

偏頭痛病例用藥討論

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Case Report - 1

Ms. T 45 y/o

OPD 2018/11/14

Subjective

- First visit at 40 y/o (2014/6/16)
 - Headache since 26 y/o, worsen frequency
 - No aura
- Migraine without aura**

✓ ≥5 attacks (12 day/ month)	✓	☆4-72 hrs (1-2 day)
	✓	☆Unilateral (Left, shifting sides)
	✓ (≥2)	☆Pulsating quality
	✓	☆Moderate or severe pain Aggravation by routine physical activity
	✓ (≥1)	☆Nausea or vomiting Photophobia and phonophobia

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Case Report - 2

Subjective

- Pain killer prn
 - ◆ Ergotamine/cafeine 1/100 mg effective?
 - ◆ Acetaminophen: Not effective in big attack
- Headache worsening during menstruation
- Headache family history: Mother
- Past history
 - ◆ Asthma
 - ◆ Mitral valve prolapse

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Case Report - 3

Objective

- BP:88/59 mmHg
- HR: 77/min
- Cr:0.66
- ALT:14
- MIDAS:66
- BDI:3
- HDAS: A=4 D=3

Migraine Disability Assessment (MIDAS)

Score	Grade	Disability
0-5	I	Little/no
6-10	II	Mild
10-20	III	Moderate
21+	IV	Severe

Beck Depression Inventory (BDI)

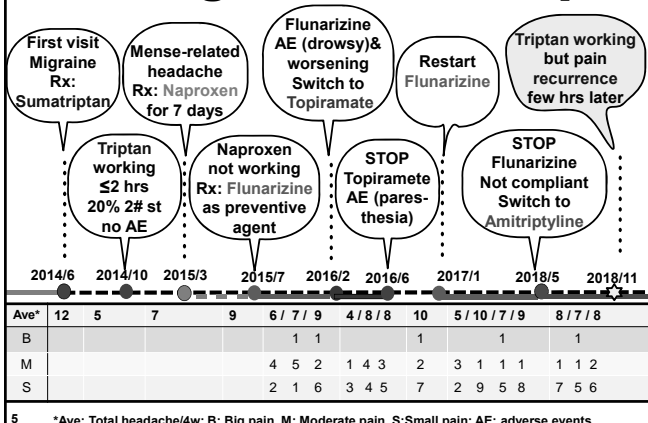
Score	Depression
0-13	Minimal
14-19	Mild
20-28	Moderate
29-63	Severe

Hospital Anxiety and Depression Scale (HDAS)

Score	Anxiety / Depression
0-7	Normal
8-10	Borderline
11-21	Abnormal

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During OPD Follow-up



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Case Report - 4

Assessment

- Migraine without aura
- Headache recurrence after taking sumatriptan (Imigran®)
- Asthma, mitral valve prolapse, gastric ulcer

Plan

- Sumatriptan (Imigran®) + celecoxib (Celebrex®) to prevent headache recurrence

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Patient Drug Profile

藥名/劑型/含量/劑量/頻次	14 06	15 02	03	07	16 02	08	17 01	04	12	18 05	11	19 01
Sumatriptan tab 50 mg 1# qdprn											
Naproxen tab 250mg 1# bid 7d	--											
Flunarizine cap 5 mg 1# qon											
Topiramete tab 25 mg 1# qn											
Amitriptyline tab 25mg 1# qn											
Celecoxib cap 200 mg 1# qdprn											
Etoricoxib tab 60 mg 1# qdprn											
Stroccain tab 1# bid 7d	--											
Headache attacks (ave./4w)	12	7	9	7	8	10	5	10	9	8	8	9

