

Why Antimicrobial Therapy for Fever and Sore Throat in Patients with Non-exudative Pharyngotonsillitis ?

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Abstract

The prescription rate and types of antimicrobial for a claim of fever and sore throat in healthy females with normal throat were determined. The general practitioners opinions for antimicrobial prescription in a presumably viral URI were also studied using a questionnaire with scenario. Antimicrobial prescription for such claim was found to be 38 (73%) of 52 visits at out-patient departments of two hospitals and three medical centres. Amoxicillin (53%) and ampicillin (13%) were the two most common antimicrobials used for therapy of the condition. Of 164 questionnaire distributed among general practitioners, 104 (63%) were available for analysis. The three most common opinions cited for antimicrobial prescription for a viral URI were as follows : Amoxicillin was used to treat silent group A streptococcal infection which may co-present in non-exudative presumably viral pharyngotonsillitis (82%). It can prevent secondary bacterial infection (81%). In addition, it can prevent rheumatic fever and acute glomerulonephritis (74%) due to possible group A streptococcal infection. (*J Infect Dis Antimicrob Agents 1996;13:43-7.*)

INTRODUCTION

Upper respiratory tract infection (URI) is frequently encountered in daily practice and clinically manifested with a wide range of well-known symptoms such as fever, headache, malaise, sneezing, nasal discharge, nasal obstruction, sore or "scratchy" throat, mild burning sensation of the eyes and cough. Viruses are undoubtedly the initiators for at least 80 percent of the total URI (1,2) and the appearance of throat for each viral infection ranges from normal to non-exudative pharyngotonsillitis though sometimes clinical clues to viral infection are also present in the throat. On the other hand, bacterial pathogens account for only 10 to 20 percent of URI cases. The only bacterial pathogen that is clinically important, is group A beta-hemolytic

streptococcus (GABHS) because infection due to this organism has been associated with increased risk of developing rheumatic fever and glomerulonephritis. Treatment with penicillin reduces the risk of developing rheumatic fever among the streptococcal sore throat (3). Of those with untreated streptococcal sore throat, 0.3-3 percent will develop rheumatic fever later (4). Thus emphasis on antimicrobial therapy is heavily placed on infection due to GABHS typically characterized by follicular or exudative tonsillitis.

However, our current observation reveals that antimicrobial prescription is still very frequent though ineffective for most URI presumed to be viral in origin, at both government hospitals and private medical clinics. In 1983, Howie discovered that 70 to 80 percent of URI

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were treated with antimicrobials. Kunin et al conducted a study on three representative hospitals in Wisconsin and found that more than half of the antimicrobials used were unnecessary and it accounted for 19 to 34 percent of the pharmacy budget of the hospitals. The situation of antimicrobial prescription has been unchanged until now in several medical centres and hospitals in Thailand and at Siriraj Hospital (5). We hypothesize that this type of practice is mainly related to the possibly common appearance of non-exudative pharyngotonsillitis most of which are caused by viruses but GABHS can not be entirely ruled out. After literature search, we are still left with unknown prevalence of infection due to GABHS in clinical setting of non-exudative pharyngotonsillitis. If such prevalence is found, we will be able to tackle or at least understand the situation of frequent antimicrobial prescription for most viral URI. Accordingly, if our hypothesis is correct, the antimicrobial prescription rate should be much lower among patients who have sore throat and fever but present with normal pharynx and tonsils most of which if not all, are caused by viruses.

Our objectives were to find the percentage and type of antimicrobials prescribed to young healthy females with normal-looking pharynx and tonsils who presented themselves to general physicians at out-patient department of hospitals and private medical clinics with a claim of sore throat and fever for two days. No underlying or concomitant disease was told to present. Opinions of another group of general practitioners to explain why amoxicillin was given to a young female patient with a diagnosis of presumably viral pharyngotonsillitis were also elucidated using a questionnaire.

MATERIAL AND METHODS

Five females volunteered to see 52 general practitioners during September 1994 to October 1995 at out-patient department of two hospitals and three private medical clinics. They presented themselves with a mock history of fever and sore throat of two-day duration. They denied any concurrent or underlying disease but symptoms of headache, myalgia and malaise could be admitted. Their pharynx and tonsils were inspected by one of the authors to assume their normal appearances with no cervical lymphadenopathy before their visits to those general practitioners. Thereafter, the prescription sheets were collected and analysed for percentage and type of antimicrobial therapy for the illness.

A questionnaire was used to elucidate opinions of general practitioners during an annual meeting of the Thai Medical Association. The questionnaire began with a scenario of a previously healthy female who had fever and sore throat for two days. Physical examination of her throat showed non-exudative pharyngotonsillitis. However, a general practitioner ordered amoxicillin for her though he thought she had viral URI. Then nine items of reason why amoxicillin was given to the patient, were offered to those general practitioners and asked for their opinions. They could agree, disagree or did not know and were requested to tick their answers at the end of each reason. The results of their answers were kept confidentially. The details of those items were showed in Table 1. In the final analysis, we counted only those who ticked "agree" to the reason. The structure and content of the questionnaire were :

A previously healthy female who had fever, sore throat, headache, myalgia and malaise for two days visited a general practitioner for treatment. Physical examination showed she had fever, injected conjunctiva and her throat showed non-exudative pharyngotonsillitis. However, the doctor ordered amoxicillin in addition to other supportive treatment though he thought she had viral URI. Your opinions to the above scenario, to explain the reason of that doctor why amoxicillin therapy was used for the illness, were offered in the following items (see details in Table 1) : Please tick whether you agree, disagree or do not know at the end of each item.

