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Do Delayed Prescriptions Reduce the Use of Antibiotics for the Common Cold?

A Single-Blind Controlled Trial

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■ OBJECTIVE To test the use of a delayed prescription compared with instructions to take antibiotics immediately in patients presenting to family physicians with upper respiratory tract infections (common colds).

■ STUDY DESIGN Randomized controlled single-blind study.

■ POPULATION Subjects were 129 patients presenting with the common cold who requested antibiotics or whose physicians thought they wanted them. All patients were in a family practice in Auckland, New Zealand, consisting of 15 physicians (9 male, 6 female) who had completed medical school between 1973 and 1992.

■ OUTCOMES MEASURED Outcomes were antibiotic use (taking at least 1 dose of the antibiotic), symptom scores, and responses to the satisfaction questions asked at the end of the study.

■ RESULTS Patients in the delayed-prescription group were less likely to use antibiotics (48%, 95% CI, 35%-60%) than were those instructed to take antibiotics immediately (89%, 95% CI, 76%-94%). Daily body temperature was higher in the immediate-prescription group. The lack of difference in the symptom score between the 2 groups suggests that there is no danger in delaying antibiotic prescriptions for the common cold.

■ CONCLUSIONS Delayed prescriptions are a safe and effective means of reducing antibiotic consumption in patients with the common cold. Clarification of patient expectations for antibiotics may result in a lower prescription rate. When the patient demands a prescription, delaying its delivery has the potential to provide gentle education.

■ KEY WORDS Common cold; antibiotics; randomized controlled trials. (*J Fam Pract 2002; 51:324-328*)

KEY POINTS FOR CLINICIANS

- Delaying the prescription of antibiotics reduces antibiotic intake in patients who insist on taking antibiotics for the common cold.
- Giving a delayed prescription and asking the patient to return to the office to fill it may reduce antibiotic consumption further.

Antibiotics continue to be commonly used to treat the common cold[1-3] despite longstanding doubts about their efficacy[4,5] or ability to prevent complications.[6] Upper respiratory tract infection (URTI) is the most common reason for a new consultation in family practice and the second most common reason for the prescribing of an antibiotic.[7] Reported prescription rates for antibiotics for treating the common cold range from 17% to 60% in the United Kingdom and United States and 78% in New Zealand.[1,8] Ineffective but widespread use of antibiotics is not only a poor use of health care funds but also a cause of morbidity (from adverse effects) and the development of resistant strains of bacteria.[8-10]

A promising technique to reduce antibiotic use is the delayed prescription. The only published randomized controlled trials of delayed prescription use examined its effect for the treatment of sore throat, acute childhood otitis media, and cough.[11-13] In the sore throat study, antibiotics were used by 99% of a group given antibiotics, by 13% of a group not offered any, and 31% of a group given a prescription to be taken after 3 days if symptoms persisted. The authors of the otitis media study noted a 66% reduction of antibiotic use in the delayed-prescription group, who had more symptoms, signs, and sleepless nights than the "take-now" group. In the study with acute cough, the use of antibiotics was reduced by 55% in the group with delayed prescriptions. Our study, undertaken in winter 2000, tested the use of a delayed prescription versus instructions to take

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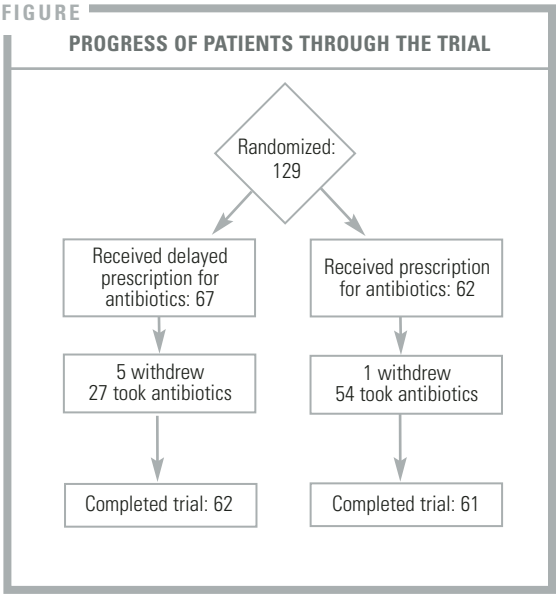
FIGURE



antibiotics immediately in patients presenting to general practitioners with URTIs.

METHODS

The 15 family physicians (FPs) who recruited patients for this study were selected primarily from a group who had reported in a previous study that they frequently gave delayed prescriptions to patients.[14] Ethical approval was given by the Auckland Ethics Committee.

