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The influence of rapid influenza diagnostic testing on antibiotic prescribing patterns in rural Thailand

Darlene Bhavnani [a,b], **Ladarat Phatinawin** [c], **Somrak Chantra** [d], **Sonja J. Olsen** [b], **James M. Simmerman** [b,*]

[a] *University of Michigan, School of Public Health, Ann Arbor, MI, USA*
[b] *International Emerging Infections Program, Thai Ministry of Public Health—US Centers for Disease Control Collaboration, Nonthaburi, Thailand*
[c] *Bureau of Epidemiology, Department of Disease Control, Thai Ministry of Public Health, Nonthaburi, Thailand*
[d] *Crown Prince Hospital, Sa Kaeo, Thailand*

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Summary
Objectives: Rapid influenza diagnostic testing is potentially a useful means to decrease inappropriate prescription of antibiotics. We studied the impact of access to rapid influenza test results on antibiotic prescribing and other patient management practices for outpatients with influenza-like illness (ILI) in a rural province in Eastern Thailand.
Methods: A medical record review was performed for 300 patients of all ages selected from five outpatient departments using a 1:2 ratio of ILI cases with and without influenza infection identified by the QuickVue® rapid test. Chi-square analysis or Fisher's exact test was used to compare patient management practices (antibiotic prescriptions, individual treatments administered, additional tests ordered, and related hospitalization) between rapid test positive and negative patients. Logistic regression was used to evaluate the effect of rapid test results on patient management practices for ILI.
Results: Eighty-two percent of all patients with ILI were prescribed antibiotics. Patients with a positive rapid test were less likely to be prescribed antibiotics than those with a negative result (73% vs. 87%, respectively, $p = 0.003$). The likelihood of antibiotic prescription for influenza positive patients was 0.41 times the likelihood for influenza negative patients (95% CI 0.23—0.74, $p = 0.003$). There was no significant difference in the frequency of other patient management practices between influenza positive and negative patients.
Conclusions: Thai outpatients with ILI are prescribed antibiotics at a frequency approximately twice that reported in the USA. Having access to a rapid influenza test result was associated with a significant decrease in antibiotic prescription. Improved access to rapid influenza testing and expanded physician education may reduce inappropriate antibiotic use and improve patient care.
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* Corresponding author. Current address: IEIP, Box 64 CDC, APO AP 96546, Thailand. Tel.: +6 62 591 1294.
E-mail address: SimmermanM@vtn.wpro.who.int (J.M. Simmerman).

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Introduction

Influenza is a highly infectious respiratory virus that causes significant morbidity and mortality worldwide.[1] Influenza outbreaks have been documented in Thailand and recent studies have identified influenza virus as an important cause of pneumonia and acute undifferentiated febrile illness.[2,3] The nonspecific presentation of influenza virus infection makes clinical diagnosis challenging.[1,4–6] At the same time, laboratory confirmation of influenza infection is seldom available in Thailand. Antibiotics are often inappropriately prescribed for patients with lower respiratory tract infections caused by respiratory viruses including influenza.[7,8] Inappropriate use of antibiotics contributes to the emergence and spread of antibiotic resistant bacteria, has the potential for adverse effects, and is associated with increased healthcare costs.[7,9,10] Data from the USA suggest that rapid diagnostic testing could potentially reduce antibiotic resistance and lower the cost of associated tests.[11,12]

Rapid influenza diagnostic tests are widely used in clinical practice in wealthy countries and in a few influenza surveillance systems.[13,14] In general these tests are simple to use, yield results in as little as 10 minutes, and offer moderate sensitivity and high specificity.[15] The QuickVue® rapid test is a lateral flow immunoassay that detects both influenza virus types A and B nucleoproteins.[16] A field study in Sa Kaeo, Thailand reported a QuickVue® rapid test sensitivity of 77% and specificity of 96% in outpatients of all ages with influenza-like illness (ILI) using viral cell culture as the gold standard. The same study showed equal sensitivity in the detection of influenza virus type A and influenza type B.[17]

Mainly due to their high cost (US$7—12/test) and limited availability, rapid influenza diagnostic tests are not widely used in Thailand.[18] In contrast, antibiotics are relatively inexpensive (less than US$5/10 day course of generic amoxicillin)[19] and widely available without a prescription.[20–22] Baseline data from Thailand suggest that frequency of over-the-counter antibiotic purchase may be as high as 75% in patients requesting amoxicillin from their pharmacy.[21]

We evaluated the impact of QuickVue® rapid test results on patient management practices (antibiotic prescribing, individual treatments administered for ILI, additional tests ordered, and any related hospitalizations) for outpatients with ILI enrolled in a protocol in rural eastern Thailand. We also examined the association between patient characteristics (age and gender) and prescription of antibiotics.

