Antibiotics for sore throat

Del Mar CB, Glasziou PP, Spinks AB


A substantive amendment to this systematic review was last made on 16 September 1999. Cochrane reviews are regularly checked and updated if necessary.

Background: Sore throat is a very common reason for people to attend for medical care. Sore throat is a disease that remits spontaneously, that is, 'cure' is not dependant on treatment. Nonetheless primary care doctors commonly prescribe antibiotics for sore throat and other upper respiratory tract infections.

Objectives: To assess the benefits of antibiotics in the management of sore throat.

Search strategy: Systematic search of the literature from 1945 to 1999, using electronic searches of MEDLINE (using the keywords, "pharyngitis", "sore throat" and "tonsillitis") after 1966, the Cochrane Library, the Cochrane collection of hand-searched trials, and the reference sections of the articles identified. Abstracts of identified articles were used to determine which studies were trials.

Selection criteria: Trials of antibiotic against control with either measures of the typical symptoms (throat soreness, headache or fever), or complications (suppurative and non-suppurative) of sore throat.

Data collection and analysis: RevMan 4.0.3

Main results: A total number of 10,484 cases of sore throat have been studied.

1. Non-suppurative complications

There was a trend for protection against acute glomerulonephritis by antibiotics, but insufficient cases were recorded to be sure of this effect.

Several studies found benefit from antibiotics for acute rheumatic fever, which reduced this complication to less than one third (OR = 0.30; 95% CI = 0.20-0.45).

2. Suppurative complications

Antibiotics reduced the incidence of acute otitis media to about one quarter of that in the placebo group (OR = 0.22; 95% CI = 0.11-0.43) and reduced the incidence of acute sinusitis to about one half of that in the placebo group (OR = 0.46; 95% CI = 0.10-2.05). The incidence of quinsy was also reduced in relation to placebo group (OR = 0.18; 95% CI = 0.08-0.43).

3. Symptoms

Symptoms of headache, throat soreness and fever were reduced by antibiotics to about one half. The greatest time for this to be evident was at about three and a half days (when the symptoms of about 50% of untreated patients had settled). About 90% of treated and untreated patients were symptom-free by one week.

4. Subgroup analyses of symptom reduction

Subgroup analysis by age; blind vs unblinded; us of antipyretics;
or results of swabs for Streptococcus yielded no significant differences.

Reviewers' conclusions: Antibiotics confer relative benefits in the treatment of sore throat. However, the absolute benefits are modest. Protecting sore throat sufferers against suppurative and non-suppurative complications in modern Western society can only be achieved by treating many with antibiotics who will derive no benefit. Antibiotics shorten the duration of symptoms, but by a mean of only about half of one day at day 3 (the time of maximal effect), and by about eight hours overall.

Background

Sore throat is a very common reason for people to attend for medical care [ABS, 1986]. Moreover, four to six times as many people suffering sore throat do not seek care [Horder, 1954; Goslings, Goslings, 1963]. Sore throat is a disease that remits spontaneously, that is, 'cure' is not dependant on treatment [Del Mar, 1992c]. Nonetheless primary care doctors commonly prescribe antibiotics for sore throat and other upper respiratory tract infections. There are large differences in clinical practice between countries and between individual primary care doctors [Howie, 1971].

Whether or not to prescribe antibiotics for sore throat is controversial. The issue is important because it is a very common disease. Therefore differences in prescribing result in large cost differences. Moreover, differences in prescribing may increase patient attendance rates, which in turn might exert an additional cost [Howie, 1978].

Objectives

To assess the benefits of antibiotics in the management of acute sore throat.

Criteria for considering studies for this review

Types of studies

Placebo controlled trials.

Types of participants

Patients presenting for primary care with symptoms of sore throat.

Types of intervention

Antibiotic or control

Types of outcome measures

At least one of the following: incidence of acute rheumatic fever within two months; acute glomerulonephritis within one month; acute otitis media; acute sinusitis; or quinsy, or measures of the following symptoms: - throat soreness; headache; or fever.

