

HIGH PREVALENCE OF RESISTANCE IN SHIGELLAE IN EUROPEAN PART OF RUSSIA

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ABSTRACT

Background: Shigellosis is an increasing cause of bacterial diarrhoea and hospitalisation in the European part of Russia. Effective antimicrobial therapy can reduce the severity and duration of illness and prevent potential complications. However data on susceptibility of *Shigella* spp. to antimicrobials in Russia are very limited. The objective of this study was the determination of the antimicrobial resistance of *Shigella* spp. isolated in the European part of Russia.

Methods: The total of 132 strains of *S. flexneri* and 69 strains of *S. sonnei* isolated in Smolensk Region and in Moscow during 1998-1999 were tested to 9 antimicrobials: ampicillin (AM), ampicillin/sulbactam (AMS), cefotaxime (CTX), tetracycline (TE), chloramphenicol (CL), nalidixic acid (NLA), norfloxacin (NOR), ciprofloxacin (CIP), trimethoprim/sulfamethoxazole (SXT) by agar dilution method. All procedures and interpretation of the results were performed according to the NCCLS guidelines.

Results: High rates of antimicrobial resistance were found in both *S. flexneri* and *S. sonnei*, respectively: SXT (97.7% and 94.2%), TE (98.5% and 92.8%), CL (93.9% and 50.7%), AM (95.5% and 26.1%) and AMS (94.7% and 23.2%). No resistance to NLA, NOR, CIP and CTX was determined. High rates of multiresistance (to 3 and more antimicrobials) were showed: 95.5% and 63.8% in *S. flexneri* and in *S. sonnei*, respectively. Among *S. flexneri* 88.6% of strains were characterized by the AM, AMS, CL, TE, SXT phenotype of resistance and 37.7% of *S. sonnei* strains had SXT, CL, TE resistance phenotype.

Conclusions: Commonly prescribing in Russia for treatment of shigellosis antimicrobials such as AM, CL, TE and SXT have lost their efficacy against *Shigella* spp. and can not be recommended for the empirical therapy of shigellosis. Quinolones and III generation cephalosporins can be considered as drugs of choice for the treatment of shigellosis.

INTRODUCTION

Bacillary dysentery is a severe inflammation of the large intestine caused by enteroinvasive bacteria belonging to the genus *Shigella*. The disease is endemic throughout the world, and one of the leading causes of the hospitalisation of patients with diarrhoea in Russia. Current epidemiological and socio-economical situation in Russia is promoting the morbidity associated with *Shigella* spp. Moreover, the incidence of severe forms and complications is also increased. Official data show the prevalence of bacterial dysentery in Russia in 1999 constituted 148.2 cases per 100,000, compared to 78.0 cases in 1998, reached 138.822 for 1999 and 99.27 versus 70.12 and 187.83 in Smolensk region in 1998 and 1999, respectively. Effective antimicrobial therapy can reduce both the severity and duration of illness and can prevent potential complications. Over the years, in many parts of the world *Shigella* spp. have acquired resistance to the commonly used antimicrobials, resulting in treatment failure and increased mortality. But for the time being there are limited data on antimicrobial resistance of shigellae in Russia.

METHODS

The total of 132 strains of *Shigella flexneri* and 69 strains of *Shigella sonnei* isolated in Smolensk Region and Moscow during 1998-1999 from hospitalised patients were included in the study. Activity of 9 antimicrobials: ampicillin (AM), ampicillin/sulbactam (AMS), cefotaxime (CTX), tetracycline (TE), chloramphenicol (CL), nalidixic acid (NLA), norfloxacin (NOR), ciprofloxacin (CIP) and sulfamethoxazole/trimethoprim (SXT) against above strains has been determined by agar dilution. All procedures and interpretation of results were provided according to NCCLS guidelines (January 2000). Reference strains *E.scherichia coli* ATCC 25922 and ATCC 35218 were used as a control strains for susceptibility testing procedures.

RESULTS

According to the study results, majority of the cases of shigellosis in Smolensk Region and Moscow are caused by *S. flexneri* 2a and *S. sonnei*. High rates of resistance to SXT (97.7% and 94.2%), TE (98.5% and 92.8%) and CL (93.9% and 50.7%) were found in both *S. flexneri* and *S. sonnei*, respectively (see Table). *S. flexneri* were significantly more resistant to AM than *S. sonnei* (95.5% vs. 26.1%). Addition of a beta-lactamase inhibitor sulbactam did not improve activity of AM - 94.7% and 23.2% of strains of *S. flexneri* and *S. sonnei* were resistant to AMS, respectively. At the same time no resistance to quinolones (NAL, NOR and CIP) and III generation cephalosporins (CTX) have been determined. Distribution of resistance of tested strains did not differ significantly in Smolensk and Moscow.

The MIC for 50% and 90% of tested strains as well as MIC ranges are given in the Table presented below.

Table. Susceptibility of *Shigella flexneri* and *Shigella sonnei* to tested antimicrobials

Antimicrobial	<i>S. flexneri</i> (n=132)				<i>S. sonnei</i> (n=69)			
	MIC ₅₀ mg/L	MIC ₉₀ mg/L	MIC ranges mg/L	R %	MIC ₅₀ mg/L	MIC ₉₀ mg/L	MIC ranges mg/L	R %
Ampicillin	256	>256	2->256	95.5	4	256	2->256	26.1
Ampicillin/sulbactam	16	128	1-256	94.7	2	32	1-64	23.2
Cefotaxime	0.12	0.12	0.015-8	0	0.03	0.06	0.015-0.12	0
Nalidixic acid	2	4	1-4	0	2	4	0.5-4	0
Norfloxacin	0.12	0.12	0.015-1	0	0.03	0.12	0.008-1	0
Ciprofloxacin	0.015	0.03	0.004-0.25	0	0.008	0.03	0.002-0.12	0
Chloramphenicol	64	256	1->256	93.9	16	256	4->256	50.7
Tetracycline	128	256	1->256	98.5	128	256	1->256	92.8
Sulfamethoxazole/trimethoprim	128	128	0.25->128	97.7	128	128	0.5->128	94.2

High rates of multiresistance (to 3 and more antimicrobials) have been observed: 95.5% and 63.8% in *S. flexneri* and *S. sonnei*, respectively. Among *S. flexneri* 88.6% of strains were characterized by AM, AMS, CL, TE, SXT phenotype of resistance and 37.7% of *S. sonnei* strains had SXT, CL, TE resistance phenotype.

DISCUSSION

The main problem in the antibacterial therapy of this disease seems to be the high level of resistance of shigellae to antimicrobials that are commonly used for treatment of bacterial diarrhoea in Russia. For instance nearly all strains now are resistant to AM, SXT, TE and CL. Surprisingly low activity of ampicillin/sulbactam can be explained by production of inhibitor-resistant beta-lactamases such as OXA and PSE, but this hypothesis is needed to be proved by molecular methods. Another problem is a high prevalence of multiresistance (to 3 and more antimicrobials): majority of strains were highly resistant to the same time to SXT, TE and CL and in addition - to AM in the case of *S. flexneri*. However, quinolones, fluoroquinolones and III generation cephalosporins remain highly active against all tested strains.

CONCLUSIONS

- ✓ Commonly prescribed in Russia for treatment of shigellosis antimicrobials such as ampicillin, chloramphenicol, tetracycline and trimethoprim/sulfamethoxazole lost its efficacy against *Shigella* spp. and can not be recommended for the empirical therapy of shigellosis.
- ✓ Quinolones and III generation of cephalosporins should be considered as drugs of choice for the treatment of shigellosis.