Ibuprofen and tension-type headache – exploring the evidence

An evidence-based summary
Introduction

Despite its high, global prevalence, headache still remains an under-recognised and under-treated condition. Around half of all headache sufferers self-manage without seeking medical advice, making headache a key area for pharmacy intervention.

Tension-type headache (TTH) is the most common type of headache, accounting for around 80% of all headaches.

Evidence in summary

- TTH is the most common of the headache disorders and it places a significant burden to society.
- The exact mechanism of TTH is not known, but referred pain from the peripheral muscles in the head and neck are believed to play a significant role, while tenderness in these muscles is also important in TTH development.
- Guidelines recommend NSAIDs, such as ibuprofen and aspirin, and paracetamol as a first-line drug treatment for episodic TTH.
- Ibuprofen provides effective and fast-acting pain relief in TTH and is more effective than paracetamol as acute therapy for TTH.
- Ibuprofen is as well tolerated as paracetamol. Ibuprofen, at OTC doses, does not need to be taken with food.

Understanding tension-type headache (TTH)

Identifying TTH

Headache is among the most common of all health conditions. The main types of headache are TTH, migraine, cluster and medication-overuse headache (MOH). Of all these types, TTH is the most common globally, with more than 80% of people affected at some time.

The symptoms of common headaches

Each of these types of headache has marked characteristics.

Table 1: International Headache Society primary headache classification

<table>
<thead>
<tr>
<th>TTH</th>
<th>Migraine</th>
<th>MOH</th>
<th>Cluster</th>
</tr>
</thead>
<tbody>
<tr>
<td>Also known as</td>
<td>Tension headache, muscle-contraction headache, stress headache, ordinary headache</td>
<td>Common migraine (without aura), classic migraine (with aura)</td>
<td>Rebound headache, drug-induced headache, medication-misuse headache</td>
</tr>
<tr>
<td>Area of head affected</td>
<td>Generally both sides, across the forehead, around the back of the head, the temples</td>
<td>Can be one side or both sides; most often one side in adults and both sides in children and adolescents</td>
<td>Can be one side or both sides</td>
</tr>
<tr>
<td>Pain severity</td>
<td>Mild-to-moderate</td>
<td>Moderate-to-severe</td>
<td>Varies through the day</td>
</tr>
<tr>
<td>Pain description</td>
<td>Pressing or tightening, non-pulsating</td>
<td>Pulsating (throbbing or banging in young people aged 12–17 years)</td>
<td>Dull pain, present and often worse on waking</td>
</tr>
<tr>
<td>Pain duration</td>
<td>30 minutes – 7 days</td>
<td>4–72 hours (adults), 1–72 hours (children and young people aged 12–17 years)</td>
<td>Not stated</td>
</tr>
<tr>
<td>Frequency of headache</td>
<td>&lt;15 days/month (episodic TTH) or a 15 days/month for ≥3 months (chronic TTH)</td>
<td>&lt;15 days/month (episodic migraine) or a 15 days/month for ≥3 months (chronic migraine)</td>
<td>Headache present on &gt;15 days per month in a patient with pre-existing headache disorder</td>
</tr>
<tr>
<td>Aura</td>
<td>None</td>
<td>Some sufferers experience aura symptoms (visual, sensory, speech/language, motor) for 5–60 minutes, with or up to an hour before headache onset</td>
<td>None</td>
</tr>
<tr>
<td>Other features</td>
<td>None, not aggravated by routine physical activity</td>
<td>At least one of the following: nausea, vomiting, aversion to light or sound. May be aggravated by routine activities of daily living</td>
<td>Regular overuse of one or more headache treatments for &gt;3 months. Can be accompanied by tiredness, irritability, feeling sick and/or difficulty sleeping</td>
</tr>
</tbody>
</table>

EVALUATE: What percentage of your patients purchases OTC analgesics for TTH and how does this disorder impact on their lives?
The implications of sensitisation of the central nervous system

The International Headache Society (IHS) states that peripheral mechanisms are associated with infrequent episodic TTH and that central mechanisms are more prominent in the development of chronic TTH. It has been shown that the central nervous system is sensitised in patients with chronic TTH. This is believed to be due to prolonged firing of the nerves in the head and neck muscles, causing sensitisation of the central pain pathways and reduction of the pain threshold, meaning normal stimuli are regarded as painful. This is thought to play a part in patients converting from an acute TTH to a chronic TTH. In short, muscles can play a role in the development of both acute and chronic TTH.