Search strategy for identification of studies

See: Collaborative Review Group search strategy

We systematically screened the literature from 1945 to 1999, using electronic searches of MEDLINE (using the keywords, "pharyngitis", "sore throat" and "tonsillitis") after 1966, the Cochrane Library (1999, Issue 2), the Cochrane ARI Group's trials register, and the reference sections of the articles identified. The abstracts of the identified articles were read to determine which studies were trials. We applied no language restriction.
Methods of the review

Data extraction was based on patient-relevant outcomes: namely the complications and symptoms listed above. Data extraction involved reading from tables, graphs, and in some cases by contacting the authors for raw data [Dagnelie, 1996; Little, 1997].

Description of studies

Studies were included if they met the criteria listed above.

Methodological quality

There were twenty-two controlled studies overall that assessed the efficacy of an antibiotic against a control. The majority of studies included in this review were conducted in the 1950s, during which time the rates of serious complications (especially acute rheumatic fever) were much higher than today. Four recent studies were found (1996-1999), perhaps signaling renewed interest in this topic.

Many of the studies were of poor quality. Only fourteen studies were double blinded: three were single blind. In most early studies subjects were randomised to treatment and control groups by methods that could potentially introduce bias (for example, air-force serial number, drawing a card from a deck, hospital bed number) or not randomised at all. The generalisability of studies can be questioned. In five studies subjects were excluded if they did not yield a positive throat-swab culture for Group A Beta-Haemolytic Streptococcus. In two studies subjects were excluded if they did yield a positive throat-swab culture for Group A Beta-Haemolytic Streptococcus [Taylor, 1977; Petersen, 1997]. The use of antipyretic analgesics was not stated in nine studies, administered routinely in five studies, and prohibited in four studies. The prohibition of analgesics might exaggerate any small symptomatic benefit of antibiotics over control if antipyretic analgesics are usually recommended in normal practice.

Results

1.
1. Non-suppurative Complications (See MetaView)

Cases of acute glomerulonephritis only occurred in the control group which suggests protection by antibiotics. However there were only two cases, and only six studies reported on acute glomerulonephritis as an end point. Therefore we estimate the protection only with a very wide 95% confidence interval, (OR = 0.07; 95% CI = 0.00-1.32) which precludes us from claiming that antibiotics protect sore throat sufferers from acute glomerulonephritis.

Several studies found benefit from antibiotics for acute rheumatic fever which reduced this complication to about one third that in the placebo group (OR = 0.30; 95% CI = 0.20-0.45). Few studies examined antibiotics other than penicillin. Use of penicillin alone resulted in little difference in protection (OR = 0.27; 95% CI = 0.18-0.41).

2. Suppurative Complications (See MetaView)

Antibiotics reduced the incidence of acute otitis media to about one quarter of that in the placebo group, (OR = 0.22; 95% CI = 0.11-0.43) and reduced the incidence of acute sinusitis to about one half of that in the placebo group (OR = 0.46; 95% CI = 0.10-2.05). Data from two studies indicate that the incidence of quinsy was also reduced in relation to placebo group (OR = 0.18; 95% CI = 0.08-0.43).
3. Symptoms (See MetaView)

At day three of illness, antibiotics reduced symptoms of sore throat (OR = 0.47; 95% CI = 0.40-0.55), headache (OR = 0.40; 95% CI = 0.28-0.56) and fever (OR = 0.56; 95% CI = 0.41-0.76). This was the greatest time of benefit because the symptoms of only half the patients had settled. At one week (6-8 days) the odds ratio of experiencing sore throat was 0.42 (95% CI = 0.32-0.56), although 85% of controls were better by this time.

4. Subgroup analysis of symptom reduction (See MetaView)

a) Blind versus unblinded studies

There was no significant difference between blinded and unblinded studies (OR = 0.41; 95% CI = 0.34-0.51; and OR = 0.58; 95% CI = 0.45-0.75 respectively). Contrary to expectation the trend was for a greater effect of antibiotics for blind studies, see MetaView.

b) Antipyretics administered versus not administered (See MetaView)

Use of antipyretics offered no significant difference between studies in which antipyretics were offered and those in which they were not (OR = 0.30; 95% CI = 0.21-0.43; and OR = 0.34; 95% CI = 0.25-0.47 respectively).

c) Streptococcus versus negative for Streptococcus versus not tested (See MetaView)

