Predictive value of antimicrobial susceptibility from previous urinary tract infection in the treatment of re-infection

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ABSTRACT

Recurrent urinary tract infections are often re-infections; therefore, antimicrobial susceptibility test results from a previous episode may guide the empiric therapy in subsequent episodes. This analysis provides predictive values of the antimicrobial susceptibility of previous *Escherichia coli* isolates for the treatment of re-infections in routine clinical practice. If resistance to ampicillin, trimethoprim, or ciprofloxacin is detected, re-prescription within 3 months is imprudent. Susceptibility to nitrofurantoin, ciprofloxacin, or trimethoprim in a previous sample supports their prescription for a re-infection within 3 months and up to a year. Resistance to nitrofurantoin is low and, once detected, decays relatively quickly. Nitrofurantoin should be considered as a first-line agent for initial and repeat treatment.

Keywords

antibiotic resistance; *Escherichia coli*; general practice; predictive value; urinary tract infection.

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INTRODUCTION

Urinary tract infection (UTI) is considered to be one of the most common bacterial infections.[1] Approximately 5% of young adults have bacteriuria at any one time,[2] with up to 50% of adult women reporting a UTI at some time in their life.[1] The incidence of UTI increases with age, at the rate of 1–2% per decade.[2] Recurrence happens frequently, in 27–48% of healthy women,[3] after spontaneous clearance as well as after antimicrobial treatment.[2,4] Prospective studies have shown that the vast majority of recurrent UTIs are re-infections by a previously identified strain.[3]

Guidelines on empirical treatment of acute uncomplicated UTI suggest that agents may not be suitable for empirical use when the community prevalence of resistance to the antimicrobial in *Escherichia coli* exceeds 10–20%.[5] Empirical antimicrobial therapy requires a balance between the need to achieve effective therapy as well as to limit the use of broad-spectrum antimicrobial agents. Antimicrobial susceptibility test results from previous episodes of UTI may guide the decision-making process in the selection of empiric therapy in a subsequent episode of UTI, and indicate the use of antimicrobials with high community resistance levels.

There are limited data to confirm or quantify the predictive value of the antimicrobial resistance pattern of previous isolates. This analysis assesses the value of the antimicrobial susceptibility of a previously isolated *E. coli* on predicting the susceptibility of a subsequent isolation of *E. coli* from a UTI in routine clinical practice.

METHOD

The laboratory at Galway University Hospital is the main regional laboratory for over 200 000 patients (of a total Irish population of around 4 million) and provides a microbiology service to GPs in the West of Ireland as well as to the hospital.

All records from general practices of patients with more than one sample of significant bacteriuria

How this fits in

Although commonly practised by GPs there is no evidence that previous episodes of UTI caused by *E. coli* can guide selection of empiric antimicrobial therapy for subsequent episodes of UTI. This database analysis of *E. coli* re-infections shows that previous episodes can provide guidance in the treatment of subsequent infections.

(>10^5 pure culture/ml), that is, recurrent infections, were extracted from the database over a 4.5-year period (April 2004 to September 2008). The first isolate during this period was identified for each patient, and the time to each subsequent isolate was calculated. A recurrence was defined as a re-infection if it was caused by the same species and if it occurred more than 2 weeks after the original UTI.[3] Relapse isolates, defined as recurrence with the same species within 2 weeks from the previous sample, were excluded from this analysis.[3] If more than one sample was given during a 3-month period, only the first of these samples was considered.

The positive predictive value (PPV) was calculated as the proportion of patients with an *E. coli* resistant to an antimicrobial at first isolate that remain resistant to this antimicrobial at the subsequent isolate. Similarly, the negative predictive value (NPV) gives the proportion of patients with an *E. coli* infection susceptible to an antimicrobial at the first isolate, who show the same susceptibility in a subsequent isolate. As the PPV and NPV are directly proportional to the prevalence of resistance in the population, a correction (Bayes theorem) is applied,[6] with a correction for the variability introduced by the prevalence according to Zou.[7] The PPV is calculated as P(disease|+test) = (sensitivity × prevalence)/([sensitivity × prevalence] + [{1 — specificity}{1 — prevalence}]). PPV and NPV and their 95% confidence intervals (CIs) were calculated using WINPEPI.[8] The prevalence was obtained from the full database (all general practice samples over the period of 4.5 years). For simplicity, PPV and NPV are only presented for re-infection within 3 months and between 9 and 12 months.

RESULTS

Over the 4.5-year period, 147 306 urine samples were analysed; in 21.3% an organism and in 14.4% *E. coli* was identified. A total of 3413 patients provided at least two *E. coli*-positive samples over the study period. The mean age of the prospective cohort was 51.7 years (standard deviation [SD] 25.7 years) and median 56.0 years. The study population consisted of 90.9% females and 11.0% were under 18 years of age. No changes in age or sex were observed over the time period.

