Pseudoephedrine and acetaminophen relieved sinus symptoms in the course of the common cold

Sperber SJ, Turner RB, Sorrentino JV, et al. ***Effectiveness of pseudoephedrine plus acetaminophen for treatment of symptoms attributed to the paranasal sinuses associated with the common cold.*** *Arch Fam Med 2000 Nov/Dec;**9**:979–85.*

QUESTION: In patients with a cold, is a combination of pseudoephedrine hydrochloride and acetaminophen (PHA) more effective than placebo in relieving sinus symptoms?

Design
Randomised {allocation concealed *}†, blinded (clinicians and patients),* placebo controlled trial.

Setting
3 university medical centres in the eastern US.

Patients
430 patients who were 18–65 years of age (mean age 28 y, 66% women), had cold symptoms of ≤48 hours in duration, and reported sinus symptoms of at least moderate severity. Exclusion criteria were diastolic blood pressure >90 mm Hg, underlying illness that might be affected by the study drugs, use of medication that might interact with the study drugs, pregnancy, or potential for pregnancy. 412 patients (96%) completed the study.

Intervention
Patients were allocated to pseudoephedrine, 60 mg, and acetaminophen, 1000 mg (n=216), or identical placebo tablets (n=214). The drugs were given in 2 doses, 6 hours apart.

Main outcome measures
Change from baseline in overall sinus symptom assessment score and a composite score of weighted averages of sinus symptoms (sinus pressure, pain, and congestion) at 2 hours after the second dose. Assessments were made using a 5 point scale (0=absent and 4=severe).

Main results
Analysis was by intention to treat. 2 hours after the second dose of medication, patients who received PHA had a greater decrease in overall sinus assessment score than did patients who received placebo ($p<0.001$) (table). Patients who received PHA also had a greater decrease in the sinus weighted score ($p<0.001$) (table). PHA recipients also had greater decreases than placebo recipients in sinus assessment score and sinus weighted score 2 hours after the first dose of medication ($p\leq 0.04$). Adverse effects were reported by more patients receiving PHA than by those receiving placebo ($p=0.04$) and included nervousness, nausea, dizziness, dry mouth, and somnolence of mild or moderate severity, except for 2 patients with severe nausea in the PHA group.

Conclusion
In patients with cold and sinus symptoms, a combination of pseudoephedrine hydrochloride and acetaminophen relieved sinus symptoms within 2 hours of the second dose of medication.

*See glossary.

†Information provided by author.

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Pseudoephedrine and acetaminophen (PHA) v placebo for relieving sinus symptoms in the course of the common cold‡

Outcomes at 2 hours after the second dose	Mean decrease from baseline: PHA (baseline)	Mean decrease from baseline: Placebo (baseline)	Difference (95% CI)
Overall sinus symptom assessment score	1.30 (2.5)	0.93 (2.6)	0.37 (0.20 to 0.54)
Weighted sinus symptom score	1.14 (2.1)	0.84 (2.2)	0.30 (0.13 to 0.47)

‡Abbreviations defined in glossary; difference and CI calculated from data in article.

COMMENTARY

The clinical significance of the trial by Sperber *et al* is in doubt for several reasons. Firstly, the patients were healthy adults rather than the children and unhealthy adults who most often present with the common cold. Secondly, the meaning of a reduction in the symptom score in relation to patient distress is uncertain. For instance, is a reduction from severe to moderately severe the same as a reduction from moderately severe to mild? The results are presented only in terms of score reductions. It would be more useful to know what proportion of patients benefited meaningfully. Thirdly, the benefits are small; reduction of symptoms of 36% by placebo is only improved to 51% by PHA.

Side effects assessed as being related to the drug occurred in 19% of patients receiving PHA compared with 11% of patients receiving placebo. The effects were severe in 2 patients and warranted stopping the drug in 2 others. The benefit risk ratio seems small.

PHA is a compound, and symptom relief may have come from either or both of its components. Because most of the adverse effects are attributed to pseudoephedrine, we do not know whether its inclusion is important in achieving the small benefits.

It is questionable whether the benefits outweigh the risks; therefore, I would not recommend the use of PHA in the patients described.

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