There was no significant difference between patients subsequently found to have cultured Streptococcus from throat swabs versus those who did not, versus those who were not tested. (OR = 0.32; 95% CI = 0.25-0.40; OR = 0.30; 95% CI = 0.18-0.50; and OR = 0.75; 95% CI = 0.58-0.96 respectively).

d) Children versus adults (See MetaView)

There were few studies that included children (~13 years of age): only 61 in total for when fever was evaluated at Day 3. There was overlap of the OR 95% confidence intervals, so that the trend for children to not experience benefits was not significantly different to adults who did (OR = 1.87; 97% CI = 0.48-7.23; and OR = 0.38; 95% CI = 0.24-0.58 respectively).

Summary of analyses

MetaView: Tables and Figures

Discussion

Natural History

Symptoms of sore throat and fever had disappeared by 3 days in about 40% and 85% respectively in the placebo groups. Eighty-five percent of patients were symptom free by one week. This natural history was similar in Streptococcus positive, negative, and untested patients. About 2% of placebo patients developed rheumatic fever, but this was largely in trials conducted in the 1950s, and the background incidence has greatly declined in most countries since then.

Benefits of Treatment

The absolute benefit of antibiotics for the duration of symptoms was very modest. The reduction of illness time is greatest in the middle of the illness period when the mean absolute reduction is about half a
about half a day at around Day 3. There are not enough data to make conclusions about children. The absolute reduction averaged over the whole illness cannot be estimated from these data. However it is a reduction in duration of symptoms over the whole illness of about eight hours [Del Mar, 1997]. Antibiotics are effective at reducing the relative complication rate of people suffering sore throat. However the relative benefit exaggerates the absolute benefit because complication rates are low and the illness is short lived. Interpretation of these data is aided by estimating the absolute benefit, which we attempt below.

In these trials, conducted mostly in the 1950s, for every 100 patients treated with antibiotics rather than placebo, there was one fewer case of acute rheumatic fever, two fewer cases of acute otitis media, and three fewer cases of quinsy. However, these figures need to be adapted to current circumstances and individuals. For example, assuming a complication rate of 5% for acute otitis media in untreated children and 1% for adults, and an odds ratio of 0.22 for treatment with antibiotics, then about 30 children and 145 adults with sore throat must be treated with antibiotics to prevent one episode of acute otitis media [Del Mar, 1992b]. Using these data, the overall complication rate for acute otitis media was 28 per 1271 (controls). The rate with antibiotic was 11 per 1967. This yields an overall number needed to treat of about 60 people treated with antibiotics to prevent one case of acute otitis media. Clinicians will have to exercise judgement in applying these data to their patients.

Adverse effects of Treatment

We were unable to present the adverse effects of antibiotic use because of inconsistencies in recording these symptoms. In other studies these were principally diarrhoea, rashes and thrush [Glasziou, 1997]. Consideration of the side effects of antibiotics would have been useful in further defining their risk-benefits.

Special Risk Groups

Acute rheumatic fever is common among people living in some parts of the world (Australian Aborigines living in poor socioeconomic conditions, for example), and antibiotics may be justified to reduce the complication of acute rheumatic fever in these settings. In other parts of the world the incidence of acute rheumatic fever is so low (one estimate is that it took twelve general practitioners' working lifetimes to encounter one new case of acute rheumatic fever in Western Scotland in the 1980s [Howie, 1985]) that the risks of serious complication arising from using antibiotics for this complication might be of the same order as that of acute rheumatic fever.

Reviewers' conclusions

Implications for practice

Acute rheumatic fever is common among people living in some parts of the world (Australian Aborigines living in poor socioeconomic conditions, for example), and antibiotics may be justified to reduce the complication of acute rheumatic fever in these settings.

For other settings where rheumatic fever is rare, there is a balance to be judged between modest symptom reduction and the hazards of antimicrobial therapy. Since ninety percent of patients are symptom free by one week (in both groups), the absolute benefit of antibiotics at this time and beyond is vanishingly small.

Assuming a complication rate of five percent for otitis media in
untreated children and one percent for adults, and an odds ratio of 0.23 for treatment with antibiotics, then about 30 children and 145 adults with sore throat must be treated with antibiotics to prevent one episode of acute otitis media.

