Efficacy and safety of over-the-counter analgesics in the treatment of common cold and flu

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SUMMARY

Rationale: Common cold and flu are the most common human illnesses, and over-the-counter (OTC) analgesics are widely used to treat the pain and fever symptoms. Despite the every day use of these analgesics there is little information available in the literature on the efficacy and safety of these medicines in treating colds and flu symptoms. The aim of this review was to determine the safety and efficacy of the analgesics, aspirin, paracetamol and aspirin for the treatment of colds and flu.

Methods: Electronic databases and a personal database were searched and the information retrieved together with information from relevant textbooks has been integrated in the review.

Results: The literature search established that there is relatively little information on the use of analgesics in treating colds and flu and that much of the safety and efficacy data must be related to other pain and fever models. The review establishes that aspirin, paracetamol and ibuprofen are safe in OTC doses and that there is no evidence for any difference between the medicines as regards efficacy and safety for treatment of colds and flu (except in certain cases such as the use of aspirin in feverish children). There is also no evidence that these medicines prolong the course of colds and flu by any effect on the immune system or by reducing fever.

Conclusion: Despite the lack of clinical data on the safety and efficacy of analgesics for the treatment of colds and flu symptoms a case can be made that these medicines are safe and effective for treatment of these common illnesses.

INTRODUCTION

The analgesics, aspirin, paracetamol and ibuprofen are widely used to treat symptoms of common cold and flu such as fever, sore throat pain, myalgia, headache, sinus pain, chilliness, and malaise, as non-prescription or over-the-counter (OTC) medicines. The OTC Directory lists 113 of a total of 263 treatments for coughs, colds and flu symptoms that contain these analgesics (1). Many of the medicines are household names (Alka-Seltzer, Anadin, Aspro, Beechams, Calpol, Day Nurse, Lemsip, Nurofen and Vicks). Despite the fact that these analgesics are the most commonly used treatments for common cold and flu, a recent review (2) on the common cold did not mention analgesics as a treatment for common cold, although mention was made of antihistamines, decongestants and anticholinergics that are also available as OTC medicines but are not as widely available as analgesics. Similarly in another review (3) on the therapy of the common cold, little mention of analgesics is made, apart from possible detrimental effects on the immune system. An explanation for lack of reference to analgesics for the treatment of colds and flu in reviews on this topic may be that there is little specific information on the safety and efficacy of analgesics in this disease state. Reviews on the safety and efficacy of OTC analgesics do provide an excellent source of information on treatment of pain and fever (4, 5) but provide little specific information on the role of analgesics in treating the symptoms of acute upper respiratory tract infections such as colds and flu.

This review will provide relevant information on the efficacy and safety of the analgesics aspirin, paracetamol and ibuprofen in the treatment of
symptoms of acute upper respiratory tract viral infection (URTI) (common cold and flu). Only placebo-controlled clinical trials will be discussed in the review for assessment of efficacy, but uncontrolled studies will be included for safety. Clinical trials that study the analgesics in combination with other medicines will be included if they also compare the efficacy of the analgesic alone against placebo. The dose ranges and safety information will be based on OTC products marketed in the United Kingdom. Common cold and flu for the purpose of this review are deemed to cover all URTI, and no differentiation is made between infections caused by common cold viruses such as rhinoviruses and influenza viruses as there is great overlap in the aetiology and symptomatology of common cold and flu syndromes, and they can all be referred to as URTI (6).

METHODS

Electronic literature searches were conducted on the PubMed database using the following terms: aspirin (acetylsalicylic acid), paracetamol (acetaminophen), ibuprofen; paired with common cold, influenza, fever, sore throat pain, safety, vaccination and review. The bibliographies of key publications were followed up, and a citation search was also conducted on ISI Web of Science database for key publications. The literature search used primarily articles in English but the abstracts and bibliographies of articles in other languages were also consulted and used in searches. The author also has an extensive database of references and this was also searched for the review as well as any relevant textbooks.