Inclusion and Exclusion Criteria

Patients of any age were eligible if they presented to their FP with a new case of the common cold and either the FP thought the patient wanted antibiotics or the patient stated that desire. For young children, the parents indicated whether or not they wanted antibiotics. FPs were provided with the diagnostic criteria for URTI from the International Classification of Health Problems in Primary Care (ICHPPC-2), which defines an URTI as including the presence of acute inflammation of the nasal or pharyngeal mucosa in the absence of other specifically defined respiratory infection.[15]

Patients were excluded if they had suspected streptococcal tonsillitis, sinusitis, bronchitis, or pneumonia. Also excluded were patients with lower respiratory signs, those who needed an x-ray, those with a past history of rheumatic fever, and those who had experienced a serious illness or any antibiotic treatment in the previous 2 weeks. Throat cultures were not required. Eligible patients were invited to participate and signed an informed consent form. Ideally, the offer to join the study was to be made to consecutive patients, but this did not occur in all practices.

Interventions

The intervention group was given a prescription for antibiotics with instructions to fill it after 3 days if symptoms failed to improve. The control group received a prescription with instructions to start taking the antibiotic medication immediately. General practitioners prescribed any antibiotic that they considered most appropriate. In both groups, patients were advised to return to see their doctor if symptoms worsened.

Data Collection

At recruitment, the patient's temperature was taken and the list of symptoms was recorded in duplicate. The patient was asked to take his or her temperature daily with a digital thermometer (Assess Diagnostics Medical Industries Australia Pty. Ltd., 148-152 Regent St., Redfern NSW 2016, Australia) that was provided. Patients were given symptom checklists to complete daily for 10 days after the visit. Symptoms listed were dry cough, night cough, sneezing, sore throat, pain on inspiration, pain when coughing, hoarse voice, headache, staying home from work or unable to do normal daily tasks, unwell, diarrhea, vomiting, and nausea without vomiting. Patients were instructed to record whether they had a runny nose with clear secretions ("clear runny nose"), stuffy (blocked) nose, or runny nose with dark secretions ("colored runny nose"). Patients further checked off whether they had clear sputum only in the morning, colored sputum in the morning, clear sputum all day, or colored sputum all day.

A point was allocated for each symptom. The maximum possible score was 15.[16] A study assistant telephoned all participants on day 3, day 7, and day 10 to ask about their temperature and symptoms. At the end of the study, the research assistant asked participants about their level of satisfaction with the consultation, using the questions and scoring system devised by Little et al.[11] Although no data were collected about revisit rates, data were collected about the patient's intention to visit a physician for the next cold.

Outcomes and Analysis

The outcomes were antibiotic use, symptom scores, and the responses to satisfaction-related questions asked at the end of the study. Outcomes of intervention and control groups were compared on an intention-to-treat basis.[17] Because of the repeated measures, the temperatures and summary scores of symptoms were determined with the general linear mixed model that uses Statistical Analysis System (SAS, Cary, N.C.), version 8, for Windows. Chi-square determinations and the Mantel-Haenszel

TABLE 1

BASELINE CHARACTERISTICS AND SYMPTOMS OF THE 2 GROUPS

	Immediate Prescription	Delayed Prescription
Characteristics		
Number of patients	62	67
Male / female	22 / 40	26 / 41
Mean age (SD)	27.9 years (3.1)	23.6 years (2.7)
Cigarettes per day	1.26 (0.47)	1.17 (0.54)
Mean temperature (SD)	36.9 (0.08)	36.7 (0.08)
Days of illness before doctor's visit	4.5 (0.5)	5.0 (0.7)
Total symptom score (SD)	5.1 (0.28)	5.4 (0.22)
Symptoms		
Dry cough	31	35
Productive cough		
Cough with clear sputum in morning	8	5
Cough with clear sputum all day	6	7
Cough with colored sputum in morning	8	7
Cough with colored sputum all day	10	16
Nasal symptoms		
Clear rhinitis	27	22
Blocked or stuff nose	21	26
Colored runny nose	12	15
Night cough	29	37
Sneezing	31	26
Sore throat	38	31
Pain in chest on breathing in	6	7
Pain on coughing	17	13
Hoarse voice	28	26
Headache	26	28
Unwell*	44*	56*
Limitation of activities	25	23
Nausea	7	6
Vomiting	5	6
Diarrhea	6	4

* Pearson chi-square 9.134, 1 degree of freedom, $P = .0025$, 2 sided.
The number of patients recruited per family physician ranged from 1 to 40.
SD denotes standard deviation.

odds ratio were performed for discrete variables using Statistical Package for the Social Sciences (SPSS), version 10, for Windows. When the final data point for continuous variables was missing, the last recorded value was analyzed as the current value. For discrete values, worst-case and best-case scenarios were performed. The sample size of 212 patients was based on a reduction from 60% of antibiotics consumed immediately to 40% in the delayed-prescription group (alpha 0.05, beta 0.2).