Methods

Sa Kaeo province in Thailand is the site for collaborative surveillance and research studies on respiratory illness between the Thailand Ministry of Public Health and the US Centers for Disease Control, International Emerging Infections Program. Beginning in August 2003, patients with ILI presenting to the outpatient departments at five of the eight hospitals in the province were approached for enrollment in a study investigating the causes of respiratory illness.[17] ILI was defined using the World Health Organization case definition of acute fever >38 °C and/or self-reported fever within the last 3 days and either cough or sore throat in the absence of another diagnosis.[23] After obtaining signed consent, a nasopharyngeal swab for viral culture and PCR testing was collected. The QuickVue® rapid influenza test was also performed using a nasal specimen according to the manufacturer's instructions. The attending physician was promptly notified of the rapid test result.[17]

For the present study we retrospectively sampled from 1092 positive and negative rapid influenza test patients of all ages with ILI who were enrolled in the prospective study between September 1, 2003 and August 31, 2004. The number of patients selected from each department was proportional to the number of positive influenza test results confirmed by QuickVue® at each of the five facilities. Since information on antibiotic prescription was not collected prospectively for all patients, this information was obtained retrospectively through a medical record review.

In order to detect a 15% difference in the frequency of antibiotic prescription between patients with a positive influenza rapid test result and those with a negative result, assuming 72% antibiotic usage in the influenza positive group, 80% power, 95% confidence and a 1:2 ratio of ILI cases with and without positive test results, a sample size of 282 was required (94 patients with a positive influenza rapid test result and 188 with a negative result). The proportion of antibiotic use in the influenza positive group was estimated using preliminary data from the study. To account for potential missing data, a sample size of 330 patients was selected (112 and 218, respectively).

Medical records were reviewed for all patients. Abstracted data included medications prescribed (antibiotics, fever medication, or decongestants), individual treatments administered for ILI (oxygen, sponge bath, nebulized albuterol, or antibiotics administered intravenously), additional tests ordered (chest radiograph, urine analysis, blood cell counts or chemistries), and any related hospital admissions. At one study hospital, Wattana Nakhon, antibiotic prescriptions were not recorded in the medical record and so prescription data were taken from the hospital pharmacy.

Comparisons of demographic characteristics and patient management practices for ILI (antibiotic prescription, individual treatments administered, additional tests ordered, and related hospitalizations) were made between patients with positive and negative rapid test results. Continuous data were analyzed using the independent sample t-test and categorical data were evaluated using Chi-square analysis or the Fisher's exact test. Continuous data were also evaluated as categorical variables as appropriate. All tests were two-sided and a p value less than 0.05 was considered significant.

To further evaluate factors predictive of patient management practices for ILI, univariate and multivariate logistic regression were carried out. Separate models considered the following dependent variables: oral antibiotic prescriptions, individual treatments administered, additional tests ordered, and related hospitalization. Independent variables were rapid test result, outpatient department, patient age and gender. Univariate logistic regression was also used to determine if patient characteristics (age and gender) were predictive of antibiotic prescription. All analyses were performed using SPSS version 12 for Windows.

Results

Medical records were available for a total of 300 patients with ILI; 106 (35%) had positive and 194 (65%) had negative

Table 1 Comparison of patient management after knowledge of influenza rapid test result

Patient care	Influenza positive (N = 106) *n* (%)	Influenza negative (N = 194) *n* (%)	Chi-square *p*-value
Antibiotic prescription by hospital			
Overall	77/106 (73)	168/194 (87)	0.003
Crown Prince	13/26 (50)	38/42 (91)	<0.001
Aranyaprathet	23/24 (96)	40/43 (93)	1.000[a]
Wattana Nakhon	20/24 (83)	35/50 (70)	0.219
Ta Praya	10/15 (67)	18/21 (86)	0.236[a]
Wang Nam Yen	11/17 (65)	37/38 (97)	0.002[a]
Individual treatments administered[b]	24/106 (23)	35/194 (18)	0.338
Additional tests ordered[c]	13/106 (12)	18/194 (9)	0.417
Hospitalization	13/106 (12)	12/194 (6)	0.069

[a] *p*-Value from Fisher's exact test.
[b] Oxygen, sponge bath, nebulized albuterol, or antibiotics administered intravenously.
[c] Chest radiograph, urine analysis, blood cell counts or chemistries.

influenza rapid test results. Patients with positive and negative test results did not differ with respect to gender (52% vs. 56% were male, $p = 0.48$) or age (median age (range), 7.5 (0—70) vs. 5 (0—86) years, $p = 0.824$). Eighty-two percent of all patients with ILI were prescribed antibiotics and 89% of these prescriptions were for amoxicillin. Ninety percent of patients were prescribed fever medication (99% acetaminophen), and 76% were prescribed decongestants. Patients with positive influenza rapid test results were less likely to be prescribed antibiotics (73% vs. 87%, respectively, $p = 0.003$, Table 1). The conclusion was the same when the analysis was limited to Crown Prince and Wang Nam Yen hospitals, which contributed 41% of the total sample. In the remaining three hospitals, there was no difference in antibiotic prescription frequencies between influenza positive and influenza negative patients (Table 1). Evaluation of other patient management variables failed to reveal any statistically significant differences between these groups. While only a minority of patients in this study were hospitalized, those with positive test results had a higher proportion of hospitalizations than patients with negative test results (12% vs. 6%, $p = 0.069$, Table 1).