Antibiotics have a small beneficial effect on both suppurative and symptom reduction. The effect is so small that clinicians must judge with individual cases whether it is clinically justifiable to employ antibiotics to produce this small effect. In other words their use appears to be discretionary rather than either prohibited or mandatory.

Implications for research

More placebo
More placebo controlled trials in modern Western societies may be helpful in further defining the benefit of antibiotics in settings in which infection poses a less severe threat to health than in the past or in socio-economically deprived communities. Trials should be conducted in socio-economically deprived societies and also in children to determine the effectiveness there of antibiotics.

Studies which use patient-centred outcome measures compatible with those presented here would be greatly beneficial, in terms of easier comparison and analysis of results, and ready inclusion of the authors work in future updates of this meta-analysis.

Few trials have attempted to measure the severity of symptoms. If antibiotics reduce the severity as well as the duration of symptoms, their benefit will have been underestimated in this meta-analysis.

Acknowledgements

Ian Thomas and Michael Thomas for research assistance.

Thanks to Beth Clewer and Katie Farmer who in January 1999 drew our attention to mistakes in the data extraction by their careful checking of original studies as part of their medical student project at the University of Bristol Medical School.

Characteristics of included studies

Table: Characteristics of included studies

Characteristics of excluded studies

Study : Bass, 1986
Study used a Likert scale to measure severity and duration of symptoms. No raw scores are available for entry into metanalysis.

Study : Bishop, 1952
Non-randomised allocation to treatment goups. (Quote) "Where an exceptionally severe case fell in the control group and it was felt unjustifiable to withhold specific treatment, the case was transferred to one of the other groups and the next case was placed in the control group." This bias was not quantified.

Study : Catanzaro, 1958
Study compared sulphonamides with other antibiotics. No control condition was used.

Study : Cruickshank, 1960
Study is another report of the data previously published by Brunfitt, 1957.

Study : Gerber, 1989
Assessed two regimes of penicillin. No control group used.
Study : Guthrie, 1988
Study did not use control condition.

Study : Haverkorn, 1971
Subjects not treated with antibiotics given antipyretics. Subjects receiving antibiotics received no antipyretics. No control condition.

Study : Herz, 1988
No patient-centred outcomes, except return visits for URIs. Poor randomisation - out of a series of 202, the first and last 50 were assigned to antibiotics, with the middle 102 assigned to control.

Study : Howie, 1970
Illness was "cold or flu-like illness", not acute pharyngitis (exclusively). Soreness of throat not an outcome measure.

Study : Marlow, 1989
Patient population highly selected (non-pregnant, negative rapid strep. test, negative throat culture, no other infection present, not allergic to erythromycin, age >12), and patient-centred outcomes not compatible with those in this meta-analysis.

Study : Massell, 1951
Study examined effect of penicillin on hemolytic streptococcal infections in rheumatic patients only, without randomisation to control condition. Infections that were not treated with penicillin for 'various reasons' were treated as controls. These reasons were not given.

Study : McDonald, 1985
No data suitable for this meta-analysis were described although symptoms were recorded. The author was approached for these data, but no reply was received.

Study : Merenstein, 1974
No data on suppurative or non-suppurative complications. No data on day three for soreness of throat, fever, or headache.

Study : Middleton, 1988
No data on suppurative or non-suppurative complications. No data on day three for soreness of throat, fever, or headache.

Study : Morris, 1956
Study observed effect of Sulfadiazine on prevention of Study observed effect of Sulfadiazine on prevention of rheumatic fever only. No control condition was used.

Study : Randolph, 1985
No data on suppurative or non-suppurative complications. No data on day three for soreness of throat, fever, or headache.

Study : Schalen, 1985
Primary complaint hoarseness, not sore throat. No patient centred outcomes apart from hoarseness.

Study : Schalen, 1993
Patients presented for laryngitis and hoarseness, not pharyngitis

Study : Schwartz, 1981
Study compared seven versus ten days of treatment with penicillin. No control group was used.

Study : Shvartzman, 1993
Study compared efficacy of amoxycillin against penicillin, no control condition was used.
Study: Todd, 1984
Primary complaint not sore throat - purulent nasopharyngitis instead

Study: Valkenburg, 1971
Study did not involve any control measures. Data only given for subjects not treated with antibiotics.

