

Dose Equivalents - Morphine

- Mg for mg - sustained equal to immediate relief
- Sustained product can be dosed q 8 or q 12

A pharmacy student ask if immediate release morphine sulfate is equivalent to sustained release morphine sulfate. Are they equivalent?

Yes they are, only the time of release is different. Sustained release products offer the patient 8n to 12 hours of relief.

用量同等性

—モルヒネ

○ Mg for mg —

速効性と持続性製剤は同量を含有する。

○ 持続性製剤は 8 から 12 時間で投与される。

Dose Equivalents - Fentanyl Patch

- Conversion from morphine to fentanyl is 3:1
 - Patch is three times more potent than oral morphine
- Patient on morphine 30 mg po q4h so 24 hour dose is 180 mg morphine
 - Fentanyl dose is 60 mg (use nearest size)

When patients want to be free of oral doses, or their intravenous ambulatory pump, what choices are there for them?

One option is patches such as fentanyl. When used, use one third the dose of the oral morphine dose. Adjust the dose as needed.

Fentanyl patches offer the patient up to three days therapy without changing the patch. Multiple patches may be used.

用量同等性

—フェンタニールパッチ

○モルヒネからフェンタニールへの変換は
3 : 1である。

パッチは経口モルヒネより3倍強力である。

○モルヒネ 30 mg 経口、4時間毎を服用している患者
の1日量は180 mgである。

フェンタニールの用量は60 mgとなる。

(近似サイズを使用する。)

Equianalgesic Doses:

•Opioid Equianalgesic Dose:

• Morphine:	30 mg po
• Dilaudid:	4-6 mg po
• Hydrocodone:	30 mg po
• Oxycodone:	30 mg po
• Codeine:	180 mg po

Basically, all routinely used narcotic analgesics can be interchanged.

Patients on a fentanyl.

Here is a table of often useful dose equivalence. Other tables are available for conversion of intravenous to oral doses.

同効性

用量：

○オピオイドの同効用量

Morphine : 30 mg 経口

Dilaudid : 4-6 mg 経口

Hydrocodone : 30 mg 経口

Oxycodone : 30 mg 経口

Codeine : 180 mg 経口

Intravenous Pain Therapy (Morphine or Dilaudid)

- **Write as continuous infusion**
- **Specify hourly rate with bolus rescue every 15 minutes**
- **Hourly rescue should equal hourly continuous infusion**

Intravenous pain therapy is often used in hospital patients or patients at home on an ambulatory pump.

Patients should always have a continuous infusion with a rescue dose available.

The hourly rescue dose should be equal to the hourly continuous infusion.

For example, when the dose of morphine is 12 mg every hour for 24 hours, the rescue dose is 3 mg every 15 minutes.

静注による疼痛治療

(MorphineまたはDilaudid)

○持続注入として記載する。

○1時間当たりの持続注入量と15分毎の追加量を示す。

○1時間毎の追加量は1時間当たりの持続注入量と同じである。

Converting PO to IV

- Calculate 24 hour narcotic total
- Divide by the appropriate conversion factor (below)
- Divide by 24 hours to obtain hourly IV rate
- (Opioid naïve - IV is 6 times more potent than po (1:6))
- (Opioid "experienced" - IV is 3 times more potent than po (1:3))

Your next patient is a cancer patient in acute pain, unable to swallow tablets. The patient has some breakthrough pain and takes rescue doses. This patient is has a projected prognosis that is very serious and is not expected to live more than one month. The decision is made to convert the patient from an oral therapy to intravenous therapy.

Given that the patient's total daily oral dose is 300 mg, what intravenous dose should be prescribed?

This patient is "experienced", meaning they have been on morphine. Their intravenous dose should be one third their oral dose to begin. After beginning the intravenous dose, adjust to patient comfort and side effects.

経口から静注への変更

- 1日当たりの麻薬の量を計算する。
- 次に示す変換係数で割る。
- 1時間当たりの持続注入量を計算する場合は24時間で割る。
- 初めて麻薬を使用する場合—
静注は経口に比較して6倍強力である。(1:6)
- オピオイドの使用経験がある場合—
静注は経口に比較して3倍強力である。(1:3)

Evaluation of Outcomes

- Hourly or daily or weekly monitoring
- Self evaluation
 - Histories
 - Scale for pain
- Prevention - of side effects
 - Laxatives and hydration
- Focus on cause of pain

Pharmacists are in a good position to work with patients, physicians and others to manage a patient's pain therapy.

Patients should be monitored hourly for pain control, daily for side effects, and weekly for opportunities for adjustment in choice of medication, and alternative therapies.

結果の評価

○時間毎、毎日、1週間毎のモニタリング

○自己評価

病歴

疼痛スケール

○副作用の予防

緩下薬、水分補給

○痛みの原因に焦点を当てる。

Adjuncts to Analgesics

- Phenothiazines
- Antihistamines
- Benzodiazepines
 - Midazolam
 - Diazepam
- Barbiturates
- Antidepressants - possibly first line

Various medications have been used as adjuncts to therapy to either relieve anxiety and stress with pain, or to synergistically aid in pain relief.