RESULTS

The searches identified a large amount of literature on pain and fever models other than URTI, and much literature on the prescription use of analgesics for treatment of chronic conditions such as rheumatoid arthritis. Much of this literature was not relevant to short courses of analgesics in OTC doses for treatment of URTI. The review therefore discusses why there is a lack of clinical data in this area, and uses the limited data on URTI trials and sore throat pain trials together with other acute pain and fever models to examine the safety and efficacy of the analgesics.

HISTORICAL PERSPECTIVE

One of the reasons that there are relatively few clinical trials and little clinical data on the effects of analgesics on the symptoms of URTI is that analgesics such as aspirin and paracetamol were used as treatments for these conditions before regulatory authorities required clinical trials to support efficacy and safety of medicines. Widespread use of aspirin for the treatment of URTI over a period of 100 years has lead to the acceptance that aspirin and similar analgesics, are effective and safe treatments, without any perceived need for further clinical trial support.

There is much clinical trial data that establishes the safety and efficacy of aspirin, paracetamol and ibuprofen in the treatment of fever and pain conditions such as postoperative dental pain (5) and it has been generally assumed that this data could be extrapolated to all forms of mild and moderate pain and fever including URTI. The assumption that inhibition of prostaglandin synthesis would help relieve all cases of fever and mild/moderate pain may also explain the lack of interest in conducting clinical trials on the efficacy of the analgesics on the treatment of fever and pain associated with URTI.

ASPIRIN

Efficacy in adults

The OTC dose range for aspirin in adults is from 325 to 1000 mg every 4–6 h with a maximum daily dose of 4000 mg (5).

Despite its present-day widespread use and the long medical history of the use of aspirin in the treatment of fever and pain associated with URTI, there is a lack of clinical data to support the efficacy of aspirin in the treatment of symptoms of URTI. The clinical trials that are available support the efficacy of aspirin in the treatment of sore throat pain associated with URTI.

Clinical studies by Schachtel et al. reported that aspirin was superior to placebo for the treatment of sore throat pain associated with URTI (7, 8). Both of the clinical trials were double blind and they
clearly demonstrated the superiority of single doses of aspirin (650 and 800 mg) above a placebo treatment, for relief of sore throat pain. The patient population studied by Schachtel et al. could be considered as having a more severe sore throat pain that normally associated with URTI in the general population seeking OTC treatments, as they were recruited from patients presenting to their family physician for treatment of sore throat pain. Thirteen of 150 patients in one trial (7) had positive throat cultures for group A beta-haemolytic streptococci but there was no suggestion that severity of sore throat pain was indicative of streptococcal pharyngitis.

In a double-blind placebo-controlled study on 279 patients suffering from sore throat pain associated with URTI a single dose of 800 mg aspirin was shown to be superior to placebo for relief of sore throat pain for up to 6 h after treatment (9). Although the clinical trial selected patients with sore throat pain associated with URTI the study demonstrated that aspirin was effective in treating other pain conditions. Headache was significantly reduced by 38%, and muscle aches and pains were significantly reduced by 38% following treatment with aspirin.

Sore throat pain has been accepted by European regulatory authorities as a suitable pain model for acute, mild–moderate pain, and therefore the results of the sore throat pain clinical trials are applicable to other forms of acute pain. Similarly the findings of a review on the efficacy of a single dose of aspirin for the treatment of acute pain should also be applicable to pain associated with URTI (10). In this Cochrane review the authors looked at the results of 72 clinical trials on post-operative pain and pain of acute trauma and concluded that ‘aspirin is an effective analgesic for acute pain of moderate to severe intensity with a clear dose response’ (10).

Aspirin has been used for over a hundred years for the treatment of fever associated with URTI and it is remarkable that there are so few clinical trials on the efficacy of aspirin in relieving fever associated with URTI. Early studies on the effects of aspirin on fever did not use a placebo control (11, 12) and this makes the interpretation of the results difficult. It is only recently that a placebo-controlled study has been conducted on the efficacy of aspirin in treating fever associated with URTI (13). Bachert et al. reported that single doses of 500 and 1000 mg aspirin were significantly better than placebo in reducing body temperature in patients with fever associated with URTI and they also reported significant relief of symptoms of headache, achiness and feverish discomfort (13).