People with episodic TTH experiencing frequent headaches are at increased risk of developing chronic TTH. It is therefore important to intervene and treat TTH as early as possible before acute headaches evolve into a chronic headache disorder.

Knowing when to refer

It is important to identify the symptoms that need referral and further investigation in any individual, especially if patients have:

- A new headache, especially in patients who:
  - Are aged >50 years or <10 years
  - Have a compromised immune system (e.g. HIV positive patients)
  - Are vomiting for no reason
  - Have a history of cancer known to metastasise to the brain
  - Are <20 years old with a history of any type of cancer
  - Not previously experienced symptoms suggestive of migraine
  - A worsening headache with fever
  - Headache that comes on suddenly, like a thunderclap, reaching maximum pain in 5 minutes
  - Headache that develops after a head injury in the past 3 months
  - A headache which differs from the normal headache experienced by the customer – i.e. is new or unexpected
  - History of, or risk factors for, HIV or cancer
  - Headache with other symptoms like muscle weakness, change in personality, reduced consciousness, difficulty concentrating or remembering
  - Headache that changes with posture
  - Headache triggered by coughing, sneezing, exercising or breathing out with the nose and mouth blocked
  - Headaches that cause waking during sleep
  - Headaches with jaw pain plus visual disturbances
  - Headache with a painful red eye or misty vision
  - Headache with aura for the first time in a customer on combined oral contraceptives
  - Persistent morning headache with nausea
  - Progressive headache that gets worse over weeks or longer

**EVALUATE:** How does this knowledge change your understanding of the source of TTH?
How do analgesics work in relieving TTH?

Ibuprofen, and other NSAIDs, work by inhibiting prostaglandin synthesis in the peripheral and central pain pathways. Prostaglandins are one of the inflammatory mediators that are the source of pain in TTH. Due to their action on the peripheral pain pathways, NSAIDs, such as ibuprofen, are able to act on the muscular sources of TTH, in addition to their central action.

In contrast, paracetamol is believed to act primarily on prostaglandin production only in the central nervous system.

### Choosing effective treatment for TTH

#### How do analgesics work in relieving TTH?

Ibuprofen provides superior pain relief to paracetamol in TTH.

**Table 2: Mode of action of ibuprofen and paracetamol**

<table>
<thead>
<tr>
<th>Action</th>
<th>Ibuprofen</th>
<th>Paracetamol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acts centrally to inhibit prostaglandin production</td>
<td>✓25</td>
<td>✓26</td>
</tr>
<tr>
<td>Has anti-inflammatory action</td>
<td>✓20</td>
<td>✘27</td>
</tr>
<tr>
<td>Acts via the central nociceptive pathway</td>
<td>✓20</td>
<td>✓26</td>
</tr>
</tbody>
</table>

How does ibuprofen compare with paracetamol?

Ibuprofen provides superior pain relief to paracetamol in TTH.

In clinical studies, ibuprofen has demonstrated superior efficacy to paracetamol in relieving the pain of episodic TTH.

A double-blind, randomised trial compared single doses of ibuprofen (400 mg, n=153) to paracetamol (1000 mg, n=151) and placebo (n=151) (see Figure 2):

- Significantly more patients experienced complete headache relief with ibuprofen than with paracetamol or placebo.
- In addition, patients randomised to ibuprofen achieved complete headache relief significantly faster than those taking paracetamol or placebo.

How does ibuprofen compare with other OTC NSAIDs?

The EFNS have stated that the clinical data show little difference in efficacy between ibuprofen and other OTC NSAIDs in TTH. The EFNS have stated that it has not been possible to clearly demonstrate the superiority of any one NSAID in treating TTH.

Ibuprofen vs aspirin

Although there is limited evidence comparing aspirin with ibuprofen, some evidence suggests that they have comparable efficacy. A study compared ibuprofen 200 mg and aspirin 500 mg with placebo in 95 patients with mild-to-moderate migraine, episodic TTH, or both, who usually self-medicated with OTC analgesics.

