
Efficacy and safety of ibuprofen and acetaminophen in children and adults: a meta-analysis and qualitative review

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CRD summary

The review found that ibuprofen was similarly or more efficacious than acetaminophen for treatment of pain and fever in adults and children and was equally safe. The authors' cautious conclusions reflected the evidence presented, but shortcomings in the review process, a lack of quality assessment and substantial clinical differences made the reliability of the conclusions unclear.

Authors' objectives

To evaluate the analgesic and antipyretic efficacy and safety of ibuprofen compared with acetaminophen in children and adults.

Searching

PubMed (to August 2009) and EMBASE (to January 2008) were searched. Searches were restricted to studies in English. Search terms were reported. Reference lists of retrieved review articles were searched.

Study selection

Eligible studies were prospective or retrospective clinical trials that included efficacy and/or safety data (adverse events) in a direct comparison of ibuprofen with acetaminophen for treatment of pain or fever. Studies that included concomitant medication use were excluded.

In the included studies, single dose ibuprofen ranged from 200mg to 600mg. Several studies used at least one dose of more than 600mg for adult pain and temperature reduction. Ibuprofen doses in children were mostly based on weight; and ranged from 5mg/kg to 20mg/kg (some studies used fixed doses). Acetaminophen doses ranged from 500mg to 1,300mg per dose in adults and from 10mg/kg to 40mg/kg per in children. For pain reduction in adults, participants had experienced a range of surgical procedures or had menstrual pain, joint pain, headache, sore throat, cancer pain or experimentally induced pain. Antipyretic treatment in adults was used mostly to reduce interferon-mediated fever and headache in participants with multiple sclerosis; it was also used for participants with acute ischemic stroke and malaria. Additional conditions in children included musculoskeletal trauma, vaccination pain and discomfort from fever. Most studies considered participants under 18 years to be children and those over 18 years to be adults. Pain, fever and adverse events were defined according to the authors of the individual studies.

The authors did not state how studies were selected for the review.

Assessment of study quality

The authors did not state whether they assessed the included studies for quality.

Data extraction

Study data were extracted and separated into paediatric and adult studies. For inclusion in meta-analysis for continuous measures of temperature or pain visual analogue scores, standardised mean differences (SMDs) were calculated with their 95% confidence intervals (CIs) for all measurement times as the acetaminophen mean minus the ibuprofen mean (where reported). For pain studies, the measurement time of two hours post first dose was used (where reported) or the post baseline time nearest to the two-hour time point. For fever studies, the four-hour time point was measured (where reported). Odds ratios (ORs) and their 95% CIs were calculated for the proportion of participants who experienced at least one adverse event and at least one serious adverse event. Where no adverse events were observed in a treatment arm, 0.5 was added to each cell of the contingency table to enable calculation of odds ratios. For all other studies not included in meta-analysis, results of the individual studies were extracted.

The authors did not state how they undertook data extraction.

Methods of synthesis

Randomised controlled trials (RCTs) were pooled in meta-analyses. RCTs in which data were summarised graphically were not included in meta-analyses. Summary odds ratios were calculated using the Mantel Haenszel estimator only if a statistical test of heterogeneity was not significant. Weighted overall SMDs were calculated according to Hedge's g_u measure. Conclusions from the other studies were pooled qualitatively in narrative format. Conclusions that indicated differences between treatments from the individual studies had to be supported by significant p values or CIs; otherwise the two treatments were considered equally efficacious and/or safe.

Funnel plots were created for the assessment of publication bias and heterogeneity.

Results of the review

Eighty-five studies were included in the review. Fifty-four studies (n=7,603 participants) assessed the effects of treatments on pain (36 in adults and 18 in children). Thirty-five studies (n=3,985) assessed the effects of treatments on fever (five in adults and 30 in children). Sixty-six studies (n not reported) assessed the adverse effects of treatments, 35 in adults and 31 in children.