References

References to studies included in this review

Bennike, 1951 {published data only}

Brink, 1951 {published data only}

Brumfitt, 1957 {published data only}

Catanzaro, 1954 {published data only}

Chamovitz, 1954 {published data only}

Chapple, 1956 {published data only}

Dagnelie, 1996 {published data only}

De Meyere, 1992 {published data only}

Denny, 1950 {published data only}
Denny, 1953

Howe, 1997 {published data only}

Krober, 1985 {published data only}

Landsman, 1951 {published data only}

Little, 1997 {published data only}

MacDonald, 1951 {published data only}

Nelson, 1984 {published data only}

Petersen, 1997 {published data only}

Pichichero, 1987 {published data only}

Siegel, 1961 {published data only}

Taylor, 1977 {published data only}
Taylor GD, McKerr M, Fergusson DM. Amoxycillin and co-trimoxazole

Wannamaker, 1951 {published data only}


Whitfield, 1981 {published data only}


* indicates the major publication for the study

References to studies excluded from this review

Bass, 1986


Bishop, 1952


Catanzaro, 1958


Cruickshank, 1960


Gerber, 1989


Guthrie, 1988


Haverkorn, 1971


Herz, 1988


Howie, 1970

Marlow, 1989


Massell, 1951


McDonald, 1985


Merenstein, 1974


Middleton, 1988


Morris, 1956

Morris AJ,

Randolph, 1985


Schalen, 1985


Schalen, 1993


Schwartz, 1981


Shvartzman, 1993

Todd, 1984


Valkenburg, 1971


Additional references

ABS, 1986


Del Mar 1992a


Del Mar, 1992b


Del Mar, 1992c


Del Mar, 1997


Glasziou, 1997


Goslings, 1963


Horder, 1954


Howie, 1971

Howie JGR, Gill G, Durno D. Respiratory illness and antibiotic use in general practice. Journal of the Royal College of General

Howie, 1978


Howie, 1985


Coversheet

Title

Antibiotics for sore throat

Reviewer(s)

Del Mar CB, Glasziou PP, Spinks AB

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Contact address :

Prof Chris Del Mar
Centre for General Practice
University of Queensland Medical School
Brisbane Queensland 4006
AUSTRALIA
Telephone: +61 7 3365 5379
Facsimile: +61 7 3365 5442
E-mail: c.delmar@mailbox.uq.edu.au

For information on the editorial group see: Cochrane Acute Respiratory Infections Review Group

Extramural sources of support to the review

No sources of support supplied

Intramural sources of support to the review

Centre for General Practice, University of Queensland Medical School

Synopsis

Antibiotics for sore throat provide modest benefit for symptoms, the incidence of suppurative and non-suppurative complications. Whether or not they are worthwhile will depend on the incidence of the complication rates for the community, and the values the patient and society places on symptom relief and avoidance of complications, balanced against the cost of the antibiotics.

Comments and criticisms

Antibiotics for sore throat

Summary of comments and criticisms

1. The objectives as they are stated in the abstract include an assessment of the harms associated with the use of antibiotics in the management of sore throat, but the objectives as stated in the text of the review no longer refer to any assessment of harm. Indeed, the review does not address any adverse effects of antibiotics [which are not unimportant] and does not provide a
reasonable explanation as to why this is not done other than to state in the discussion that this was not possible because of inconsistencies in the way these data were recorded. In the absence of RCT data on harmful effects the authors might have considered whether usable information could be provided by other study designs.

2. Reviews on this subject should treat adults and children separately, but this review does not attempt to do this.

3. All clinically important outcomes have not been addressed by the review and others such as resource use, re-attendance and time off school or work are probably at least as important as those that were selected. It may have been more helpful to have collected data on all available outcomes provided that they are free from detection bias.

4. The question addressed by the review is not sufficiently well defined to allow the review to be executed systematically. Clear definitions are not given for the key elements of the question.

Most importantly, clear definitions of what is meant by primary care and sore throat are not given, leading to confusion around inclusion and exclusion decisions. Many of the control groups of the included studies do not involve a placebo but instead simply compare treatment with antibiotics to no treatment, so that some excluded studies would be eligible for inclusion, such as Catanzaro 1958 which was excluded because it compared antibiotics with sulfadiazine.

