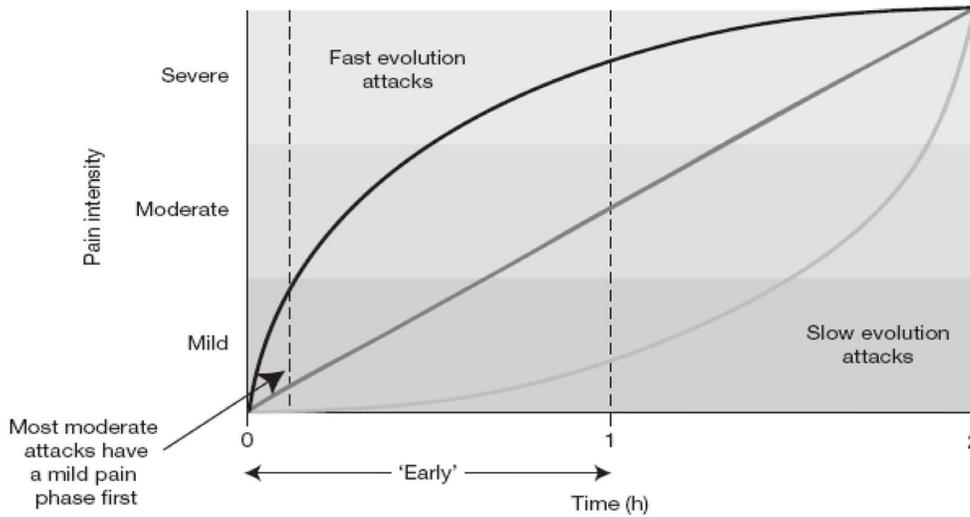
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- 국내 판매 : Cafergot (ergotamine 1 mg + caffeine 100 mg), 크래밍정
- 작용시간이 길므로 재발이 흔한 환자에 유용하나 약물과용, 오용이 매우 흔하므로 주의해야 한다.