A total of 1092 of patients had a re-infection within 3 months, 693 patients had a re-infection between 3 and 6 months after the first sample, 543 between 6 and 9 months, and 450 between 9 and 12 months. Little difference was found between age and sex when comparing the full database from the 4.5-year period to the re-infection database (Table 1). Table 2 gives an overview of the PPV and NPV of the first sample when the subsequent sample is within 3 months and between 9 and 12 months; the PPV and NPV for the periods in between (3–6 months and 6–9 months) declines gradually between these periods.

There is an 84.6% probability that a patient with an ampicillin-resistant *E. coli* in a previous sample will still have an ampicillin-resistant *E. coli* in a subsequent episode of bacteriuria within 3 months.

Table 1. Comparison of full and re-infection database.

	Full database	Re-infection database
n	14 495	3413
Mean age, years	46.8	51.7
Sex, %		
Female	86.4	90.2
Male	9.1	8.2
Unknown	4.5	1.6

Table 2. Overview of prevalence of resistance, positive predictive value and negative predictive value and 95% confidence interval for each antimicrobial for a re-infection within 3 months and after 9–12 months.

	Prevalence of resistance, %	Within 3 months				9–12 months			
		PPV	95% CI	NPV	95% CI	PPV	95% CI	NPV	95% CI
Co-amoxiclav	23.9	54.5	49.8 to 59.1	87.3	85.7 to 88.7	43.1	35.9 to 50.4	82.4	80.0 to 84.7
Ampicillin	60.7	84.9	82.2 to 87.2	77.6	74.2 to 80.7	75.9	71.4 to 80.0	60.1	54.7 to 65.2
Ciprofloxacin	5.7	83.8	71.7 to 90.7	98.3	97.8 to 98.7	43.4	30.1 to 56.9	96.8	96.0 to 97.5
Nitrofurantoin	2.6	20.2	12.3 to 31.3	98.0	97.6 to 98.3	5.7	1.5 to 26.3	97.5	97.1 to 97.9
Trimethoprim	26.4	78.3	73.1 to 82.5	91.3	89.9 to 92.5	59.2	51.9 to 66.0	86.3	83.6 to 88.6

NPV = negative predictive value. PPV = positive predictive value.

PPVs are obtained for ciprofloxacin (83.8%) and trimethoprim (78.3%). The probability of a nitrofurantoin resistant re-infection within 3 months if the previous isolate is resistant is particularly low (20.2%). The probability that a re-infection between 9 months and a year remains resistant is high, at 75.9% for ampicillin and 59.2% for trimethoprim. In contrast, the probability that a re-infection within 3 months and up to a year is susceptible if the initial *E. coli* was susceptible is nearly 100% for ciprofloxacin and nitrofurantoin, and 86.3% for trimethoprim.

DISCUSSION

Summary of main findings

If a patient presents with a recurrent UTI within 3 months and their previous sample showed an *E. coli* resistant to ampicillin, trimethoprim, or ciprofloxacin, this recurrent UTI is most likely associated with an organism that is still resistant. If a patient with a recurrent UTI was diagnosed in the previous year with an *E. coli* that was susceptible to nitrofurantoin, ciprofloxacin, or trimethoprim, the organism associated with this recurrent episode is likely to be still susceptible.

Limitations of the study

The use of routine laboratory urine samples as the basis for this analysis may influence the results due to varying request behaviour or changes in laboratory procedures. However, the number of urine samples submitted did not change over time (data available from authors). Also, the GPs' follow-up of patients with a laboratory-confirmed UTI as well as its potential effect on the data is unknown.

Comparison with existing literature

Occurrences of re-infection are common and clinicians often look at the results of previous urine testing to help guide their antimicrobial choice when patients represent. To the authors' knowledge there has been no research, to date, which either supports or opposes this practice.

Implications for clinical practice and future research

These results may help GPs to conserve broad-spectrum agents by using antimicrobial test results from previous episodes of UTI to prescribe more narrow-spectrum agents such as trimethoprim, even when community resistance levels are high. The high PPV of previous ampicillin, trimethoprim, and ciprofloxacin resistance warrants against the re-prescription of these agents within 3 months, while the high NPV indicates prescription of these antimicrobials if susceptibility for these antimicrobials was shown in a previous sample of the patient. The low prevalence of resistance and high NPV of nitrofurantoin at both 3 and 12 months promotes nitrofurantoin as a beneficial first-line agent for initial and repeat presentations.

More in-depth research into patients presenting with another positive *E. coli* UTI, in particular within 3 months, would be of interest to further improve prescribing practice. An ongoing prospective study will address these concerns (www.antibiotics.nuigalway.ie).

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Ethical approval

Ethical approval was granted by the Irish College of General Practitioners.

Competing interests

The authors have stated that there are none.

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