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RESEARCH ARTICLE

Sexually Transmitted Infections in the PReP Era. Are Family Doctors Ready to Give Advice?

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Abstract:

Background:

Pre-exposure prophylaxis (PrEP) for human immunodeficiency virus (HIV) as a method of HIV prevention is not without controversy, and there has been concern that it may lead its users to think that they no longer need other preventive measures such as condoms. Thus, healthcare providers are convinced that PrEP decreases condom use and increases sexually transmitted infections (STIs). This treatment has been studied in men who have sex with men, men and women in heterosexual HIV-discordant couples, and heterosexual men and women.

Objective:

The objective of this study was to review the current state of evidence on the association of PrEP with condom use, the incidence of STIs, and the change in sexual behaviours in populations with risky practices.

Materials and Methods:

PubMed (National Center for Biotechnology Information, Bethesda, MD, USA), Science Direct (Elsevier Ltd., Oxford, UK), and Google Scholar (Google Inc., Mountain View, CA, USA) search engines were used during the study. We used the terms HIV, PrEP, sexually transmitted infections (STIs), MSM, condom, heterosexual men / women to search the databases.

Results:

Here, we present evidence that daily oral treatment is safe and effective in these populations studied, especially when medication adherence is high. STI testing should include extra-genital testing regardless of PrEP use to prevent health deficits and onward transmission.

Conclusion:

Despite this safety and efficacy, we strongly advise that patients continue to use condoms as a prophylactic measure against other sexually transmitted diseases. This update addresses the benefits and precautions that must be taken when establishing PrEP treatment, focusing mainly on family doctorswho are best positioned to provide follow-up and advice to patients and their relatives.

Keywords: VIH, Pre-exposure prophylaxis (PrEP), Sexually transmitted infections, Syphilis, Gonorrhea, Chlamydia, Vulvovaginitis, Family Doctors.

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1. INTRODUCTION

Infection with the human immunodeficiency virus (HIV) continues to be a major sanitary, social, economic, and human health problem in the world. Recently, the so-called "pre-exposure prophylaxis" (PrEP) has been developed as a preventative strategy in which uninfected individuals with a high exposure or vulnerability to HIVare administered pharmaceutical therapy intended to prevent infection [1].

The use of antiretroviral drugs to prevent HIV infection in at-risk, uninfected individuals was initially based on efficacy demonstrated in animal models. The implementation of this strategy must be based on the scientific evidence provided by controlled clinical trials. In these trials, it is essential to pay attention to both the efficacy and the safety of a preventive intervention directed at a healthy population [2].The FDA recently approved the HIV antiretroviral drug emtricitabine/tenofovirdisoproxilfumarate as PrEP therapy for adults at high risk for sexually-acquired HIV infection [2].

The use of HIV PrEP, where seronegative individuals with high-risk sexual practices are administered with anti-retroviral drugs, could also be a contributing factor to the transmission of other STIs. We believe that such practices may lead to a significant increase in the manifestation of STIs as ulcers, such as in syphilis. Thus, a STI poses a significant public health risk in all demographic groups; all physicians should maintain a high level of awareness and should avoid stereotyping patients [3].

2. MATERIAL AND METHODS

We carried out a comprehensive search of the Cochrane Central Register of Controlled Trials, MEDLINE (PubMed), and Embase databases for articles published from March 2010 to March 2016, using the following search terms: VIH, pre-exposure prophylaxis (PrEP), sexually transmitted infections, syphilis, gonorrhea, chlamydia, and vulvovaginitis. We performed an exhaustive review of the published articles and the bibliographies of the selected manuscripts.

3. RESULTS AND DISCUSSION

The PrEP dosage is a single, once-dailytablet (emtricitabine 200 mg and tenofovir- disoproxilfumarate 300 mg). The drug is taken orally, with or without food. In addition to the medication, which should not be prescribed in more than a 90-day supply, the patient should be educated about risk reduction strategies, particularly consistent use of condoms during every sexual encounter [4].