Allocation and Masking

The unit of randomization was the patient. N.K., who was not a recruiter, generated the allocation schedule with Excel 97. Letters containing instructions for the intervention strategy pertaining to each patient or allocating the patient to the control group were placed in opaque envelopes and sealed. The study number was written on the outside of the envelope according to the randomization schedule. The envelopes were then given to the research assistant, who placed them in a large brown envelope with the consent forms and information sheets for recruiting family physicians. The recruiters opened each envelope immediately after recruitment of each patient.

Patients were told only that they would be given 1 of 2 sets of instruction about taking antibiotics for their colds. Participants read an information sheet and then completed a consent form. Thus, patients were blind to what the other group would take. The research assistant asked the participants not to tell her which instructions they had been given for taking antibiotics. If both types of blinding had been followed correctly, this study could be described as double blinded. However, because we cannot confirm the effectiveness of blinding the research assistant, we prefer to call this study single blinded. One copy of the allocation schedule was kept in the office of N.K.; another was kept by the departmental secretary.

RESULTS

The Figure shows the trial profile summarizing participant flow. The baseline characteristics of the patients in both groups were similar (Table 1).

Patients in the delayed prescription group were less likely to use antibiotics (48%, 95% CI, 35%-60%) than those in the "take antibiotics now" group (89%, 95% CI, 76%-94%). The odds ratio for not using antibiotics was 0.12 (95% CI, 0.05 to 0.29) using intention-to-treat analysis. By antibiotic use, we mean that the patients consumed at least 1 dose of the antibiotic medication.

Table 2 shows the outcomes for temperature and symptom score using an intention-to-treat model. The general linear model for repeated measures found average temperature significantly higher (by 0.2°C) in the immediate antibiotic use group ($P = .039$) and no significant difference for the symptom score ($P = .29$). Reanalyzing with only collected data (without intention to treat) found no significant differences from the intention-to-treat analysis. The power to detect a difference in symptom score of 30% is 80% for an alpha of 0.05, assuming that the study gives measures of variation of the symptom score that are close to the real values. There were no significant adverse effects from taking antibiotics or not. Patients' beliefs and intentions were not affected by the interventions (Table 3).

TABLE 2

OUTCOMES AT BASELINE AND ON DAYS 3, 7, AND 10

	Immediate Prescription	Delayed Prescription
Temperature (C)*		
Baseline	36.9 (0.1)	36.7 (0.1)
Day 3	36.4 (0.1)	36.2 (0.1)
Day 7	36.4 (0.1)	36.1 (0.1)
Day 10	36.3 (0.1)	36.1 (0.1)
Symptom Score (1 point for each of 15 symptoms in Table 1)*		
Baseline	5.1 (0.3)	5.4 (0.2)
Day 3	2.9 (0.2)	3.6 (0.3)
Day 7	1.8 (0.2)	2.0 (0.3)
Day 10	1.4 (0.2)	1.5 (0.2)

*The general linear model for repeated measures found the significantly higher temperature of 0.2°C in the immediate-use antibiotic versus that in the delayed-use group (P = .039) and no significant difference for the symptom score (P = .29).

DISCUSSION

We believe that this is the first published randomized controlled trial of delayed prescriptions for antibiotics for the common cold. Asking patients to wait for 3 days before taking their medication reduced consumption of antibiotics from 89% to 48% (P = .0001). The 41% reduction is smaller than that found in the study by Little and colleagues[11] of 1% in the take-now group and 69% in the delayed-prescription group. Patients in the UK study returned to the office in 3 days to pick up their prescription, whereas the New Zealand group received the prescription with instructions to wait 3 days before filling it. If the third day had occurred on a weekend, the patients would have had to seek assistance from an after-hours clinic, thereby incurring a direct patient charge.

Our study assessed only the effect of delayed prescriptions, whereas the study by Little and colleagues tested the combined effect of a delayed prescription and the barrier of having to return to the clinic to obtain the prescription. Furthermore, our approach may be more acceptable to a wider group of doctors and patients, although at the expense of a higher consumption rate.