## 효능을 높이는 급성기 치료전략

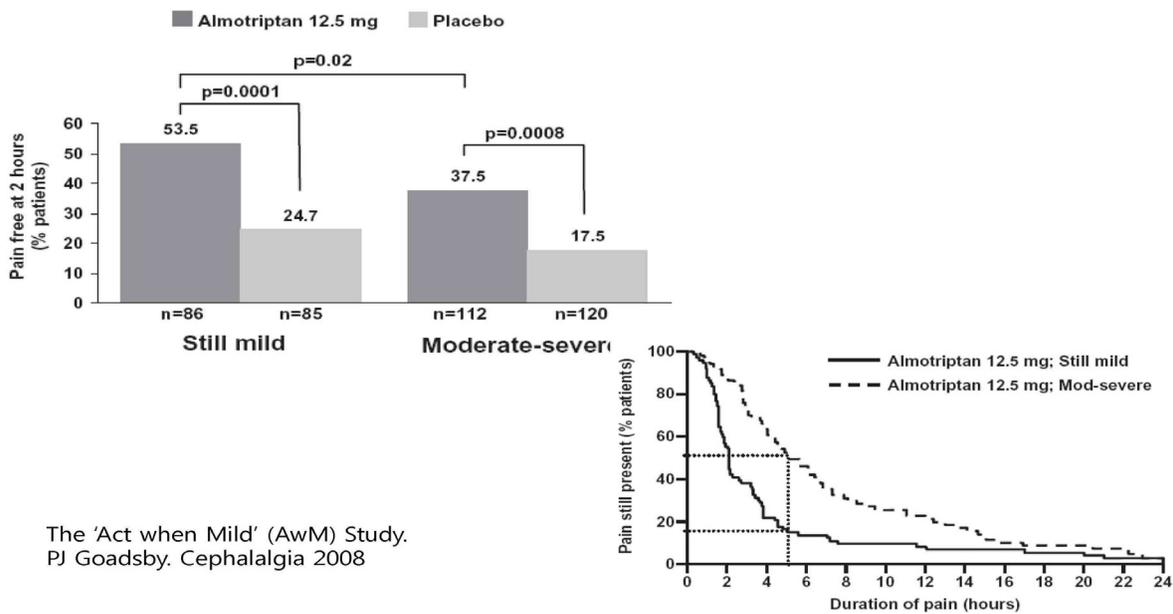
빨리 복용  
복합약물  
다른 투여경로

## 교육: 언제 triptan을 복용하나?

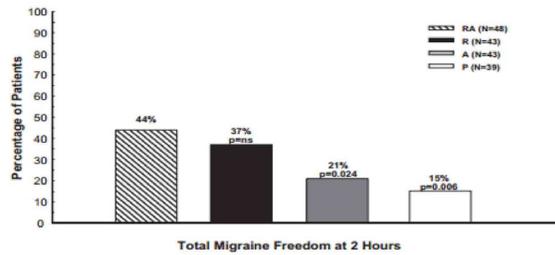
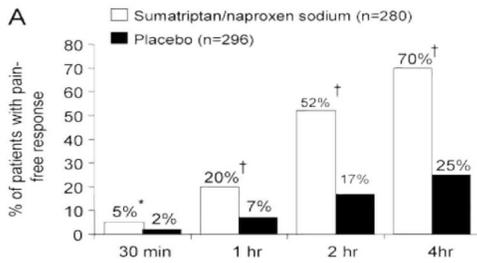


Gendolla A. Cephalalgia 2008 Epub

## 'Act when Mild (AwM)'



### Multi-mechanism therapy - Triptan/NSAID combination tablet



Sumatriptan 85 mg + naproxen 500 mg  
Silberstein SD. Neurology 2008

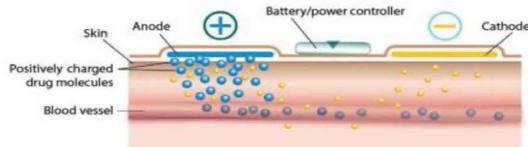
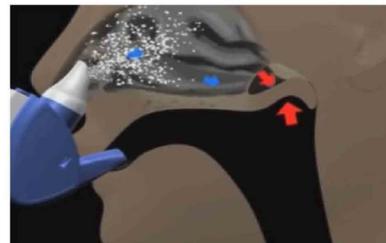
Rizatriptan 10 mg + AAP 1000 mg  
Freitag F. Headache 2008

High pain-free rate  
Low recurrence

Frovatriptan+dexketoprofen  
Allais G, Neurol Sci 2015 May

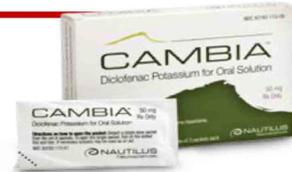
### 다양한 투여경로 - triptans

- 7 triptan tablets
- 2 fast-melt tablets, 2 nasal sprays, 3 types of injection
- Sumatriptan: SC, oral, rectal, nasal spray
- Various generic formulations of sumatriptan : Needle-free injection
  - Lingual spray
  - Intranasal powder (OptiNose apparatus)
  - Patch (Zelix)



## 다양한 투여경로 - Non-triptan drugs

- Diclofenac powder for solution (Cambia®)



- Intranasal ketololac tromethamine (Sprix®)



- DHE inhaler (Levadex®)



## ED and inpatient treatment of status migrainosus

Continuum 2015 Aug

- Adequate **fluid** hydration and combination **IV** therapy with multiple nonopioid medications from **multiple drug** classes

**TABLE 4-2 Typical Emergency Department Treatment Strategy<sup>a</sup>**

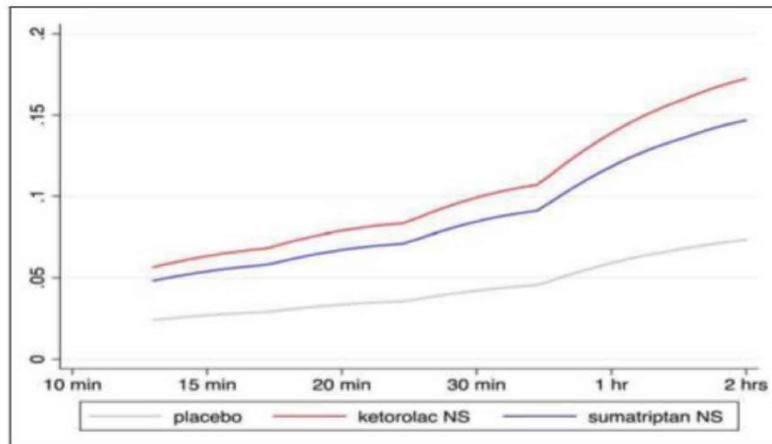
1. IV fluids, normal saline 2–3 L bolus or 80–100 cc/h for as long as patient is in emergency department
2. IV diphenhydramine 12.5–25 mg
3. IV dopamine receptor antagonist medication (typically use metoclopramide 10 mg or prochlorperazine 10 mg)
4. IV magnesium sulfate 500 mg–1 g
5. IV ketorolac 30 mg
6. If patient does not improve, other options include IV sodium valproate (500 mg), IV levetiracetam (500 mg), or IV methylprednisolone (200 mg)
7. IV dihydroergotamine 0.5–1.0 mg may be used if patient has not used a triptan within 24 hours and no contraindications exist

IV = intravenous.