Apparent errors in inclusion and exclusion decisions have arisen probably as a result of the general lack of clarity discussed above. Specifically, the lack of a clear definition of what is meant by primary care appears to have led to the inclusion of an odd assortment of studies. For example, a couple of the included trials studied only people with sore throat who were admitted to hospital (Siegal 1961 and Bennike 1951). In addition, there appears to be an issue around the definition of a sore throat particularly in relation to positive or negative Streptococcus throat swabs. Streptococcal sore throats are a small sub-set of the total population of sore throats and the failure of the reviewers to address this in the inclusion criteria means that the results of pragmatic trials of sore throat are mixed in with those of streptococcal sore throat.

There is a failure to always faithfully report the detailed results of the included studies, and there are several numerical errors in the data abstracted. For example, in Bennike 1951 the baseline numbers include patients in the "ulcerative tonsillitis" group even though most outcomes are not reported for this group.

5. The search strategy is restricted to a Medline search, a search of the Cochrane Library and citation checking. No attempt appears to have been made to search other databases. The reviewers are not explicit about the details of their searching activities nor about how they used the work of the Cochrane Acute Respiratory Infections Group.

6. References to the included and excluded studies were incomplete. Specifically they were not provided for Dagnelie 1996, Howie 1997, Little 1997 and Peterson 1997 (included) and Herx 1988, Howie 1970, Marlow 1989, McDonald 1985, Schalen 1993 and Todd 1984 (excluded).

7. Given the nature of the data presented, it is possible that a formal meta-analysis was inappropriate. A descriptive analysis may have been more appropriate and more informative.
8. There is considerable uncertainty around the effectiveness of antibiotics on sore throat on the basis of the existing research examined by this review and this is not emphasised by the authors. Particular problems exist around the relevance of the trials to the present day with regard to the outcomes examined (rheumatic fever and glomerulonephritis), the poor quality of the majority of the included trials and the generalisability of the trials with regard to the study populations (e.g. United States airforce recruits).

Reviewer's reply

1. This is valid criticism: we need to describe the inadequacies of the information in the trials (after checking again) in the text.

2. A subgroup analysis on the basis of age is a good idea, and we will attempt this at the next major review.

3. This is a good idea, and we will attempt this at the next major review.

4. Certainly the issue of definitions is particularly difficult in this group of illnesses. One of us has written a paper on these difficulties (Del Mar C. Managing sore throat: a literature review. I. Making the diagnosis. Med J Aust 1992;156:572-5.). There is a particular difficulty in the fact that primary care doctors use the terms 'sore throat' tonsillitis and pharyngitis in slightly different ways, including interchangably. Moreover the notion that patients with positive swabs for Streptococcus have a different illness can be challenged. Nevertheless a subgroup analysis for this with swab-positive and swab-negative is a good idea which we will incorporate with our next review.

Thank for pointing numerical errors out to us, and we will check on this. Please could you detail other numerical errors for us?

5. We are explicit about our search method. At the time we undertook the search the Cochrane Acute Respiratory Infections Group had no material to assist us. This will be reviewed at the next major update.

6. Thank you for drawing our attention to this.

7. As is often the case, there is considerable variation in the population groups, treatments, outcomes measures, etc in these trials. This does not make a synthesis inappropriate, but rather allows us to examine whether these factors appear to make a difference. We also felt it important to specifically attempt to calculate the SIZE of the benefits, as this is what clinicians are interested in, and what will persuade them to modify their practice. It is then important to recognise that the size of the effect will vary in different populations: as we point out, in groups at high risk of rheumatic fever - such as Australian aboriginals - the prevention of RF is important; we are also interested in trying to better predict which sub-groups will experience the most or least symptom relief, and plan to detail this in the next update.

8. We think we have discussed this in the Review. However we will reconsider what we have written in the overhaul.

Contributors to comment

Jackie Young (on behalf of an interdepartmental critical appraisal workshop based in the Department of Public Health and Epidemiology, The University of Birmingham, UK) Email: j.m.young.20@bham.ac.uk

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