The external validity (generalizability) of this study is difficult to assess. As with the study by Little and colleagues,[11] the FPs had different rates of recruitment. One investigator in the current study (B.A.) kept a list of all patients who presented to him with symptoms of the common cold. Of the 44 who were potentially eligible, 4 refused to be part of the study and 10 had other medical problems (eg, heart transplant, previous lung removal) that would have made inclusion potentially hazardous. Thus, 88% of those who had a common cold and were eligible may have participated in the study.

We do not know how many patients were excluded or refused to participate; the recruiting physicians did not supply this information as requested. There was no systematic difference in symptom scores for patients of the different recruiting doctors. As with the study by Little and colleagues, the doctors found themselves too busy to enroll patients. Such problems are always an issue in general practice research.[18] Little and colleagues checked the internal validity of their telephone information; therefore, we did not repeat this. In an earlier study,[14] the recruiting family physicians' preference for using delayed prescriptions may have made them more supportive of the delayed prescription than of the immediate prescription. This issue cannot be resolved, since we needed doctors who would prescribe either a delayed prescription or an immediate prescription in order to recruit enough patients.

TABLE 3

SATISFACTION, ATTITUDES, AND BELIEFS

	Immediate Prescription	Delayed Prescription	*P*
Satisfaction with the consultation; ie, score (1+2) / (1+2+3+4)	58 / 62 (94%)	64 / 67 (96%)	.71 *
Doctors dealt with worries	58 / 62 (94%)	64 / 67 (96%)	.71 *
Likely to see doctors for next common cold	40 / 62 (65%)	49 / 67 (73%)	.343 †
Antibiotics are effective	47 / 62 (76%)	51 / 67 (76%)	1.0 †
Importance of seeing doctor to have time off from work or school	19 / 62 (31%)	13 / 54 (19%)	.16 †
Importance of seeing doctor to explain illness to friends and family	6 / 62 (10%)	7 / 60 (12%)	1.00 †

* Fisher's exact test. † Chi-square test.

1= very satisfied; 2 = moderately satisfied; 3 = slightly satisfied; 4 = not at all satisfied. For this table, groups responding 1 and 2 have been combined and groups responding 3 and 4 have been combined.

The strength of this study lies in the blinded nature of the intervention delivery to the patient, the analysis by intention to treat, and the study's originality. Our intervention had no impact on patients' satisfaction, concerns, or the likelihood of seeing a doctor for next illness (Table 3). In contrast, Little[11] found that antibiotic use predicted future consultations for sore throat and the

belief that antibiotics were effective for sore throat.[11,19] The differences may relate to the different patient symptoms and geographical differences (common cold in New Zealand versus sore throat in the UK) or the fact that all patients in our study left with a prescription. Another possible reason is that the patients knew they were participating in a study, whereas in the Little study, the instructions were more vague.[11]

Doctors often misinterpret patient expectations. Improving communications between patient and doctor may be central to reducing patients' demand for antibiotics. Britten makes the claim that "all the misunderstandings were associated with lack of patients' participation in the consultation in terms of voicing of expectations and preferences or the voicing of responses to doctors' decisions and actions."[20] The need for delayed prescriptions had been highlighted as a solution. We know that the common cold presents no great diagnostic dilemma but can produce enormous treatment dilemmas.[21] Barry believes that by changing doctors' views and helping patients to explain what they want from the office visit may lead to changes in treatment patterns.[22] We concur with Little that unless patients are very ill, general practitioners should consider exploring their concerns, explaining the natural history of their illness, and avoiding or delaying prescribing antibiotics.[11]

We were pleased to see a reduction of antibiotics consumed (89% to 48%). However, 48% still represents a high proportion of patients who consumed antibiotics for an illness that is most unlikely to respond to those drugs. More placebo-controlled randomized trials of antibiotics for respiratory tract infections in the primary care setting are needed. We suggest that FPs clarify patients' expectation for antibiotics and not prescribe them unless the patient insists. For patients who expect to take antibiotics and cannot be persuaded otherwise, a delayed prescription may be the first step in educating them that these medicines are not routinely required.

CONCLUSIONS

Delayed prescriptions are a safe and effective means of reducing antibiotic use in patients with the common cold who want antibiotics. The additional barrier of asking the patient to pick up the prescription from the office if symptoms persist after 3 days may reduce antibiotic use even further. When the patient demands a prescription, delaying its delivery has the potential to provide gentle education that antibiotics are an unnecessary treatment.

JFP

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