

Reducing Antibiotic Treatment Failure- a focus on tetracycline and fluoroquinolone antibiotics interaction

Raising awareness of the interaction between tetracycline and fluoroquinolone antibiotics with multivalent cation-containing products to improve antimicrobial stewardship

Key messages:

- Concomitant oral administration of tetracycline (e.g. doxycycline) and fluoroquinolone (e.g. ciprofloxacin) antibiotic with multivalent cations (iron, calcium, magnesium, aluminium, zinc or sucralfate- often contained in antacids and nutritional supplements), lanthanum or sodium bicarbonate can result in the formation of insoluble chelation complexes in gut. Co-prescription orally can result in
 - Loss of antibiotic absorption and treatment failure
 - Potential unnecessary escalation to broader antibiotic cover including intravenous therapy
 - Development of antimicrobial resistance
- Serum level of doxycycline are reduced as much as 90% to 100% by this interaction. Ciprofloxacin plasma levels can be reduced by over 50% by the simultaneous administration of enteral feeds and oral nutritional supplements (e.g. Ensure® Fortisip® products)

Summary of interactions and recommended suggestions:

Situation Actions	Co-administration with multivalent cation containing product (i.e. iron, calcium, magnesium, aluminium, zinc, antacids*, sucralfate), lanthanum, sodium bicarbonate, or patients on enteral feeding/oral nutritional supplements	Co-administration with dairy products	Co-administration with food
Fluoroquinolones			
Ciprofloxacin	AVOID: Give Abx 2hrs before or 4 hours after these products ^{1,2} For enteral feed: Break of 2 hours before and 2 hours after Abx is acceptable ³ <i>Potential 50-90% reduction in Abx plasma levels</i>		OK <i>Dietary calcium as part of meal does not significantly affect absorption¹</i>
Levofloxacin Ofloxacin	AVOID**: Give Abx 2 hours before or after ^{1,2} For Lanthanum: Give 2 hours before of 4 hours after ⁶ For Enteral feed: Break of 2 hours before and 1 hour after Abx is acceptable ³ <i>Potential 20-40% reduction in Abx plasma levels</i>		OK <i>Dietary calcium as part of meal does not significantly affect absorption¹</i>
Tetracyclines			
Doxycycline	AVOID**: Give Abx 2hrs before or 2 hours after ^{1,2} For enteral feed: Break of 2 hours before and 1 hour after Abx is acceptable ³ Use dispersible tablets as capsules as contents are irritant <i>Potential 90-100% reduction in Abx plasma levels</i>		OK <i>Taking with food can lessen nausea but avoid dairy products⁴</i>
Tetracycline Oxytetracycline	AVOID: Give Abx 2hrs before or 2 hours after ^{1,2} Enteral feed: Break of 2 hours before and 1 hour after Abx is acceptable ³ <i>Potential 90-100% reduction in Abx plasma levels</i>		AVOID. Best taken on an empty stomach 1 hour before or 2 hours after food¹
Lymecycline Minocycline	AVOID: Give Abx 2hrs before or 2 hours after ^{1,2} Enteral feed: review need to continue. No info but best practice to dose space as above <i>Potential 90-100% reduction in Abx plasma levels</i>	OK Not affected by moderate amount of dairy products ¹	OK <i>Taking with food can lessen nausea or risk of oesophageal irritation or ulcers⁴</i>

- *Antacids: Peptac & Gaviscon liquid both contains Calcium carbonate 16 mg per 1 ml⁵
- H₂ receptor antagonists and proton pump inhibitors do not require to be spaced apart from oral tetracycline or fluoroquinolone antibiotics

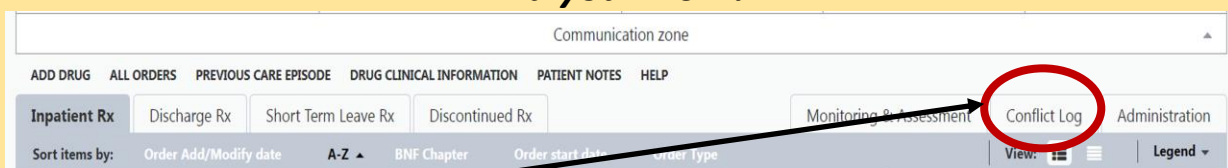
Caveats to note:

- Note that while some references (e.g. SPC/ BNF) for levofloxacin and doxycycline does indicate that calcium salts/ milk has a minimal effect on oral absorption of these antibiotics, other references (e.g. Stockley, NEWT, Sanford Guide) suggest that interactions can occur and potentially lower antibiotic concentrations in the body, hence consensus to err on the side of caution and avoid co-administration with calcium containing products
- **BNF cautionary advice on ciprofloxacin: recommends 2 hours apart for majority of medicines; when manufacturer advises a different time period as they do in SPC, this can be followed and should be explained to the patient


3. Action for Clinical Teams

- When possible, multivalent cation-containing products should be withheld/stopped in patients receiving oral tetracyclines or fluoroquinolones until the antibiotic treatment course is completed (especially for short course antibiotics)
- If tetracycline or fluoroquinolone group and cation-containing product must be prescribed together:
 - ✓ Administration times should be spaced apart as far as possible to improve antibiotic absorption (as per table above)
 - ✓ Review if able to reduce the dose frequency of multivalent cation-containing product for the duration of the antibiotic course to make dose spacing more manageable
 - ✓ For oral nutritional supplements, multiple sips throughout the day should be replaced with set administration times to enable adequate spacing from oral antibiotic
 - ✓ Dose spacing is recommended if patient is receiving containing cation-containing enteral feed (as per table above)
 - ✓ Consider adding a note on HEPMA to **'appear on charting'** to alert nurses during administration rounds
- Patients should be made aware as soon as able of the need to avoid multivalent cation-containing products and should be discuss the concomitant use of any other OTC products with their GP or pharmacist. Patients should be reminded of food and dairy restrictions, if applicable

Did you know?



ON HEPMA – there is a **'CONFLICT LOG'** tile that you can click on to show if there are any interactive medicines with the antibiotic(s) prescribed

For Pharmacy Team- On your PHEW tool, the  icon denotes that there are antibiotic interactions found

References

1. SPC for individual antibiotics www.medicines.org.uk
2. Sanford guide
3. NEWT guideline www.newtguidelines.com
4. The NHS website www.nhs.uk
5. BNF online www.bnf.nice.org.uk
6. Stockley Drug Interaction www.medicinescomplete.com