While amitriptyline and other antidepressants do work, others probably do not work to directly relieve pain.

鎮痛補助薬

- フェノチアジン誘導体
- 抗ヒスタミン剤
- ベンゾジアゼピン誘導体
 - Midazolam
 - Diazepam
- バルビタール誘導体
- 抗うつ薬
 - 第一標準

Adjuncts to Analgesics

- Midazolam (Versed)
 - Benzodiazepine
 - Much like diazepam
 - Less pain on injection
 - Amnesic effect
 - Water soluble base
 - Lower doses than diazepam

A patient in the clinic you work in is going to have oral surgery. The patient asks you the day before if you can discuss using midazolam with her oral surgeon. She has read that the two work well together. What do you tell her? When benzodiazepines are used, they are primarily used to relieve anxiety prior to a procedure, and not to enhance pain relief.

鎮痛補助薬

○Midazolam (Versed)

ベンゾジアゼピン誘導体

Diazepam類似

注射時の痛みが少ない

健忘効果

水溶性基材

Diazepamより低用量

Headache

• Pathophysiology

- Vascular theory - stimulation of sensory nerves in large cerebral arteries and meningeal circulation
- Neuronal theory - interaction of 5th cranial nerve and several mediators

A patient comes to your pharmacy complaining of frontal headaches that occur daily at the end of the work day. They are described as “dull pain”, and “throbbing”. You inquire further and find out the patient does not experience any loss of vision, and does not have an aura. The headaches are not associated with consumption of alcohol.

This is the classic signs of vascular headaches. Most often they are resolved with non-steroidal anti-inflammatory medications or aspirin, which act by reducing prostaglandins.

頭痛

○病態生理

血管説

大脳動脈および髄膜循環における感覚神経刺激

○神経説

第5頭蓋神経と幾つかのメディエーターの相互作用

Pathophysiology

- 5HT on platelets drops significantly, which binds to receptors and causes vasoconstriction
- Other
 - Monosodium glutamate
 - Tyramine metabolites
 - 5HT reuptake block (antidepressants)
 - Altered platelet aggregation by estradiol
 - Vasodilation with nitroglycerin or alfentanil

Since we also know 5HT is reduced, other medications have been used to treat vascular headaches, most often when aspirin does not work well.

Other causes of vascular headache are listed on the slide.

病態生理

○血管収縮作用を有するセロトニンが血小板で減少している。

○その他

グルタミン酸

チラミン代謝物

セロトニン取り込み阻害（抗うつ薬）

エストラジオールによる血小板凝集の変化

ニトログリセリン、ニフェジピンによる血管拡張

Migraine Headache-Clinical Presentation

- Without aura 85%
- With (classic) aura 10%
- Other 5%
- Usually in early daytime with peak within 1 hour
- Unilateral mostly and temporal
- Sensitivity to stimuli
- Duration 4-72 hours

The next patient in your clinic experiences early morning headaches associated with seeing spots in her peripheral fields of vision. This patient says she must stop what she is doing, and seeks a dark place to go to avoid noise and other stimuli. She says even taking four adult aspirin doesn't work to stop the pain. She knows when a headache is starting because she smells "something burning". Each day she has a headache like this, it lasts a day.

These are classic migraine headache characteristics.

片頭痛—臨床症状

- 前兆なり 85%
- 前兆あり 10%
- その他 5%
- 通常、昼間早期より起こり
起床後1時間をピークとする。
- 片側性で側頭である。
- 刺激に対する感受性
- 持続時間 4-72時間

MHA-Treatment

• **Abortive - AT ONSET -**
works in 50-80% of
patients

- **Aspirin or acetaminophen**
 - if infrequent and relatively mild
- **NSAIDS** - works to inhibit prostaglandin synthesis, platelet aggregation, reduces serotonin release and with menstruation
- **Ergotamine** - vasoconstrictor of smooth muscle, fast, p.o. iv, or inhalation
 - Side effects are numerous including rebound

What will abort a migraine headache? What is used to effectively treat a migraine headache?

High dose aspirin works only sometimes.

Non-steroidal anti-inflammatory agents work best when the headaches are associated with menses and serotonin release, but are not always effective.

Most of the time, ergotamine like agents.

片頭痛－治療

○頓挫療法

50-80%の患者で有効である。

Aspirinまたはacetoaminophen

もしそれほど頻回ではなく比較的軽度であれば

NSAID－プロスタグランジン合成と血小板凝集抑制、

セロトニン放出抑制および月経を伴う

Ergotamine－平滑筋の血管収縮

種々の副作用

MHA-Treatment

- Sumatriptan (Imitrex) - 5HT_{1B} receptor agonist to cause vasoconstriction, and blocks extravasation and inflammation.
- Rizatriptan (Maxalt-MLT) - 5HT_{1B} tablet; a selective serotonin like receptor agonist
- Midrin - vasoconstrictor/sedative/analgesic
- Metoclopramide - nausea and vomiting
- Narcotics - as above

Are 5HT_{1B} agents effective in preventing the occurrence of a migraine headache?

