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Case Report

Pharmacology Section

Garenoxacin in Skin and Skin Structure Infections Sustained due to Road Traffic Accident

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ABSTRACT

Skin and soft tissue infections represent a continuum of symptoms that range from uncomplicated cellulitis to the potentially lethal entity necrotizing fasciitis that is often considered to be microbial invasions of the epidermis, dermis and subcutaneous tissues. Garenoxacin, a newer oral des-fluoroquinolone having potent antimicrobial activity against wide variety of common pathogens involved in skin and skin structure infections (SSTIs), including the resistant strains offer the advantage of broad spectrum of coverage including gram positive, gram negative and anaerobic organisms. This case study indicates the utility of garenoxacin in treating skin and soft tissue infections caused by road traffic accidents.

Keywords: Broad-spectrum antibiotic, Newer fluoroquinolone, Resistance, SSTI, Wounds

CASE REPORT

A male aged 30-years weighing 55 kgs presented to a Surgeon at Dr. Ulhas Patil Medical College and Hospital, Jalgaon, Maharashtra, India in December,'13. The patient presented with nasal and upper lip wounds due to a road traffic accident leading to disfigurement of the face [Table/Fig-1a]. Patient was conscious, moderately built and had vital parameters including temperature, pulse rate and respiratory rate within normal limits. He had no history of any chronic illnesses like Diabetes mellitus or tuberculosis in the past. There was no icterus or generalized lymphadenopathy observed during examination. Local examination suggested wound contaminated with soil. After thorough wash with hydrogen and betadine a reconstructive surgical procedure was performed on the same day with an excision sample sent for further analysis and culture. The culture report showed *Staphylococcus aureus* on the third day. As surgical prophylaxis patient received Cefuroxime 1.5 mg injection intravenously every 8 hourly for two days. On 3rd day a healthy granulation tissue was seen and then the patient was taken for graft. A switch over therapy with Garenoxacin 400 mg once a day was then started for the next 10 days, after obtaining consent from patient. Excellent response was observed with the use of garenoxacin in the postoperative period. The response of the patient was graded on the basis of reduction in the swelling, redness and discharge. Clinically inflammatory response subsided in three days followed by total regression of wound up to scar formation in 7 days. There was no gaping or wound dehiscence or suture abscess. On 12th postoperative day the wound was found to be dry and the suture removal was done [Table/Fig-1b]. Upon completion of treatment with Garenoxacin, no side effects/adverse effects were noted.

[Table/Fig-1]: Before and after treatment with Garenoxacin along with surgical repair

DISCUSSION

Skin and skin structure infections (SSTIs) are classified by the FDA as either "uncomplicated" or "complicated". Uncomplicated SSTIs are defined as those that respond to either a simple course of antibiotics alone or simple drainage alone and include superficial cellulitis, folliculitis, furunculosis, simple abscesses, and minor wound infections. Complicated SSTIs are defined as those that involve the invasion of deeper tissues or require significant surgical intervention or occur in the presence of a significant underlying disease state that complicates the response to therapy. Complicated SSTIs remains a therapeutic challenge since most of the times they are accompanied by polymicrobial invasions. Hence, choosing an appropriate antibiotic with a wide spectrum of activity is essential.

These infections include complicated abscesses, infected burn wounds, infected ulcers, infections in diabetics, and deep space wound infections.

Additionally, the definitions of the various categories of these infections are indistinct and overlapping [1-3].

Injuries sustained on the face are an important cause of cosmetic disfigurement. Infection of these wounds is common perhaps due to the excellent blood supply to the face. Provision of proper wound care is essential for good outcomes and to reducing the infection risk in patients who undergo wound closure. When reconstructive procedures are performed, extensive irrigation, wound debridement, avoidance of deep sutures (if possible), institution of prophylactic antibiotic therapy and close follow up are indicated. A common approach involves initial IV therapy until infection is resolving followed by oral therapy to complete the course of 10 to 14 days.

Aggressive wound management is believed to decrease the infection rate [4]. Cleansing of the wound with a few hundred ml of high pressure saline is usually effective. Removal of devitalized tissues is also important to prevent a nidus of infection.

A number of antibiotics have been tried in the past. Currently the widely prescribed antibiotics in the treatment of SSTIs include Amoxicillin-Clavulanate (875/125 mg twice a day po), Dicloxacillin (250 mg 4 times a day po), Cephalexin (250 mg 4 times a day po), Erythromycin (250 mg 4 times a day po), Clindamycin (300-400 mg 3 times a day po). In case of SSTIs where MRSA (Methicillin-

resistant *S. aureus*) is encountered the choice of the antibiotic shifts to Vancomycin (30 mg/kg/day in 2 divided doses iv) or Linezolid (600 mg every 12 hours iv or 600 mg twice a day po) or Daptomycin (4 mg/kg every 24 hours iv) [5].

Garenoxacin, a novel des-fluoroquinolone is one of the most active fluoroquinolone active against various gram positive, gram negative and anaerobic organisms. It has a broad antimicrobial coverage including resistant organisms like methicillin resistant *S. aureus*, *S. epidermidis* and ciprofloxacin resistant *S. pneumoniae*. It has also been found to be active against various fastidious organisms like *mycoplasmas*, *ureaplasmas*, *chlamydiae*, CIP-nonsusceptible *gonococci* and *B. burgodorferi* [Table/Fig-2]. Evidences also suggest the utility of garenoxacin against *Enterobacter*iaceae and most nonfermenters. Hence garenoxacin is used in the treatment of various infections [6]. Drugs Controller General India (DCGI) has approved the use of Garenoxacin on 07/06/13 for the treatment of bacterial respiratory tract infections [7] with permission no. MF-131/13 in Form 46 under Drugs & Cosmetic Acts & Rules thereunder.

