

Pre and post-exposure prophylaxis with doxycycline: Exploring promises for prevention of sexually transmitted infections in the Indian context

Dear Editor,

Sexually transmitted infections (STIs) pose a significant global public health challenge, with over 1 million newly acquired cases daily worldwide. In India, despite limited centralised data, an estimated 6% of adults contract STIs annually and syphilis emerges as the predominant STI among men in the clinical data of STIs, with a prevalence ranging from 12.6% to 57%, followed by chlamydia (20%–30%), chancroid (9.9%–34.7%) and gonorrhoea (8.5%–25.9%). Recent studies also underscore concerning trends, including high vaginal discharge rates, low condom usage, increasing gonococcal infection-related urethritis, and rising syphilis prevalence. Rising use of geosocial networking apps among the Indian population again has implications for HIV/STI transmission.

Despite the availability of antibiotics for the treatment of symptomatic bacterial STIs, the high prevalence of asymptomatic infections poses great challenges to combat the spread of HIV and other STIs. Asymptomatic STI is particularly worrisome when present among those with a high potential to cause dissemination, especially in the presence of limited sexual health literacy and barriers to healthcare access. Traditional contact tracing methods face limitations in identifying anonymous partners and are also bound by resource constraints, stigma, and socio-cultural factors.

STI prevention has traditionally focused on early detection and adequate treatment. Pre-exposure prophylaxis (PrEP) for populations at higher HIV risk is an important and established strategy in STI prevention. Notably, doxycycline, an affordable, broad-spectrum tetracycline antibiotic, has emerged as a promising option for bacterial STI prevention, both as pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP). The Centers for Disease Control and Prevention (CDC) has recommended a 7-day doxycycline course for chlamydia prevention since 2014. Recent research

expanded its role as PEP, with a single 200-mg dose taken within 24 hours after unprotected sex substantially reducing the risk of bacterial STIs.³ Among men who have sex with men (MSM) and transgender women, PEP with doxycycline reduced combined gonorrhoea, chlamydia, and syphilis cases by two-thirds compared to standard care.⁴

In a pilot clinical trial, daily 100 mg doxycycline as PrEP significantly reduced bacterial STIs in MSM living with HIV over 48 weeks, outperforming other incentives for staying STI-free.⁵ Ongoing trials, the daily doxycycline in HIV and for syphilis PrEP (DaDHS) and the dual daily HIV and syphilis pre-exposure prophylaxis (DuDHS) aim to evaluate the efficacy of doxycycline in preventing syphilis and other STIs among MSM.⁶ Recognising the mounting burden of bacterial STIs, various global health authorities recommend PEP with doxycycline, especially for high-risk groups like MSM, transgender women, and commercial sex workers (CSWs) with previous bacterial STIs.⁷

Current Indian National AIDS Control Organisation (NACO) guidelines 2021 for STI PEP in sexual assault victims recommend azithromycin and cefixime for chlamydia and gonorrhoea, along with metronidazole or tinidazole for trichomoniasis and bacterial vaginosis. For hepatitis B virus (HBV) exposure, they suggest hepatitis B immunoglobulin, and for HIV prevention, a triple-drug antiretroviral regimen. In light of recent evidence, Indian guidelines may contemplate including self-administered doxycycline as an option for PEP, especially in high-risk groups. This approach aligns with India's diverse population facing barriers to consistent condom use and healthcare access. PEP with doxycycline particularly serves as a valuable tool for individuals who may not have control over barrier contraceptives, such as CSWs and others at high risk for STIs. The ready availability, affordability, and tolerability of doxycycline make it a safe STI prevention choice, though caution is advised for pregnant

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or individuals trying to conceive. Single-dose doxycycline PEP offers flexibility for those with irregular sexual activity, mitigating STI stigma in India with a discreet and accessible prevention method.

Yet, there are concerns regarding potential over-reliance on PEP with doxycycline, possibly diminishing the emphasis on condom use and regular STI testing. Daily dosing requirements can be challenging, especially for those with frequent sexual activity. Additionally, the ideal duration of PEP with doxycycline remains uncertain, raising questions about prolonged use and associated risks like antibiotic resistance and subclinical infections. The chronic, intermittent use of antibiotics, such as doxycycline, also raises concerns about impacting the normal microbiome and favouring multidrugresistant bacteria, such as gonococci and methicillin-resistant *Staphylococcus aureus*. While PEP with doxycycline shows promise, its successful implementation must carefully consider these complexities and drawbacks within the broader framework of a comprehensive STI prevention approach.

In conclusion, PEP and PrEP with doxycycline emerge as promising strategies to mitigate the substantial burden of bacterial STIs in India; however, they face a series of distinctive challenges. Crucially, addressing low sexual health literacy is necessary, as misconceptions about of the purpose and scope of PEP with doxycycline can hinder its effectiveness. Robust randomised controlled trials in the Indian population, particularly among high-risk groups, are crucial before incorporating PrEP/PEP with doxycycline into national guidelines. Emphasising the necessity for comprehensive assessments of safety and efficacy, including thorough monitoring of potential side effects, is imperative for ensuring the suitability of doxycycline in the specific context of the Indian population. Healthcare authorities and policymakers should also consider revising NACO guidelines to integrate PrEP and PEP with doxycycline for high-risk populations, such as MSM, CSWs, and transgender women with recent STIs while ensuring efficient resource allocation. Concurrently, we must bolster surveillance for antimicrobial resistance and improve resource availability, including selftesting kits, point-of-care tests, and STI vaccines.

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