# The Trends of Common Pathogens of Nosocomial Infection and Changes of Resistance to Quinolones

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**Abstract:** To investigate the distributions of common pathogenic bacteria and the changes of the resistance to quinolones isolated from inpatients during the past 5 years, and explore their resistance mechanisms to guide the clinic doctors to use antimicrobial drugs. Results showed that 5303 strains of bacteria had been detected during Jan. 2007 to Dec. 2011 in hospital. The top five kinds of bacteria were illustrated as follows: Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa,Pneumonia klebsiella, Acinetobacter baumannii., the total situations of distribution were little changed each year. It could be seen from the results of antimicrobial susceptibility test, resistance of five kinds of bacterial to quinolones were rising year by year. So we should strengthen the monitoring of drugs resistance of pathogens.The clinical doctors should choice the rational antimicrobial drugs according to the results of clinical antimicrobial susceptibility test.

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**Key words:** pathogens; nosocomial infection; quinolones; drug resistance; antimicrobial susceptibility test

## 1. Introduction

Quinolones drugs have wide antibacterial spectrums, strong antibacterial activities, low resistance crossing and small side effects. To Gram-positive bacteria and Gram-negative bacteria, they have shown lots of better antibacterial activities. In recent years, with the increasing using of quinolones drugs in clinic, some unreasonable using have also led to increasing drugs resistance and changing of drugs resistance spectrums (QuLiang, 2010). By retrospective analysis, ciprofloxacin (CIP), levofloxacin (LEV), pefloxacin (PFLX) and gatifloxacin (GAT) were selected respectively as represent medicine of 3, 4, generation of quinolone in this test, so that we can investigate the changes of the resistance to quinolones of pathogenic bacteria isolated from inpatients during the past 5 years, and explore their resistance mechanism, and guide the clinic doctors to use antimicrobial drugs reasonable.

## 2. Material and Methods

2.1 Source of specimens: 5303 strains bacteria isolated from inpatient's specimens from January 2007 to December 2011, including blood, phlegm, throat swabs, wound secretions, etc. All kinds of specimens met the requirements.

2.2 Isolation and identification of bacteria: strictly according to the third edition of The National Clinical Operation Procedure, Vitek 32 automatic measurement system for microbial bacteria was used. Some of them used K-B antimicrobial susceptibility test. Results would be interpretated according to the clinical laboratory standards formulated by standardization committee (CLIS).

2.3 Quality control: Pseudomonas aeruginosa ATCC27853, Staphylococcus aureus ATCC25923, Escherichia coli ATCC25922 provided by the Chinese pharmaceutical and biological products.

2.4 Statistical analysis: WHONET 5.6 software for statistical analysis was used.

## 3. Results

3.1 The distributions of main strains: from January 2007 to December 2011, the total number of pathogenic bacteria was 5303, the number of bacteria of Gram-negative bacteria was the dominant position, the top five bacteria were illustrated as follows: Escherichia coli (E.coli), Staphylococcus aureus (St.aureus), Pseudomonas aeruginosa (P.aeruginosa), Klebsiella pneumoniae (K. pneumoniae), Acinetobacter baumannii (Ac.baumannii). Each year, the total situation of distribution was little changed. The distributions of main bacteria will be illustrated in Table 1.

3.2 The resistance to quinolones of main five bacteria will be illustrated respectively in Table 2 to 4.

**Table 1** The composition of main isolated bacteria for five years (%)

| Pathogens | 2007 (n=818) | 2008 (n=1019) | 2009 (n=1134) | 2010 (n=1057) | 2011 (n=1280) |
|---|---|---|---|---|---|
| **E.coli** | 16.25 | 14.82 | 17.02 | 16.31 | 16.17 |
| St.aureus | 15.40 | 19.23 | 20.90 | 19.39 | 20.00 |
| P.aeruginosa | 13.57 | 12.07 | 11.99 | 11.61 | 13.04 |
| K.pneumoniae | 12.96 | 10.99 | 10.14 | 11.31 | 9.80 |
| Ac.baumannii | 11.12 | 9.12 | 4.94 | 8.17 | 7.57 |

**Table 2** The resistance of E. coli and klebsiella pneumonia bacillus to quinolones(%)

| years | Escherichia coli | | | | Klebsiella pneumonia | | | |
|---|---|---|---|---|---|---|---|---|
| | LEV | PFLX | GAT | CIP | CIP | PFLX | GAT | LEV |
| 2007 | 48.84 | 28.76 | 21.43 | 48.72 | 48.33 | 21.62 | 20.91 | 39.77 |
| 2008 | 53.66 | 30.80 | 25.74 | 58.99 | 50.84 | 26.57 | 24.46 | 41.23 |
| 2009 | 62.99 | 43.34 | 37.42 | 63.15 | 64.07 | 38.22 | 39.52 | 58.87 |
| 2010 | 64.56 | 47.70 | 42.58 | 78.03 | 72.90 | 42.57 | 47.19 | 69.82 |
| 2011 | 80.14 | 51.76 | 49.73 | 89.06 | 81.53 | 51.59 | 49.85 | 80.64 |
| $X^2$ | 87.05 | 55.80 | 77.58 | 163.58 | 81.454 | 58.44 | 67.72 | 121.91 |
| Pvale | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 |