RESULTS

Of 52 visits, 38 (73%) doctors prescribed an antimicrobial to treat the illness claimed by our normal volunteers. Paracetamol or acetylsalicylic acid and throat lozenges were also prescribed in 98 and 50 percent of the visits respectively. Among the prescribed antimicrobials, amoxicillin was accounted for 53 and ampicillin 13 percent. Penicillin V, co-amoxiclav, erythromycin, spiramycin, roxithromycin, cefaclor, cephalexin, cefuroxime axetil were also used in 5, 5, 3, 5, 5, 3, 3 and 3 percent respectively.

Of 164 questionnaires distributed, 104 (63%) were sent back for analysis. Sixty percent were male and 61.7 percent worked in government hospitals. Overall, more than 50 percent agreed with all the reasons offered with the exception of patient's demand for an antimicrobial which 49 percent of the doctors agreed. The top two

Table 1. Percentage of agreement by general practitioners for each item.

No.	Item	Yes (n = 104)
1.	Such clinical manifestation was not useful to discriminate viral from bacterial URI.	68%
2.	Amoxicillin can shorten the duration of illness.	66%
3.	Amoxicillin can prevent secondary bacterial infection such as otitis media, sinusitis and pneumonia.	81%
4.	Amoxicillin therapy was used because the physician did not want to miss even a single case of non-exudative pharyngotonsillitis possibly due to group A streptococcal infection.	82%
5.	Amoxicillin can prevent rheumatic fever and glomerulonephritis which may complicate the illness.	74%
6.	Amoxicillin was quite safe though prescribed for therapy of viral URI.	66%
7.	Amoxicillin is very cheap compared to other antimicrobial though prescribed for therapy of viral URI.	55%
8.	Patient's demand for an antimicrobial to treat sore throat, is high and very common.	49%
9.	Overall, the doctor would like to provide the best treatment.	68%

reasons which 82 and 81 percent of the responders agreed were items no. 3 and no. 4 which showed that physicians believed that antimicrobial could prevent secondary bacterial infections such as otitis media, sinusitis and pneumonia and another aim of amoxicillin therapy was not to miss even a single case of non-exudative pharyngotonsillitis possibly due to GABHS. The percentages of agreement to each item were showed in Table 1.

DISCUSSION

Our study revealed that antimicrobial prescription for adults with history of fever and sore throat was 73 percent though the appearance of their throats were normal. In 1987, Nirun Vanprapar found 83 percent of children with acute respiratory tract infection were given an oral antimicrobial at Siriraj Hospital. According to our verbal surveillance, the antimicrobial prescriptions for non-streptococcal URI at various hospitals and medical centres varied within the range of 70-98 percent. Since the antimicrobial prescription rate in our study also fell in this range, we were inclined to believe that the appearance of throat in URI was not critical for physician to order an antimicrobial. Symptoms such as sore throat and fever were much more crucial and perhaps automatically direct to the antimicrobial prescription for the patient. Whether our preliminary conclusion is correct awaits to be proven in another study. However, it is very interesting to know the prevalence of streptococcal infection in URI manifested as normal throat and non-exudative pharyngotonsillitis. In addition, if

there is any clinical clue to discriminate viral from streptococcal sore throat in patients who have fever and sore throat but exhibit normal throat or non-exudative pharyngotonsillitis, the question of whether antimicrobial prescription under the condition is in deed overused or appropriate, can be answered.

With regards to types of antimicrobial prescribed for our normal volunteers, it can be seen that the target organism was GABHS since amoxicillin, ampicillin, penicillin V and other antimicrobials are active against the organism. Reasons given by general practitioners supported the above explanation since most of them believed that clinical manifestation alone was not useful in discriminating viral from bacterial URI and infection due to GABHS may co-exist in undifferentiated URI or in URI with normal throat. The commercial kit designed to rapidly detect group A streptococcal antigen is still relatively expensive for most Thai patients and offers only marginal advantage over clinical picture of URI. Thus it is not practical to be used in Thailand and is not popular up to now. Other antimicrobials such as co-amoxiclav, erythromycin, spiramycin, roxithromycin, cefaclor, cephalexin, cefuroxime axetil were used possibly due to their broader antimicrobial spectrum than that of amoxicillin in order to treat or prevent bacterial complications of URI. If they occur, the responsible bacteria are generally *S. aureus* or anaerobes which required oral broad-spectrum antimicrobial. In addition, it is customarily for many Thai patients to acquire some kind of antimicrobial sold freely over the

