



Evaluation and Clinical Impact of Concomitant Administration of Polyvalent Cations with Oral Fluoroquinolones

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Background

- In vitro data demonstrates reduced absorptivity and bioavailability when fluoroquinolones (FQ) are administered concurrently with polyvalent cations (PVC)
- Reduced FQ concentrations may be associated with treatment failure
- Limited data exists assessing clinical impact of concurrent administration

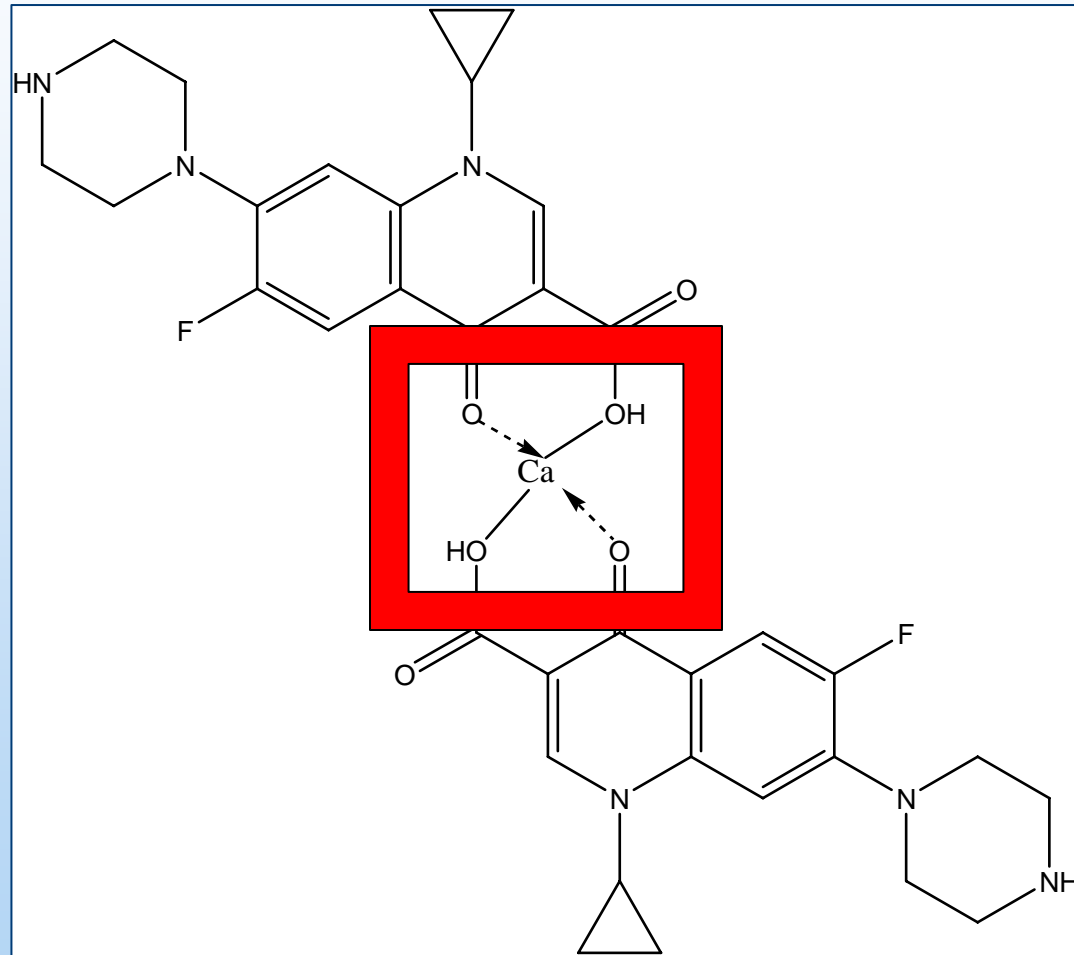
J Antimicrob Chemother. 1994 Oct;34(4):465-83.

J Pharm Biomed Anal. 1999 Jan;18(6):1057-67.

Drugs 1993; 45 Suppl 3:65-72.

Pharm World Sci 2005. 27:81-82.