Pathogen	MIC90 (µg/ml)
Methicillin susceptible *S. aureus*	0.03
Methicillin resistant *S. aureus*-Ciprofloxacin sensitive	0.12
Methicillin resistant *S. aureus*-Ciprofloxacin resistant	4
Methicillin resistant *S. aureus*	2
Group B Streptococci	0.12
E. Coli	0.06
Serratia spp.	1
Pseudomonas aeruginosa	16

[Table/Fig-2]: In-vitro activity of Garenoxacin against common organisms causing SSTI [6]

In a study done by Kirby et al., [8], the role of garenoxacin was evaluated in 2,537 skin and soft tissue infection (SSTI) isolates from the SENTRY Antimicrobial Surveillance Program. Strains isolated in 2000 from Europe, North and Latin America was tested at a central laboratory using reference broth microdilution methods. The rank order of the seven most frequent SSTI pathogens was: *Staphylococcus aureus* (39.9%),*Pseudomonas aeruginosa* (12.1%), *Escherichia coli* (9.7%), *Enterococcus* spp. (7.7%), *Klebsiella* spp. (5.8%), *Enterobacter spp*. (5.6%) and coagulase-negative *staphylococci* (CoNS; 4.2%).

Garenoxacin exhibited a four-fold greater activity (MIC90, 0.06 µg/ml) compared to levofloxacin (MIC90, 0.25 µg/ml) against oxacillin-susceptible *S. aureus*; and oxacillin-resistant *staphylococci* were more susceptible to garenoxacin (≥90.5%) at ≤4 µg/ml than ciprofloxacin or levofloxacin. *Enterococcus* spp. were more susceptible to garenoxacin and gatifloxacin (MIC50, 0.5 µg/ml) than ciprofloxacin or levofloxacin (MIC50, 2 µg/ml).

Considering garenoxacin for the treatment of pathogens that commonly cause SSTIs appears to be warranted [8].

In another study done by Rennie et al., [9], the role of garenoxacin was evaluated against 1,404 bacterial isolates recovered from SSTIs from hospitalized patients in 24 sites in the United States (US) and 5 Canadian medical centers as part of the SENTRY Antimicrobial Surveillance Program. Isolates were collected between October and December, 2000. The rank order of pathogens was: *Staphylococcus aureus* (45.9%), *Pseudomonas aeruginosa* (10.8%), *Enterococcus* spp. (8.2%), *Escherichia coli* (7.0%), *Enterobacter* spp. (5.8%) and *Klebsiella* spp. (5.1%). The same order was observed in the US and Canada. Of note, almost 30% of *S. aureus* were oxacillin-resistant. Vancomycin resistance among enterococci was low (7.8%) representing a marked decrease from earlier SENTRY Program reports.

In a case study by Pukar et al., [10], Garenaxacin was used in the skin and soft tissue infection sustained after a bear bite. Garenoxacin was found to be extremely effective in treating *P. aerugonisa* and *S. aureus* which was found in the culture report of wound tissue.

Garenoxacin is also found to be extremely safe at daily dose of 400 mg [11]. In one study done by Gajjar et al., Garenoxacin was found to be well-tolerated by healthy adult subjects at oral doses of up to 1200 mg/day for up to 14 days [12].

A PMS (Post-marketing surveillance) study had been conducted at Japan by Hori et al., [11] on 6,412 cases from May 2008 to March 2010. The PMS study suggested 277 incidents of side effects in 221 cases and the rate of incidence was 3.45 % (221 cases / 6, 412 cases). The main side effects were 0.87 % (56 cases) of gastrointestinal disorders such as diarrhoea, which was followed by 0.72 % (46 cases) of abnormalities in laboratory values in increased alanine amino transferase and no specific peculiarity of this drug was recognised. The rate of incidence of adverse effects/side effects in the elderly persons above 65 years of age was 4.29% (100 cases / 2,331 cases), cases with low body weight (< 40 kgs) were 4.32% (6 cases / 139 cases) and cases with advance renal dysfunction with creatinine clearance < 30 ml/min were 4.55% (2 cases / 44 cases).

In a study done by Takagi et al., [13], the clinical safety was evaluated in all 702 patients who were treated with GRN in all clinical studies. Adverse events were observed in 244 patients (34.8%) and drug related adverse events were observed in 89 patients (12.7%).A committee of independent physicians looked at the adverse events and judged two to be serious; one case of Clostridium-related colitis and one case of rash. The most frequent drug related events were diarrhoea (2.4%), loose stool (1.3%), nausea (1.0%) and headache (1.0%). All of these events were mild or moderate in severity. No adverse events specific to Garenoxacin were seen. There was no correlation between QTc prolongation and different dosages of Garenoxacin (100–600mg) or plasma concentration in a phase I study of healthy adult subjects [14].

CONCLUSION

Garenoxacin is found to have an outstanding antimicrobial coverage against major pathogenic bacteria with superior safety profile. High improvement at an early stage of treatment also suggests the excellent antimicrobial activity of garenoxacin. Garenoxacin with high potency, low MICs against common SSTI pathogens, superior safety profile and a convenient once a day dosage offers better patient compliance and a suitable option in the treatment of SSTIs.

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