How effective are treatments other than antibiotics for acute sore throat?

MICHAEL THOMAS

CHRIS DEL MAR

PAUL GLASZIOU

SUMMARY

To estimate the benefits of treatments other than antibiotics for acute sore throat, and the differences between non-antibiotic interventions and controls in patient-perceived pain of sore throat, a systematic review of controlled trials in Medline and the Cochrane Library was carried out. Sixty-six randomised controlled trials (with or without additional antibiotics) were identified and 17 met the selection criteria. Twenty-two non-antibiotic managements for sore throat were compared. Their efficacy relative to placebo ranged from no effect to 93%. Some non-antibiotic treatments may be more effective than anti-biotics; however, publication bias may have exaggerated the benefits. These treatments should be investigated further with respect to efficacy, safety, and side-effects as potential firstline management options for acute sore throat.

Introduction

PATIENTS frequently attend general practices in the industrial western world with the complaint of sore throat.[1,2] Although the illness is usually self-limiting, it is such a common reason for attending the doctor that its treatment is of considerable interest. Treatment has always been controversial, with most debate concerning whether antibiotics should be used.[3-7]

The facts are largely undisputed. The benefits of antibiotics are modest, shortening the symptoms of the illness by about half a day (from 3.3 to 2.7 days).[8,9] Antibiotics also provide protection against acute rheumatic fever, an illness that has become so rare in the western world that the risk it poses may be of the same order as misadventure from the antibiotics themselves.[8,9] They protect patients from some secondary bacterial infections (principally acute otitis media) but the effect is small and many patients have to be treated for only one to benefit.[9] Treating sore throats with antibiotics, especially broad spectrum, poses a risk to society by accelerating the evolution of resistant organisms.[10]

The question is whether the modest benefits outweigh the risks. One approach is to test the opinion of our patients to ensure we have accommodated their values.[11] Another is to use effective alternatives. Killing microorganisms that may, or may not,[12] trigger the inflammatory process has conceptual neatness but might not necessarily be the most effective strategy. We thought it worth examining the literature to investigate treatments other than antibiotics for sore throat.

M Thomas, BSc, medical student; C Del Mar, FRACGP, FAFPHM, professor; and P Glasziou, PhD, FAFPHM, reader, Centre for General Practice, Graduate School of Medicine, University of Queensland, Australia.
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Method

We searched for relevant randomised controlled trials from 1966 onwards within the Cochrane Controlled Trials Registry on CD-ROM and Medline using the key words 'tonsillitis' *or* 'pharyngitis' *or* 'sore throat' and (in Medline) 'randomised controlled trial' *or* 'drug therapy' *or* 'therapeutic use' *or* 'random'. We obtained the full text if the abstract indicated a controlled trial of any non-antibiotic intervention, written in any language. Outcome measures were limited to patient-centred sore throat symptoms.

We attempted to score each symptom on the same scale, giving each a score of 100 at baseline. Efficacy was defined as the percentage change of symptom score in the intervention group relative to placebo at the reference time. The reference time was any time used in the trial: when there was a choice we used Day 3 to enable comparison with antibiotics data.[8,9]

Results

The search yielded 66 potentially eligible papers. The full texts of three were not available in Australia. We excluded 46 of the remaining for the following reasons: acute sore throat was not investigated (30); active treatment was an antibiotic (8); not in a clinical setting (2); excessive dropouts (1); guideline only (1); no suitable control (2); no treatment (1); and both unclear randomisation and blinding (1). Some papers had more than one reason for exclusion. This left 17 papers reporting 22 randomised, at least single-blinded, controlled trials. The heterogeneous nature of the interventions precluded a formal quantitative summary of the results (meta-analysis).

