Doxycycline to help prevent bacterial STIs

FACT SHEET

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What are doxyPEP and doxyPrEP?

Doxycycline post-exposure prophylaxis (doxyPEP) is one way to take the antibiotic doxycycline to help prevent bacterial sexually transmitted infections (STIs). With doxyPEP, a person takes 200 mg of doxycycline after they have a condomless sexual encounter. It should be taken as soon as possible after sex but can be taken up to 72 hours after. Research shows that doxyPEP can help to prevent bacterial STIs among gay, bisexual and other men who have sex with men (gbMSM) and among transgender women. It is most effective at preventing syphilis and chlamydia, but it also may provide some protection against gonorrhea.

Doxycycline pre-exposure prophylaxis (doxyPrEP) is another approach to taking doxycycline as STI prevention. With doxyPrEP, a person takes 100 mg of doxycycline every day. The evidence on the effectiveness of doxyPrEP is limited, but studies are ongoing.

What is doxycycline?

Doxycycline is an antibiotic that is used to treat or prevent a variety of infections. It is commonly used in Canada to treat chlamydia, and it is sometimes used to treat syphilis. It is not a recommended treatment for gonorrhea because some strains of gonorrhea are resistant to it. Doxycycline is also used to treat various other types of infections, such as respiratory tract and skin infections.

While it is most often used as treatment after a person has an infection, this antibiotic and others from the same family have long been used to help prevent infections such as malaria and Lyme disease.

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How does doxycycline work to prevent STIs?

Doxycycline works by preventing the growth and spread of bacteria that can cause STIs. When a person takes doxycycline, the drug gets into their bloodstream and into the tissues and mucus of their genitals, rectum and throat. When a person is exposed to certain bacterial STIs through sex, doxycycline may prevent the bacteria from multiplying and establishing an infection. Doxycycline only helps to prevent some bacterial STIs. It does not help to prevent viral STIs such as HIV, herpes and human papillomavirus (HPV).

How effective is doxyPEP at preventing STIs?

Four large studies have looked at doxyPEP. The first was an open-label randomized controlled trial (RCT) done in France. This study was a substudy of the IPERGAY HIV PrEP trial, which looked at on-demand HIV PrEP. This substudy included 232 gbMSM who reported having condomless sex with men. Half were randomly assigned to take doxyPEP and the other half did not receive any STI prophylaxis. People taking doxyPEP were 47% less likely to be diagnosed with any bacterial STI (i.e., syphilis, gonorrhea or chlamydia) during follow-up than people not on doxyPEP. People taking doxyPEP were 70% less likely to be diagnosed with chlamydia and 73% less likely to be diagnosed with syphilis than those not taking doxyPEP. Taking doxyPEP did not make a significant difference for gonorrhea in the study.

Another open-label RCT was done in Seattle and San Francisco. This study enrolled 501 gbMSM and transgender women who have sex with men, who were either living with HIV or taking HIV PrEP, and who had been diagnosed with a bacterial STI at least once in the past year. Two-thirds of participants were randomly assigned to take doxyPEP, and the remaining third did not receive STI prophylaxis. Among the cohort of people taking HIV PrEP, doxyPEP reduced the risk of syphilis by 87%, chlamydia by 88% and gonorrhea by 55%. Similarly, among the cohort of people living with HIV, doxyPEP reduced the risk of syphilis by 77%, chlamydia by 74% and gonorrhea by 57%.

A third open-label RCT called DOXYVAC was done in France. This study included 502 gbMSM who were taking HIV PrEP and who had been diagnosed with an STI in the past year. Two-thirds of participants were randomly assigned to receive doxyPEP and the remaining third did not receive any STI prophylaxis. Compared with those not taking it, people taking doxyPEP were 79% less likely to be diagnosed with syphilis, 89% less likely to be diagnosed with chlamydia and 51% less likely to be diagnosed with gonorrhea.

Only one open-label RCT has looked at doxyPEP among cisgender women. This study was done in Kenya and included 449 women who were already taking HIV PrEP. Half of the participants were assigned to receive doxyPEP and the other half received regular care, including STI screening and treatment. The study did not find any significant difference in the number of STI diagnoses between the two groups. This means that doxyPEP did not significantly lower the risk of getting a bacterial STI in this study. This may have been because many of the women who were assigned to take doxyPEP did not take doxycycline consistently after each time they had sex. The results from this study may not be generalizable to Canada. Promisingly, a small study that looked at concentrations of doxycycline in the vaginal tissue of people who had taken 200 mg of doxycycline suggests that doxyPEP should be effective in cisgender women if it is taken as prescribed. More research is needed to determine whether doxyPEP could help prevent bacterial STIs among cisgender women in Canada.

In each of the doxyPEP studies, not everyone who was assigned to take doxyPEP reported perfect adherence (taking the medication exactly as prescribed). For example, in the trial done in Seattle and San Francisco, 71% of participants assigned to take doxyPEP said that they never missed a dose of doxycycline after having condomless sex. The doxyPEP studies did not assess to what extent varying levels of adherence impacted the study outcomes. Research is needed to determine how much the risk is reduced for individuals who take doxyPEP with perfect adherence.

How effective is doxyPrEP at preventing STIs?

DoxyPrEP has not been as well studied as doxyPEP. Two pilot studies have found promising results, but neither of these studies had a large enough sample size to draw firm conclusions.