Proposed mechanism of PVC and FQ chelation



Primary Objective

Characterize scheduling errors

- Ciprofloxacin, Levofloxacin, or Moxifloxacin

and
- Aluminum, Calcium, Iron, Magnesium, Zinc, or Multivitamins with cation content

Secondary Objective

Identify treatment failures associated with concurrent FQ and PVC

- Change in antibiotic regimen
- Change to IV FQ while the patient continues other oral medication
- Isolates initially susceptible to a FQ and subsequently non-susceptible or new isolates emerging during therapy that demonstrate FQ non-susceptibility

- Retrospective cohort analysis
- Inclusion Criteria
 - All adult inpatients (≥ 18 years old) admitted to Medical University of South Carolina
 - Prescribed oral FQ for > 48 hours between 1 January 2007 and 30 June 2007
- Exclusion Criteria
 - Received PVC for part of but not the entire FQ course
 - Schedule of target drugs altered during therapy

- Cohort A: Concurrent
 - Received PVC for entire duration of FQ
- Cohort B: FQ only
 - Did not receive any PVC during FQ therapy
 - Randomly selected from FQ only group using random numbers table
- T-test, Fisher's exact test and chi-square analysis were used depending on variable structure
- Significance was determined at the 0.05 level
- SAS V9.1 used for statistical analysis

Definitions

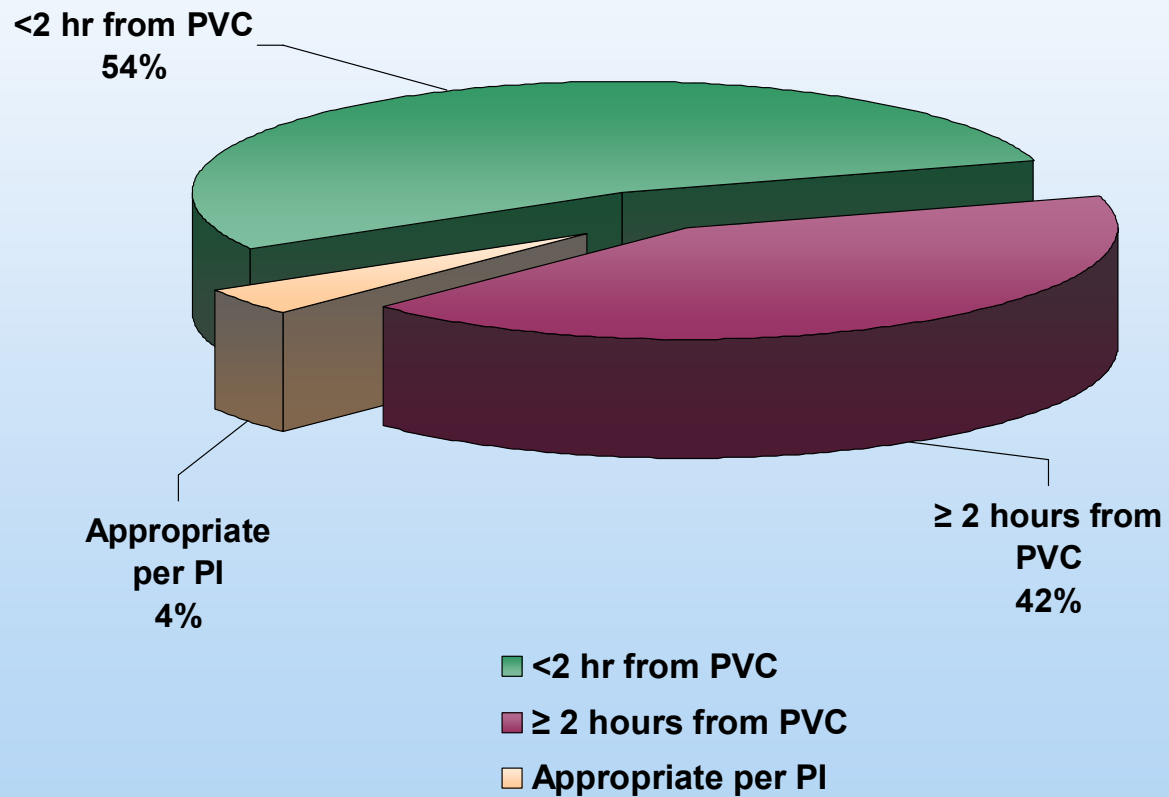
- Appropriate: scheduling of PVC and FQ according to prescribing information
- Inappropriate: scheduling of PVC and FQ *not* according to prescribing information
- Hospital policy: scheduling of all PVC ≥ 2 hours before or after FQ

