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Case report

GARENOXACIN IN UNCOMPLICATED URINARY TRACT INFECTION – A CASE STUDY REPORT

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ABSTRACT

Urinary tract infection (UTI) is a global problem which has increased the morbidity and mortality in both men and women. Strategies which are proposed in the management of UTIs include the use of empirical antibiotics with a broader spectrum of coverage. Urine specimen culture is of significant importance to evaluate the organism responsible in the pathogenesis. Garenoxacin, a newer fluoroquinolone with unique structural advantage appears to be a suitable drug in the treatment of UTIs.

Keywords: Urinary tract infection, Garenoxacin, fluoroquinolone, PK/PD, E.coli

INTRODUCTION

A urinary tract infection (UTI) is defined as microbial infiltration of the otherwise sterile urinary tract and is one of the most common bacterial infections occurring worldwide. UTIs include infections of the urethra (urethritis), bladder (cystitis), ureters (ureteritis), and kidney (pyelonephritis)¹.

Uncomplicated UTIs are those occurring in healthy premenopausal, non-pregnant women with no history of an abnormal urinary tract. These include acute cystitis and pyelonephritis². Longer courses of treatment are often recommended for persons with complicated urinary tract infections.

CASE REPORT

A female aged 34 years weighing 57 kgs approached a consultant surgeon at a tertiary care hospital at Vadodara complaining of burning micturition, difficulty in urination and increased urinary frequency since 3 days. The patient was well built, well-nourished and was in a stable condition. She was afebrile and her vital parameters like pulse rate, respiratory rate and blood

pressure were within the normal limits. There was no generalized lymphadenopathy. There was no history of any chronic illnesses like Diabetes mellitus or tuberculosis. The patient's urine specimen was sent to the microbiology department for urine culture. Garenoxacin 400 mg OD (200 mg X 2 tablets stat) for 5 days was prescribed to the patient along with a urinary alkalizing agent. The patient was also advised to consume plenty of water. She was asked to come back to the OPD for the follow up. After 2 days the urine culture reported *E. coli*. The patient returned to the OPD on the third day and admitted to the doctor about the relief of urinary symptoms. After 5 days of therapy another urine specimen was sent to the microbiology department. The urine culture report was found to be negative for *E. coli*.

DISCUSSION

UTIs are the most frequent bacterial infection seen in the outpatient setting. 1 in 3 women will develop a UTI requiring antibiotic treatment by age 24, and 50%

experience at least 1 UTI during their lifetime³. The incidence of cystitis is found to be significantly higher in women than men, which might be the result of anatomic difference. Among young, healthy women with cystitis, the infection recurs in 25% of women within 6 months after the first urinary tract infection, and recurrence rate increases with more than 1 prior urinary tract infection. Acute uncomplicated pyelonephritis is much less common than cystitis (estimated ratio, 1 case of pyelonephritis to 28 cases of cystitis) with a peak annual incidence of 25 cases per 10,000 women 15 to 34 years of age².

Management guidelines:

Aims of treatment⁴:

There are two predominant aims in the treatment of both uncomplicated and complicated UTIs

1. Rapid and effective response to therapy and prevention of recurrence in the individual patient treated
2. Prevention of emergence of resistance to chemotherapy in the microbial environment or at least prevention of further increase of resistance.

Current therapeutics for the treatment of UTI in adults include: 1. -lactams (like Amoxicillin/Clavulanate, Ampicillin/Sulbactam, and Cefixime etc.) 2. Fluoroquinolones (like Norfloxacin, Levofloxacin, and Ciprofloxacin etc.)3. Oxazolidinones (like Nitrofurantoin, Linezolid) and 4.Pyrimethamines(like Trimethoprim/Sulfamethoxazole)

Garenoxacin: Garenoxacin is a novel desfluoroquinolonethat lacks fluorine at the C-6 position⁵ but has fluorine incorporated through a C-8 difluoromethyl ether linkage. It has been shown to have activity against a wide range of clinical isolates. The activity of garenoxacin has been further assessed against strains of *S. aureus* with specific topoisomerase mutations, and more recently, it has been shown that garenoxacin has similar potency against both topoisomerase IV and DNA gyrase (dual-targeting quinolone)⁶, thus requiring mutations in both topoisomerases for resistance to occur. Although horizontal transfer is a major reason for the spread of ciprofloxacin-resistant strains, the role of antimicrobial selection may also play an important role⁷. In vitro profile of Garenoxacin against the UTI pathogens⁷.⁸:Garenoxacin is found to have lower MIC₉₀ values (Fung Tomc) to the common UTI pathogens. For the fact that Garenoxacin is excreted in the unchanged form in the urine it is believed to exert its antibacterial

properties against the UTI pathogens⁸. For antibacterial like fluoroquinolone which exhibit concentration dependent killing, increasing the AUC/MIC ratio would increase the bactericidal activity. Today AUC/MIC ratio values of 125-150 h for gram negative and 30-40 h for gram positive organisms are recommended not only for the microbiological outcome but also to prevent resistance⁹.

Table 1: In-vitro profile of Garenoxacin against common UTI pathogens

| Pathogen | MIC ₉₀ (µg/ml) | AUC/ MIC | Cmax/ MIC |
|--------------------------------|------------------------------|-------------|--------------|
| <i>E. coli</i> | 0.06 | 1678.3 | 123.8 |
| <i>Klebsiellapneumoniae</i> | 0.5 | 201.4 | 14.9 |
| <i>Proteus mirabilis</i> | 1 | 100.7 | 7.4 |
| <i>Enterococcus faecalis</i> | 0.5 | 201.4 | 14.9 |
| <i>Streptococcus agalactis</i> | 0.12 | 839.2 | 62 |

MIC₉₀, AUC, MIC, Cmax,

Garenoxacin was also found to be superior in terms of safety profile. Garenoxacin was found to be well tolerated by healthy adult subjects at oral doses up to 1,200 mg/day for up to 14 days¹⁰. A Post-marketing surveillance (PMS) study done at Japan by Hori et al.¹¹ in 6,412 patients confirmed the superior tolerability profile of Garenoxacin.

CONCLUSION

UTI is found to be a common problem worldwide, especially in reproductive women. Need of the hour is to start the therapy with an empirical antibiotic with a broad spectrum of coverage. Garenoxacin with its superior efficacy and safety profile appears to be a suitable choice among the currently available antibiotics for the treatment of UTIs. The excellent PK/PD profile also adds up to the advantage of preventing selection of resistant mutants. Convenient once a day dosing schedule has improved the patient compliance.

Conflict of interest: Nil.

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