

EXPERIMENTAL STUDY

Eradicative effect of cotrimoxazole and quinolones on non-typhoid salmonellae

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Abstract

Opinions on antibiotic treatment of salmonella gastroenteritis are still different. Many authors support an opinion that antimicrobial treatment has no effect on salmonella elimination. The authors of the study have tried to prove that fluoroquinolones shorten the elimination of salmonellae and therefore they are useful not only for the treatment of salmonella gastroenteritis in immunocompromised patients to prevent sepsis and extraintestinal manifestations of the infection, but also for eradication of salmonellae in food industry workers, whose carrier state might exclude them from their work. (Tab. 3, Ref. 10.)

Key words: salmonella, carrier state, quinolones, antimicrobial agents, food industry workers.

Salmonellosis is one of the most frequent zoonoses in Slovakia. The disease is caused by a number of non-typhoid salmonellae: *S. enteritidis*, *S. typhimurium*, *S. gallinarum-pullorum*, *S. montevideo*, *S. dublin*. Salmonellosis in humans is caused most frequently by *S. enteritidis*, *S. typhimurium*, etc. Since the mid-eighties the portion of *S. enteritidis* has markedly increased in comparison with *S. typhimurium*. The reservoirs of infection are warm-blooded and cold-blooded vertebrates. The most frequent sources of infection in our conditions are the products containing raw or half-raw eggs (1, 5). Eggs can be contaminated either via egg-shell pores with hen's droppings, or transovarially before the formation of egg-shell (2, 3).

There is a considerably high infectious dose in salmonellosis (10^5 – 10^9 bacteria), and therefore the interhuman transmission is practically impossible, except newborns and immunocompromised individuals, in whom the manifest illness can be induced even by a dose of 10^3 bacteria (4). As to the transmission of infection in young children, an important role is played probably not only by alimentary transmission, but also by a contact (5). In 1994 there was recorded in the U.S.A. an outbreak of epidemic in consumers of ice-cream, in which the concentration of bacteria had been very low, only 6 cells per 65 g of ice-cream (half a cup of ice-cream) (6).

Carriage of non-typhoid salmonellae is a clinically silent form of salmonella infection. In contrast to *S. typhi*, this carrier state usually results in spontaneous recovery without any treatment. As a rule, it lasts for several weeks or months.

The carriage of non-typhoid salmonellae is very important from a viewpoint of epidemiology in workers of canteens, restaurants, kitchens and food industries. These workers might, especially if the personal hygiene requirements had not been fulfilled, conta-

minate the food, in which the number of salmonellae might increase up to the necessary infectious dose.

Clinical course of salmonella infection varies from the asymptomatic carrier state' through the gastroenteritic form to rare forms, as the typhoid form, whose course is similar to that of typhoid fever caused by *S. typhi*, or the septic form. This last form occurs especially in patients with other severe underlying diseases, such as diabetes mellitus, hepatic cirrhosis, cancer, collagenoses, AIDS, and is usually associated with extraintestinal organ manifestations, e.g. osteomyelitis, endocarditis.

The most frequent form of the manifest illness is gastroenteritis. Incubation period lasts for 6–48 hours. Symptoms of the disease are fever, malaise, the aqueous, green, frequent stools. The disease usually recedes spontaneously within 5 days, in case of symptomatic treatment even sooner. Reactive arthritis may occur as a late complication following salmonella gastroenteritis (7).

The most important aspect of treatment is the fluid and mineral replacement. Antibiotic treatment is recommended in immu-

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nocompromised patients to prevent extraintestinal complications (8, 9), as well as in workers of food industries and services (8) for preventing the salmonella carriage. Some authors are of the opinion that antibiotics do not influence the elimination of salmonellae (4). Antibiotic treatment is fully indicated in typhoid and septic forms (4).

The second-generation fluoroquinolones (ciprofloxacin, ofloxacin) are the first choice treatment. In addition to quinolones, also the third-generation cephalosporins (cefotaxime, ceftriaxone) are very useful, especially for the treatment of extraintestinal forms (8, 9). *S. enteritidis* is still sensitive to the majority of antibiotics used. The increasing resistance of *S. typhimurium*, particularly of the phage type DT 104, to ampicillin, sulfamethoxazole, tetracycline, chloramphenicol and streptomycin has become a worldwide problem. This phage type has been isolated in our country, too (7).

Methods

In this retrospective study the authors have compared eradication effects of quinolones and cotrimoxazole on salmonellae in the group of 394 patients with acute gastroenteritis of salmonella etiology, who had been admitted to the Clinic of Infectious Diseases of the University Hospital with Policlinic in Trnava for the period from 1.1.1997—1.11.1999. Reported data are based on the patient records.

The effect of antimicrobial agents — cotrimoxazole, ofloxacin and pefloxacin on salmonella eradication was analyzed. The antimicrobial agents were administered to 188 patients, i.e. 123 women (65.2 %) and 65 men (34.8 %). Ofloxacin, pefloxacin and cotrimoxazole were administered per os in recommended dosage 5 days. 206 patients (100 women — 48.6 % and 106 men — 51.4 %) were treated only symptomatically without antibiotics. Children and adolescents under 18 years of age were not administered quinolones (7).