Prescribing Information Scheduling Recommendations for Concurrent PVC

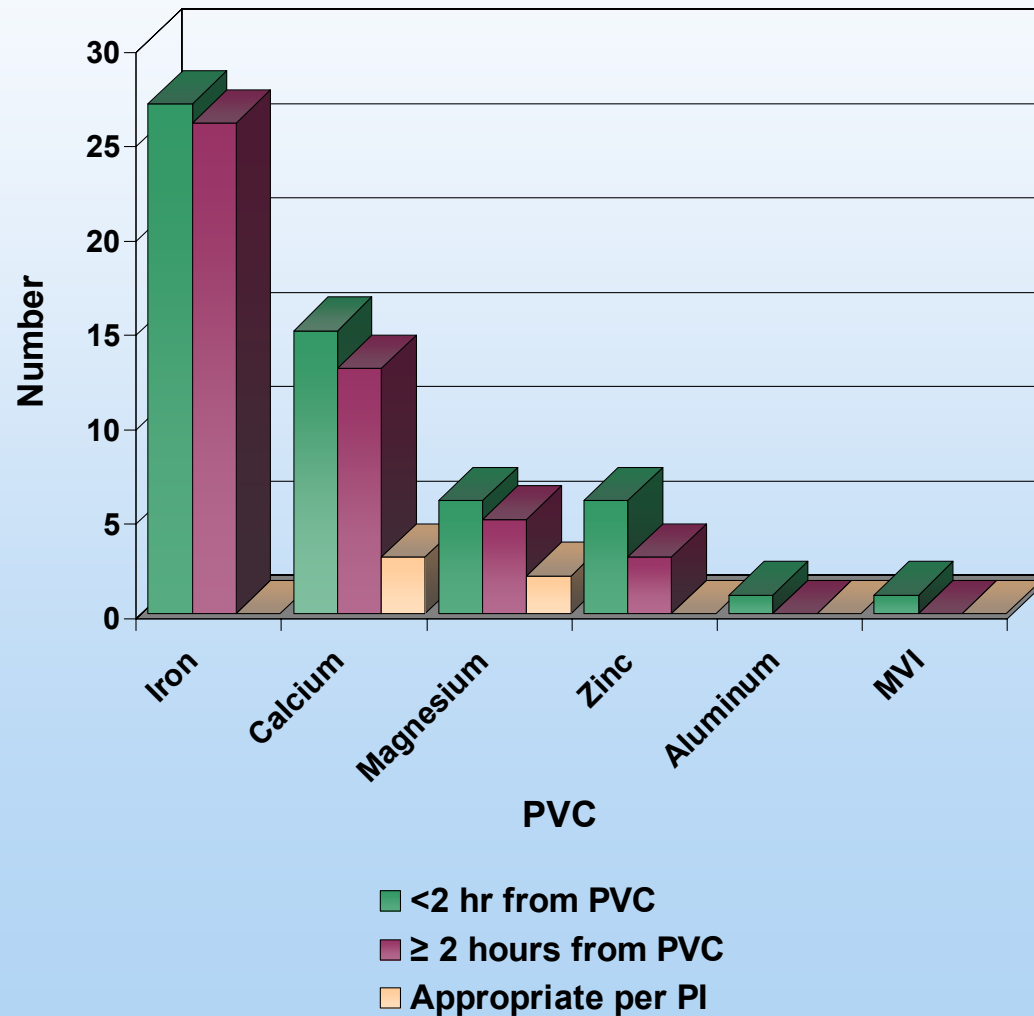
FQ	Schedule
Ciprofloxacin	6 hours before or 2 hours after FQ
Levofloxacin	2 hours before or 2 hours after FQ
Moxifloxacin	8 hours before or 4 hours after FQ

- **Characterize scheduling errors**
- Cohort A: 95 patients received concurrent PVC and FQ
 - Inappropriate scheduling occurred with a frequency of 96%
 - 40 (42%) were scheduled for administration at least 2 hours apart
 - Iron and calcium accounted for 81 (76%) of prescribed PVC

Scheduling of FQ with Concurrent PVC



Appropriateness of Concurrent PVC and FQ Scheduling by Cation



- Identify treatment failures associated with concurrent FQ and PVC
- 190 patient charts were reviewed

Patient Demographics		
	Cohort A (number)	Cohort B (number)
Total	95	95
Female	52	51
Male	43	44
Median age	58	57

Patient Outcomes			
	Cohort A (number)	Cohort B (number)	p-value
New antibiotics	19	8	0.0223
Switch to IV FQ (other meds by mouth)	5	0	0.0592
Emergence of FQ non-susceptible isolate	4	1	0.3683
Any treatment failure	25	8	0.0011

Limitations

- Retrospective chart review dependent on reliable documentation
- Surrogate endpoints used as markers for treatment failure
- Patients may have received ciprofloxacin as prophylaxis rather than treatment
- Tube feeds administered concurrently in a small number of patients
- 50 patients reviewed had no repeat cultures

Conclusions

- High frequency of scheduling FQ and PVC inappropriately
- Concomitant administration of FQ and PVC appears to be associated with treatment failure
- Healthcare practitioners must maintain vigilance to avoid these drug interactions to preserve antimicrobial activity in an era of increasing drug resistance
- Recommendations

Acknowledgements

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