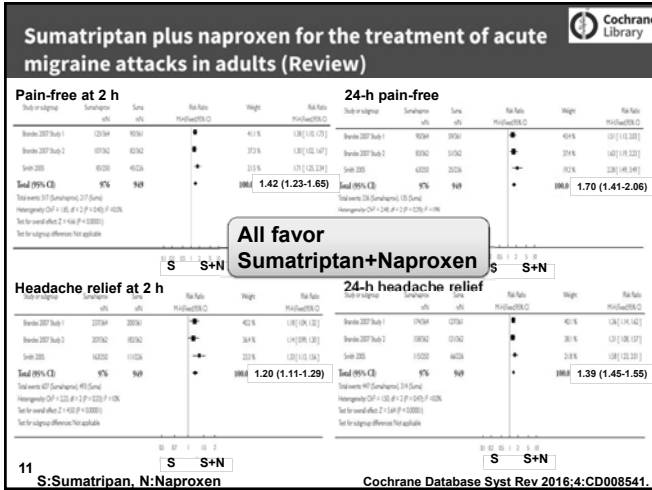
Less recurrence

Try Arcoxia (longer T_{1/2}: 22hr) F/u at 2019/4

- ## Discussion
- Acute treatment of migraine
 - Triptan-NSAID combination
 - Preventive treatment of migraine
 - Current available agents in Taiwan
 - New treatment options
 - Menstrual migraine
 - Short-term prevention
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- ## Acute Treatment of Migraine
- Mild to moderate attacks
 - NSAIDs (aspirin, diclofenac, ibuprofen, naproxen)
 - Acetaminophen
 - Caffeinated analgesic combinations
 - ◆ AAC: aspirin + acetaminophen + caffeine
 - Moderate or severe attacks (or poorly response to NSAIDs or caffeinated combinations.)
 - Triptans (first choice)
 - ☆ Sumatriptan (50 mg tab, 20 mg nasal)
 - ◆ Rizatriptan (5 mg tab, 10 mg tab)
 - ◆ Almotriptan, eletriptan, frovatriptan, naratriptan, zolmitriptan
 - Dihydroergotamine
- Acetaminophen Not effective in big attacks
- Sumatriptan tab 50 mg (or 100 mg)
- pain recurrence
- Headache 2019;59:1-18; Headache 2015;55:3-20

- ## Headache Recurrence
- Definition: Initially headache relief after treatment but return within 24 hr
 - Management
 - Take triptan earlier
 - ◆ Still mild and <1 hr of onset
 - Second dose of the same triptan
 - ◆ Repeat after ≥2 hr
 - Consider eletriptan or frovatriptan (longer T_{1/2})
 - ◆ Not available in Taiwan...
 - Combination
 - ◆ Triptan-based combination
- 2015/11/11 OPD:
HA becomes longer (2-3day)
Take Imigran® ASAP
- Cephalalgia 2008;28:383-91
Cephalalgia 2008;28:36-41
Headache 2000;40:792-7
Cephalalgia. 2014;34:258-67
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- ## Triptan-NSAID Combination-1
- Sumatriptan-naproxen (85/500 mg) TREXIMET®
 - 2008/4 FDA approved for adult
 - Sumatriptan-naproxen (10/60 mg) TREXIMET®
 - 2015/5 FDA approved, ≥12-17 y/o
 - Different mechanism and less pill burden
- Sumatriptan**

 - 5-HT_{1D/1B} agonist
 - Trigeminal system
 - Vasoconstriction and reduces neurogenic inflammation

Naproxen

 - COX inhibition
 - Meninges
 - Reduces inflammation
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- Drugs 2016;76:111-21

Triptan-NSAID Combination-2

- Clinical indicated
 - ☆ Headache recurrence
 - Partial working of triptans
 - Reduction of the single drug dosage
- Other NSAID is used empirically
 - PK: Half life, rapid- or slow-release
 - Side effects: ☆ Gastric, cardiovascular
 - If one is ineffective, may try a different one

Imigran® + Celebrex® (T_{1/2}: 11 hr), less recurrence.
 → Imigran® + Arcoxia® (T_{1/2}: 22 hr), f/u at 2019/4.

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Headache 2012;52:636-47

Preventive Treatment of Migraine-1

- ☆ Frequent attacks (≥4MHD)
- ☆ Attacks significantly interfere daily routines despite acute treatment
- To acute treatments
 - Contraindicated
 - Intolerant
 - ☆ Failure
 - Overuse

Attacks: 5-12/month
 MIDAS: 66 (severe disability)
 Headache recurrence

MHD: Migraine headache days

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Headache 2019;59:1-18

Preventive Treatment of Migraine-2

1. Drowsiness, alopecia, tremor, edema, wt. gain, liver or CBC abnormality. 2. Paresthesia, wt. loss, cognitive dysfunction, glaucoma, kidney stone

Drowsiness, fatigue, erectile dysfunction **MS.T**

Anti-epileptics
 1. Valproate
 2. ☆ Topiramate

Beta-blockers
 • Propranolol
 • Metoprolol
 • Atenolol

Asthma
DM
Depression

Anti-depressants
 • Amitriptyline
 ☆ Venlafaxine

Calcium channel blockers
 ☆ Flunarizine

Parkinson disease

Drowsiness, xerostomia, constipation, blurred vision, urinary retention, tachycardia

Drowsiness, wt. gain, extrapyramidal reaction

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Lancet 2017;390:1211-59
 Headache 2013;53:644-55
 Cephalalgia 2017;37:470-85

New: CGRP-Targeted Treatment

mAbs Prevention

5-HT_{1B} or 5-HT_{1D} receptors, Triptans, Anti-CGRP antibody, CGRP, Adenylate cyclase, Gαq, cAMP, Protein kinase A, Vasodilation, Gepants Acute, Cerebrovascular smooth muscle cell.