The first pilot study on doxyPrEP was done in Los Angeles. This open-label RCT included 30 HIV-positive gbMSM who have sex with men who had been diagnosed with syphilis two or more times since their HIV diagnosis. Study participants were randomly assigned to either a doxyPrEP group that took daily doxycycline for 36 weeks or a contingency management group that did not receive doxyPrEP but were given financial compensation if they tested negative for STIs at three different time points. At 48 weeks' follow-up, those in the doxyPrEP group were 73% less likely to have been diagnosed with any bacterial STI (syphilis, chlamydia or gonorrhea) than those who did not take doxyPrEP.

Another pilot open-label RCT investigated the feasibility of combining daily HIV PrEP with doxyPrEP in HIV-negative gbMSM and transgender women in Vancouver. The Dual Daily HIV and Syphilis Pre-Exposure Prophylaxis (DuDHS) study recruited 52 participants who had been diagnosed with syphilis at least once in the last three years. All of the participants received HIV PrEP for 48 weeks. Half were randomly assigned to take doxyPrEP immediately and the other half were assigned to begin taking it after 24 weeks. In the first 24 weeks of the study, participants taking doxyPrEP were 82% less likely to be diagnosed with any bacterial STI than those not taking it.

Adherence to doxyPrEP was not perfect in either of these trials. Further research is needed to determine if the risk reduction is higher among people who take doxyPrEP consistently as prescribed.

Given the promising results of these small studies, more research on doxyPrEP is underway.

How can people access STI prophylaxis?

Doxycycline needs to be prescribed by a healthcare provider. Some healthcare providers may not be aware of this approach, and some may not support it. A person who wants to take STI prophylaxis needs to find a healthcare provider who is knowledgeable about it (or willing to learn) and who is willing to prescribe doxycycline and provide the necessary follow-up.

Who can consider taking STI prophylaxis and what is involved?

There are currently no pan-Canadian guidelines on the use of doxycycline as STI prophylaxis. However, some health regions in Canada and other high-income countries have provided guidance and considerations for prescribers. The only guidance that exists in Canada is a position statement from the British Columbia Centre for Disease Control (BCCDC). It advises that doxyPEP can be considered for gbMSM and transgender women who have had a bacterial STI in the previous year.

The position statement says that people taking doxyPEP should take 200 mg of doxycycline within 72 hours after having condomless sex and should not take more than 200 mg per day. It outlines follow-up care that people taking doxyPEP should receive. This includes regular testing for STIs (e.g., every three months) and treatment if necessary. People taking doxyPEP who are HIV negative should receive counselling on ways to reduce their risk for HIV, including HIV PrEP as an option. Follow-up should also include monitoring for drug side effects and relevant testing (e.g., routine blood work, renal and liver function tests).

The BCCDC does not provide recommendations about doxyPrEP because of the limited evidence available.

What side effects are associated with doxycycline as STI prophylaxis?

Doxycycline is generally well tolerated by people who take it to treat an STI and by people who take it on a longer-term basis (e.g., as prophylaxis for malaria). Many people do not experience side effects, but among those who do, the most common side effects are gastrointestinal disturbances and skin issues such as developing a rash. This suggests that ongoing use of doxycycline as STI prophylaxis should be tolerated by most people.

Limited data from STI prophylaxis trials show that side effects are more common in people taking STI prophylaxis than in those not taking it, with gastrointestinal issues being the most commonly reported. Side effects led some participants to withdraw from the studies, but the majority of people who experienced side effects remained on STI prophylaxis. In studies where people were taking HIV PrEP or HIV treatment in addition to doxycycline, it is impossible to determine which drugs caused the side effects.

Are there safety concerns associated with doxycycline as STI prophylaxis?

The two main safety concerns that have been raised are the potential for antibiotic resistance and undesirable changes to the microbiome.

Antibiotic resistance

One concern about STI prophylaxis is that its widespread use could increase the chance that chlamydia or syphilis might develop resistance to doxycycline. If this were to happen, it would limit treatment options for these STIs, which doxycycline is currently very effective at treating. There have not yet been any doxycycline-resistant strains of chlamydia or syphilis found anywhere in the world, and some experts don't consider this likely to occur, on the basis of what is known about resistance. Since strains of doxycycline-resistant gonorrhea are already common, doxycycline is not used to treat gonorrhea in Canada.

There is also concern that doxycycline used as STI prophylaxis could lead to greater levels of resistance in other organisms that doxycycline is used to treat (such as bacteria that cause respiratory tract infections). The risk of this happening is not well understood because there has not yet been a lot of research in this area. More research is needed to understand the impact that STI prophylaxis could have on antibiotic resistance.

Changes to the microbiome

Broad-spectrum antibiotics like doxycycline can affect beneficial bacteria that are part of a healthy microbiome. The microbiome refers to the microorganisms that live in or on a person's body, including bacteria, viruses and fungi. These microorganisms are important for the healthy functioning of a person's immune system and their health generally. There are concerns that long-term use of doxycycline could cause changes in a person's microbiome that could lead to undesirable health outcomes. Some research suggests that doxycycline has minimal effects on the microbiome. More research is underway to better understand this issue.

Resources

Chlamydia – *CATIE fact sheet*

Syphilis – *CATIE fact sheet*

Gonorrhea – *CATIE fact sheet*

Syphilis: What you need to know – *CATIE brochure*

Position statement

The BCCDC Position Statement on Doxycycline as Prophylaxis for Sexually Transmitted Infections

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Author: Harrigan M

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