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THE DYNAMICS OF RESISTANCE TO QUINOLONES IN GRAM NEGATIVE BACTERIA ISOLATED FROM HOSPITALIZED PATIENTS

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Abstract: *Quinolones are one of the largest classes of antimicrobial agents, including synthetic drugs frequently used worldwide. The study group has included all the Gram negative bacilli isolated from the pathological products of the patients hospitalized in the Clinical County Emergency Hospital of Brasov during a period of two years (2008 and 2010). The aim of the study has consisted in the evaluation in dynamics of the resistance to quinolones of the isolated germs. The results showed that resistance to quinolones was present in all tested bacterial genre. In dynamics, we have found an increase of the level of resistance of non fermentative gram negative bacilli to ciprofloxacin. There were also recorded increases in the percentage of resistance of Enterobacter strains to norfloxacin and to nalidixic acid in case of Proteus strains. The relative high level of resistant strains to quinolones shows the necessity of a rational policy in prescribing these antibiotics in hospitals*

Key words: *antibiotic resistance, quinolones, gram negative bacilli.*

1. Introduction

Quinolones are one of the largest classes of antimicrobial agents, including synthetic drugs frequently used worldwide [2, 5, 15].

It is generally accepted that nalidixic acid was the first quinolone drug, introduced in 1962. The first generation of quinolones is rarely used today. From 1998, nalidixic acid is considered a carcinogen drug [9]. There have been developed a second- , third- and fourth-generation of fluoroquinolones and the action spectrum has been expanded from the Gram negative to Gram positive organisms, from aerobic to anaerobic germs [4, 9, 14].

Clinical applications of fluoroquinolones include infections with various localizations: genitourinary, respiratory, gastrointestinal, skin infections, and other [7, 9].

The induction of resistance to quinolones involves mutations in genes (*gyr*A, *par*C) that codify the production of some enzyme with role in DNA replication (DNA gyrase, topoisomerase IV) or porins synthesis from outer-membrane. Another mechanism is the reduction of intrabacterial concentration by

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efflux pumps that eliminate the antibiotic molecules from the bacterial cell [6, 9]. All these changes are chromosomally mediated. In present, a significant concern is plasmid-mediated resistance to quinolones, the gene that is responsible being *qnr* [1, 4, 9, 12].

In Enterobacteriaceae there are implicated all the presented resistance mechanisms [4, 6]. In Pseudomonas species, the most frequent implicated mechanisms are impermeability of the outer membrane and efflux pumps. Additionally, mutations of target enzymes occur [4, 8]. In Acinetobacter, the quinolones resistance is usually due to the mutations of DNA-gyrase. Rarely, efflux pumps may also contribute [4, 11].

The quinolones resistance is a phenomenon encountered also in community but with higher levels in hospitals, as shown in many published studies [3, 5, 6, 7, 10, 13].

2. Material and Methods

Our study was retrospective, based on data provided by the laboratory records.

The study group has included all the Gram negative bacilli isolated from the pathological products of the patients hospitalized in the Clinical County Emergency Hospital Brasov during a period of two years (2008 and 2010).

In the studied period, in the Department of Bacteriology of the hospital there have been isolated different glucose fermentative and non fermentative Gram negative bacilli.

For the isolation of the germs there were used Oxoid culture media. The identification of the isolated germs was carried out using classical biochemical techniques (Triple Sugar Iron Agar, S.I.M. Agar, Urea Agar, Citrate Agar), API galleries and the system VITEK 2 COMPACT. The testing of strains to the antibiotics was performed by the difusimetric Kirby Bauer method, interpreted based on CLSI (Clinical and Laboratory Standards Institute) or using VITEK 2 COMPACT system.

The quinolone constantly tested for Gram negative bacteria from pathological products was ciprofloxacin, to which there were added, in the case of the strains isolated from urine, norfloxacin and nalidixic acid.

The objective of the study was to assess the dynamics of resistance to quinolones of the Gram negative strains involved in the infections of hospitalized patients.

3. Results and discussions

We have initially analyzed the susceptibility of all the isolated Gram negative bacilli to ciprofloxacin.

In Figure 1 is represented the dynamics of the resistance of Enterobacteriaceae strains to ciprofloxacin from one year of study to the other.

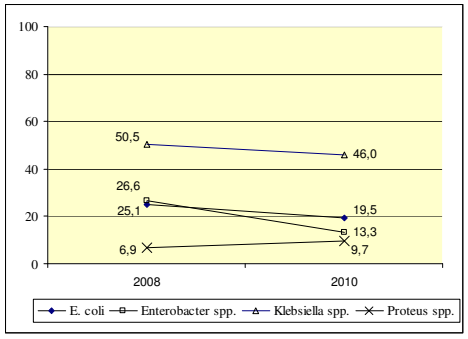

Fig.1. *The dynamics of resistance to ciprofloxacin of Enterobacteriaceae strains*

Figure 2 shows the graphical representation of the dynamics of resistance to ciprofloxacin of non fermentative gram negative bacilli.