Ten trials measured very short-term outcomes (less than 24 hours) (Table 1);[13-18] seven used our preferred assessment time at Day 3 (after 48 hours of therapy); and one used the time to 'complete lack of pain'. Four trials of prophylactic treatments used follow-up times of up to two years (Table 2).[19]

The non-steroidal anti-inflammatory drug (NSAID) ibuprofen appeared to have immediate efficacy, reducing throat pain in adults by between 32% and 80% relative to placebo after two to four hours, and 70% at six hours.[14] In children it had a lower efficacy (25% after two hours),[15] although after two days there was a 56% reduction in patients still with sore throat.[22] Morniflumate suppositories (another NSAID) were no better than placebo at Day 3, although after four days there was a 34% reduction in pharyngeal pain.[25]

Better doctor–patient communication (in the form of increased courtesy from the doctor, with an increase in consultation time to 10 minutes from six minutes, and offering a prognosis) in addition to prescribing antibiotics improved symptoms by Day 3, especially in patients whose cultures were positive for β-haemolytic streptococci.[26]

Three trials looked at prevention of episodes. Vaccination against both influenza and pneumococcus showed significant reductions in the number of future episodes of acute sore throat (27% and 18% respectively).[19,20] Similarly, spraying the throat to colonise it with less pathogenic streptococcus appeared to reduce sore throat recurrences.[23,29]

Table 1. Alternative treatments to antibiotics for sore throat. Short-acting (24 hours or less).

Author, year, reference	Nature of active treatment(s)	Definition of illness	Enrolled patient characteristics, setting, country	Blinding	Active/ Control	Estimate of treatment effect (relative effect compared with control)[a]	P-values
Schachtel 1991[13]	NSAID (aspirin) 800 mg plus caffeine 64 mg, single dose	Acute sore throat (onset within 4 days) with defined severity	139 adults aged 18–83 years in one general practice, USA	Double	70/69	75% decrease in sore throat pain at 1 hour	<0.01
Schachtel 1991[13]	NSAID (aspirin) 800 mg, single dose	Acute sore throat (onset within 4 days) with defined severity	137 adults aged 18–83 years in one general practice, USA	Double	68/69	55% decrease in sore throat pain at 1 hour	<0.01
Schachtel 1988[14]	Paracetamol 1000 mg, single dose	Upper respiratory infection with acute sore throat (onset within 4 days) severity above a threshold on an objective scoring instrument	81 adult patients at Medical Department, Whitehall Laboratories, USA	Double	40/41	50% peak decrease in throat pain after 3 hours 20% decrease after 6 hours	<0.01 <0.01
Schachtel 1988[14]	NSAID (ibuprofen) 400 mg, single dose	Upper respiratory infection with acute sore throat (onset within 4 days) severity above a threshold on an objective scoring instrument	80 adult patients at Medical Department, Whitehall Laboratories, USA	Double	39/41	80% peak decrease in throat pain after 4 hours 70% decrease after 6 hours	<0.01 <0.01
Schachtel 1993[15]	NSAID (ibuprofen) 10 mg/kg, single dose	Acute sore throat of severity above a threshold on an objective scoring instrument	78 children aged 3.5–12.5 years at Medical Department, Whitehall Laboratories, USA	Double	39/39	25% decrease in throat pain after 2 hours 22% decrease after 6 hours	<0.05 NS
Schachtel 1993[15]	Paracetamol 15 mg/kg, single dose	Acute sore throat of severity above a threshold on an objective scoring instrument	77 children aged 3.5–12.5 years at Medical Department, Whitehall Laboratories, USA	Double	38/39	31% decrease in throat pain after 2 hours 7% decrease after 6 hours	<0.05 NS
O'Brien 1993[16]	Corticosteroid (dexamethasone) 10 mg intramuscular injection plus oral antibiotics	Severe sore throat with tonsillar exudate and either fever or cervical adenopathy	51 patients aged 12–65 years at an urban community hospital emergency department, USA	Double	26/25	38% decrease in mean pain score at 24 hours; 58% decrease in time (from 35 hours to 15 hours) to complete lack of pain	<0.05
Bernstein 1974[17]	Aspirin-containing gum	Acute sore throat, clinical evidence of inflammation	20 males in one industry aged 20–56 years	Double	10/10	53% decrease in time to relief initially; 50% after repeating in 2 hours	≤0.001
Schachtel 1994[18]	NSAID (ibuprofen) 400 mg, single dose	Acute upper respiratory tract infection with sore throat for <5 days, severity greater than defined score	20 healthy adults aged ≥18 years, Canada	Double	10/10	47% decrease in throat pain after 2 hours	<0.05
Schachtel 1994[18]	NSAID (ibuprofen) 200 mg, single dose	Acute upper respiratory tract infection with sore throat for <5 days, severity greater than defined score	18 healthy adults aged ≥18 years, Canada	Double	9/10	32% decrease in throat pain after 2 hours	<0.05