**Efficacy in children**

Although there are some older studies on the efficacy of aspirin in children (14, 15), because of the risk of Reye’s syndrome (see below) aspirin is not recommended for use in children under 16 except on medical advice.

**PARACETAMOL**

**Efficacy in adults**

The OTC dose range for paracetamol in adults is from 325 to 1000 mg every 4–6 h with a maximum daily dose of 4000 mg (5).

Despite the introduction of many new analgesics, paracetamol is still one of the most widely used analgesic–antipyretic agents. Paracetamol is a first-line choice for many clinicians for pain management and control of fever in a variety of patients, including children, pregnant women, the elderly, and those with osteoarthritis (16). There is increasing support by clinicians for ibuprofen to replace paracetamol as a first-line treatment for fever in infants and children (17).

Paracetamol has been shown to be effective in relieving mild to moderate pain such as headache, toothache, dysmenorrhoea, and a variety of post-surgical pain in a dose range of 650–1300 mg in a wide variety of controlled clinical trials (5, 18–20).

Paracetamol has been shown to be effective in the symptomatic relief of sore throat pain and fever associated with URTI. In a double-blind placebo-controlled clinical trial on subjects with sore throat pain associated with URTI, Schachtel et al. demonstrated that a single dose of paracetamol of 650 mg in 13 subjects caused a highly significant reduction in subjective scores of sore throat pain with no reported adverse effects (7). In a similar double-blind placebo-controlled clinical trial on subjects with sore throat pain associated with URTI, Schachtel et al. demonstrated that a single dose of 1000 mg paracetamol in 40 subjects caused
a highly significant reduction in subjective scores of sore throat pain with no adverse effects (21). In the latter trial the 1000 mg dose of paracetamol was shown to provide subjective relief from sore throat pain for up to 6 h.

Bachert *et al.* reported that single doses of 500 and 1000 mg paracetamol were significantly better than placebo in reducing body temperature in patients with fever associated with URTI and they also reported significant relief of symptoms of headache, achiness and feverish discomfort (13).

**Efficacy in children**

Paracetamol is especially useful for the treatment of pain and fever in infants and children, where it has a superior safety record to aspirin as regards Reye’s syndrome (16). Typical recommended doses for paracetamol in the United Kingdom for infants and children are given in Table 1. Most of the clinical data regarding the efficacy of paracetamol in the treatment of fever in children has been generated from clinical trials aimed at comparing the efficacy of the newer antipyretic ibuprofen with that of the established children’s antipyretic paracetamol (22, 23). In a double-blind placebo-controlled trial on children aged 2–12 years, a single dose of paracetamol 15 mg/kg was shown to be superior to placebo for treatment of sore throat pain and fever associated with URTI (24). In a review of the first 40 years of paracetamol use in children the authors state ‘paracetamol remains the first-choice OTC treatment for analgesia and antipyresis in children’ (25).

**IBUPROFEN**

Ibuprofen has a relatively short history as treatment for URTI as the medicine only achieved OTC status in the United Kingdom in 1983. Despite its short history as an OTC medicine it has quickly achieved popularity as a treatment for URTI in both adults and children, both as a single ingredient and in combination with pseudoephedrine. Although the efficacy of ibuprofen has been established in various pain and fever models there is very little information available as regards its efficacy in treating pain and fever specifically associated with URTI.

**Efficacy in adults**

The OTC dose range for ibuprofen in adults is from 200 to 400 mg every 4–6 h with a maximum daily dose of 1200 mg (5).

The efficacy of ibuprofen as an analgesic has been shown in a range of pain models such as post-surgical dental pain where there is a clear dose–response relationship between 200 and 400 mg doses (5, 26). Analgesic efficacy has also been demonstrated in sore throat pain associated with URTI, and in fever and pain symptoms associated with naturally acquired URTI. A single dose of ibuprofen 400 mg was shown to provide superior relief to placebo for sore throat pain associated with URTI for up to 6 h (21). In a clinical trial on 80 patients with naturally acquired URTI ibuprofen 400 mg three times daily was shown to cause a significant reduction in symptom severity of headache, earache, muscle/joint pain, and sneezing as well as a reduction in body temperature (27).