<sup>a</sup> Medications are given in succession separated by 15 to 20 minutes.

### 응급실 치료: Ketorolac NS vs Sumatriptan NS vs Placebo NS

Rao AS, Headache 2016 Feb



Time-to-pain-relief

### 응급실 치료: IV valproate vs SC sumatriptan

Ghaderibarmi F, Acta Med Iran 2015 Dec

- Randomized 37 patients
- 6 mg SC sumatriptan
- 15 mg/kg of IV valproate – **faster, more effective**  
without any recurrence and remarkable side effects

Mean pain score	Sumatriptan	Valproate
baseline	8.3	8.3
1 hr after Tx	4.7	2.2

## 응급실 치료: IV valproate vs IV dexamethasone

Mazaheri S, PLoS One 2015 Mar

- 104 patients
- Both drugs were highly effective.
- However, dexamethasone was not effective in patient with migraine with aura.

VAS	valproate	dexamethasone
baseline	8.2	8.5
2 hr after tx	3.7	3.6

## 응급실치료: haloperidol IV vs metoclopramide IV

Gaffigan ME, J Emerg Med 2015 Sep

- IV haloperidol is as **safe and effective** as metoclopramide for the ED treatment of migraine headaches
- 31 pts with HPD 5 mg vs 33 pts with METO 10 mg
- No QT prolongation

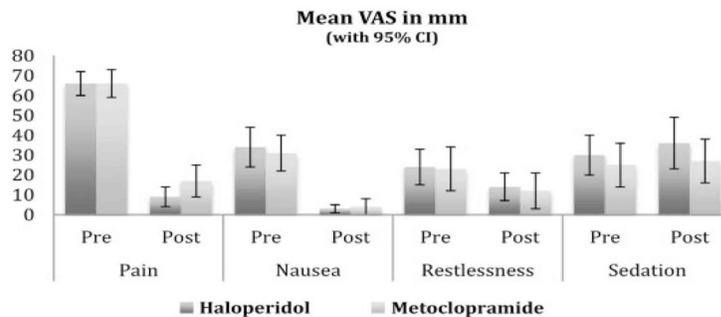


Figure 2. Mean visual analog scale (VAS) in mm with 95% confidence intervals (CI).

## 비약물치료: Acupuncture for acute migraine

Du R, BMJ Open 2015 Apr

- 7 databases from MEDLINE, EMBASE, Cochrane, and 4 Chinese databases (~ 2015 Feb)
- RCTs in English or Chinese
- This systematic review will evaluate published RCT evidence for the effectiveness and safety of acupuncture for acute migraine attacks in adults.

## 비약물치료: HBOT for migraine

Cochrane review 2015 Dec

- 11 trials with 209 participants
- 5 HBOT vs. sham for acute migraine,
- 3 NBOT vs. sham or ergotamine for cluster HA
- 2 HBOT for cluster HA
- 1 NBOT vs. sham for a mixed HA



### Hyperbaric oxygen therapy for the relief of acute migraine

**Patient or population:** Acute migraine  
**Setting:** Hospital care  
**Intervention:** HBOT (2.0 to 2.4 ATA for 40 to 45 minutes)  
**Comparison:** Sham therapy (air at pressure or 100% oxygen at 1 ATA)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Number of participants (trials)	Quality of the evidence (GRADE)	Comments
	Risk with sham therapy	Risk with HBOT				
Chance of obtaining substantial headache relief (Relief). Assessed with: Patient self-assessment	111 per 1000	663 per 1000 (162 to 1000)	RR 6.21 (2.41 to 16.00)	58 (3 RCTs)	Low <sup>1</sup>	We included 3 small RCTs but all showed large effect size with HBOT compared to either air or 100% oxygen sham

\*The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).  
 Abbreviations: CI: confidence interval; RR: risk ratio; OR: odds ratio; ATA: atmospheres absolute; HBOT: hyperbaric oxygen therapy.

## 비약물치료: GON for acute migraine

- **Hemiplegic migraine**  
Rozen T, Headache 2007  
Casas-Limon J, Headache 2015
- **Basilar type migraine**  
Baron EP, Headache 2010

## 비약물치료: sTMS

Bhola R, J Headache Pain 2015 Jun

- 62% pain relief
- At 3 months – HA days reduction from 12 to 9 (EM),  
from 24 to 16 (CM)