[a]Some figures are estimated from graphs or transformed from study data.

Table 2. Alternative treatments to antibiotics for sore throat. Outcomes estimated more than 24 hours after starting treatment.

Author, year, reference	Nature of active treatment(s)	Definition of illness	Enrolled patient characteristics, setting, country	Blinding	Active/ Control	Estimate of treatment effect (relative effect compared with control)[a]	P-values
Nichol 1995[19]	Trivalent subvirion influenza vaccine injection	Upper respiratory infection (sore throat plus either fever or cough) for at least 4 hours	849 healthy working adults aged 18–64 years, USA	Double	422/424	25% decrease in episodes of acute sore throats during the influenza season	<0.001
Christensen 1985[20]	14-valent pneumococcal vaccine	Acute tonsillo-pharyngitis (clinical diagnosis)	405 children aged 0.5–5 years in day care centres, Sweden	Double	198/207	18% decrease in episodes of acute tonsillitis/pharyngitis over the 2-year follow-up	Not given
Sauvage 1990[21]	NSAID (niflumic acid) 1000 mg daily for 4–5 days	Acute diffuse pharyngitis or acute tonsillitis with fever over 38°C and dysphagia	230 adults aged 18–65 years in 30 general ractices, France	Double	118/113	17% decrease in patients with pain after 2 days 33% decrease after 4 days	<0.05 <0.05
Bertin 1991[22]	Paracetamol 10 mg/kg three times daily for 2 days	Sore throat for less than 48 hours being treated as tonsillitis and pharyngitis with penicillin	154 children aged 6–12 years (outpatients), France	Double	78/76	34% decrease in children with sore throat after 2 days	<0.01
Bertin 1991[22]	NSAID (ibuprofen) 10 mg/kg three times daily for 2 days	Sore throat for less than 48 hours being treated as tonsillitis and pharyngitis with penicillin	153 children aged 6–12 years (outpatients), France	Double	77/76	56% decrease in children with sore throat after 2 days	<0.01
Roos 1996[23]	Super-colonisation with a-streptococcal bacteria (oral spray twice daily for 10 days)	Culture confirmed recurrence of group A streptococcus sore throat	130 patients aged 3–59 years in 12 centres, south and west Sweden	Double	51/61	42% decrease in total recurrences of GAS within 8 weeks of completing antibiotics	0.064
Benarrosh 1989[24]	NSAID (tiaprofenic acid) for 5 days plus antibiotics	Acute tonsillitis of viral or bacterial origin, duration <24 hours	106 children aged 6–10 years in 13 centres, France	Double	50/56	14% decrease in children with pain after 2 days 93% decrease after 5 days	0.001 0.001
Manach 1990[25]	NSAID (morniflumate suppository) 400 mg twice daily for 4 days plus antibiotics	Acute diffuse pharyngitis or acute tonsillitis ≥38C, at least moderately severe	101 children aged 6–10 years, France	Double	49/52	1% increase in children with pharyngeal pain after 2 days 34% decrease after 4 days	NS <0.05
Olsson 1989[26]	Greater attention to patients (offering prognosis, longer communication, and physical examination) plus antibiotics	Acute streptococcal tonsillitis (clinical diagnosis, excluding mononucleosis) of whom 65% returned positive throat swabs for streptococcus	Patients aged >16 years, health centre, Sweden	Single	50/50	40% decrease in the number of patients not better after 2 days	<0.005
Benarrosh 1989[27]	NSAID (tiaprofenic acid) for 5 days plus penicillin V	Acute tonsillitis present for <48 hours, severity greater than defined score	60 adult patients at six centres, France	Double	25/30	20% decrease in pain score after 2 days 81% decrease after 5 days	0.09 0.004
Whiteside 1982[28]	Benzydamine HCL (analgesic and anti-inflammatory) 0.15% oral rinse 3-hourly	Sore throat from tonsillitis or viral respiratory illness	51 patients aged 17–74 years in one general practice, UK	Double	25/26	42% decrease in Day 3 mean score pain score	<0.001
Roos 1993[29]	Super-colonisation with a-streptococcal bacteria (oral spray twice daily for 10 days)	Culture confirmed recurrence of group A streptococcus sore throat	36 patients aged 5–40 years, Sweden	Double	17/19	90% decrease in patients with bacteriological-confirmed clinical recurrences of GAS within 3 months	<0.001