Results from the univariate logistic regression analysis demonstrated that a positive influenza rapid test result was protective for antibiotic prescription (OR 0.41, 95% CI 0.23—0.74, $p = 0.003$, Table 2). In contrast, patient age and gender were not associated with antibiotic prescription (Table 2). These analyses also failed to demonstrate significant relationships between rapid test results and other patient management practices (data not shown). Similarly, a multivariate logistic regression model (independent variables: rapid test result, outpatient department, patient age and gender) found that only rapid test result was protective of antibiotic prescription ($\beta = -0.88$, $p = 0.004$). The likelihood of antibiotic prescription for influenza positive patients is 0.42 times the likelihood for influenza negative patients holding age, gender, and outpatient department constant (95% CI 0.23—0.76). Multivariate models evaluating other patient management variables as the dependent variable failed to show significance of rapid test results (data not shown).

Table 2 Univariate logistic regression models for factors predictive of antibiotic prescription

Variable	Estimate	OR (95% CI)	*p*-Value
Rapid test result	−0.89	0.41 (0.23—0.74)	0.003
Patient age	0.097	1.1 (0.75—1.63)	0.63
Patient gender	0.19	1.2 (0.67—2.16)	0.54

OR, odds ratio; CI, confidence interval.

Discussion

Eighty-two percent of outpatients with ILI in this rural Thai population received antibiotics. However, when a rapid influenza test was used at the point of care and positive results were immediately communicated to physicians, the frequency of antibiotic prescription was significantly lower. These results varied by hospital, probably reflecting the prescribing habits of individual physicians. Influenza positive patients treated at the two largest hospitals were significantly less likely to receive antibiotics than influenza negative patients. This could partly be explained by the greater number of specialist physicians working at these facilities who may have had a greater awareness of judicious antibiotic use.[24,25]

The USA has pursued aggressive campaigns to promote the judicious use of antibiotics[26] and there has been a subsequent decrease in antibiotic use and resistant organisms.[27—29] Recent studies from the USA have documented rates of oral antibiotic prescription in influenza patients without secondary bacterial infections from 26% to 38%.[7,8] In this study, 73% of patients with rapid test confirmation of influenza infection received antibiotics suggesting that Thai physicians may be less familiar with the issues surrounding inappropriate use of antibiotics and increasing antimicrobial resistance. Although we do not know if any of these patients developed secondary bacterial infections, all patients were seen as outpatients and only 8% were hospitalized after being seen in the outpatient department.

Physicians at three hospitals did not change their antibiotic prescribing behavior even when they were notified of a positive rapid test result. This could reflect the physician's lack of confidence in the rapid test as these physicians were given an initial briefing but not provided any additional formal training on the rapid test. Alternatively, physicians may have been influenced by patient expectations to receive antibiotics.[30,31] The universal healthcare scheme recently adopted in Thailand reduced the patient's out-of-pocket cost for antibiotic prescriptions, a factor which may encourage overuse.[18] In addition, physicians in the study sites provide care for more than 100 patients during an average clinic day. A study from the USA found that antibiotic prescriptions were associated with shorter patient visit times in adults with upper respiratory tract infections, and data from Hong Kong reveal that physicians in public practice over-prescribe antibiotics to save time.[30,32] Similar patient-care dynamics may also be in effect in Thailand. Finally, the physician may have decided that the severity of the illness and risk of a secondary bacterial infection warranted antibiotic therapy. However, no increase in laboratory tests ordered, such as a blood culture, or hospitalization was observed in patients who received an antibiotic.

Antibiotic prescription data were not recorded in medical charts at Wattana Nakhon hospital and therefore pharmacy records were used to identify this information. Given the potential for information bias, we repeated the analysis excluding patients from this hospital and the conclusions were unchanged. Illegible writing and misinterpretation by our data collection team may have resulted in misclassification in some cases, but this was likely to be equally distributed among persons with and without positive rapid influenza tests. At all hospitals, information on chronic or concurrent disease was often missing and therefore no meaningful analysis could be done with regard to comorbidities. Furthermore, previous studies suggest that certain physician specialties are associated with a lower frequency of antibiotic prescription.[32,33] However, we were unable to investigate physician characteristics in this study. Due to hospital administration concerns about the identification of individual physicians we were not authorized to collect potential physician identifiers. Despite these limitations, we found that access to positive influenza rapid test results in the outpatient department was associated with a lower frequency of antibiotic prescription.

Inappropriate antibiotic use in Thailand is common. Our findings suggest that access to rapid testing may be a useful tool to address this problem. Instructional aids to accompany rapid test kits should be developed to help increase their impact on patient management. Expanded physician training on the judicious use of antibiotics is needed and educational campaigns to promote appropriate management of influenza should be targeted for physicians and patients in Thailand.

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Conflict of interest: No conflict of interest to declare.

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