



Die Hausarztmedizin ist nicht nur ein praktisches Fach, sondern auch ein akademisches. In der Schweiz gibt es seit Jahren zwei Sponsor-Gesellschaften, die herausragende Forschungsarbeiten oder Forschungsprojekte zu Themen der Allgemeinen Inneren Medizin (AIM) auszeichnen: Das Kollegium für Hausarztmedizin (KHM) mit Fokus auf die ambulante AIM und die Schweizerische Gesellschaft für Allgemeine Innere Medizin (SGAIM) mit ihrer Forschungsstiftung «SGAIM Foundation». In dieser Serie möchten wir Ihnen in zusammengefasster Form die Ergebnisse oder die geplanten Forschungsvorhaben der Preisträger*innen 2020 vorstellen. Weil die Sprache der wissenschaftlichen Literatur englisch ist, erscheinen die meisten dieser Artikel auf Englisch. Die Preisträger*innen wurden von uns angehalten, in ihren Artikeln Bezug auf die Praxisrelevanz ihrer Arbeit zu nehmen.

Prof. Dr. med. Stefan Neuner-Jehle, Chefredaktor PHC

Does the current resistance situation allow the empirical use of Bactrim[®] in patients with urinary tract infections?

Andreas Plate^a, Andreas Kronenberg^b, Martin Risch^c, Yolanda Mueller^d, Stefania Di Gangi^a, Thomas Rosemann^a, Oliver Senn^a

^a Institute of Primary Care, University and University Hospital of Zurich, Zurich, Switzerland; ^b Swiss Center for Antibiotic Resistance, Institute for Infectious Diseases, University Bern, Bern and Medix General Practice Network, Bern, Switzerland; ^c labormedizinisches zentrum Dr Risch Ostschweiz AG, Buchs, St. Gallen; ^d Department of Family Medicine, Center for Primary Care and Public Health (Unisanté), University of Lausanne, Switzerland

Introduction

This report is a summary of a previously published original publication [1].

Urinary tract infections (UTIs) are frequent reasons for consultation in primary care and the choice of empirical antibiotic therapy is determined by the local resistance patterns of the causative uropathogens. However,

in the nationally established passive surveillance for monitoring antibiotic resistance, uropathogens of complicated infections are overrepresented and therefore do not reflect the everyday situation in practice. The aim of this study was to determine the resistance patterns of uropathogens in patients with UTI by means of active surveillance.

Background

Trimethoprim-sulfamethoxazole (TMP/SMX, Bactrim®) is recommended by many guidelines for the empirical therapy of uncomplicated urinary tract infections (uUTIs) [2–4]. However, clinicians need to be aware of the local resistance patterns as guidelines

Guidelines recommend Bactrim® as empirical therapy for uncomplicated UTI only in areas where local resistance rates do not exceed 20%.

recommend Bactrim® only in areas where resistance rates do not exceed 20%. Since urinary cultures are not recommended for uUTI and many doctors refrain from a microbiological analysis of the urine before empirical therapy of uUTI, resistance data from the national passive surveillance (Swiss Centre for Antibiotic Resistances, ANRESIS, www.anresis.ch) may have a significant selection bias, as resistance patterns of uropathogens in urine samples from complicated UTI or recurring UTI are overrepresented. The aim of the study was to determine by active surveillance the resistance patterns of uropathogens in patients with UTI in Swiss primary care.

Methods

The study was conducted between June 2017 and August 2018 in 163 primary care practices. Patients ≥ 18 years of age with the diagnosis of lower UTI (cystitis) could be included in the study. Pregnant woman and patients with pyelonephritis were excluded. A urine specimen, as well as basic clinical and epidemiological data, were obtained from all patients. All urine samples were analysed centrally in one laboratory (laboratory Risch) and in the event of microbial growth, antimicrobial resistance tests were performed. The local ethics committee of Zurich approved the study (BASEC Number: 2016-01918) and all patients signed a study-specific informed consent form.

Results

The final analysis included 1352 patients, of whom 1210 had a diagnosis of uUTI and 129 had a diagnosis of com-

plicated UTI. Overall, 94.9% of the patients were female and the mean age was 53.8 years (standard deviation 20.8). Positive urine cultures were reported for 87.1% of the urine samples. Urine samples with detection of three or more bacteria (140 cases, 11.9%) were considered contaminated and excluded from the following analyses. Gram-negative rods were detected in 86.8% of all samples, gram-positive bacteria (excluding enterococci) in 19.4% and enterococci in 6.9%. *Escherichia coli* (*E. coli*) (74.6%) was the most commonly detected single bacterium. No statistically significant differences were found in the distribution of bacteria in patients with uncomplicated and complicated UTI. Resistance patterns for *E. coli* are reported in table 1. We found a high proportion of *E. coli* isolates to be susceptible to Bactrim® (85.66%, 95% confidence interval [CI] 85.58–85.74%), nitrofurantoin (99.48%, 95% CI 99.47–99.5%) and fosfomycin (99.35%, 95% CI 99.34–99.37%). Compared with the resistance patterns provided by ANRESIS, we found significant higher rates of susceptibility of *E. coli* to Bactrim® and ciprofloxacin (table 1).

The rates of resistance to Bactrim® were below 20% and Bactrim® is thus an adequate choice as empirical therapy for uncomplicated UTI.

In multivariate logistic regression analysis, patient age (odds ratio [OR] 1.01, 95% CI 1.00–1.02; $p = 0.042$), antimicrobial exposure during the past 3 months (OR 1.84, 95% CI 1.17–2.87; $p = 0.007$) and a history of recent travel to Africa (OR 3.16, 95% CI 1.24–7.45; $p = 0.011$) were identified in patients with an uUTI as independent predictors for resistance to Bactrim®, fosfomycin or nitrofurantoin.