The efficacy and safety of PrEP have been demonstrated in clinical trials and confirmed in observational studies, following the implementation of specific programs in different countries. The data are obtained from studies conducted in men who have sex with men (MSM) [5], heterosexual serodiscordant couples(regardless of the infected limb), and in users of parenteral drugs. Studies have been conducted almost exclusively with the combination of emtricitabine (FTC) and tenofovirdisoproxilfumarate (TDF), administered continuously or in intermittent patterns related to contact risk. Clinical trials and observational studies have shown that PrEP with FTC/TDF has great benefitin preventing HIV transmission, though the efficacy is highly dependent on adherence to the prescribed regimen. All studies have also analyzed the following potential drawbacks of this strategy: 1) Toxicity, whereby patients receiving FTC/TDF experience more digestive intolerance than those taking the placebo. Additionally, in those receiving FTC/TDF there is significant loss of bone mineral density and decreased clearance of creatinine, although these effects are not clinically relevant during the observed period, and are reversible after the suspension of the drugs. 2) Development of resistance; has occurred at exceptionally high rates of prophylaxis who subsequently acquire HIV infection. 3) Increase in the development of STIs whose number and type are not higher than those presented before PrEP. As reflected in the manuscript published by Lal *et al.* [6] where the authors conclude that the decrease of condom use brings with it an increase in STIs, the prevention, early detection, and treatment of STIs should be a priority in the current era of HIV PrEP.

In another study published by Hoornenborg *et al.* [7], the authors assessed 375 HIV-negative MSM enrolled in Amsterdam PrEP and detected high levels of hepatitis C virus RNA from three different genotypes (1a [73%], 4d [20%], and 2b [7%]). Therefore, the authors warn of the importance of detection and prevention of hepatitis C owing to the high rate of promiscuity in these patients.

Therefore, the benefits and risks evidenced in the PrEP studies support their administration to individuals at high risk of acquiring HIV [8].

In this study from Calabrese *et al.*, 20 healthcare providers were interviewed.The interviews were conducted by the PI in person or by telephone between September 2014 and February 2015, and the duration of each interview was between 60 and 90 minutes. The interviews were semi-structured, following an organized thematic guide that included questions about leadership and follow-up suggestions [9].

Primary topics included PrEP experience, PrEP attitudes and prescribing intentions, patient / provider communication about sex, fair PrEP provision, and training experiences and recommendations.

In this manuscript from Krakower *et al*. [10],during January and February 2015, all primary care clinicians at a community health center in Boston that specializes in the care of sexual and gender minorities were invited to complete surveys regarding 35 anonymous items evaluating their experiences with the provision of PrEP. The surveys evaluated provider demographics, practice characteristics, experiences and practices with PrEP provision, perceptions about feasibility, and future prescribing intentions. Half of the respondents indicated that financial barriers had prevented patients from using PrEP [10].

In this meta-analysis Fonner *et al.* [11] encompassed eighteen studies, which included data from 39 papers and six conference abstracts. The results show that PrEP is attractive for people in heterosexual relationships because of their lower cost, greater availability, and lower risk of drug resistance. Regarding safety, PrEP showed no evidence of an increase in the proportion of adverse events. However, two studies reported small decreases in kidney function among those taking PrEP.

As Sheth *et al.* [12] reported, women are very vulnerable to HIV infections, whether due to sexual, social, or biological factors. Strategies are needed to prevent the emergence of new cases, which in the United States account for 20% of HIV cases. The World Health Organisation and Centers for Disease Control and Prevention recommend PrEP with Truvada antiviral (tenofovir/emtricitabine) in combination with protective measures to prevent infection in people at high risk of infection.

Several studies have found a 70-90% reduction in the risk of acquiring HIV in women administered oral PrEP. The adhesion is between 30% and 50% (determined by tenofovir levels in plasma). The use of gels with 1% tenofovir or vaginal rings with dapivirine has not been as effective as the use of oral PrEP. In the case of gels (application before and after having sex), the risk of acquiring HIV was reduced by up to 76% in one of the studies. In the case of vaginal rings, protection was low, but increased in women over 21 years of age.

Several factors should be considered with regard to PrEP. One is that tenofovir concentrations are higher in the rectal than in the vaginal tissue, so women should take higher doses to prevent infections. Other factors are age, presence of other sexually transmitted diseases, or viral load of sexual partners. It is also important to consider kidney and bone toxicity in long-term treatments. There appears to be no interaction between contraceptive use and prophylactic treatment with tenofovir.

One of the goals of PrEP according to Haberl [13] is to increase the perception of risk among women, since in some studies, more than 50% of women perceived being at low risk or of not being at risk of contracting HIV. A communication campaign is needed as several studies have shown that a high percentage of women had not heard of PrEP or did not know what it was.

Factors such as effectiveness, cost, side effects, and whether the doctor is guiding therapy are determinants of good adherence to this type of prophylactic treatment.

Regarding pregnancy, PrEP does not appear to affect the effectiveness of hormonal contraception. As Davey *et al.* [14] reported, in countries where HIV acquisition during pregnancy and postpartum periods remains high despite increased access to and initiation of antiretroviral therapy in sub-Saharan Africa, a strict follow-up of adherence by these patients is required to make PrEP a success.

