

## A Short Note on Pharmacokinetic Properties of Chloramphenicol

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### DESCRIPTION

Chloramphenicol is an antibiotic that is used to treat bacterial infections. This includes its application as an eye ointment to treat conjunctivitis. It is used to treat meningitis, plague, cholera, and typhoid fever by taking it or injecting it into a vein. It is only recommended for use by mouth or injection when safer antibiotics are unavailable. During treatment, it is recommended to monitor both medication and blood cell levels every two days.

Chloramphenicol is a small molecule that is extremely lipid-soluble and remains relatively unbound to protein. It has a large apparent volume of distribution and effectively penetrates all body tissues, including the brain. The distribution is not uniform, with the highest concentrations found in the liver and kidney and the lowest concentrations found in the brain and cerebrospinal fluid. Even when the meninges are not inflamed, the concentration achieved in the brain and cerebrospinal fluid is around 30% to 50% of the overall average body concentration; this increases to as much as 89% when the meninges are inflamed. Chloramphenicol improves iron absorption.

### Participation in affected citizens

The liver converts chloramphenicol to chloramphenicol glucuronate (which is inactive). In cases of liver impairment, the dose of chloramphenicol must be reduced. There is no standard dose reduction for chloramphenicol in liver impairment; the dose should be adjusted based on measured plasma concentrations.

The kidneys excrete the majority of the chloramphenicol dose as the inactive metabolite chloramphenicol glucuronate. Only a small amount of chloramphenicol is excreted unchanged by the kidneys. Plasma levels in patients with renal impairment should be monitored, but this is not required. Chloramphenicol succinate ester (an intravenous prodrug form) is excreted unchanged by the kidneys more readily than chloramphenicol base, which is why blood levels of chloramphenicol are much

lower when given intravenously rather than orally. Whereas chloramphenicol passes into breast milk, it should be avoided if possible during breastfeeding.

### Dose monitoring

Chloramphenicol plasma levels must be monitored in neonates and patients with abnormal liver function. All children under the age of four, the elderly, and patients with kidney failure should have their plasma levels checked. Because chloramphenicol efficacy and toxicity are related to maximum serum concentrations, peak levels (one hour after the intravenous dose is given) should be 10-20 g/ml with toxicity greater than 40 g/ml; trough levels (taken immediately before a dose) should be 5-10 g/ml.

### Drug interactions

Sequential administration of chloramphenicol with bone marrow depressant drugs is not recommended, though concerns about aplastic anaemia caused by ocular chloramphenicol have been mostly dismissed.

In the liver, chloramphenicol inhibits the cytochrome *P450* isoforms *CYP2C19* and *CYP3A4*. If antidepressants, antiepileptics, proton-pump inhibitors, and anticoagulants are given concurrently, inhibition of *CYP2C19* causes decreased metabolism and thus increased levels of, for example, antidepressants, antiepileptics, proton-pump inhibitors, and anticoagulants. Calcium channel blockers, immunosuppressants, chemotherapeutic drugs, benzodiazepines, azole antifungals, tricyclic antidepressants, macrolide antibiotics, SSRIs, statins, cardiac antiarrhythmics, antivirals, anticoagulants, and *PDE5* inhibitors are all affected by *CYP3A4* inhibition.

### Drug antagonistic

Most cephalosporins are antagonistic to chloramphenicol, so treating infections with both should be avoided.

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