[a]Some figures are estimated from graphs or transformed from study data.

Discussion

This review of treatments for acute sore throat suggests there are effective alternatives to antibiotics for symptom relief. A meta-analysis found that antibiotics reduce the proportion of patients suffering sore throat on Day 3 from 63% with placebo to 44% with antibiotics.[8,9] In other words, they were 29% effective. Thus, in the absence of data comparing these alternatives directly with antibiotics, these results suggest that antibiotics may be among the least effective treatments tested for symptom relief in acute sore throat.

Symptom relief from analgesics such as paracetamol and NSAIDs seems to be very effective. How is treatment in the trials described different from usual practice? Perhaps especially in that the drugs were administered regularly and in large doses, rather than as required. We could effectively incorporate this difference in drug administration in our clinical practice.

In addition, activities aimed at preventing sore throats could perhaps be investigated more seriously as an alternative to antibiotics — especially for people troubled by repeated acute sore throats. Adoption of these managements should be cautious until any benefits are confirmed, as to curb the immune response might create problems in some patients. In addition, every drug has side-effects, drug interactions, allergies, contraindications, and other complications that must be carefully considered before contemplating changes to prescribing behaviour, and which may not have been adequately documented in the trials summarised here.

The trials have several weaknesses. There may be a publication bias: some treatment trials with non-significant results may not have been submitted for publication. The wide variation in time points used by authors means that outcomes are difficult to compare, as the degree of symptom relief changes with time. Some of the most effective therapies were not tested for more than a few hours, meaning we cannot know if the effect lasted or decreased the illness duration. Confidence intervals on efficacy rates could not be easily calculated.

Nevertheless, if we are to adopt the main empirical principle of evidence-based medicine, we should prepare to change our clinical behaviour by choosing these effective alternative treatments ahead of less effective ones.

- Effective short-term (less than 24 hours) alternative treatments to antibiotics for sore throat treatments include steroids and NSAIDs, caffeine, and paracetamol.
- Longer-term (more than 24 hours) effective treatments include paracetamol, NSAIDs, super-colonisation with benign bacteria, better communication skills, and vaccination against influenza and pneumococcus.
- The effect size was as large as 93% — greater than for antibiotics.
- Some alternative treatments were additional to antibiotics.
- Further exploration of these alternatives seems indicated.

Box 1. Keypoints.

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Address for correspondence

Professor Chris Del Mar, Centre for General Practice, Graduate School of Medicine, University of Queensland, Herston, Queensland 4006, Australia. E-mail: c.delmar@mailbox.uq.edu.au