counter from any drug store. If they failed to improve from self-medication, then they came to seek medication from doctor at a private clinic or hospital. This pattern of patient's behaviour can explain why some general practitioners used oral broad-spectrum antimicrobial as empiric treatment since they believed the patient has failed from recent self-treatment with an antimicrobial such as amoxicillin. Another reason obtained from few physicians who work in luxurious medical centres owned by big banks, is that medical service offered to workers of the banks, must be of highest standard with no limit of financial resource. In general, single shot and rapid recovery is the rule to assure those workers that the highest quality of medical care is being offered at the centre. If symptom such as sore throat due to a minor illness like URI, failed to improve after single treatment, the responsible physician or medical care are then, perceived by those workers as non-qualified physician or substandard care. On the physician's side, they would also like to use the most expensive and "presumably best" drug to defend themselves in case that if those workers fail to improve, it is not their faults since they have provided their patients the best and "most expensive" care no matter their prescriptions were rational or not. Those expensive antimicrobials given to our volunteers came from these centres.

Reasons to use an antimicrobial for a viral URI on the physicians' opinion can be summarized into three main categories which are not different from what other study have found (6). The first one is not to miss even a case of group A streptococcal infection and its serious complications such as rheumatic fever and glomerulonephritis could be reduced or prevented. The second reason is to prevent bacterial complication or shorten the duration of illness. The third one is the relatively low price and safety of amoxicillin administration and most physicians believed there was no significant economic loss for prescribing amoxicillin. The demand of patients for an antimicrobial to treat URI was accepted by 49 percent which was least agreed by the responders. After literature review, we could not find any study that addressed the issue of prevalence of group A streptococcal infection in non-exudative pharyngotonsillitis. No data available to examine how many cases of non-exudative pharyngotonsillitis, subsequently developed acute rheumatic fever and glomerulonephritis. The existing evidence do not also support the second reason. As shown by numerous papers, antimicrobials did not

shorten the course of URI, prevent complications (7-9), reduce pathogens in the nasopharynx or exert any beneficial effect (10-16). Although many of the studies had flaws e.g. failure to have a placebo control in some and inadequate sample size in the majority, which detract from their validity, all were consistent in finding antimicrobials to be without benefit. For the third reason, the prevalence of adverse reaction may be high as 29 percent most of which were minor and severe reactions occurred in roughly 2 percent of treated children (17). From a society's viewpoint, irrational use of antimicrobial is associated with an unnecessary increase in bacterial resistance sometimes at the alarming rate. Even with newer fluoroquinolones which are completely synthetic agents and had been introduced into market worldwide for less than fifteen years, gram-negative bacteria are very smart to develop resistance to the drugs. Since fluoroquinolones interfere with bacterial DNA synthesis, transmission of resistance *via* plasmid is never expected and spreading of quinolone-resistant bacteria is possible through mutation only. Hence development of bacterial resistance should be at a very slow pace. However, recent report contradicts our anticipation (18). When these agents are used too often, quinolone-resistant bacterial pathogens begin to emerge. The resistance spreads to such an extent that in some developed country where drug prescription is expected to be mostly rational, susceptibility of *E. coli* to fluoroquinolones can no longer be taken for granted (18). It is also a burden to the whole country because the total annual cost for unnecessary antimicrobials prescribed for the condition is enormous. If a minimal average cost for the entire course of antimicrobial therapy using the locally manufactured drugs is 10 bahts and Thai people have an average of 3 episodes of URI annually two of which are viral in origin, then for 60 million population like Thailand, at least 1,200 million bahts are wasted unnecessarily in only one year.

In a time of spiralling health care cost in Thailand, the justification of antimicrobial administration in non-exudative pharyngotonsillitis possibly due to presumed viral URI is worthy of reassessment. We need to know the prevalence of group A streptococcal infection in patients with non-exudative pharyngotonsillitis. If possible, we also need to know the prevalence of serious complications due to group A streptococcal infection that arise from this group of patients. The effectiveness of amoxicillin over placebo in non-exudative pharyngo-

tonsillitis may need just another rigorous evaluation for an unbiased estimate of its effectiveness in shortening the duration of the illness in the current situation. In order to minimize the problem of emerging resistant pathogens with limited financial resources, all these data are urgently needed to show that routine antimicrobial therapy for fever and sore throat is justified or not. Since antimicrobial resistance rate is rapidly increased in Thailand, it is also important to aim control of resistant bacteria at the most cost-effective areas. In fever and sore throat due to non-exudative pharyngotonsillitis, if previous data about effectiveness of amoxicillin administration holds true for the present situation, it means that antimicrobials should be used when its clinical presentation strongly indicates bacterial infection. They can also prevent our country to be a victim of neglected and hefty economical loss due to excessive use of antimicrobials now and in the future.

In conclusion, antimicrobial prescription for non-exudative pharyngotonsillitis presumably due to viral infection is very common. Amoxicillin is the most frequent drug used for the condition. Common reasons given by general practitioners to explain this practice pattern were not to miss even a case of group A streptococcal infection, to prevent rheumatic fever and glomerulonephritis, to prevent bacterial complication and to shorten the duration of illness.

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