Pain in adults: Twenty-six studies concluded that ibuprofen was superior to acetaminophen and 10 reported no significant difference between treatments. In the meta-analysis of RCTs, ibuprofen was associated with a significantly lower pain score than acetaminophen at two hours post dose (SMD 0.69, 95% CI 0.57 to 0.81; nine studies), which corresponded to a medium effect size using Cohen's rule of thumb.

Pain in children: Six studies concluded that ibuprofen was superior to acetaminophen, 11 studies reported no significant difference between treatments and one study found a significant difference for ibuprofen only on the day of surgery and not at later time points. In the meta-analysis of RCTs, ibuprofen was associated with a significantly lower pain score than acetaminophen at two hours post dose (SMD 0.28, 95% CI 0.10 to 0.46; six studies), consistent with a small effect size according to Cohen's rules.

Fever in adults: Three studies concluded that ibuprofen was superior to acetaminophen and two studies reported no significant difference between treatments (five studies). No meta-analysis was performed.

Fever in children: Fifteen studies concluded that ibuprofen was superior to acetaminophen and 15 studies reported no significant difference between treatments. In the meta-analysis of RCTs, ibuprofen was associated with significantly lower fever scores at four hours post dose (SMD 0.26, 95% CI 0.10 to 0.41; seven studies), consistent with a small effect size using Cohen's rules.

Adverse events in adults: No studies found evidence of a significant difference between ibuprofen and acetaminophen in the incidence of one or more adverse events (35 studies). In the meta-analysis of RCTs, ibuprofen was associated with a lower (but not statistically different) incidence of adverse events than acetaminophen (OR 1.12, 95% CI 1.00 to 1.25; 25 studies), consistent with a small effect size using Cohen. One study found no difference in the rate of serious adverse events between treatments.

Adverse events in children: Twenty-nine studies found no evidence of a significant difference between ibuprofen and acetaminophen in the incidence of one or more adverse events. One study concluded that acetaminophen was safer or better tolerated than ibuprofen. In the meta-analysis, there was no evidence of a difference in the rates of adverse events between ibuprofen and acetaminophen (OR 0.82, 95% CI 0.60 to 1.12; 19 studies). Two studies found no evidence of a difference in the rate of serious adverse events between treatments.

Authors' conclusions

Ibuprofen was similarly or more efficacious than acetaminophen for treatment of pain and fever in adults and children and was equally safe.

CRD commentary

The review addressed a clear research question. Broad inclusion criteria appeared appropriate. A range of relevant sources was searched with appropriate search terms for studies published in English; language bias could not be excluded. The authors stated that funnel plots were performed for assessment of publication bias, but did not report the results of these analyses and investigators did not contact authors for missing information in the individual studies;

publication bias could not be excluded. Methods for study selection, quality assessment and data extraction were not reported; reviewer error and bias could not be ruled out. No quality assessment was performed, which made it difficult to determine the reliability of the conclusions. Participants had a wide range of conditions that warranted treatment. There was wide variation in doses and timing of treatments. No subgroup analysis was performed to determine differential effects. Adverse effects were defined and reported in different ways in the studies, which added to the difficulty of quantitative assessment of the proportion with one or more adverse events. The included studies used variable time points for the assessment of effects of treatments; the authors chose early time points (two hours for pain effects and four hours for fever effects post dose) based on the inclusion of the maximum number of studies in the analyses.

The authors performed meta-analyses with RCTs and presented both the results of the meta-analyses and a narrative synthesis of all studies by reporting the proportion of all studies that found significant differences between treatments and the proportion that did not find statistical evidence of a difference. The quantitative assessments by meta-analyses were mostly based on studies of short duration, which made reliable conclusions about safety over longer time points difficult. The authors reported that statistical heterogeneity was assessed for the meta-analyses, although neither the test used nor the results were reported. One of the authors was employed by Cumberland Pharmaceuticals in Nashville, Tennessee.

The authors' cautious conclusions reflected the evidence presented, but shortcomings in the review process, a lack of quality assessment and substantial clinical heterogeneity made the reliability of the conclusions unclear.

Implications of the review for practice and research

The authors did not state any implications for practice and research.

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