**Efficacy in children**

Ibuprofen is now widely used for the treatment of pain and fever in children and the efficacy of ibuprofen has been mainly established by comparison with treatment with paracetamol rather than in placebo-controlled trials. Typical recommended doses for ibuprofen in the United Kingdom for infants and children are given in Table 2. In a double-blind study, multiple doses of ibuprofen

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**Table 1.** Paracetamol. Typical doses for infants and children

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose (mg)</th>
<th>Doses/day frequency</th>
<th>Maximum dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 months&lt;sup&gt;a&lt;/sup&gt;</td>
<td>60</td>
<td>2</td>
<td>120</td>
</tr>
<tr>
<td>&lt;3 months</td>
<td>60</td>
<td>2</td>
<td>120</td>
</tr>
<tr>
<td>3 months to &lt;1 year</td>
<td>60–120</td>
<td>4</td>
<td>480</td>
</tr>
<tr>
<td>1 to &lt;6 years</td>
<td>120–240</td>
<td>4</td>
<td>960</td>
</tr>
<tr>
<td>6–12 years</td>
<td>250–500</td>
<td>4</td>
<td>2000</td>
</tr>
<tr>
<td>&gt;12 years</td>
<td>500–1000</td>
<td>4</td>
<td>4000</td>
</tr>
</tbody>
</table>

<sup>a</sup>May be given for fever following vaccination at 2 months. Two doses may be given for other causes of pain or fever if infant is >4 kg body weight and not born before 37 weeks of gestation. Medical advice should be sought for further doses.
20 mg/kg/24 h were compared with paracetamol 50 mg/kg/24 h given at six hourly intervals, and the study concluded that ibuprofen suspension was as effective and well tolerated as paracetamol in treatment of fever in young children aged between 0.2 and 12 years (28). This result is supported by several other comparative studies (22, 23). In a double-blind placebo-controlled trial on children aged 2–12 years, a single dose of ibuprofen 10 mg/kg was shown to be superior to placebo for treatment of sore throat pain and fever associated with URTI (24).

**SAFETY**

In considering the safety of the analgesics for treatment of symptoms of URTI it is necessary to understand that much of the concern over the use of non-steroidal anti-inflammatory drugs (NSAIDs) such as aspirin and ibuprofen is related to long-term therapy with higher doses than available for OTC use, for example in the treatment of rheumatoid arthritis. Similarly concerns about the safety of paracetamol are often linked to alcohol abuse and overdose. Because of the limited number of trials on the use of analgesics in patients with URTI it is necessary to rely on safety data gathered from trials on other indications than URTI. These data will not be dealt with in detail as the reader can obtain the relevant safety data from comprehensive review articles (4, 5) and textbooks (29, 30). Only general concerns about safety of OTC doses of analgesics for treatment of URTI will be highlighted in this review. In one of the few reports to provide information on the safety of aspirin, paracetamol and ibuprofen when used in the treatment of cold and flu symptoms the authors report that ‘ibuprofen used at OTC doses is as well tolerated as paracetamol and much better tolerated than aspirin’ (31). However, the conclusions need to be qualified as the report is part of a sub-set analysis on 1705 patients from a larger study on 8677 patients (32) and the report is directed towards demonstrating the greater tolerability of ibuprofen above aspirin in OTC doses (31). In general the report provides support for the tolerability of all three analgesics for treatment of cold and flu symptoms, as the incidence of significant adverse events is similar for the three analgesics (aspirin 15.7%, ibuprofen 12%, and paracetamol 12.3%).

Hypersensitivity reactions to analgesics (e.g. asthma, rhinitis, angiodema or urticaria) are rare but can be serious, and patients are more likely to exhibit these responses to NSAIDs than paracetamol. NSAIDs, because of their peripheral inhibition of COX, are also more likely than paracetamol to have effects on the renal system. NSAIDs such as aspirin and ibuprofen may produce mild renal side-effects, such as the generation of peripheral oedema in up to 5% of the general population (33).

