Headache and OTC analgesics

Learning objectives
After completing this activity, pharmacists should be able to:

- Identify risk factors for adverse drug events with analgesics
- Differentiate between types of chronic headache syndromes
- Appraise patients for medication overuse headaches
- Counsel patients on risks of overuse of analgesics and anti-migraine products

The competency standards addressed by this activity include (but may not be limited to)
3.2.2, 6.1.1, 6.1.2, 6.1.3, 6.2.1, 6.2.2, 6.2.5, 6.3.2.

The National Pain Strategy identified that less than 10% of patients gain access to effective management of chronic pain and up to 80% are missing out on treatment that could improve their health and quality of life.

The availability of over-the-counter (OTC) analgesics provides ready access to consumers who experience either intermittent or chronic headaches to self-treat their pain. It has been shown that up to 70% of the Australian population uses OTC analgesics regularly for headaches or musculoskeletal pain.

Chronic pain
Chronic pain is a complex biopsychosocial phenomenon that can have a profound impact on people’s lives. The condition persists beyond the normal time of healing and is conservatively defined as pain experienced every day for three months or more in the previous six months.

Chronic pain is a common condition in Australia. In 2007, around 3.2 million Australians (1.4 million males and 1.7 million females) are estimated to experience chronic pain. For many people in the community their chronic persistent pain is not well controlled or managed.

Pharmacological treatments can be effective in reducing symptoms but are not always needed and may not be sufficient alone to improve functional status. There are concerns that over-reliance on pharmacological treatments can lead to poorer functional outcomes and substance-related problems.

The inappropriate and overuse of OTC analgesics is an important consideration for pharmacists. Community pharmacists have a professional responsibility to address the judicious and appropriate use of OTC analgesics. With the recent changes in pack sizes for combination analgesic products, pharmacists have an important role to play in raising consumer awareness, pharmacovigilance and appropriate referral to general practitioners (GPs).

Adverse drug events
An Australian retrospective audit of over 100,000 adult patients screened for contraindications, warning or precaution to the use of paracetamol, ibuprofen, or aspirin. The study found that paracetamol was suitable for use by 98% of adults, but 23% had a documented reason to indicate ibuprofen was inappropriate. Over 80% of patients had no contraindications, warning or precautions to the use of aspirin.
Screening criteria for suitability of these medicines included:

- History of, or current, gastric or duodenal ulceration
- Allergic reaction to ibuprofen, aspirin or other NSAIDs
- History of asthma
- Renal, hepatic or cardiac impairment
- Concomitant anticoagulant
- Pregnancy
- OA/RA (and being treated with a NSAID)
- Hypersensitivity to paracetamol
- Severe liver or kidney disease

These findings highlight the need for intervention by pharmacists and referral to the patient’s GP in many cases, particularly with OTC use of NSAIDs.

Medicines known to increase the risk of adverse events with NSAIDs include:

- Anticoagulants (e.g. warfarin)
- Other NSAIDs or COX-2 inhibitors
- Corticosteroids (e.g. prednisone, prednisolone)
- Antihypertensives (especially ACE inhibitors and angiotensin receptor blockers together with a diuretic)

**Dependency**

The psychotropic side-effects of analgesics such as sedation or mild euphoria and their stimulating action may lead to drug dependency. Codeine, dextropropoxyphene and other opioids as well as caffeine are most likely to have this effect.

Pharmacists should ask patients about their caffeine taking behaviour when counseling on analgesic use and misuse. Caffeine withdrawal symptoms include irritability, nervousness, restless and ‘caffeine withdrawal headache’. These symptoms may last for several days.

**Chronic headache**

Chronic daily headache affects approximately 3 to 4% of the general population. It is defined as headaches that occur on greater than or equal to 15 headache days per month, for 4 hours or more per day, for at least 3 months.

The International Classification of Headache Disorders describes several types of headaches:

- New daily persistent headache – daily unremitting headache with sudden onset
- Chronic tension-type headache – headache that lasts for hours or may be continuous
- Chronic migraine – headache (tension-type or migraine) on ≥15 days/month for ≥3 months in the absence of medication overuse
- Medication overuse headache – headache on ≥15 days/month that has developed or markedly worsened with regular medication overuse for > 3 months

Many patients with chronic headache are overusing medications, which contribute to the resistance to control of the headache and are refractory to most treatments. Analgesics can cause rebound or drug-induced headaches if overused.

