Acetaminophen and ibuprofen for prevention of adverse reactions associated with childhood immunization

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CRD summary
This review investigated use of acetaminophen and ibuprofen for prevention of adverse reactions associated with childhood immunisation. The authors concluded that acetaminophen and ibuprofen may prevent adverse events in young infants receiving diphtheria-tetanus toxoids-whole pertussis vaccine. No benefits were demonstrated for the diphtheria-tetanus toxoids acellular pertussis vaccine. The conclusions may not be reliable due to methodological limitations.

Authors' objectives
To evaluate prophylactic use of acetaminophen and ibuprofen for prevention of adverse reactions associated with childhood immunisation.

Searching
MEDLINE (1966 to February 2007), PubMed (1966 to March 2007) and EMBASE (1980 to 2007) were searched without language restrictions. Search terms were reported. Retrieved articles were cross-referenced and bibliographies checked.

Study selection
Studies of infants and children were eligible for inclusion. Randomised controlled trials that investigated prophylactic acetaminophen or ibuprofen compared with placebo or control for the diphtheria-tetanus toxoids-whole pertussis (DTwP) vaccine or diphtheria-tetanus toxoids-acellular pertussis (DTaP) vaccine were included. Various doses and dosing regimens were reported. Acetaminophen or ibuprofen were given before and after vaccination in most studies. Study participants were between two months and six years old.

The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors stated neither how the data were extracted for the review nor how many reviewers performed the data extraction.

Methods of synthesis
The studies were combined in a narrative synthesis by type of prophylaxis and type of immunisation. The study details were also presented in tables.

Results of the review
Five randomised controlled trials (n=1,625) were included in the review.

Three randomised controlled trials (n=997) investigated the difference in adverse effects between acetaminophen and placebo for the DTwP vaccine; two studies found that in infants aged two to six months the overall incidence of fever (at least 38°C) and fussiness (irritability) were significantly decreased with acetaminophen. One trial reported a significant decrease in the overall incidence of high fever (at least 39°C), local redness greater than 2 cm, crying, moderate to severe pain and anorexia. One trial found no difference in fever or any other adverse reactions between placebo and treatment groups.
One randomised open-label study that investigated prophylactic ibuprofen versus control for the DTwP vaccine (n=256) found ibuprofen was associated with a significant improvement in crying, pain, fussiness, drowsiness and induration. The incidence of fever, redness, oedema, vomiting, diarrhoea and anorexia was no different between groups.

The one randomised controlled trial (n=372) that investigated acetaminophen and ibuprofen for the DTaP vaccine found no significant difference in adverse reactions between either treatment and placebo in the two days following vaccination. There was no difference in itchiness between groups during the six days after vaccination.

**Authors' conclusions**

Prophylactic acetaminophen and ibuprofen may reduce the incidence of adverse events in young infants receiving DTwP vaccine. No benefits have been demonstrated for the DTaP vaccine.

**CRD commentary**

The review question was clear with regard to participants, but there were no inclusion criteria for study design or intervention which may have led to subjective decisions during study selection. Several databases were searched in any language, reducing the risk of language bias. The authors did not report searching for unpublished studies, which may have introduced publication bias. The authors also did not report any assessment of study quality. Details of the review process were not reported, so it was not known whether steps were taken to minimise bias and error. The applicability of the results to infants was limited as significant results were only found for infants aged two to six months. Details of how the outcomes were measured were not provided, so it was not known how objective these were. The clinical relevance of the vaccines investigated may also be questionable as DTwP has been replaced with DTaP in practice in North America and DTaP was investigated in only one study. The methodological limitations suggested that the authors' conclusions may not be reliable.

**Implications of the review for practice and research**

Practice: The authors stated that individuals at high risk for seizures may warrant special consideration for use of prophylactic acetaminophen and ibuprofen, as recommended by the ACIP (Advisory Committee on Immunization Practices) and AAP (American Academy of Pediatrics). Acetaminophen and ibuprofen can be used to treat adverse reactions and parents should be counselled to monitor infants for vaccine-related adverse events and to treat them if they occur.

Research: The authors stated that more research was needed to determine the effectiveness of prophylactic acetaminophen and ibuprofen for adverse reactions associated with currently available childhood vaccines.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.