**Aspirin**

Gastrointestinal irritation, nausea and vomiting may occur in sensitive subjects, and gastrointestinal bleeding is associated with aspirin use, especially when taken with alcohol (5). Although aspirin is often implicated in gastrointestinal bleeding, the risk attached to aspirin consumption needs to be kept in perspective, as considering the widespread use of aspirin, the number of cases of gastrointestinal bleeds is very small with only 700 cases per annum in the United Kingdom (34). Hypersensitivity to aspirin may occur in some individuals and in persons with asthma. Prevalence of aspirin-induced asthma is 21% for adults and 5% for children according to a systematic review (35). Aspirin should not be used by patients with a bleeding tendency, i.e. with severe hepatic damage, hypoprothombinaemia, vitamin K deficiency or haemophilia (36, 37). Individuals with gout should avoid using aspirin as it may antagonize the action of gout medications (37).

<table>
<thead>
<tr>
<th>Age</th>
<th>Dose (mg)</th>
<th>Dose frequency (per day)</th>
<th>Maximum dose (mg)/24 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>3–6 months</td>
<td>50</td>
<td>3</td>
<td>150</td>
</tr>
<tr>
<td>6–12 months</td>
<td>50</td>
<td>3</td>
<td>150</td>
</tr>
<tr>
<td>1–3 years</td>
<td>100</td>
<td>3</td>
<td>300</td>
</tr>
<tr>
<td>4–6 years</td>
<td>150</td>
<td>3</td>
<td>450</td>
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<tr>
<td>7–9 years</td>
<td>200</td>
<td>3</td>
<td>600</td>
</tr>
<tr>
<td>8–12 years</td>
<td>200</td>
<td>3–4</td>
<td>800</td>
</tr>
<tr>
<td>&gt;12 years</td>
<td>200–400</td>
<td>3–4</td>
<td>1200</td>
</tr>
</tbody>
</table>

*Not suitable for infants <3 months unless advised by a doctor.

*bLeave at least 4 h between doses.
**Paracetamol**
At OTC doses, paracetamol is well tolerated, and seldom causes adverse events (16). With doses of 4000 mg/day paracetamol there is no evidence of any adverse effect on the liver but overdose of paracetamol is known to be hepatotoxic (38). Hepatotoxicity is a complication of both chronic alcohol use and paracetamol overdose, and some labels recommend ‘that patients who consume three or more alcoholic drinks per day contact their physician before ingesting paracetamol’ (5).

**Ibuprofen**
It is a generally held view among clinicians including gastroenterologists that all NSAIDs pose a risk to the gastrointestinal tract (GIT), but NSAIDs vary greatly in their adverse event profile, and in general ibuprofen is well tolerated in OTC doses and is ranked lowest amongst prescription NSAIDs for its effects on the GIT (39). The literature does not indicate that there is any risk of serious GIT bleeding and damage with short courses of OTC doses of ibuprofen (5, 39, 40). OTC ibuprofen has an excellent side-effect profile in multiple-dose use, with a frequency of gastrointestinal adverse events comparable to a placebo (40) and less than paracetamol (41). In a sub-set analysis on patients with cold and flu symptoms from a larger study (described above), the authors conclude that ibuprofen is as well tolerated as paracetamol and much better tolerated than aspirin (31).

**Pregnancy and lactation**
There is no evidence to indicate any specific contraindications to the use of paracetamol during pregnancy and therapeutic doses do not seem to present a risk to nursing infants (5, 20). However, as with all drugs, paracetamol should be used in pregnant or lactating women only on the advice of a physician. Aspirin and ibuprofen should be avoided during pregnancy.

**Children**
Paracetamol and ibuprofen are the medicines of choice for use in children and aspirin is not recommended. Considerable evidence implicates aspirin as an important factor in the severe hepatic injury and encephalopathy observed in Reye’s syndrome (42, 43). Reye’s syndrome is a very rare but frequently life-threatening disease typically observed after a virus infection (especially chickenpox or influenza).

