Effectiveness of oral vs rectal acetaminophen: a meta-analysis

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CRD summary
The authors concluded that oral and rectal acetaminophen had comparable effects on temperature reduction. Given the unclear quality of the included trials and the small numbers of participants included for analysis, the reliability of the authors' conclusions is unclear.

Authors' objectives
To compare the effectiveness of oral versus rectal acetaminophen as a treatment for fever and pain.

Searching
PubMed (1950 to October 2007) and the Cochrane Database of Systematic Reviews (2007) were searched for articles published in any language with an English abstract. Search terms were reported. References of major pharmacological textbooks, relevant reviews and the included studies were handsearched.

Study selection
Randomised (RCT) or quasi-randomised controlled studies comparing oral and rectal acetaminophen, measuring reduction in temperature or pain and specifying the time of these measurements, were eligible for inclusion. Studies of combined treatments or investigating other drugs were excluded.

Included studies were of single dose oral acetaminophen in doses of 15 to 20mg/kg for children and 325 or 650 mg in adults compared to single dose rectal acetaminophen in doses of 15 to 35mg/kg in children and 650 or 1300mg in adults. Included studies were of children aged three months to 13 years and adults aged 23 to 96 years. Inclusion criteria for rectal temperature ranged from greater than 38.3 degrees centigrade to greater than 39 degrees centigrade. Outcomes reported in the review were reduction of temperature at one and three hours, maximum decline in temperature, and time taken to a reduction in temperature of one degree centigrade.

Studies were initially selected for review by one reviewer, with a subsequent selection performed independently by two reviewers; disagreements resolved through consultation with a third reviewer.

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

Data extraction
The mean differences between the groups were extracted for each outcome.

Data were extracted independently by two reviewers using structured data collection tables, with disagreements resolved by discussion.

Methods of synthesis
Weighted mean differences (WMD) with 95% confidence intervals (CI) were calculated using a random-effects model. Statistical heterogeneity was assessed using the $\chi^2$ statistic and quantified using the $I^2$ statistic.

Results of the review
Four RCTs were included for review (n=241 participants), of which one was double-blind, double-dummy (n=51 participants) and one was double dummy (n=83 participants). There was a discrepancy between the number of participants reported for the trials and the number included for analysis, which was unexplained by the authors.

There was no significant difference between oral and rectal acetaminophen in temperature reduction at one (WMD -0.14 degrees centigrade, 95% CI: 0.36 to 0.08; four RCTs, n=124 participants) or three hours (WMD -0.10 degrees...
centigrade, 95% CI: -0.41 to 0.21; four RCTs, n=124 participants) after administration, in the maximum temperature reduction achieved (WMD -0.10 degrees centigrade, 95% CI: -0.24 to 0.04; two RCTs, n=81 participants) or in the time taken to a temperature reduction of one degree centigrade (WMD -0.06 degrees centigrade, 95% CI: -1.34 to 1.23; two RCTs, n=71 participants). There was evidence of significant statistical heterogeneity for time taken to temperature reduction (p<0.001, I²=94.8%) but no evidence of significant statistical heterogeneity was found for the other outcomes.

Only one trial was found measuring pain, so a meta-analysis of pain reduction was not performed.

Authors’ conclusions
Oral and rectal acetaminophen had comparable effects on temperature reduction.

CRD commentary
The review addressed a clear question with well-defined inclusion criteria for intervention, study design and outcomes. Inclusion criteria for participants were broad. Only two databases were searched, so relevant data may have been missed. There did not appear to have been any attempt to search for unpublished material, so publication bias cannot be ruled out. However, appropriate steps were taken to minimise language bias. Appropriate steps were taken to minimise reviewer error and bias in the data extraction stages of the review. A validity assessment did not appear to have been carried out, so it was not possible to ascertain the methodological quality of the included trials. A suitable method of pooling results was used and statistical heterogeneity was assessed. However, it was unclear why some of the participants in the included trials were omitted from the meta-analysis. Given the unclear quality of the included trials and the small numbers of participants included for analysis, the reliability of the authors’ conclusions is unclear.

Implications of the review for practice and research
Practice: The authors stated that the American Academy of Pediatrics recommendation that rectal acetaminophen should not be used in children should possibly be revised.

Research: The authors stated that further studies are required comparing the toxic effects of rectal and oral acetaminophen.

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