In this double-blind, double-dummy trial:

- Ibuprofen was at least as effective after 150 minutes in the 65 patients who completed the study (see Figure 3).

Another randomised, double-blind trial of 108 patients with TTH compared ibuprofen 400 mg, ibuprofen 800 mg, aspirin 650 mg and placebo for 4 successive headaches, when a single dose was taken at the onset of the headache:

- Patients taking either ibuprofen dose or aspirin reported significant improvement in their pain scores 3 hours after taking the drug compared to placebo.
- The physician’s global assessment of overall efficacy of the trial medication based on responses to all 4 headaches indicated that both doses of ibuprofen were significantly superior to placebo.
Figure 3: Ibuprofen is as effective as aspirin in relieving migraine, TTH, or both headache types for up to 2 hours (as measured by patient-rated visual analogue scale).

Fast-acting formulations

Is a rapid onset of action important when treating TTH?

There are two reasons to consider time to onset of action when recommending an OTC analgesic for TTH:

- Treatment should be taken at the first sign of symptoms of an acute headache episode to gain relief as early as possible. Second only to efficacy, a fast-acting treatment is one of the most important functional benefits that patients want from their analgesics when treating headache (n=2000).8 Second only to efficacy, a fast-acting treatment is one of the most important functional benefits that patients want from their analgesics when treating headache.

- Treating an acute TTH early may also help prevent prolonged sensitisation of the central nervous system, which is thought to play a key role in the development of chronic TTH.8,9

What are the benefits of fast-acting formulations?

Fast-acting ibuprofen formulations, e.g. sodium ibuprofen and liquid-filled capsules, enhance ibuprofen absorption with earlier peak concentrations than standard formulations.10 This is due to the ibuprofen salts having a faster solubility than standard ibuprofen in studies of healthy individuals, increasing the rate of absorption into the bloodstream.11 Data show fast-acting ibuprofen formulations are absorbed twice as fast as standard ibuprofen.11,12

This also impacts on pain relief. As fast-acting formulations are absorbed into the bloodstream quicker, they provide faster onset of pain relief than standard ibuprofen.8,10

A systematic review published in 2014 compared single-doses of fast-acting formulations with standard ibuprofen tablets for acute pain. Results indicated that the fast-acting formulations:

- Achieved a faster onset of pain relief after dosing
- Ensured fewer patients needed additional pain relief within 6 hours of dosing
- Did not result in an increase in the number of patients reporting side-effects

Fast-acting formulations of ibuprofen demonstrated more rapid absorption, faster initial pain reduction, but with no higher rate of patients reporting adverse events

Moore – 2014

Figure 4: A meta-analysis indicated NNTs for fast-acting ibuprofen formulations are lower than with standard ibuprofen when compared with placebo in dental pain.

Adapted from Moore et al., 2014

Colour density change indicates the point estimate. Width of the bar indicates the 95% confidence interval (CI) of the NNT.

NNT = Number needed to treat, where 1 is the ideal analgesic
How does ibuprofen’s safety profile compare to other analgesics?

Ibuprofen has the lowest risk of GI side effects compared with all other OTC NSAIDs. At OTC doses up to 1200 mg/day, ibuprofen has a good GI safety profile and is better tolerated than aspirin, naproxen and diclofenac. In terms of cardiovascular (CV) effects, OTC dose ibuprofen and naproxen are least likely to increase CV risk among the widely used NSAIDs.

Ibuprofen, as well as other NSAIDs, is recommended by headache experts based on its efficacy and favourable safety profile.

In practice, this means that recommending a fast-acting ibuprofen formulation can deliver faster overall pain relief, compared to standard ibuprofen at the same dose.

EVALUATE: How does this information alter your perception of the safety of ibuprofen compared to paracetamol at OTC doses?
What is the recommended treatment for TTH

Simple analgesics are recommended as the first-line treatment choice in international and UK guidelines for acute TTH.2,4–8,12 Analgesic options available OTC include:38

- NSAIDs
  - ibuprofen
  - aspirin
  - naproxen
  - diclofenac
  - ketoprofen
- Paracetamol

What do the UK guidelines recommend?