In a review on the literature of the first 40 years of paracetamol use in children the authors conclude that ‘paracetamol remains the first-choice OTC treatment for analgesia and antipyresis in children’ and that ‘when used in the recommended doses, it has few side-effects and is remarkably well tolerated’ (25).

Reports on the safety of ibuprofen in children indicate that the medicine is safe and well tolerated. A meta-analysis of 17 clinical trials concluded that ‘in children, single doses of ibuprofen (4–10 mg/kg) and acetaminophen (7–15 mg/kg) have similar efficacy for relieving moderate to severe pain, and similar safety as analgesics or antipyretics’ (22). In a comprehensive review on the safety of paracetamol and ibuprofen 10 clinical trials are listed on 544 children between 4 and 15 years age, dosed for 1–5 days, and the only striking feature of the data was a higher adverse event rate in children under 4 years of age, with several of these events being febrile seizures, which the medicines were being taken to prevent (4). In a general practitioner-based randomized clinical trial a total of 27 065 children less than 2 years of age were treated for fever with either; paracetamol (12 mg/kg), ibuprofen (5 mg/kg) or ibuprofen (10 mg/kg) and the authors concluded that the risks of serious adverse events were small with these treatments (44). This study represents the largest randomized clinical trial on the safety of paracetamol and ibuprofen in children less than 2 years old and it provides reassuring safety data on these medicines in this age group (44).

In one of the few studies on children (2–14 years) with URTI and fever, the authors conclude that paracetamol (10 mg/kg) and ibuprofen (10 mg/kg) when given three times a day for 5 days were remarkably well tolerated, and there were no drug-related side-effects recorded, including haematological abnormality and hepatotoxicity (45). This study was a small, uncontrolled trial, involving only 30 patients in each treatment group but it does provide some reassuring safety data specific for URTI.
Elderly

Most of the information about the safety of analgesics in the elderly is related to chronic use for treatment of pain, particularly osteoarthritis and other musculoskeletal disorders. There is also information regarding the use of low-dose aspirin. Although the elderly may differ from younger adults in the rate of metabolism and excretion of analgesics (46), no information has been found in the literature to indicate that there are any increased risks in using these analgesics in the elderly in OTC doses for short courses for treatment of URTI symptoms. In a comprehensive review on the safety of paracetamol and ibuprofen three clinical trials are listed on 58 patients over 60 years of age using the analgesics for up to 7 days and no adverse events are reported (4). Interactions with concomitant medications may be more of a problem in the elderly because of the greater number of medications taken by the elderly compared with younger adults, but no specific problems have been raised in the literature, assuming that the patients follow the normal label contraindications.

EFFECTS ON THE IMMUNE SYSTEM AND COURSE OF URTI

High doses of NSAIDs have a depressant action on the immune response and this is beneficial in diseases such as rheumatoid arthritis where the autoimmune response causes damage to joints. However, a depressant action on the immune system would not be beneficial in the treatment of URTI, and analgesics are sometimes implicated in prolonging the course of infections, especially when the infection is associated with fever (47). A study using rhinovirus challenge as a model of URTI has reported that aspirin and paracetamol in OTC doses suppress the serum neutralizing antibody response but do not influence viral shedding (48). In the same study OTC doses of ibuprofen had no effect on the antibody response (48). Studies on effects of analgesics on viral shedding in rhinovirus challenge models have produced conflicting results with one study reporting that aspirin increases viral shedding (49) and others showing no effect (11, 48). There is no evidence that paracetamol and ibuprofen influence viral shedding.

In a study using rhinovirus challenge in healthy volunteers daily doses of aspirin (325 or 650 mg) did not influence the course of infection or the incidence of seroconversion, but there was some evidence that aspirin enhanced the production of the cytokines interferon-gamma and interleukin-2 (50).

There is no evidence that treatment with analgesics interferes with the natural recovery from URTI but there are reports that aspirin and paracetamol may increase the severity of the symptom of nasal obstruction associated with URTI. A single dose of 900 mg aspirin has been reported to cause an increase in nasal resistance to airflow in healthy volunteers (51) and there is one report that daily doses of 4000 mg aspirin and paracetamol caused nasal congestion when used by volunteers infected via rhinovirus challenge (48).