CGRP mAbs

Episodic migraine	>50% reduction in migraine days (% of patients)
Erenumab	46%
Eptinezumab	61%
Galcanezumab	63%
Fremanezumab	53%

Legend: Placebo (white), Active (grey)

CGRP: calcitonin gene-related peptide
 mAb: Monoclonal Antibody

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Nat Rev Neurol 2018;14:338-50

CGRP Monoclonal Antibodies

Drug	FDA approved	Target	Dosing	Peak	Metabolism	Adverse events	Cost
Erenumab Aimovig® Amgen/Norvatis	2018/5/17 Prevention EM, CM	CGRP receptor	SC QM	~6d	Proteolysis	Injection site 575 reaction, constipation (3%)	*
Fremanezumab Ajovy® Teva	2018/9/14 Prevention EM, CM	CGRP ligand	SC QM/ Q3M	5-7d	Proteolysis	Injection site 575 reaction	*
Galcanezumab Emgality® Eli Lilly	2018/9/27 Prevention EM, CM (FDA priority review: eCH)	CGRP ligand	SC QM	5d	Proteolysis	Injection site 575 reaction	*
Eptinezumab Alder	Submitted Prevention EM, CM	CGRP ligand	IV Q3M	hrs	Proteolysis	URI (9%)	N/A

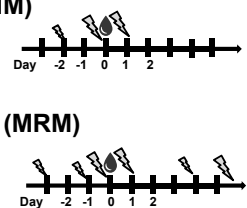
CGRP: Calcitonin gene-related peptide; CM: Chronic migraine; eCH: Episodic cluster headache; EM: Episodic migraine; URI: Upper respiratory tract infection. * USD/month

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Nat Rev Neurol 2018;14:338-50

Menstrual Migraine

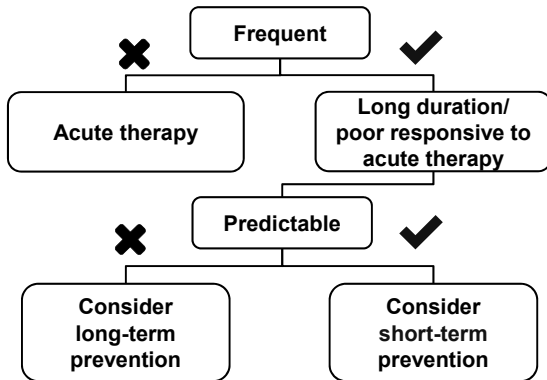
- **Menstrual migraine (MM)**
 - 22% female migraineurs
 - More severe and longer-lasting than non-MMs.
- **Pure menstrual migraines (PMM)**
 - ≥2 attacks in day 0±2
 - AND ≥3 menstrual cycles
- **Menstrually related migraines (MRM)**
 - ≥2 attacks in day 0±2
 - AND ≥3 menstrual cycles
 - AND other times



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Cephalalgia. 2014;34:280-8.
 Cephalalgia. 2013;33:629-808
 Headache 2017;57:194-208

Treatment Algorithm of MM



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MM: Menstrual migraine

Headache 2017;57:194-208

Short-term Prevention of MM

Drug	Dose	Start	Duration (day)	Note
Frovatriptan	2.5 mg qd or bid	Day-2	6	RCT, Level A rating
Naproxen	250-500 mg bid	Day -7~-1	5~14	RCT
Dihydro-ergotamine	3.5 mg bid	Day-2	5	Open label trial
Magnesium	120 mg tid	Day15 of the cycle	Until the next cycle	RCT
Estradiol gel	1.5 mg	Day-2	7	Efficacy +/-, withdrawal effect, stroke risk
Estradiol patch	<100 ug/d	Day10 after ovulation	Until day 2	

MM: Menstrual migraine

20 RCT: Randomized controlled trial

Headache 2017;57:194-208
Neurology 2012;78:1337-45

Take Home Message

- Triptan-NSAID for acute migraine
 - Headache recurrence
 - Partial working of triptan
 - Reduction of the single drug dosage
- Preventive treatment of migraine
 - ABCD and CGRP-targeted treatment
- Short-term prevention of MM
 - Start from day-2, total 5-7 days
- Select effective acute/prevention therapy
- Make sure pts understand the medications

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Thanks
for Your Attention