**Medication overuse headache**

Medication overuse headache is defined as a headache that is present on 15 or more days of the month and developed or worsened whilst the patient has been taking regular analgesics or anti-migraine medications for more than 3 months. Prior to 2004, it was referred to as rebound headache.
It is the third most frequent type of headache. The prevalence in the general population is around 1 to 1.4\%. Women may be more prone to medication overuse headache, with peak prevalence in women in their 50s.

Simple analgesics and combination analgesics account for more than 90% of medication overuse. Discontinuation of analgesics can lead to clinical improvement.

**Definition**
Medication overuse headache is defined by:

- Regular overuse for ≥3 months of ergotamine, triptans, opioids or combination analgesic medication on ≥10 days/month on a regular basis for ≥3 months; or
- Simple analgesics or any combination of ergotamine, triptans, analgesics or opioids on >15 days/month on a regular basis for ≥3 months without overuse of any single class alone.

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Chronic tension-type headache</th>
<th>Chronic migraine (without aura)</th>
<th>Medication overuse headache</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>≥ 15 days/month on average for &gt; 3 months</td>
<td>≥ 15 days/month on average for &gt; 3 months</td>
<td>≥ 15 days/month with regular overuse for ≥ 3 months</td>
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<tr>
<td>Duration</td>
<td>Hours or may be continuous</td>
<td>Intermittent</td>
<td>Constant</td>
</tr>
<tr>
<td>Location Quality</td>
<td>Bilateral</td>
<td>Unilateral Pulsating quality</td>
<td>Varies</td>
</tr>
<tr>
<td>Intensity</td>
<td>Mild to moderate intensity</td>
<td>Moderate to severe intensity</td>
<td>Varies in severity</td>
</tr>
<tr>
<td>Precipitants</td>
<td>Not aggravated by routine physical activity such as walking or climbing stairs</td>
<td>Aggravation by physical activity</td>
<td>Headache has developed or markedly worsened during medication overuse</td>
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<tr>
<td>Nausea and/or vomiting</td>
<td>No (anorexia may occur)</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

**Medications causes**
All medicines used for the treatment of headache can cause medication overuse headache. This includes aspirin, paracetamol, opioids, triptans, NSAIDs and ergot alkaloids, alone or in combination with caffeine or benzodiazepines.

It is important that headaches due to overuse are distinguished from those which are caused directly by some medications, such as nitrates.

Medication overuse headache may be restricted to those who are already headache sufferers. Patients can fear a headache prior to work or a social event and take analgesics prophylactically, compounding the problem. This may be especially relevant to patients with migraine with aura or the headache phase of a migraine attack.
Migraine and tension-type headache have a higher potential for medication overuse headache. Patients with cluster headache almost never develop medication overuse headache.

Frequent use of medication for the treatment of acute migraine attacks may also cause medication overuse headache. The delay between first intake and symptoms of medication overuse headache is shortest for the triptans (1-2 years), longer for ergots (3-5 years) and longest for analgesics (5-10 years). This is mainly due to the differing timeframes for receptor and enzyme downregulation that occurs with frequent administration of different classes of analgesics.

**Risk factors**
People at risk for medication overuse headache include:

- patients with frequent migraine or tension-type headache
- patients with other morbidities such as arthritis
- patients with familial history of headache or genetic predisposition

**Questionnaire**
A questionnaire has been validated to detect medication overuse and dependence-like behaviour in people with chronic headache. These questions are designed to measure psychological dependence. Each item is scored on a 4-point scale (0-3) and the total maximum score is 15. A score of 4 for men and 5 for women can predict medication overuse.

1. Do you think your use of headache medication is out of control?
2. Does the prospect of missing a dose make you anxious or worried?
3. Do you worry about your use of your headache medication?
4. Do you wish you could stop?
5. How difficult would you find it to stop or go without your headache medication?

Taking a comprehensive medication history and exploring the psychosocial aspects is an important part of identification of medication overuse headache. The progression from intermittent headache to continuous or frequent, at least second daily, headache is a key aspect.