Yes they are, such as sumatriptan or rizatriptan.

Other, older agents are somewhat effective for pain, but are no longer considered at the medication of choice.

片頭痛－治療

○Sumatriptan (Imifrex)－血管収縮を誘発するセロトニンアゴニスト、extravasationと炎症などを抑制する。

○Rizatriptan (Maxalt-MLT)－
選択的セロトニンレセプターアゴニスト

○Midrin－
血管収縮作用／鎮静作用／鎮痛作用

○Metoclopramide－吐き気、嘔吐

○麻薬性鎮痛剤

MHA-Treatment

• **Prophylactic** - moderate severity more than twice monthly or refractory or predictable

• **Beta blockers** - do not use

• **Antidepressants** - NE block

• **Calcium channel blockers** - inhibit initial vasoconstriction

• **Cyproheptadine** - Periactin 5HT₂ receptor antagonist

Can treatment be offered continuously, or days before the apparent causative event to prevent headache?

Yes, there are good results using beta blocking agents such as propranolol, antidepressants such as amitriptyline, calcium channel blocking agents, and cyproheptadine, a 5HT₂ receptor antagonist.

片頭痛－治療

○予防療法

月に2回以上の中程度の発作または難治性
または予測可能なもの

β-ブロッカー－使用しない

抗うつ薬－NEブロック

カルシウムチャンネルブロッカー－

初期の血管収縮を抑制する。

Cyproheptadine－

Periactin 5-HT₂レセプターアンタゴニスト

MHA-Treatment

- Anticonvulsants - various
- Methysergide - (Sansert)
5HT receptor antagonist;
intermediate term use only
- Reserved for patients refractory
to other medications

Other medications are available if these are ineffective, however, they cause more side effects in most patients.

片頭痛—治療

○抗けいれん薬

○Methysergide- (Sansert)

セロトニンアンタゴニスト

中期的使用に限る

その他の治療薬に対して難治性の患者のみ

Cluster Headaches

- Pathophysiology
 - Decreased blood flow in supraorbital and frontal arteries, followed by vasodilation, and other mechanisms
- Triggers
 - Vasodilators
 - Hypoxemia
 - High altitude hypoxia

Our next patient comes to our attention with migraine headaches, but the headaches are multiple and occur over a two to four day period. They cause the patient to stay home from work.

These are often considered cluster headaches.

群発頭痛

○病態生理—

血管拡張やその他の反応に引続いて起こる
眼窩上および前頭葉動脈における血流減少

引き金：

血管拡張

低酸素症

高空低酸素症

Cluster Headaches

• Clinical presentation

- Unilateral
- Localized - eyes or temples
- Agitation
- Ipsilateral (same side) effects
 - lacrimation
 - nasal stuffiness
 - etc.

There are other characteristics of cluster headaches that can be determined by the pharmacist as he or she completes their assessment and plan. These are listed on the slide.

群発頭痛

○臨床症状

片側性

局在性—目またはこめかみ

興奮、精神障害

同側の効果

流涙、鼻づまり

CHA-Treatment

• Treatment

• Abortive

- Ergotamine effective
- Oxygen
- Sumatriptan - 25

• Prophylaxis

- Lithium - effective 300-1200mg/d
- Ergotamine - 1-2 mg in 1 or 2 daily doses
- Methysergide - usually effective in shortening course
- Corticosteroids - last choice

Is treatment the same for cluster headaches?

Yes quite similar. Agents used are listed on the slide.

群発頭痛

○治療

頓挫療法

Ergotamine 効果的

酸素

Sumatriptan

予防療法

Lithium - 効果的 300-1200mg/d

Ergotamine - 1 - 2 mg

Methysergide - 通常効果的

コルチコステロイド - 最後の選択

CHA-Outcomes

- Evaluation of outcomes
 - Evaluate frequently
 - Adjust treatment as needed

Cluster headaches and migraine headaches are a chronic situation and should be monitored over long periods of time. Medications should be changed as needed. The pharmacist is in an ideal position to know the patient's history and to make recommendations for improvement.

群発頭痛－結果

○治療結果の評価

度々評価する

必要により治療を調節する

Neuropathic Pain

• Pathophysiology

• Peripheral nervous system

- damage to nerves + ectopic discharges
- probably not due to changes in myelination

• Sympathetic nervous system

- abnormal communication + an increase in ectopic impulse generation

The next patient is a 34 year old female who was referred to the pain clinic for treatment of pain of unknown cause (onset about 2 weeks after a motor vehicle accident).

This patient describes her pain as "burning and tingling, from my toes to my knees on both sides." Pain is constant, rated a 7-8 of 10 most days, sometimes helped by acetaminophen, and significantly impairs functioning.

This is likely neuropathic pain, caused by nerve damage or abnormal impulse generation.

神経障害性疼痛

○病態生理

末梢神経系

神経への障害

異所性発射

ミエリンの変化によるものではない。

交感神経系

異常な伝達

異所性インパルスの増加