Treatment of renal abscesses caused by *Staphylococcus aureus MW2*, using delafloxacin and moxifloxacin

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Abstract

Background and Objectives
Abcesses are a common type of infection that often involves methicillin-resistant *S. aureus*. Antibiotics are in general poorly effective in treatment of abscesses, at least in part because of reduced activity against bacteria in a stationary phase of growth, in an acidic environment, and with physiologic overproduction of efflux pumps, conditions that all occur in the abscess environment. Delafloxacin (DFX), a new quinolone under development, exhibits distinctive properties that suggest it may offer advantages against bacteria that have formed an abscess, notably activity against stationary phase bacteria and increased activity under acidic conditions. We tested the activity of delafloxacin (DFX) in comparison to that of moxifloxacin (MFX) against renal abscesses formed by *S. aureus* MW2 in a murine model of systemic infection.

Methods
On day 0, 7- to 8-week old male Swiss-Webster mice were injected intravenously with *S. aureus* MW2. On days 4, 5, and 6, by which time renal abscesses had developed, twice daily treatment with DFX, MFX (10 and 30 mg/kg), or vehicle was administered, and kidneys were harvested, homogenized, and plated quantitatively on day 7. In addition, a 2-day early-treatment regimen was begun 24 h after injection and renal bacterial load measured in a similar manner.

Results
Renal abscesses formed reliably by 4 days after systemic injection with *S. aureus* inocula in the range of 3-6×10^5 CFU. Both DFX and MFX at 10 mg/kg significantly reduced bacterial load (1.7-10^6 and 8.1-10^5 CFU/g kidney, p<0.0003 and 0.0002, respectively) compared to controls (8.8-10^6 CFU/g kidney). The reduction of bacterial load by DFX was significantly greater than that by MFX (p<0.0212). The bacterial load in mice given 30 mg/kg DFX was reduced significantly relative to controls (2.0-10^6 to 5.0-10^5 CFU/g kidney, p<0.0003). MFX at this dose also reduced the CFU, but the effect did not reach statistical significance (2.0-10^6 to 1.0-10^5 CFU/g kidney, p=0.0541). In the early treatment regimen, both DFX and MFX (10mg/kg) showed a significant reduction in bacterial load (1.1-10^5 to 5.0-10^5 CFU/g kidney, p<0.0039 and 0.0007, respectively), compared to that in controls (2.3-10^5 CFU/g kidney).

Conclusion
*S. aureus* MW2 reliably produces renal abscesses in mice when injected intravenously. Both DFX and MFX were effective in reducing the bacterial load in established renal abscesses, with DFX superior to MFX. DFX and MFX showed similar efficacy in an early treatment regimen wherein mice were treated prior to the formation of mature renal abscesses.

Methods and Results

Bacteria and Chemicals. *S. aureus* MW2, a commonly associated MRSA, was cultivated in tryptic soy broth (TSB). Moxifloxacin HCl (MFX) (M W 437.9) was prepared in phosphate buffer pH 7.4 with 5% DMSO and 5% Tween 80. Delafloxacin (DFX) (the N-methylglycine salt MW 635.95) was prepared in 0.9% saline (pH 7.4) with 5% DMSO and 5% Tween 80. *S. aureus* MW2 was grown in TSB to OD_600_ to 0.8 as measured in a Thermo Scientific Spectrophotometer at 600nm.

**Inocula and bacterial load in renal abscesses.** Medians and interquartile range of renal CFU on day 4 were shown.

**Methods of treatment.** Both DFX and MFX at 10 mg/kg significantly reduced bacterial load in renal abscesses on day 4. Delafloxacin (DFX) at 10 mg/kg showed superior activity compared to moxifloxacin (MFX) against renal abscesses formed by *S. aureus* MW2 (p<0.0003). In the early treatment regimen, both DFX and MFX (10mg/kg) showed a significant reduction in bacterial load (1.1-10^5 to 5.0-10^5 CFU/g kidney, p<0.0039 and 0.0007, respectively), compared to that in controls (2.3-10^5 CFU/g kidney).

Conclusions

1. *S. aureus* MW2 reliably produces renal abscesses after intravenous injection in the murine model.
2. Both delafloxacin and moxifloxacin are effective in treating renal abscesses.
3. Delafloxacin was superior to moxifloxacin in reducing bacterial counts in established renal abscesses in the murine model.
4. Delafloxacin and moxifloxacin have similar efficacy in reducing bacterial recovery in kidneys prior to formation of renal abscesses.

Bibliography


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