**Signs and symptoms**
Several features are helpful in identifying the occurrence of analgesic rebound headache:

- Headaches are refractory and occur daily or nearly daily
- Headache varies in severity, type and location from time to time
- Physical or intellectual effect may bring on headache
- Accompanied by asthenia, nausea or vomiting, restlessness, anxiety, irritability, memory problems, depression and concentration difficulty
- Evidence of tolerance (progressively higher doses needed)
- Withdrawal symptoms experienced when abruptly stop medications
- Spontaneous improvement with discontinuation
- Concomitant prophylactic medications relatively ineffective

Patients are less likely to have cravings or to escalate the quantity of medications taken as seen in drug dependency.
Behavioural change
Techniques such as motivational interviewing can explore and resolve ambivalence with patient behaviours. The patient recognises the risks but balances this out by saying the overuse helps with their pain. Some patients find it difficult to accept that the medication they use to treat their headaches is actually making it worse. Often attempts at drug withdrawal can perpetuate use.

Behavioural therapies may have a positive influence on the rate of headache recurrence. Psychotherapy, biofeedback, stress management, regular aerobic exercise or relaxation training may be beneficial.

Treatment
Treatment of medication overuse headache is withdrawal of the offending medication or medications. Abrupt drug withdrawal, which may need to be under medical supervision, is considered the treatment of choice for medication overuse headache.

A prospective study of a 2-month drug-free period showed that 45% of the patients has a reduced headache frequency, 48% had no worsening and only 7% experienced aggravation of the headache. In this study the original headache types leading to overtreatment included migraine (10%), tension-type headache (33%), both migraine and tension-type headache (43%), and other (14%). Patients with migraine had a better response to medication withdrawal.

Withdrawal symptoms typically last for 2 to 10 days and include withdrawal headache, nausea, vomiting, tachycardia, sleep disturbances, restlessness, anxiety and nervousness.

Patients may require drug treatment to alleviate withdrawal symptoms. This may include adequate hydration and anti-emetics, and short-term regular medications from a different class to the overused medication if unable to tolerate the withdrawal symptoms. Tricyclic antidepressants can be used to cover withdrawal of treatment from tension-type headaches (e.g. amitriptyline 10-25mg at night).

Prevention
The most important preventive measure is proper information and education to patients, and appropriate surveillance of patients. Regular follow-up is an important means of preventing recurrence. Pharmacists and pharmacy assistants should display a caring and encouraging attitude.

Relapse may be prevented through education of patients, use of headache diaries, extended medical supervision, restrictions on the intake of headache medications, primary headache prophylactic drugs and use of behavioural therapies. Relapse is most likely in the first 12 month following withdrawal. Patients overusing combination products are more likely to relapse.

Summary
Pharmacists and pharmacy assistants have a duty of care to ask patients about any other medicines they are using and to satisfy themselves that there are no contraindications to the use of OTC analgesics. All consultations with patient with headaches for OTC analgesic products require awareness of the possibility of developing medication overuse. Pharmacists should have a high index of suspicion in patients requesting frequent medications for headaches and support them appropriately.

Debbie Rigby
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MCQs

1. Which of the following statements regarding medication overuse headache is most appropriate?
   
a. Patients who complain of daily headaches may have medication overuse headache
   b. Medication overuse headache occurs in 10% of the population
   c. Autonomic symptoms are frequently associated with medication overuse headache
   d. Withdrawal of offending medications should occur slowly over extended periods of time

2. Which of the following set of symptoms best describes chronic tension-type headache?
   
a. Unilateral, throbbing pain worsened by activity
   b. Unilateral with severe excruciating pain
   c. Bilateral, pulsating pain of moderate to severe intensity
   d. Bilateral, non-pulsating pain of mild to moderate intensity

3. Risk factors for medication overuse headache include all of the following, except:
   
a. Frequent migraines
   b. Osteoarthritis
   c. Family history
   d. Obesity

4. Which of the following medications is most likely to be associated with medication overuse headache over a 1 to 2 year period of frequent use:
   
a. Paracetamol/codeine combination products
   b. Sumatriptan
   c. Ergotamine/caffeine
   d. Ibuprofen

5. Treatment of medication overuse headache includes:
   
a. Abrupt withdrawal of overused medication
   b. Low dose tricyclic antidepressant for withdrawal of treatment for tension-type headaches
   c. Antiemetics for management of nausea or vomiting
   d. All of the above
References