**Table 3** The resistance of pseudomonas aeruginosa and acinetobacter baumannii to quinolones(%)

| years | Pseudomonas aeruginosa | | | | Acinetobacter baumannii | | | |
|---|---|---|---|---|---|---|---|---|
| | PFLX | LEV | GAT | CIP | PFLX | CIP | GAT | LEV |
| 2007 | 28.54 | 41.34 | 21.45 | 52.13 | 35.43 | 41.64 | 31.52 | 40.93 |
| 2008 | 33.68 | 43.41 | 25.72 | 53.37 | 42.59 | 46.59 | 35.06 | 49.99 |
| 2009 | 37.13 | 44.29 | 37.48 | 55.84 | 48.46 | 48.23 | 40.13 | 58.16 |
| 2010 | 50.24 | 51.78 | 42.53 | 64.20 | 53.36 | 62.50 | 47.77 | 60.74 |
| 2011 | 59.39 | 61.77 | 49.70 | 69.25 | 67.82 | 71.55 | 58.63 | 69.83 |
| $X^2$ | 73.25 | 33.14 | 62.99 | 25.78 | 45.05 | 45.81 | 35.89 | 36.31 |
| Pvale | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 |

**Table 4** The resistance of staphylococcus aureus to quinolones(%)

| years | Staphylococcus aureus | | | |
|---|---|---|---|---|
| | CIP | PFLX | GAT | LEV |
| 2007 | 33.22 | 18.72 | 15.23 | 26.78 |
| 2008 | 41.36 | 20.85 | 21.76 | 31.35 |
| 2009 | 45.52 | 33.38 | 31.97 | 40.43 |
| 2010 | 55.76 | 37.75 | 37.72 | 49.57 |
| 2011 | 59.99 | 41.78 | 41.52 | 50.30 |
| $X^2$ | 68.76 | 71.75 | 79.36 | 66.68 |
| Pvaule | <0.01 | <0.01 | <0.01 | <0.01 |

## 4 Discussion

As can be seen from the monitoring in past five years, the drugs resistance of bacteria to quinolones were rising year by year, especially Gram-negative bacteria were more apparent, which may be related to resistance mechanisms of unique membrane permeability declining. Resistant rate of E. coli to ciprofloxacin and levofloxacin increased respectively from 48.72% and 48.84% in 2007 to 89.06% and 80.64% in 2011, even if resistant rate of the 4th generation gatifloxacin also reached to 49.73% in 2011, which may be related to the extensive drags using in human and animal. Given its high resistance of quinolone drugs, which implied that they cannot serve as treatment drugs of E. coli . The basic trend of Gram-positive coccus resistance to quinolone was rising. The resistant rate of levofloxacin and ciprofloxacin staphylococcus aureus reached to 59.99% and 59.99% respectively in 2011.

The mechanism of bacterial resistance to quinolone drugs was complex, the most main reason is related to changes of topoisomerase gumming points mediated by chromosome and reducing of the intracellular drug accumulation or the Qnr protein protection mechanism encoded by plasmid. (1) Bacteria resist to quinolone drugs by interfering with bacterial DNA replication, its targeted point is enzyme and DNA topoisomerase Ⅳ, both belong to the topoisomerase Ⅱ type.To Gram-negative bacteria such as E. coli, DNA promoting rotary enzymes was targeted as primary point to quinolones. When gene of topoisomerase coding is mutational, the ability of quinolones combining with DNA topoisomerase will be reduced, unable to stop DNA replication, and lead to the development of drugs resistance; To Gram-positive bacterium, topoisomerase Ⅳ changing is the main mechanism (Giraud E, 2006). The studies of Jinke, etc (Jinke, 2009) have found that the resistance of Pseudomonas aeruginosa is that gyrA gene codon generate mutations.So it lead to droping of affiniting between lelequinolones and topoisomerase Ⅱ. ParC sever as another gumming of quinolones. From its gene

sequence analysis, we can find the mutation of codon in 87th aminoacid so that it results in the decrease of drug affinity. Two provious situations led to resistance of Pseudomonas aeruginosa to quinolones alone or togother.(2) It was only found Gram- negative bacteria that the declining of outer membrane permeability lead to resistance to quinolone at present. Bacteria can change the outer membrane protein or the number of LPS or change the permeability, and cause low resistance to quinolones (QuLiang, 2010), which is also some nonspecific chromosome mutations. The research of Xu Hongtao (Xu Hongtao, 2007) and other researches found that the important mechanism of resistance to quinolone was also involved in the Pseudomonas aeruginosa. (3) The bacterica that are mediated by plasmid resist to quinolone: plasmid will be transfer after joint, lead to the zygote resistance to quinolone increased, and resistant mutant strains to quinolone are easy to choose, QNR genes encoding proteins can protect bacteria DNA helicase and topoisomerase Ⅳ from attacking by quinolones (NingYongzhong, 2007).

Because quinolone drugs were widely used in clinical, drug-resistant to bacteria is a combination of specific and non-specific resistance mechanisms. Clinicians should strictly master the principle of quinolone drugs using to reduce the selective pressure of antibiotics. By the dynamic monitoring of the bacteria resistance to quinolone drugs and understanding the mechanism of drug resistance, it will guide clinicians to use drugs rational as possible.

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