

Pharmacist Guidelines and Considerations for the Treatment of *C.difficile*

Ali Chaudhry*

Shoppers Drug Mart, Canada

*Corresponding Author: Ali Chaudhry, Shoppers Drug Mart, Canada.

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Clostridium difficile (*C.difficile*) is a major gastro-intestinal infection, that is caused by the use of antibiotics, more specifically clindamycin, fluoroquinolones, and second, third and fourth generation cephalosporins.^{1,2,4} Even though this gram positive bacteria, which can form spores, is normally found in the gut, is inhibited from multiplying from the normal gut flora. [1,4] However when antibiotics are used, they disrupt the gut flora, providing opportunity for the bacteria to multiply. [1,3] *C.difficile* uses toxin A and B to bind to specific targets of the mucosal cells, and begins apoptosis. [1-3] *C.difficile* is usually obtained from

Diagnosis of *C.difficile* is usually from a single stool sample, which are then put through antigen test or nucleic acid amplification tests. [1,4] *C.difficile* can be then sub-divided into mild to moderate, severe, or severe and complicated. [1,3,4] Signs and symptoms of mild to moderate infection include diarrhea, fever, abdominal pain with cramps, whereas severe infection includes all of the signs and symptoms of mild to moderate, but an increase in white blood cell count and a decrease in serum albumin. [1-4] Severe and complicated *C.difficile* infections have signs and symptoms of mild to moderate, and similar to severe, except the white blood cell count is nearly doubled that of severe, and also the patient will suffer from hypotension, mental status changes and a very high fever. [1,3]

As *C.difficile* is spread from the fecal-oral route and can be deadly, there are several steps that must be taken before pharmacological treatment can be started. [3] Protocols that must be taken include, having the patient isolated to their own room with their own wash-room, staff must wear gloves and an apron when in contact with the patient to ensure that the infection does not spread, strict hand washing must be practiced, as hand sanitizer will not remove the bacteria from hands. [1,4] Also all prescribed antibiotics must be stopped and stool samples are checked for blood. [2,3]

When looking to treat mild to moderate *C.difficile* infection, oral metronidazole 500mg three times for 10 days or oral vancomycin 125mg four times daily for 10 days are considered the first line option. [1,3,4] However if treatment is started with metronidazole and there is no improvement after 5-7 days, then it is recommended to switch to vancomycin. [2,3] On the other hand, when treating severe *C.difficile* infections, oral vancomycin 125mg four times daily for 10 days is recommended. [1] When treating severe complicated cases of *C.difficile* oral vancomycin 500mg four times daily, intravenous metronidazole 500mg every 8 hours, along with vancomycin 500mg in 500mL of saline rectally. [1,2,4]

Metronidazole mode of action entering a bacterial or protozoa cell and damages their deoxyribonucleic acid. [1,3] Vancomycin works by inhibiting the cell wall synthesis, and may possible inhibit the permeability of the cell wall and selectively inhibits ribonucleic acid synthesis. [2,4] Side effects from metronidazole include abdominal pain, dry mouth, dizziness and has a metallic taste, where side effects from vancomycin include nephrotoxicity, bitter taste, deafness, muscle pain, etc. [1,3]

When deciding which antibiotic to use for patients with mild to moderate *C.difficile* infections, it is important to firstly consider the patient allergy status. If the patient is allergic to metronidazole, then the use of vancomycin would be appropriate, and vice versa. [1,2] Patient medications should also be considered as metronidazole will interact with warfarin and lithium, whereas vancomycin will interact with non-steroidal anti-inflammatory drugs. [1,2,4] Patients who consume alcohol, should not be given metronidazole because it will cause nausea, headache, vomiting, abdominal pain and cramps. [2,3] Also female patients who are pregnant or nursing should not be given metronidazole. [4]

These antibiotic regimes are effective with treating *C.difficile* infections, with metronidazole having a cure rate of approximately 76% and vancomycin has a cure rate of 97%. [3] However with the increase in rate of recurrent infections, other antibiotics are being explored as possible cures, such as rifamycin and fidaxomicin. [1] However the effectiveness of these antibiotics still requires further investigation.

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