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CASE REPORT

Nitroxoline: an option for the treatment of urinary tract infection with multi-resistant uropathogenic bacteria

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Abstract
The number of multi-resistant uropathogens is increasing. A multi-morbid patient developed a symptomatic urinary tract infection with two multi-resistant bacteria, namely *Klebsiella pneumoniae* and *Proteus mirabilis*. Nitroxoline was the only drug active against both uropathogens. Obviously, nitroxoline can be an option for the therapy of a urinary tract infection with multi-resistant uropathogens.

Keywords Urinary tract infections · Multi-resistant uropathogens · Nitroxoline

Introduction

Nitroxoline is principally scheduled for the oral therapy as well as prophylaxis of acute or recurrent uncomplicated urinary tract infections, respectively [1], because it disposes antimicrobial activities against a broad range of bacteria [2] and even yeasts [3]. Especially isolates from *Escherichia coli* were fully susceptible. Furthermore, high concentrations of nitroxoline and especially of the predominant, antimicrobial active metabolite nitroxoline sulfate are achieved in the urine after oral application [4]. In addition, in a meta-analysis, the drug has been shown to be well tolerated [5].

Here we describe a case, when nitroxoline was the only drug which could be recommended for therapy of a urinary tract infection with multi-resistant bacteria.

Case report

During a previous stay in a hospital in Serbia, a 68-year-old patient with multi-morbidity had attracted rectal colonization with several multi-resistant bacteria, namely *Klebsiella pneumoniae, Providencia stuartii, Acinetobacter baumanii* and vancomycin-resistant *Enterococcus faecium*. Since he suffered from a left-sided hemiplegia and dysphagia after a stroke in his medical history, he was provided with a gastric feeding tube. After a coughing attack, he developed swallowing problems and increasing fever, so that he had been admitted to a pulmonology department of the hospital. In X-ray photographs there were, however, no signs of aspiration pneumonia.

The clinical examination provided in fact evidence for a symptomatic urinary tract infection with turbid urine, proteinuria and massive leukocytosis triggered by an indwelling catheter (Table 1).

The microbiological examination of the mid-stream urine revealed the presence of two bacteria, namely *Klebsiella pneumoniae* and *Proteus mirabilis* in each case in high numbers, i.e. $> 10^6$ per ml. Their in vitro susceptibilities were tested routinely by VITEK2 (Biomérieux, Nürtingen, Germany). The susceptibility of the *Klebsiella* strain to ceftolozane/tazobactam was tested by E-test. In addition, the susceptibility of both isolates to nitroxoline was determined by a disk diffusion test (content of discs 30 µg) and validated according to EUCAST breakpoints. The complete antibiograms—obtained finally only after a delay of 4 days—showed that nitroxoline was the only drug active against both uropathogens (Table 2). The presence of carbapenemase OXA48 in the *Klebsiella* isolate was approved by PCR.

After removal of the urinary catheter, the clinical symptoms improved definitely, so that the patient could be

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Table 1 Laboratory results

Blood	
Leukocytes	24.89/nl
C-reactive protein	185 mg/l
Urine	
pH	8
Leukocytes	+++
Nitrite	Positive
Protein	++++

Table 2 Antibiograms of two multi-resistant bacteria isolated from a mid-stream urine in high numbers, i.e. > 10^6 per ml

	I	II
Ampicillin	res	res
Ampicillin/sulbactam	res	res
Amoxicillin/clavulanic acid	res	res
Piperacillin	res	res
Piperacillin/tazobactam	res	res
Imipenem	int	sus
Meropenem	int	sus
Cefuroxime	res	res
Cefixime	res	res
Cefotaxime	int	res
Ceftazidime	int	res
Ceftolozane/tazobactam	res	not tested
Gentamicin	res	res
Levofloxacin	res	res
Ciprofloxacin	res	res
Tigecycline	sus	res
Cotrimoxazole	res	res
Nitrofurantoin	res	res
Fosfomycin	res	sus
Nitroxoline	sus	sus

Strain I: *Klebsiella pneumoniae* carbapenemase (OXA 48) positive. Strain II: *Proteus mirabilis*

delivered at home with an advice for an oral antibiotic treatment of the observed uropathogens for 5 days.

Discussion

The prevalence of urinary tract infections with multi-resistant and even pan-resistant uropathogens is increasing [6–10]. Especially patients with indwelling catheters are at risk [11]. Obviously, resistance traits against various common antibiotics are often coupled on the same transmissible genetic elements [8], so that parallel-resistance to several, chemically different antibiotic groups is observed in clinical isolates.

This above-described case demonstrates that nitroxoline is an option for the treatment of patients infected with multi-resistant uropathogens, because resistance to nitroxoline is obviously not concomitantly expressed with resistance to other antibiotics. The use of reserve antibiotics or the combination of drugs which is recommended sometimes in case of infection with multi-resistant bacteria [12] could be avoided. Indeed nitroxoline, which is given orally and eliminated predominantly via the urinary tract, disposes of a broad spectrum of activities even against bacteria resistant to many other antibiotics [2, 3, 13–15] and is—by the way—also active against bacteria in biofilms [16], which will emerge during urinary tract infections, especially on indwelling catheters or intraluminal foreign bodies [11].

In addition, nitroxoline may be useful to prevent urinary tract infections with multiresistant pathogens, since this drug is recommended for prophylaxis, too.

Compliance with ethical standards

Conflict of interest The authors declare that they do not have any conflicts of interest.

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