Discussion

In this study, we determined by active surveillance actual susceptibility patterns of uropathogens in patients with acute UTI presenting to primary care physicians. Antibiotic susceptibility rates of the most common uropathogen *E. coli* to the recommended first-line antibiotics were high and we found higher rates of susceptibility as compared with data reported by the

Table 1: Susceptibility rates of *E. coli* in our cohort compared with data provided by Swiss passive surveillance.

	Fosfomycin			Nitrofurantoin			Bactrim®			Ciprofloxacin		
	Study	ANRESIS	p-value	Study	ANRESIS	p-value	Study	ANRESIS	p-value	Study	ANRESIS	p-value
Total N = 774	99.4	98.8	0.140	99.5	99.2	0.543	85.7	77.5	<0.001	88.9	83.3	<0.001
		n = 35644			n = 36286			n = 36343			n = 35329	

Data shown in percentages. Study: susceptibility rates in our cohort. ANRESIS: susceptibility rates (2018) provided by the Swiss national resistance centre.

national passive surveillance system. With the exception of the Geneva region (76.5%), the proportions of *E. coli* isolates susceptible to Bactrim® were above the 80% margin in our study. However, the number of urine samples studied in the Geneva area was small (n = 17) and therefore this sub-analysis must be considered with caution.

Recent antimicrobial exposure and recent travel to Africa were independent predictors for Bactrim® resistance.

Bactrim® is therefore an adequate antibiotic for the empirical therapy of uUTI according to the current guidelines [2, 3]. We were able to confirm the risk factors for antibiotic resistance known from the literature [5, 6]. Accordingly, patients with a risk factor (prior antibiotic exposure, or history of recent travel) must be assumed to have a higher resistance rates and an alternative antibiotic can be considered.

Although the susceptibility rates of *E. coli* to the quinolone antibiotics were high, we must emphasise that quinolone antibiotics should not be used for empirical therapy of uUTI. On the one hand, quinolone antibiotics have a wide range of serious side effects and, on the other hand, the overuse of quinolones in UTI leads to an increase in resistance not only of

urinary, but also of non-urogenital pathogens. As quinolone antibiotics are of particular importance in the treatment in non-urogenital infections, an increase in resistance rates should be avoided [4]. With Bactrim®, nitrofurantoin and fosfomycin, three effective and well tolerated alternative antibiotics are available. Accordingly, quinolone antibiotics should only be used in selected cases where the use of another antibiotic is contraindicated.

Conflict of interest

All authors declare no conflict of interest.
This study was awarded with the KHM Research Award 2020.

Funding

The study was supported with project-related grants from the following institutes: SwissLife, Blumenau-Léonie Hartmann Foundation, and Innova Foundation. ANRESIS is funded by the Swiss Federal Office of Public Health and the University of Bern. None of the funders had influence over the study design, study results, analysis and interpretation of the data and publication.

Acknowledgement

We would like to thank all representatives of the Institutes of Family Medicine and the Physicians' Networks for their support in recruiting study physicians. We thank all study physicians for recruiting patients and patients for participating in our study. Special thanks to the staff of the Laboratory Risch for performing all the urine analyses. Finally, we would like to thank all general practitioners who contributed to the initiation of this project through their suggestions and discussions. In the spirit of: "from the practice – for the practice".

Photo credit

© Tomert | Dreamstime.com

References

- 1 Plate A, Kronenberg A, Risch M, Mueller Y, Di Gangi S, Rosemann T, et al. Active surveillance of antibiotic resistance patterns in urinary tract infections in primary care in Switzerland. *Infection*. 2019 Dec;47(6):1027–35.
- 2 Hasse B, Huttner A, Huttner B, Egger M, Zanetti G, Marschall J, et al. Behandlung von unkomplizierten Harnwegsinfektionen. 2014. [Internet] [cited June 2021]. Available from: https://www.sginf.ch/files/behandlung_von_unkomplizierten_harnwegsinfektionen.pdf
- 3 SSI Guideline – Harnwegsinfekt (HWI) 2020.
- 4 Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis*. 2011 Mar 1;52(5):e103–20.
- 5 Brown PD, Freeman A, Foxman B. Prevalence and Predictors of Trimethoprim-Sulfamethoxazole Resistance among Uropathogenic *Escherichia coli* Isolates in Michigan. *Clin Infect Dis*. 2002;34(8):1061–6.
- 6 Wright SW, Wrenn KD, Haynes M, Haas DW. Prevalence and risk factors for multidrug resistant uropathogens in ED patients. *Am J Emerg Med*. 2000 Mar;18(2):143–6.

Correspondence:
Andreas Plate, MD
Institute of Primary Care,
University of Zurich
Pestalozzistrasse 24
CH-8091 Zurich
[andreas.plate\[at\]usz.ch](mailto:andreas.plate[at]usz.ch)

Key messages

- Urinary tract infections are a frequent reason for patient consultations in primary care and GPs have to select appropriate empirical antibiotic therapy without knowledge of urinary culture results.
- Bactrim® is a well-tolerated antibiotic frequently used for the treatment of urinary tract infections. However, according to national passive surveillance, resistance rates are >20% and guidelines recommend avoiding Bactrim® as empirical therapy in such areas.
- New findings of this study: resistance rates collected by means of active surveillance in practice showed that the rates of resistance to Bactrim® in Switzerland are below 20% and that Bactrim® is therefore an adequate choice as empirical therapy.
- Despite low resistance rates, quinolones should not be used for empirical therapy because of their high collateral damage.