Acute rhinosinusitis and systemic corticosteroids

I read with interest the *CMAJ* article by Venekamp and colleagues,[1] but I disagree with the authors' findings that suggest systemic corticosteroid monotherapy had no clinically important benefit in acute rhinosinusitis. The proportion of patients with resolution of facial pain or pressure on day 7 was 62.5% in the prednisolone group and 55.8% in the placebo group (absolute risk difference 6.7%). Studies with possible clinical importance have 95% confidence intervals (CIs) that include the value of the minimal clinically important difference (MCID) and a MCID greater than the point estimate of the efficacy.[2] Based on this, the 95% CI (–7.9% to 21.2%) obtained for the point estimate included both the point estimate (6.7%) and the MCID used for the study (20%).

Also, the proportion of patients with resolution of severe facial pain or pressure on day 7 was significantly higher among those receiving prednisolone compared with those receiving placebo (absolute risk difference 10.6%, 95% CI 1.0% to 20.2%). Furthermore in Table 2, which shows the proportion of patients with resolution of symptoms on day 7, the prednisolone group shows a tendency toward an overall beneficial effect compared with placebo.[1]

One reason why the full effect of systemic corticosteroids cannot be elicited from the study is lack of patient selection. The Infectious Diseases Society of America guidelines distinguish clinically between acute bacterial/viral rhinosinusitis and acute rhinosinusitis due to other causes based on illness pattern and duration.[3] There was no attempt to identify patients in the sample who might benefit from other treatment approaches. It is possible that the short-term benefits are higher among those with acute rhinosinusitis due to other causes compared with patients with acute bacterial rhinosinusitis who might require antibiotic therapy.[3] A previous guideline suggests that systemic corticosteroids be reserved for those with nasal polyps, severe nasal swelling due to inflammation of the mucous membrane, or for whom other treatment approaches have failed.[4]

I thank the authors for the study, but I believe the clinical importance of systemic corticosteroids for treating acute rhinosinusitis should not completely be discarded until we identify the subgroups of patients who will benefit from them.

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The author responds

We sincerely thank Dr. Ukwaja[1] for his commentary on our *CMAJ* article.[2] To the best of our knowledge, no sign, symptom or test has been identified that can accurately differentiate viral from bacterial infection in patients with clinically diagnosed acute rhinosinusitis. Clinical practice guidelines' recommendations to differentiate between viral and bacterial acute rhinosinusitis based on illness pattern and/or duration of symptoms are mostly based on consensus rather than scientific evidence. To enhance the generalizability of our trial findings, we included the broad population of patients with clinically diagnosed acute rhinosinusitis encountered in primary care.[2]

Both our primary and secondary outcomes revealed small but clinically unimportant differences between the systemic corticosteroid and the placebo group. We are therefore confident that our main conclusion "lack of effect of systemic corticosteroids in patients with clinically diagnosed acute rhinosinusitis" is justified. However, we agree with Ukwaja's final statement that there may be a subgroup of patients who do benefit from systemic corticosteroids. The magnitude of the effect size found in our study is in agreement with the effect sizes reported in previous trials on antibiotics in acute rhinosinusitis.[3] There might be a subgroup of patients that could benefit from antibiotics and an individual patient-data meta-analysis has been performed.[3] Unfortunately, no clinical sign or symptom could be detected to predict beneficial effects of antibiotics. Finding subgroups of patients who really benefit from antibiotics is challenging, and it is likely that this will also be the case for detecting subgroups who will benefit from systemic corticosteroids. Future research is needed to identify those subgroups that do benefit from either antibiotics or corticosteroids. Until then, we recommend refraining from these treatment options in patients with uncomplicated clinically diagnosed acute rhinosinusitis, because symptoms are self-limiting in the majority of patients within 2 to 4 weeks.

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Antimicrobials in farming

I wish to applaud Barbara Sibbald for her editorial on antimicrobial use in agriculture and its implications for human health.[1] I was interested to learn about the degree to which Canada lags behind other countries in regulating the agricultural use of antimicrobials.

I have 2 comments on the editorial: With respect to the article's statement that

"…quinupristin–dalfopristin, [is] our last line of defence if *Staphylococcus aureus* or *Enterococcus* infections develop resistance to vancomycin,"[1] I note that vancomycin-resistant *Enterococcus* has been recognized for over 2 decades;[2] strains of *S. aureus* with intermediate-level resistance to vancomycin were described in 1997, and high-level vancomycin resistant *S. aureus* was described (outside the laboratory) in 2002.[3] The role that agricultural use of avoparcin played in the genesis of vancomycin-resistant *Enterococcus* in humans is controversial, but recognition of the potential links between avoparcin and vancomycin-resistant *Enterococcus* likely contributed to European decisions to remove this antibiotic from feeds, as mentioned in the article.[4] Fortunately, however, quinpristin-dalfopristin is not the only agent with activity against multiresistant gram positive microbes. Daptomycin and linezolid are available in Canada, and other agents, such as ceftaroline, have been approved in the United States and await approval in Canada.

The editorial did not mention multidrug resistant gram negative pathogens, including *Acinetobacter* species, *Pseudomonas aeruginosa*, and the Enterobacteraceae, including recently described strains with a novel plasmid-borne carbapenemase, some of which have actually reached a point of being effectively pan resistant to available antimicrobials.[5] Such microbes are environmentally abundant in agricultural runoff, surface waters and sewage. Particularly given the tendency of resistance determinants to cluster at the microbial level, the environmental contamination associated with agricultural antibiotic use provides a source of selective pressure that gives a competitive advantage to resistant microbes.

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I have just read the *CMAJ* editorial by Barbara Sibbald in which she concludes that the agricultural industry is primarily responsible for the superbug phenomenon.[1] Not being an expert on this issue, I will avoid generalizations on responsibility; however, I encourage *CMAJ* readers to look up reviews on the subject as well as presentations given at a 2011 forum on this issue.[2]

I would like to correct Sibbald's statement that only the province of Quebec has taken a legal stand on antimicrobial use in the agricultural industry. In Newfoundland and Labrador, selling directly to a consumer an antibiotic for animal use that is for injection or for oral, intramammary or intrauterine administration is illegal without a prescription from a veterinarian. The sole exemption is if the antibiotic is used in conformity with the federal Feeds Act.[3]

I presume that the intent of the editorial was to generate debate; I'm sure it will.

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