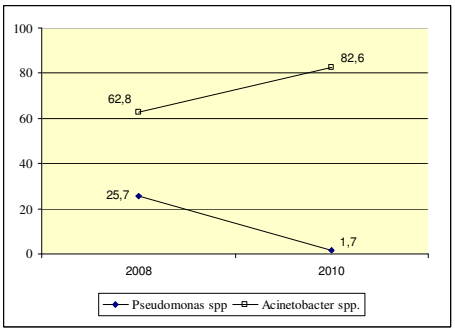

Fig. 2. *The dynamics of resistance to ciprofloxacin of non fermentative bacilli*

In the case of E. coli, there was found a decrease in the percentage of resistance to ciprofloxacin but this can be also correlated with the reduced numbers of isolated bacilli in 2010.

The decrease of the resistance percentage is higher in Enterobacter spp., appearance probably due to a more judicious antibiotic use.

In Klebsiella species, the resistance level was relatively constant in the study period and in the case of Proteus species, there was observed a discrete increase of the percentage of resistant strains to ciprofloxacin in 2010 compared to 2008.

In the case of the isolated non fermentative gram negative bacilli (Pseudomonas species and Acinetobacter species), the percentage of the resistant strains has increased in 2010 compared to 2008.

The Enterobacteriaceae strains which were isolated from urine have been also tested to urinary quinolones (norfloxacin, nalidixic acid), as shown in Figures 3-6.

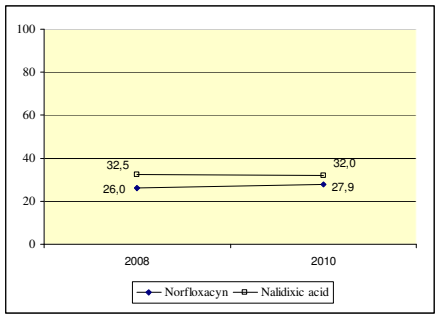

Fig. 3. *The dynamics of resistance to urinary quinolones in E. coli*

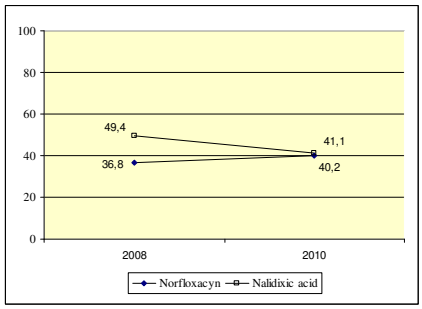

Fig. 4. *The dynamics of resistance to urinary quinolones in Enterobacter spp.*

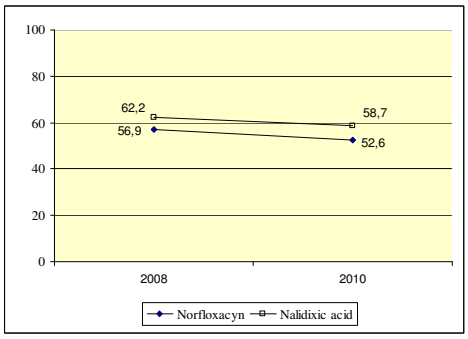

Fig. 5. *The dynamics of resistance to urinary quinolones in Klebsiella spp.*

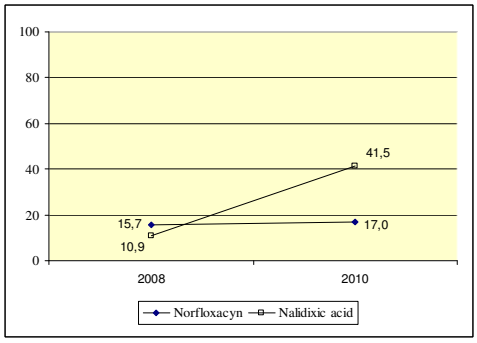

Fig. 6. *The dynamics of resistance to urinary quinolones in Proteus spp.*

In E. coli, the level of resistance to the two urinary quinolones was relatively constant. We have observed an increased percentage of Enterobacter species strains resistant to norfloxacin, the variation being insignificant for nalidixic acid. The level of resistance in the isolated Klebsiella spp. strains was relatively constant to both quinolones. The share of Proteus spp. strains resistant to nalidixic acid has illustrated a significant increase while in case of norfloxacin the level was relatively constant.

4. Conclusions

1. The results of the study show that resistance to quinolones was present in all tested bacterial genre.

2. In dynamics, we have found an increase of the level of resistance of non fermentative gram negative bacilli to ciprofloxacin.
3. There were also recorded increases in the percentage of resistance of Enterobacter strains to norfloxacin and to nalidixic acid in case of Proteus strains.
4. The relative high level of quinolones resistant strains shows the necessity of a rational policy in prescribing these antibiotics in hospitals
5. However, there can be observed that this class of antibiotics, if used judiciously, under the control of the antibiogram, may still be the therapeutic solution for infections at various sites.

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