Antibiotics were ineffective for the common cold unless bacteria were present in nasopharyngeal secretions

Kaiser L, Lew D, Hirschel B, et al. **Effects of antibiotic treatment in the subset of common-cold patients who have bacteria in nasopharyngeal secretions.** Lancet. 1996 Jun 1;347:1507-10.

Objective
To determine the efficacy of co-amoxiclav for adults with common cold symptoms and a low probability of sinusitis.

Design
5-day randomised, double-blind, placebo-controlled trial.

Setting
An outpatient infectious disease clinic of a Swiss hospital.

Patients
314 adults (mean age 31 y, 52% men) who had sought treatment for common cold symptoms (history of acute nasal congestion or rhinorrhoea and clinical evidence of upper respiratory tract infection with nasal congestion, rhinorrhoea, or pharyngitis) during the autumn and winter were studied. Exclusion criteria were clinically confirmed sinusitis, infections that required antibiotics, recent antibiotic use, allergy to aminopenicillin, immunosuppression, or pregnancy.

Intervention
314 patients were randomised, and 288 were followed up. Of these patients, 142 had been allocated to placebo and 146 to co-amoxiclav (amoxicillin and clavulanate), 375 mg 3 times/d for 5 days. Nasopharyngeal secretions were aspirated from the posterior nasopharynx by suction catheter to detemine infection status.

Main outcome measures
Physician assessment of cure or persistent or worsening symptoms and patient-reported symptoms.

Main results
58 patients (20%) had positive cultures for *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Streptococcus pneumoniae*, and 230 (80%) had negative cultures. For patients who had negative cultures, the groups did not differ for rates of cure (35% for co-amoxiclav vs 41% for placebo, {95% CI for the 6% difference, –6.7% to 18%}*), persistent symptoms (61% vs 52%, {CI for the –9% difference, –21% to 4.2%}*), and worsening symptoms (4% vs 7%, {CI for the 3% difference, –3.6% to 9.5%}*) (P = 0.39 for the distribution). For the subgroup of patients who had positive cultures, more patients who received co-amoxiclav reported being cured (27% vs 4%, P = 0.001). {This 23% absolute risk improvement means that 4 patients who had positive cultures would need to be treated with co-amoxiclav (compared with placebo) for 5 days to have 1 additional patient report being cured (CI 2 to 19); the relative risk improvement was 646%, CI 35%* to 4374%.}* However, the absolute risk improvement in cure for all patients in the trial was zero.

Conclusions
Patients who had common cold symptoms and positive cultures for *H. influenzae*, *M. catarrhalis*, or *S. pneumoniae* reported higher cure rates after co-amoxiclav. Patients who had negative cultures did not report any benefits from co-amoxiclav.

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*Numbers calculated from data in article.

Commentary

Kaiser and colleagues have shown that a subset of patients with symptoms of upper respiratory tract infection and positive bacterial cultures can achieve faster symptom relief if given co-amoxiclav. These results might be important for the subset of patients who will probably return 5 days after initial assessment feeling worse or unimproved.

Nevertheless, I do not believe that a blanket policy of treating symptoms of upper respiratory tract infection with antibiotics in primary care is justified from these results. No overall benefit was found for the entire trial group, and primary care practices may have a lower prevalence of bacterial infections than the 20% prevalence seen in this infectious disease clinic. In addition, nasopharyngeal aspiration and culture are not practical in primary care settings.

Because of these limitations, future studies should focus on finding a method for the rapid and inexpensive identification of patients with combined cold symptoms and bacterial infection. If this group could be identified, then treating 4 patients with positive cultures would achieve a cure at the 5-day point for 1 additional patient. This benefit, however, would be offset by side effects in 1 out of every 5 patients treated. (A 20% rate of side effects was found in the group of patients treated with co-amoxiclav.)

Could similar benefits be achieved with a different antibiotic? Co-amoxiclav is substantially more expensive than amoxicillin. Could amoxicillin achieve the same benefits at less cost? Also to be resolved is whether a cold with a positive bacterial culture is a new clinical entity or merely a predictor of which patients will develop sinusitis.

This study opens up a line of investigation that may provide practical guidance for busy practitioners who see patients who are worried that their cold will not go away. Particularly if a rapid and inexpensive method for identifying the subgroup with bacterial infections can be developed, this group of patients may be offered some help in the future.

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