Ildikó Gágyor, Jörg Haasenritter, Jutta Bleidorn, Warren McIsaac, Guido Schmiemann, Eva Hummers-Pradier and Wolfgang Himmel

Predicting antibiotic prescription after symptomatic treatment for urinary tract infection:

development of a model using data from an RCT in general practice

A clinical prediction model for the diagnosis of urinary tract infection, including positive tests for nitrite, leucocytes and erythrocytes, moderate-to-severe urgency frequency, and impairment of regular daily activities, may be valuable in making decisions about antibiotic prescribing

Address for correspondence

Ildikó Gágyor
Department of General Practice, Göttingen University Medical Center, Humboldtallee 38, 37073 Göttingen, Germany.
E-mail: igagyor@gwdg.de

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BACKGROUND

Urinary tract infection (UTI) is often treated with antibiotics, resulting in increasing resistance levels. Lowering antibiotic prescription rates in general practice is a promising approach to reduce antimicrobial resistance. A recently published randomised controlled trial showed that symptomatic treatment could substantially reduce the number of antibiotic courses in females with uncomplicated UTI. In the symptomatic treatment group, only one-third of the females subsequently required antibiotics in the following 28 days.

The aim of this study was to investigate whether there are differences between females with a UTI who were subsequently prescribed antibiotics and those who recovered with symptomatic treatment alone, and to develop a model to predict those who can safely and effectively be treated with symptomatic treatment alone.

METHOD

This is a subgroup analysis of females assigned to ibuprofen in a UTI trial in general practices. For the current analysis the ibuprofen group was split into two subgroups: patients who recovered without antibiotics (the No Antibiotic group) and patients who received an antibiotic for UTI within the following 28 days (the Antibiotic group).

The outcome to be predicted was whether or not a female subsequently received an antibiotic within 4 weeks of initial presentation in the practice. Predictors were considered that were available at initial presentation to the practice, such as age, number of previous UTIs, symptom duration at inclusion, UTI symptoms (dysuria, urgency or frequency of micturition, and low abdominal pain), activity impairment, and results of dipstick tests (nitrite, erythrocytes, and leucocytes).

Absolute and relative frequencies of each potential predictor were determined in both subgroups and odds ratios (ORs), and corresponding 95% confidence intervals (CI) were calculated. Multiple logistic regression was performed and the least absolute shrinkage and selection operator (LASSO) was used to select variables for a prediction model. Its discriminative value was estimated by the area under the receiver operator curve (AUC), and the effects of different thresholds were calculated on prediction of initial antibiotic prescription and need for follow-up visits. Bootstrapping was used to calculate an optimism-corrected AUC.

A linear score was constructed and for several cut point values the sensitivity and specificity were determined. To evaluate clinical utility, for each of these cut point values the proportions of patients were estimated who would receive antibiotics at presentation according to the model and who would be initially classified as not requiring antibiotic treatment but subsequently return to the practice because of symptomatic treatment failure.

RESULTS

Of the 235 females in the ibuprofen group included in the current analysis, 79 (34%) were prescribed an antibiotic prescription for UTI-related symptoms within 28 days of the initial consultation and 156 (66%) were not. The final model included five predictors: urgency/frequency (with a score of 50 points), impaired daily activities (19 points), and positive dipstick test results for erythrocytes (94 points), leucocytes (75 points), and nitrite (56 points). The sum of scores ranged from 0 to 294 points. The AUC of the model was 0.73 (95% CI = 0.67 to 0.80), the optimism-corrected AUC was 0.69. As shown in Table 1, a cut-off value of ≥210 for antibiotic initiation would result in 58% of females presenting with UTI being treated with antibiotics. Of the remaining females, 6% would return to the practice because of persistent or recurrent symptoms. A higher threshold reduces the use of antibiotics but increases the risk of symptomatic treatment failure.

Table 1. Measures of classification accuracy for several cut-off values to predict an antibiotic need

Cut-off point value	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Antibiotics[a] prescribed, % (95% CI)	Returning[b] patients, % (95% CI)
≥60	100.0 (95.4 to 100.0)	5.8 (3.1 to 10.6)	96.2 (92.9 to 100.0)	0.0 (0.0 to 1.6)
≥120	97.5 (91.2 to 99.3)	17.9 (12.7 to 24.7)	87.2 (82.4 to 91.0)	0.9 (0.02 to 3.0)
≥165	88.6 (79.8 to 93.9)	39.1 (31.8 to 46.9)	70.2 (64.1 to 75.7)	3.8 (2.0 to 7.1)
≥210	83.5 (73.9 to 90.1)	55.1 (47.3 to 62.7)	57.9 (51.5 to 64.0)	5.5 (3.3 to 9.2)
≥220	59.5 (48.5 to 69.6)	73.1 (65.6 to 79.4)	37.9 (31.9 to 44.2)	13.6 (9.8 to 18.6)
≥230	55.7 (44.7 to 66.1)	76.9 (69.7 to 82.8)	34.0 (28.3 to 40.3)	14.9 (10.9 to 20.0)
≥240	25.3 (17.0 to 35.9)	93.6 (88.6 to 96.5)	12.8 (9.1 to 17.6)	25.1 (20.0 to 31.0)

Cases are classified by the model as 'negative' if point score < threshold; cases are classified by the model as 'positive' if point score ≥ threshold. [a]Antibiotics prescribed refers to the number of positive cases (= patients that the model predicted will receive an antibiotic) in relation to all patients. [b]Returning patients refers to the number of false-negative cases (= patients that the model falsely predicted will not receive an antibiotic) in relation to all patients.

DISCUSSION

The present prediction model included five factors: positive test results for nitrite, leucocytes, and erythrocytes, moderate to severe urgency or frequency, and impairment of regular daily activities. A reasonable threshold for antibiotic treatment yielded a high accuracy in prediction with a significant reduction of antibiotic prescriptions and a small number of females who would return to the practice.

This is the first follow-up study of females who initially received symptomatic treatment with ibuprofen for a UTI and the first model to predict those who can safely and effectively be treated with symptomatic treatment and vice versa.

Limitations of the study are the setting of a randomised controlled trial with several inclusion and exclusion criteria, as well as lack of information about the reasons for GPs' decisions to subsequently prescribe antibiotics.

Knowledge of the urine culture results could have influenced GPs' and patients' decisions, resulting in overestimation of the predictive performance of the model. Data on vaginal discharge, smelly and cloudy urine, or back pain were not collected in the immediate versus conditional antibiotic treatment for women with UTI (ICUTI) trial and were not evaluated in the present analysis.

GPs and patients may consider the prediction model when discussing different treatment approaches. If both favour symptomatic treatment, they could arrange a wait-and-see approach, combined with appropriate information for the patient, or with delayed prescribing of antibiotics. In cases where culture of urine samples is necessary, symptomatic treatment could bridge the time until results are available and combat pain, the most important symptom of UTI.

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