



Q/ Does lowering a fever >101°F in children improve clinical outcomes?

EVIDENCE-BASED ANSWER

A/ IT DEPENDS ON WHICH OUTCOMES YOU LOOK AT. Treating fever significantly increases comfort, activity, feeding, and fluid intake and decreases the patient's temperature compared with placebo (strength of recommendation (SOR): **A**, multiple randomized controlled trials [RCTs]). It doesn't shorten or prolong the overall duration of illness or reduce the recurrence of febrile seizures (SOR: **A**, multiple RCTs). In patients with varicella,

reducing fever prolongs the time it takes for lesions to crust, but doesn't appear to cause group A streptococcal necrotizing fasciitis (SOR: **B**, multiple prospective cohorts).

Ibuprofen and acetaminophen reduce fever effectively and safely; their side effect levels are similar to placebo (SOR: **A**, multiple RCTs). Physical methods of cooling also are effective for lowering fever (SOR: **A**, high-quality meta-analysis).

Evidence summary

The possible risks and benefits of lowering fever with antipyretics have prompted much discussion in the medical literature. Most evidence supporting the useful effects of fever comes from animal models. A few human studies in special populations (patients with brain trauma) suggest that antipyretics may worsen certain aspects of disease processes.¹ However, many studies show that antipyretics do clinically benefit, and don't harm, the typical child with an upper respiratory illness.²⁻⁴

Acetaminophen improves some symptoms, but doesn't shorten fever

A double-blind, randomized, placebo-controlled trial of 210 children with upper respiratory illness showed that giving acetaminophen significantly increased short-term temperature reduction compared with placebo (0.36°F vs 0.09°F/hr; $P<.001$). Acetaminophen also improved subjective symptoms at 6 hours over placebo: activity (60% vs 16%; $P<.001$), alertness (58% vs 21%; $P<.001$), comfort (37% vs 7%; $P<.001$), mood (36% vs

12%; $P<.001$), appetite (20% vs 1%; $P<.001$), and fluid intake (22% vs 2%; $P<.001$).² Total time until complete resolution of fever (defined as no fever with or without medication) didn't differ between treatment and placebo groups (32 hr for acetaminophen vs 36 hr for placebo; $P=.23$).²

A similar study failed to show a statistically significant difference between acetaminophen and placebo in fever clearance time (34.7 vs 36.1 hr), mood, comfort, or appetite. However, the study did find significant improvement in activity (38% vs 11%; $P=.005$) and alertness (33% vs 12%; $P=.036$) based on parents' reports.³

Ibuprofen is a better antipyretic than acetaminophen

A meta-analysis (N=84,192) comparing acetaminophen with ibuprofen found both drugs to be equally efficacious analgesics; ibuprofen was a more effective antipyretic. Both drugs had the same level of adverse outcomes when compared with each other and placebo.⁵

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Treating fever significantly increases comfort, activity, feeding, and fluid intake, but doesn't reduce recurrence of febrile seizures.

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➤ **An RCT involving children with varicella found that acetaminophen increased the time for lesions to crust compared with placebo.**

Lowering fever doesn't reduce recurrence of febrile seizures

Antipyretics don't appear to affect the recurrence of febrile seizures. In a well-designed, randomized, double-blind, placebo-controlled trial, 230 patients 1 to 4 years of age with 1 or more risk factors for febrile seizures were randomized to fever reduction with ibuprofen or placebo. The estimated 2-year probability for recurrent febrile seizure was 32% in the ibuprofen group and 39% for the placebo group. The difference between the groups was not significant (relative risk=0.9; 95% confidence interval [CI], 0.6-1.5).⁶

Varicella lesions crust more slowly with acetaminophen

An RCT involving 68 children with varicella found that acetaminophen increased the time for lesions to crust compared with placebo (6.7 days for acetaminophen vs 5.6 days for placebo) and that acetaminophen didn't alleviate itching or improve appetite. However, patients taking acetaminophen were more active by day 2.⁷

NSAIDs don't cause necrotizing fasciitis

A case-control study of 48 children with varicella suggested an association between ibuprofen and increased incidence of necrotizing soft tissue infections (odds ratio [OR]=11.5; 95% CI, 1.4-96.9),⁸ but larger reviews haven't borne out this finding. A review of 5 prospective studies of nonsteroidal anti-inflammatory drugs and invasive soft-tissue infections (N=912; 114 cases of necrotizing fasciitis) failed to show any connection. The largest study (474 cases) suggested a trend that was

not statistically significant (OR=3.5; 95% CI, 0.8-16).⁹

Nonpharmacologic measures also lower fever

A Cochrane review showed that cool water sponging caused fever reduction similar to antipyretics at 1 hour; sponging combined with ibuprofen reduced the proportion of patients still febrile at 1 hour. Common side effects of sponging included goose pimples and shivering. The antipyretic effect didn't last beyond a few hours.¹⁰

Recommendations

Concerning treatment of fever, *Nelson's Pediatrics* states, "Fever with temperatures less than 39°C (102.2°F) in healthy children generally does not require treatment. As temperatures become higher, patients tend to become more uncomfortable and administration of antipyretics often makes patients feel better. Other than providing symptomatic relief, antipyretic therapy does not change the course of infectious diseases. Antipyretic therapy is beneficial in high-risk patients who have chronic cardiopulmonary diseases, metabolic disorders, or neurologic diseases and in those who are at risk for febrile seizures. Hyperpyrexia (>41°C [105.8°F]) indicates greater risk for severe infection and should always be treated with antipyretics."¹¹

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