Fever is often associated with URTI, especially in infants, and analgesics are usually taken to control the severity of the fever. Fever is a normal physiological response to infection (52) and a case can be made that antipyretics by reducing body temperature may prolong an infection by interfering with normal host defences (53). Despite much interest in the role of fever and antipyretics such as aspirin, paracetamol and ibuprofen in the course of infections, there is still no clear consensus of opinion on the benefits and risks of antipyretic therapy (53). In a review on the toxicity of antipyretics the author concluded ‘Given the frequency of antipyretics use for the treatment of fever and the relative paucity of adverse events associated with such therapy, treatment of fever with antipyretic agents should be considered as safe’ (54). However, the author gave the usual caveats about care regarding the use of aspirin and Reye’s syndrome and cautions as regards use in patients with liver or renal failure (54).

Studies on the antibody response to influenza vaccination have not shown any effect of a single dose of 650 mg paracetamol on the immune response (55).

DISCUSSION

Paracetamol, aspirin and ibuprofen are probably the most frequently used medicines throughout the world, and are commonly used for the treatment of pain and fever associated with URTI. There is
relatively little clinical data on the use of these analgesics in URTI but the efficacy and safety of the medicines can be established from other pain and fever studies in adults and children. The transferability of efficacy data from one pain/fever model to another is possible because the analgesics have a common mode of action on pain and fever. Analgesics that are efficacious in the treatment of dental pain are also likely to be efficacious in the treatment of pain associated with sore throat, and similarly fever associated with chickenpox can be treated with analgesics in the same way as fever associated with influenza. The same transferability of safety data can be used to establish safety for short courses of analgesics in the treatment of URTI but there are some caveats and precautions necessary. Aspirin is safe for treatment of fever in adults but is not recommended for treatment of fever in children because of the rare but serious consequences of Reye’s syndrome.

**Which analgesic is the best?**

Aspirin was the only treatment available for treatment of URTI for the first 50 years of the 20th century. With the licensing of paracetamol for OTC use in the 1960s aspirin was displaced as the first-line treatment for pain and fever by paracetamol, which became the dominant OTC analgesic, especially for children and infants. Ibuprofen has subsequently competed with paracetamol as the first-line treatment in children for pain and fever. Its longer duration of action than paracetamol (56) makes it especially suitable for night-time dosing. Ibuprofen has also competed with aspirin as the first-line OTC NSAID, as due to its transition from a prescription NSAID to an OTC medicine, it is perceived to have have anti-inflammatory properties even if these are not substantiated with clinical data at OTC doses.

There are several studies comparing the relative efficacy of the analgesics in pain (57–59) and fever (28, 60–62) models, and although some studies show superiority of one analgesic above the other for either pain or fever relief, there is no consistent superiority of one above the other.

Aspirin and ibuprofen are often viewed as causing gastrointestinal irritation and bleeding whereas paracetamol is viewed as a safer option, especially in any patients with a history of gastrointestinal bleeding. The interactions of aspirin and ibuprofen with anticoagulants also mean that these medicines are contraindicated in patients on anticoagulant therapy. Hypersensitivity reactions such as asthma and rhinitis are more common with aspirin and ibuprofen than paracetamol.

Analgesics, because of their OTC status are sometimes overdosed in attempts of self-harm or suicide. This has brought about regulatory control over the maximum number of doses of paracetamol available in single packs (63). Because of the hepatotoxicity of paracetamol, overdose with this medicine is of particular concern.

**CONCLUSIONS**

There is little specific clinical data on the safety and efficacy of analgesics for treatment of cold and flu symptoms, but the efficacy and safety of the medicines can be established from limited studies in the disease state and from other pain and fever studies in adults and children. No convincing case can be made for a difference in efficacy between the analgesics in the treatment of pain and fever associated with URTI. There is also little evidence for any difference in overall safety between the analgesics, although special cases can be made for contraindications such as for aspirin in children, and for paracetamol in cases of excess alcohol intake.

**REFERENCES**


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