Bazzi *et al*. [15] discussed the need to extrapolate the connotations acquired in African countries to serodiscordant couples in the United States.

Nevertheless, as Callagan *et al.*, it appears to interfere with oral contraceptives, and unwanted pregnancies were found among users of oral contraceptives who had received PrEP [16].

Outstanding studies from Silawaspan *et al.* [17], exist in the scientific literature about attitudes, intentions, and behaviors related to PrEP, as well as concerns and obstacles by primary care physicians to prescribe PrEP. In addition, one study used a clinical case to illustratethe use of PrEP. Another study by Di Biagio *et al.* [18] was conducted in Italy, a European country in which the use of PrEP based on tenofovir and emtricitabine has not yet been approved, although in Europe, it already has the approval of the European Medicine Agency. In this study, the responses to a 21-item survey conducted among physicians at Italian centres that treat HIV patients, was analysed. The survey was conducted between 1 April and 30 May 2015.

After analysing the answers, it was found that despite the majority being familiar with PrEP, almost 47% were not clear that there was sufficient evidence supporting its use. Most believed that its use could be dangerous if it was not done properly and safely. There were also limitations in terms of its use for a specific group of people. Half of the respondents asked for more research on PrEP that could better define its role.

To date in our country, we have not found any publications concerning PrEP.

As Avuvika *et al.* [19], sexually transmitted infections (STIs) represent a public health concern due to their wide distribution and potential to lead to serious health conditions. STIs are preventable, diagnosable, and treatable. STIs most commonly occur in adolescents and young adults, and are associated with various health problems and complications in this population [20]. Elderly patients [21], particularly those who do not have a partner, have been found to be a novel group of patients. Other patient groups with high-risk practices include MSM and female sex workers. Furthermore, couples that appear to be monogamous, but in fact one individual practices sex with other partners, can also acquire an STI.

Patients seeking treatment for an STI account for a large number of Family Physician (FP) visits per year. Moreover, FP patients are reported to have a high rate of asymptomatic STIs [22].Hence, most of these patients remain undiagnosed until admission by family health services to STI units at advanced stages, by which time the infection has been disseminated and contributes to the epidemiological chain. Hence, patients with suspected STIs during an FP visit should be asked if they have a new partner, multiple partners, recent contacts, or if they are involved in high-risk sexual practices. Moreover as Rajalakshmi *et al.* [23], physicians should assess the symptomatology, including that in the genital area, and check for the presence of ulcers, vesicles,and pustules, in addition to genital, rectal, or eye discharge. Furthermore, the skin should be examined for the presence of rash or scaling, and the physical exam should include assessment for lymphadenopathy, hepatosplenomegaly, and joint pain. All patients should also undergo the required tests to exclude STIs, including HIV,hepatitis B, and possible co-infections [23].Women should undergo a pelvic examination and a pregnancy test. Also, reinforcement of human papilloma virus and hepatitis B vaccination where appropriate should be performed. Thus, a trial conducted in Spain by Hidalgo-Tenorio *et al.* [24] showed significantly higher anti-high-risk human papillomavirus antibody titres in vaccinated individuals than in unvaccinated controls.

Of more than 30 viruses, bacteria, and parasites that are reportedly transmitted through sexual contact, Rahimzadeh *et al.* [25] identified 8 species linked to the highest incidence of sexually transmitted diseases (Table **1**). We begin with the STIs presenting with urethritis or cervicitis. For this, it is helpful to divide patients into two groups: those presenting with complaints consistent with urethritis or cervicitis, and those with genital ulcers. The primary pathogens responsible for urethritis and cervicitis are *Chlamydia trachomatis* and *Neisseria gonorrhoeae*, though *Trichomonasvaginalis*, *Mycoplasma*, and *Ureaplamsa* havebeen implicated as well. Urethritis is more visible in male patients, and the mucus-purulent exudate is characteristically accompanied by dysuria and pollakiuria. Cervicitis presents with redness of the cervix and mucopurulent leucorrhoea [26].

Table 1. Common STI syndromes, their pathologies, and their etiological agents.

Clinical syndromes	Associated pathologies	Etiological agents
Urethral discharge	Urethritis	*Neisseria gonorrhoeae* *Chlamydia trachomatis* *Mycoplasma genitalium* *Ureaplasma urealyticum*
	Epididymitis	
Vaginal discharge	Cervicitis	*Neisseria gonorrhoeae* *Chlamydia trachomatis* *Candida albicans* *Trichomonas vaginalis*
	Vulvovaginitis	
	Bacterial vaginosis	*Gardnerella vaginalis*

(Table 1) contd.....