<table>
<thead>
<tr>
<th>Organisation</th>
<th>Recommendation</th>
<th>Key quote</th>
</tr>
</thead>
<tbody>
<tr>
<td>The British Association for the Study of Headache (BASH)</td>
<td>Ibuprofen 400 mg Aspirin 600–900 mg</td>
<td>“Symptomatic treatment is appropriate for TTH occurring on less than 2 days per week”</td>
</tr>
<tr>
<td>The UK National Institute for Health and Care Excellence (NICE)</td>
<td>NSAIDs Aspirin Paracetamol</td>
<td>“…taking into account the person’s preference, comorbidities and risk of adverse events”</td>
</tr>
</tbody>
</table>

Table 3: UK guideline recommendations for first-line treatment of TTH

What do the European guidelines recommend?

The European Headache Federation (EHF) and the European Federation of Neurological Societies (EFNS) state that paracetamol may be less effective than NSAIDs.13 Data show that a 400 mg dose of standard ibuprofen tablets can start relieving TTH from 15 minutes.13 Ibuprofen 200–400 mg should be considered as a treatment of choice for TTH, provided NSAIDs are not contraindicated.

Combination treatments for TTH

A combination of aspirin + paracetamol + caffeine is recommended in some guidelines.6,11 Combination analgesics plus caffeine have been shown to increase the efficacy of analgesics.6,7 However, European guidance advises it is used only as a second-line option as caffeine-containing combinations are believed to be more likely to induce MOH than single OTC analgesics.8 These guidelines also state that codeine combinations should also be avoided for TTH for the same reason.2,6

The UK BASH guidelines consider analgesics containing caffeine and codeine to have an increased risk for the development of MOH.13

Simple analgesics and NSAIDs are the mainstays in the acute therapy of TTH. Paracetamol 1000 mg is probably less effective than the NSAIDs...

Ibuprofen 400 mg may be recommended as drug of choice amongst the NSAIDs

EFNS – 2010

How do patients believe about TTH management?

RB global market research has found that some individuals who suffer from TTH believe that medication should only be used when it affects their ability to concentrate, or that treating a headache may make them reliant on analgesics or negate their efficacy for more serious pain.41 Understanding more about patient behaviours can help pharmacy staff intervene more effectively.

Common mistakes patients make when treating their TTH

Since half of those who suffer from headache will opt to self-treat their headache without any consultation with a healthcare professional, it is important to consider what treatment decisions they may be making.

Treatment choice:

A survey of 2000 UK patients shows that twice as many people use paracetamol over ibuprofen as their TTH-relieving analgesic.28

The impact of TTH?

TTH affects both adults and children and although there is limited data and estimates vary with the latter, one 2007 review suggested that 1 in 3 children/adolescents suffer from TTH.22 Episodes commonly start in children at 7 years of age.20 Peak prevalence is between the age of 30–39 years and decreases slightly with age.5 Females are marginally more affected than men.5

TTH is estimated to exert a greater global burden with much larger disability worldwide compared with migraine.13 TTH, like other headaches, has a significant impact on quality of life; affecting family and social life and reducing productivity at work.38 A study showed that depression and anxiety have also been shown to be associated with migraine and non-migraine headaches, compared with headache free individuals.40

What do patients believe about TTH management?

Many patients want fast and effective pain relief for their TTH.28 In spite of this, a survey of 961 customers with headache, demonstrated that more than half of customers with headache delay taking analgesics until the pain is unbearable.28 In a UK survey of 2000 adults, 84% wait at least 20 minutes before taking any medication.43

Taking analgesics with food:

Ibuprofen is a pain reliever that can be taken with or without food, even on an empty stomach.20,44 Paracetamol can also be taken without food. However, other NSAIDs (e.g. diclofenac) do require administration with food.45,46

Understanding patients
There is also a broader socioeconomic and healthcare burden associated with TTH. European data found that the mean per person annual costs for TTH were €303.47. Indirect costs, such as reduced productivity and absenteeism from work, accounts for 92% of the cost of TTH.

Can pharmacy play a pivotal role in the management of TTH?

The management of TTH also places a large burden on healthcare systems. In Europe, outpatient care was listed as the top contributor to the direct costs of this type of headache.