A rectal swab was taken from all the patients and microbiologically examined at the Department of Clinical Microbiology of University Hospital with Policlinic in Trnava. Isolated salmonella was tested by qualitative method — the disk diffusion test — for the sensitivity to following antimicrobial agents: ampicillin, chloramphenicol, tetracycline, cotrimoxazole, cefalotin, cefuroxim, ofloxacin and gentamicin. Control microbiological examinations were done after 3 weeks from the onset of disease. The patients who failed to come to the control examinations, were omitted.

Chi-Quadrat-Test was used for statistical analysis. Comparison of the treatment with ofloxacin and pefloxacin was evaluated by Fischer Exact Test. The tests were done at the $\alpha = 0.05$ level of significance.

Results

Of 394 cases of culture-confirmed salmonellosis, the most frequently classified serotype was *S. enteritidis*, occurring in 390 cases (99 %). *S. typhimurium* was detected in 3 cases (0.7 %) and *S. montevideo* in 1 case (0.2 %). All detected Salmonella strains were sensitive to cotrimoxazole and to fluoroquinolones as well.

Of 206 patients without antimicrobial therapy, spontaneous eradication of salmonellae occurred in 97 patients (47.1 %), elimination of salmonellae persisted in 109 patients (52.9 %) (Tab. 1).

Tab. 1. Comparison of successfulness of salmonella eradication in patients with and without antibiotic treatment.

	Patients with antibiotic treatment	Patients without antibiotic treatment
Eradication of salmonellae	155 (82.4 %)	97 (47.1 %)
Unsuccessful eradication	33 (17.6 %)	109 (52.9 %)

Tab. 2. Comparison of successfulness of salmonella eradication in patients treated with fluoroquinolones and cotrimoxazole.

Antibiotics used	Fluoroquinolones (ofloxacin, pefloxacin)	Cotrimoxazole
Eradication of salmonellae	114 (95.8 %)	41 (59.4 %)
Unsuccessful eradication	5 (4.2 %)	28 (40.6 %)

Tab. 3. Comparison of successfulness of salmonella eradication with ofloxacin and pefloxacin.

Antibiotics used	Ofloxacin	Pefloxacin
Eradication of salmonellae	52 (94.5 %)	62 (96.9 %)
Unsuccessful eradication	3 (5.5 %)	2 (3.1 %)

Of 69 patients treated with cotrimoxazole, eradication was successful in 41 patients (59.4 %), unsuccessful in 28 patients (40.6 %) (Tab. 2).

55 patients were treated with ofloxacin; eradication of salmonellae was successful in 52 of them (94.5 %), unsuccessful in 3 (5.5 %). Of 64 patients treated with pefloxacin, salmonellae were successfully eradicated in 62 patients (96.9 %) and eradication failed in 2 patients (3.1 %) (Tab. 3).

Statistical analyses showed the significant effect of antimicrobial treatment on eradication of salmonellae ($\chi^2=53.31$; $p<0.001$). Eradicative effect of fluoroquinolones was statistically significant in comparison with the effect of cotrimoxazole ($\chi^2=39.94$; $p<0.001$).

No statistically significant difference has been found between the effects of ofloxacin and pefloxacin ($p=0.661$).

High percentage of patients in the group treated with antimicrobial agents is due to the fact that hospitalization is necessary only in patients with severe clinical form of gastroenteritis.

The present study has confirmed opinions of cited authors supporting the use of the second-generation fluoroquinolones as first-choice drugs for salmonella infections, eradicating successfully salmonellae. At the same time it has been confirmed that cotrimoxazole, in spite of its good effectiveness on salmonellae *in vitro*, has less eradication effect in patients than quinolones. It is another example of discrepancy between efficacy of antibiotics *in vitro* and *in vivo* (10). Comparing the effectiveness of 2 fluoroquinolones used, no significant differences were found. In agreement with data from literature (7), good sensitivity of *S. enteritidis* was confirmed to the majority of used antibiotics also in our group of patients.

Our results show that antimicrobial treatment is indicated not only in patients with a severe underlying immunocompromising disease, but it is also indicated and successful in workers of food

industry and services to prevent their working incapability. Patients and salmonella carriers must be administered adequate antimicrobial agents, as the second-generation fluoroquinolones, whose effect has been confirmed also in the present study.

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GEROVA M: COMMENT TO THE ARTICLE

Holomanova A, Ivanova A, Brucknerova I, Benuska J:

Andreas Vesalius — the reformer of anatomy

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It is to appreciate the endeavour of A.Holomáňová and co-workers to acquaint the Slovak medical public with such a personality as Andreas Vesalius was. I, myself, met the work of A.Vesalius when searching the roots of knowledge on coronary arteries. In his “De humani corporis fabrica” A.Vesalius provided the anatomical drawing of the heart, with “Coronales Arteriae” running on the surface of the heart, as well as the drawing of the arterial tree — the aorta and its main branches. It was only in the next century when W.Harvey (1628) described the functional role of coronary arteries.

I would like to note that Jan Stefan Kalkar shared in anatomical drawings of the heart and coronary arteries and arterial tree. Even the portrait of A. Vesalius presented in the article of A. Holomáňová et al. was made by J.S. Kalkar (1). J.S. Kalkar himself used to work in the Titian school.

Finally, evidently as a matter of misprint, the lifespan of Vesalius was 50 years and not 30 years as given in the article.

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