Clinical syndromes	Associated pathologies	Etiological agents
Low abdominal pain	Acute pelvic inflammatory disease	*Neisseria gonorrhoeae* *Chlamydia trachomatis*
Genital ulcers	Herpes	*Herpes simplex virus* type 2 (HSV-2) and herpes simplex virus type 1 (HSV-1)
	Syphilis	*Treponema pallidum*
	Chancroid	*Haemophilus ducreyi*
	Lymphogranuloma venereum	*Chlamydia L1, L2 (serovariant L2b) y L3*
Genital Warts	Condylomata acuminata	Human papillomavirus (HPV)
	Condyloma syphilitic plane	*Treponema pallidum*
STIs that do not manifest initially at the genitals	HIV/AIDS	*VIH*
	Hepatitis B	*VHB*
	Acute cytomegalovirus infection	*CMV*
	Disseminated gonorrhoeae:	*Neisseria gonorrhoeae*
	Secondary syphilis	*Treponema pallidum*
	Lymphogranuloma venereum, Extragenital	*Chlamydia L1, L2 y L3*
	Proctoenterocolitis	*Neisseria gonorrhoeae* *Chlamydia trachomatis serotypes D-L* *Treponema pallidum* *Herpes virus* HPV
	Arthritis	*Chlamydia trachomatis* *Neisseria gonorrhoeae*

The diagnosis of non-specific urethritis is established by the presence of >5 leukocytes per gram on Gram staining (×1000) and ruling out both *N. gonorrhoeae* and *C. trachomatis*as the causative agents. Although the clinical significance is unclear, culture formycoplasma detection or nucleic acid detection by polymerase chain reaction (PCR) of *M. genitalium*, *M. hominis*, and *U. urealyticum* is recommended (Tables **2** and **3**) [27].

The diagnosis of non-specific cervicitis is established by the presence of >20-30 leukoctyes per gram on Gram staining (x1000). In this scenario, in addition to the tests already mentioned in the Table **3**,it is advisable to performculturing for Mycoplasma detection or nucleic acid detection by PCR for *M. genitalium*, *M. hominis*, and *U. urealyticum*, particularly when the investigation of *N. gonorrhoeae* and *C. trachomatis* yields a negative result [26].

It is impossible to clinically distinguish infections caused by chlamydia from those caused by gonorrhea, and they often exist as coinfections. Hence, the Centers for Disease Control and Prevention recommend the use of presumptive treatment for both chlamydia and gonorrhea in men with urethritis. In women aged <25 years with cervicitis, and women with new or multiple sexual partners, the Centers for Disease Control and Prevention also recommend presumptive treatment for chlamydia and gonorrhea. This guideline should be particularly adhered to when patient follow-up cannot be ensured [27].

Organisms that can cause genital ulcers include chancroid, herpesgenitalis, syphilis, and the lymphogranulomavenereum (LGV) serotype of *C. trachomatis*.In genital herpes, the ulcer is painful and often presents with painful, bilateral inguinal adenopathies [27]. The ulcer associated with chancroid ulcer is also painful, but painful adenopathy is unilateral. Differently, the ulcer associated with primary syphilis is painless, and though the adenopathies are bilateral,they too are painless. Finally, the ulcer associated with lymphogranuloma venereum is painless, though the associated adenopathy is painful and unilateral [28]. Syphilis can be diagnosed by darkfieldmicroscopy, PCR, or direct immunofluorescence [29]. Girometti *et al.* [30] showed the importance of the diagnosis of early syphilis as it entails a high HIV seroconversion rate and its detection should be prioritised before PrEP is prescribed.

For genital herpes, chancroid, and LGV, diagnosis is by culture, or direct immunofluorescence or PCR, if available [31].

Lymphogranuloma Venereum (LGV) is caused by specific serotypes of *C. trachomatis* and occurs sporadically in the United States. A recent increase in cases was noted in Europe, with the majority of cases affecting MSMs who were also co-infected with HIV. These patients were frequently presented with severe proctitis [32].

Genital warts should be considered, as they are common and have a strong relationship with intraepithelial squamous lesions. If a lesion is suspected (possibility of dysplasia), a biopsy should be performed under local anesthesia. This biopsy can be used either for histological analysis or for the detection of human papillomavirus via

nucleic acid identification,with subsequent typing [33]. In high-income countries, accurate STI diagnostic tests are widely used, and such tests are particularly useful for diagnosing asymptomatic infections [27].

Table 2. Request for tests on men.