The majority of customers with headache have a positive attitude towards OTC medications and feel that they are more adequate for acute headache than prescription medication. Ultimately, half of headache sufferers will opt to self-treat their headache without any consultation with a healthcare professional.

Although the pharmacist is well-placed to provide first-line advice on the management of the different types of headache, recent UK research (involving 2000 adults) revealed around half of sufferers have rarely or never sought advice from a pharmacist.

Better communication, through specific techniques, such as motivational interviewing, may increase patient engagement and encourage patients to seek advice from the pharmacy in the future. Pharmacy has a key role in improving patient care and reducing healthcare costs associated with TTH.

How can pharmacy make a difference?

A UK survey of 2000 adults revealed 86% of patients may be influenced by advice from their pharmacist. Furthermore, around three-quarters of people said they would change their treatments if they understood more about their headache. This allows the pharmacy team the opportunity to work with patients to optimise TTH management.

Pharmacists can suggest non-pharmacological options that can help reduce the likelihood of future headaches (e.g. avoiding triggers, relaxation techniques, improving posture).

Another key part of the pharmacist’s role in helping patients manage their TTH is to enquire about their current analgesic usage and emphasise the importance of avoiding MOH, i.e. ensuring the safe and appropriate use of any medications.

It is important to be aware of MOH and refer any customer you suspect might be affected to the pharmacist or their GP for further help. MOH is a chronic headache which results from taking too many analgesics routinely for a period of time. Customers regularly taking simple OTC pain relievers on 15 or more days per month or codeine-containing analgesics on 10 or more days per month are at risk of developing MOH.

In addition, pharmacists can signpost patients to their GP if there is evidence of any ‘red-flag’ symptoms that require further investigation (see page 5).

Helping patients choose appropriate treatment

In addition to gaining an accurate picture of the patient’s symptoms and concerns, another aspect is to understand what is motivating patient behaviours. Using motivational interviewing skills can help. This uses open-ended questions based around the following key principles:

- Expressing empathy with the patient’s suffering – this will require the pharmacy team to first determine that the analgesic being purchased is for TTH
- Identifying behaviours that may explain why relief is not optimal e.g. analgesic choice, delaying treatment (taking effective analgesics early in the course of a headache is important to relieve the pain before it becomes established)
- Not all patients will be happy to implement behaviour change at the pharmacist’s initial suggestion, but this can be discussed further in later consultations
- Supporting self-care

The role of the pharmacy

Alleviating the burden

Can pharmacy play a pivotal role in the management of TTH?
**Essential information:**

**Nurofen Express 400 mg Liquid Capsules:** Each capsule contains ibuprofen 400 mg. **Nurofen Express Soluble 400mg Oral Powder:** Each sachet contains 400mg ibuprofen (spirophylline). **Indications:**

**Nurofen Express Liquid Capsules:** For symptomatic relief of non-steroidal anti-inflammatory drug (NSAID)-induced, rheumatic or muscular pain, backache, neuralgia, migraine, headache, dental pain, dysmenorrhoea, feverishness, colds and influenza.

**Nurofen Express Soluble Oral Powder:** For the relief of mild to moderate pain associated with headache, migraine, fever, backache, period pain, dental pain, rheumatic and muscular pain, cold and flu symptoms such as sore throat and cough.

**Nurofen Express Soluble Oral Powder:** Adults, the elderly and children over 12 years: Initial dose – one sachet. Then, if necessary, one sachet up to three times a day as required. Dissolve the contents of the sachet in a glass of water, stir, and then drink immediately. Leave at least six hours between doses. Do not exceed more than 3 sachets (1200mg) in any 24 hour period. The patient should consult a doctor if symptoms persist or worsen, or if the product is required for more than 5 days for treating pain and 3 days for treating fever. Not for use by children under 12 years of age.

**Contraindications:** Known hypersensitivity to ibuprofen or other ingredients. History of bronchospasm, asthma, rhinitis, or urticaria, associated with aspirin or other non-steroidal anti-inflammatory drugs (NSAIDs).

**Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Reckitt Benckiser Healthcare (UK) Ltd on: 0500 455 456.**

**References:**