

Macrolides Side Effects

Macrolides are a group of antibiotics whose activity stems from the presence of a macrolide lactone ring. Commonly used macrolides include erythromycin, azithromycin and clarithromycin. As a class, these drugs bind to the 23S rRNA of the 50S prokaryotic ribosomal subunit and inhibit protein synthesis via blocking of translocation. These antibiotics are considered to be bacteriostatic and are commonly used against gram- positive cocci, atypical pneumonias, and infections caused by chlamydia. Bacteria can become resistant to macrolides via alteration of the 23S rRNA binding site, usually by post-transcriptional methylation. Macrolides are potent inhibitors of the cytochrome P450 system, especially CYP3A4. Therefore, macrolides can cause elevations of other drugs metabolized by the P450 system. One particular combination that should be avoided due to this interaction is macrolides with statins, used for lowering cholesterol, which can lead to debilitating myopathy. Macrolides, especially erythromycin and clarithromycin, also have an effect on QT prolongation, which can lead to torsade de pointes if untreated. These drugs exhibit enterohepatic recycling, meaning the drug is absorbed in the gut and sent to the liver where it is excreted back into the duodenum in bile. This form of recycling can lead to a buildup of the product and cause nausea and GI distress, such as diarrhea. There is also a strong association between macrolides and hepatotoxicity. The pathogenesis of hepatotoxicity with macrolide exposure involves both a direct cytotoxic effect as well an immunoallergic reaction. Hepatotoxicity caused by an immunoallergic reaction is typically accompanied by peripheral eosinophilia and skin rash.



PLAY PICMONIC

Side Effects

Diarrhea

Toilet

GI disturbances like diarrhea, nausea, vomiting, and abdominal pain are common with macrolide use like erythromycin because it is a motilin agonist, encouraging hypermotility and the unpleasant collateral damage. These GI disturbances are commonly the cause of patients' noncompliance and preference toward discontinuation.

Prolonged QT Interval

Stretched QT-heart

Macrolides, especially erythromycin and clarithromycin, adversely perpetuate the QT interval and can progress to a potentially fatal torsade de pointes if untreated.

P450 Inhibitor

Pea 450 Inhibited in handcuffs

Macrolides are potent inhibitors of the cytochrome P450 system, especially CYP3A4, potentially causing elevations of other drugs metabolized by the P450 system. One particular combination to be avoided due to this interaction is macrolides with statins, HMG-CoA reductase inhibitors used for lowering cholesterol, as this combination can lead to debilitating myopathy. Other important interactions include the potential serum elevation of PT/INR in patients on oral anticoagulants, and delayed clearance of theophylline.

Cholestatic Hepatitis

[Collie-static and Happy-tie-liver](#)

Cholestasis, the impairment of bile flow or production, is a well recognized presentation of macrolide-induced liver disease. Laboratory evaluation typically manifests with elevations in alkaline phosphatase, bilirubin and hepatic transaminases. Specific to the transaminases ALT and AST, these two components are capable of elevations up to 10 times the upper limit of normal during hepatic inflammation.

Skin Rash

[Skin Rash being examined by dermatologist](#)

As part of the pathophysiology involving hepatotoxicity secondary to macrolide use: a direct cytotoxic effect and an immuno-allergic reaction occur producing a peripheral eosinophilia accompanied with a skin rash.

Eosinophilia

[Eosinophilia-eagle](#)

The pathogenesis of hepatotoxicity with macrolide exposure involves both a direct cytotoxic effect as well an immuno-allergic reaction. Macrolide-induced hepatotoxicity aroused by an immuno-allergic reaction is typically accompanied by the release of eosinophils from their mostly tissue-based habitat, resulting in peripheral eosinophilia. This is also associated with skin eruptions primarily in the form of maculopapular exanthems.