

Introduction

- Dicloxacillin inhibits bacterial cell wall synthesis by binding to penicillin binding proteins which are essential to the final step of building the peptidoglycan structure used in the bacterial cell wall.
- This medication is commonly used to treat mastitis while breastfeeding. A typical dose is 500 mg PO every 6 hours for 7-14 days and 1% to 10% can expect some side effects of abdominal pain, diarrhea, nausea, or a hypersensitivity reaction¹.
- Previous studies show that dicloxacillin is present in breast milk². The relative infant dose (RID) of dicloxacillin is 0.09% to 0.18% when calculated using the highest breast milk concentration located and compared to an infant therapeutic dose of 25 to 50 mg/kg/day.
- The present case study measured the transfer of dicloxacillin into human milk collected from 3 lactating women over 6 hours.

Case Report

Three patients volunteered to donate their milk samples after administration of dicloxacillin 500 mg taken every 6 hours for treatment of mastitis. Breast milk was donated on or after the 4th day of the antibiotic course and therefore blood levels were at steady state. All the infants had a normal gestation age and weight gain.

Patient 1: A 33-year-old woman breastfeeding her 6-month-old infant was prescribed dicloxacillin for mastitis. She was already taking Synthroid for hypothyroidism and prenatal vitamins. She donated her milk on the 7th day of therapy.

Patient 2: A 34-year-old woman breastfeeding her 1-month old infant was prescribed dicloxacillin for mastitis. She was also taking flax supplements. She donated her milk on the 4th day. Patient missed her hour 5 sample donation.

Patient 3: A 39-year-old women breastfeeding her 3.5-month-old infant was prescribed dicloxacillin for mastitis. She was also taking lactase, ranitidine, iron, and vitamin supplements. She donated her milk on the 4th day. Patient missed her hour 3 sample donation.

Methods:

Quantification of dicloxacillin was determined using an Agilent 1260 Quadrapole mass spectrometer. A Phenomenex Luna C-18 column, 50 x 2 mm, 3-micron particle size was used. Isocratic elution was followed using water and acetonitrile with a flow rate of 0.5 mL/min. Single ion Monitoring for dicloxacillin at m/z 470 was analyzed.

Extraction from milk was accomplished using protein precipitation with acetonitrile. Blank milk was spiked with appropriate concentrations of dicloxacillin for determining the calibration curve.

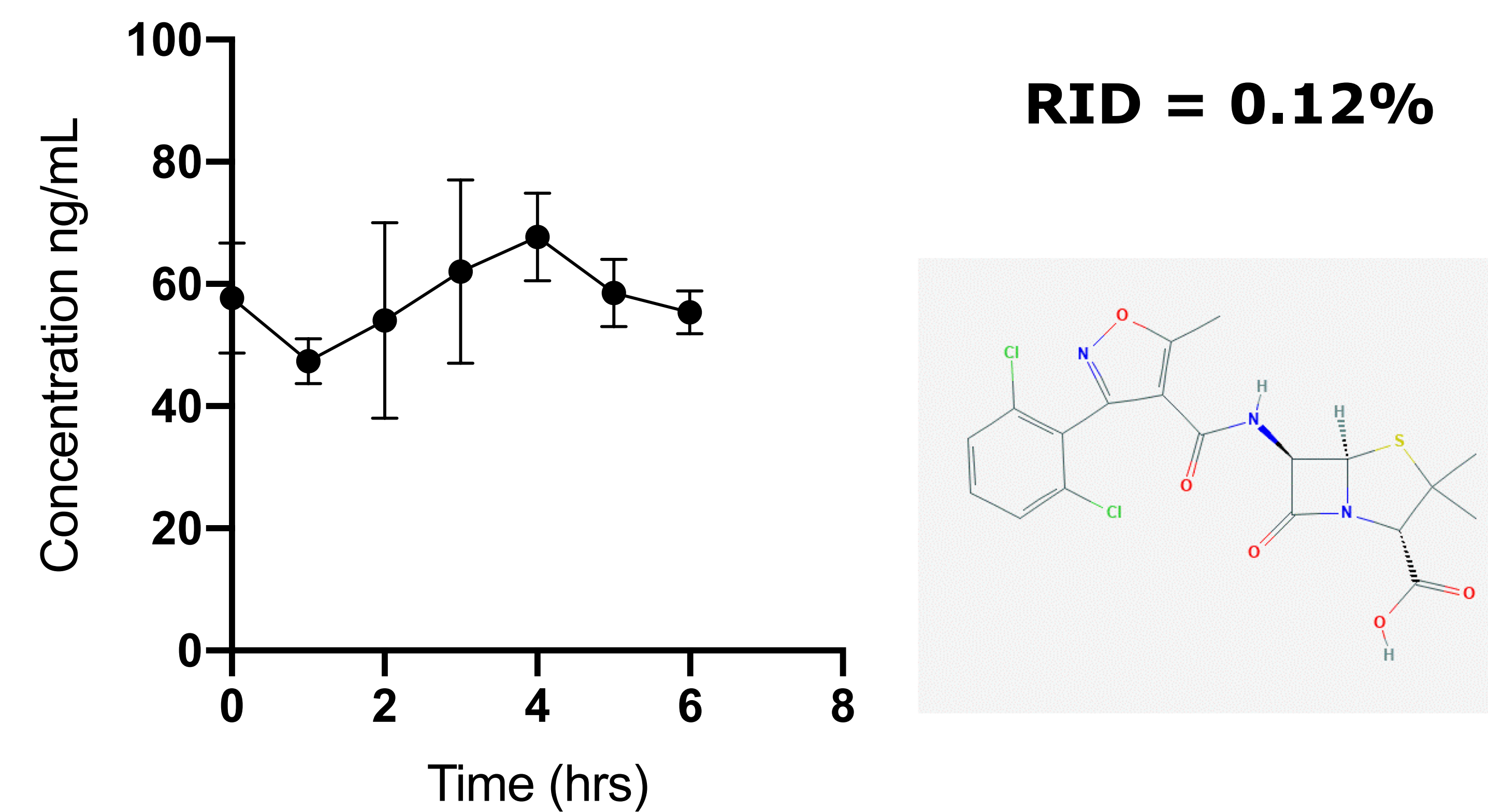


Figure 1: Mean milk concentration-time profile of dicloxacillin following the oral administration of 500 mg taken every 6 hours daily dose (n=3).

Parameters (units)	Value
AUC (ng.hr/mL)	346
C _{avg} (ng/mL)	57.67
C _{max} (ng/mL)	67.6
T _{max} (hr)	4
Infant dose (mg/kg/6hrs)	0.002
RID%	0.03
RID (24 hours)	0.12

Table 1: The pharmacokinetic parameters are summarized above.

Antibiotic	Relative Infant Dose	RID Range
Dicloxacillin	0.12%	
Cephalexin	0.49%	0.39-1.47%
Clindamycin	1.36%	0.9-1.8%
Erythromycin		1.4-1.7%

Table 2: Comparison of Relative infant dose (RID) and RID range for common antibiotics that are used to treat mastitis.

Results

- The maximum concentration of Dicloxacillin in milk was 67.6 ng/mL and was observed at 4 hours. The average concentration was 57.65 ng/ml. The concentration of dicloxacillin was relatively stable over the six-hour time course as evident in figure 1.
- Based on the assumption of infant's daily milk intake of 75 ml/kg/6hr, the infant dose from patient 1 was calculated at 0.002 mg/kg/6hr.
- The relative infant dose (RID) for 24 hours was calculated to be 0.12%, well below the standard theoretical level of concern of 10%. based on the assumption of infant's daily milk intake of 150 ml/kg/day.

Discussion

- Dicloxacillin has rapid but incomplete absorption in the gut with a bioavailability of 49% to 76%¹. It is mostly bound to albumin in the serum (95% to 99%). It is excreted by the feces and has an elimination half-life time of ~0.7 hours and the time to peak, serum is 1 to 1.5 hours.
- The Penicillins, as a class of medications are considered safe for breastfeeding mothers and their infants when using typical dosing. Table 2 shows the relative infant dose for other medications commonly used for mastitis. Of this group we find that Dicloxacillin is the lowest relative infant dose.
- Other studies have reported antibiotics may produce slight changes in gut flora, so it is important to monitor for GI disturbances.

Conclusion

- This case report on three lactating mothers add to the growing body of evidence, suggesting a clinically insignificant transfer of the drug into milk.
- The relative infant dose for dicloxacillin is 0.12%, which is below the theoretical level of concern (RID of <10%)⁴. This case report suggests that the RID is similar to previously reported (0.09-0.18%)
- There is a low risk of infant toxicity. However, as this is only three patients, additional studies are required to verify our findings and to document any effect of dicloxacillin on breastfeeding infants.
- We recommend that the infant be monitored for issues such as gastrointestinal side effects and hypersensitivity reactions.

References

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