Location of the sample	Gonorrhea	Chlamydia	Non-specific urethritis [1]	Trichomonas	Candida	Observations
Urethral [2,3]	Gram staining + Culture	Detection of nucleic acids	Gram staining + cultivation and/or detection of nucleic acids for *M. genitalium*, *M. hominis*, and *U. urealyticum*	Culture	Not recommended	If the sample is not directly seeded, the Stuart-Amies transport medium should be used, which is the universal medium for the transport of chlamydia and viruses. The processing of the samples should be conducted within 4–6 hours at room temperature, and if this is not possible, the samples should be stored in a refrigerator at 2–8°C, following which the sample will be valid for up to 24 hours after being obtained. The sample should be assessed according to the patient's sexual practices, similar to the indication used for the urethral sample. This sample is not recommended for heterosexual men
Rectal [4]	Culture	Culture and/or detection of nucleic acids	Not recommended	Not recommended	Not recommended	
Pharyngeal [5]	Culture	Culture/PCR	Not recommended	Not recommended	Not recommended	The sample should be obtained according to the patient's sexual practices. The same indications should be followed, as for the urethral sample.

[1] As a general rule, the patient should remain without urinating for 2–4 hours prior to the urethral dose. The following materials are required for the sample protocol indicated: 3 Dacron urethral swabs, including 1 with Stuart-Amies transport medium or a similar medium (for cultivation of gonococcus and other general pathogens);another for *C. trachomatis*, which is convenient to use as a swab with the UTM (Universal Transport Medium, Copan, Italy) or a similar medium (although the technique of each manufacturer in each laboratory should be followed); and another that will serve as an extension of the Gram stain, with subsequent inoculation with Roiron or Diamond medium for the culture of trichomonas. If possible, direct seeding of the shoot should be performed on a selective agar for gonococcal isolation (GC-LECT agar or similar medium). The culture plates should be maintained at 37°C in an atmosphere with 5% CO2.

[2] It is preferable to obtain a urethral sample with a swab than a urine sample due to the greater sensitivity. Instead, Its use is relegated to: 1) population screening studies; 2) locations without laboratories that can care for the samples with minimum guarantees of quality for proper processing; and 3) cases where the patient cannot tolerate the sample study due to its invasive nature. However, it should be noted that in urine samples, only the indication of infection by *N. gonorrhoeae* and *C. trachomatis* is supported by a nucleic acid detection test.

[3] The following materials are required for the sample protocol indicated: 2 Dacron swabs, slightly moistened with physiological saline, including 1with Stuart-Amies or similar medium and another with the UTM medium. If possible, direct seeding of the shoot should be performed on a selective agar for gonococcal isolation (GC-LECT agar or similar medium). The culture plates should be maintained at 37°C in an atmosphere with 5% CO2.

[4] The following materials are required for the indicated sample protocol: 2 dry Dacron swabs, including 1 with Stuart-Amies or similar medium and another with the UTM medium. In case of direct seeding of the shoot, blood agar, Saboraud-Chloramphenicol agar, and selective agar should be used for gonococcal isolation (GC-LECT agar or similar medium). The culture plates should be maintained at 37°C, and the chocolate agar and GC-LECT agar should also be maintained at 37°C in an atmosphere with 5% CO2.

Table 3. Request for tests on women.

Location of the sample	Gonorrhea	Chlamydia	Vaginosis	Trichomonas	Candida	HPV	Observations
Urethral [1]	Not recommended	Not recommended	Not recommended	Not recommended	Not recommended	Not recommended	Only recommended in women who report symptomatology compatible with urethral syndrome
Vaginal [2,3]	Not recommended	Not recommended	Gram +/- fresh	Gram +/- fresh	Gram staining+ Gram staining +/- fresh	Not recommended	Use of Stuart-Amies medium + Roiron or Diamond medium for the cultivation of *T. vaginalis*
Endocervical [4,5,6]	Gram staining + culture	Detection of nucleic acids	Not recommended	Not recommended	Not recommended	HPV cytology and detection	Use of Stuart-Amies medium + UTM medium. Processing for <4-6 hours at room temperature, if not stored in a refrigerator at 2-8°C

(Table 3) contd.....

Location of the sample	Gonorrhea	Chlamydia	Vaginosis	Trichomonas	Candida	HPV	Observations
Rectal [7]	Culture	Culture and/or detection of nucleic acids	Not recommended	Not recommended	Not recommended	Liquid cytology in HIV patients or those with cervical cancer	Include the sample according to the patient's sexual practices. Same indications as for the urethral sample
Pharyngeal	Culture	Culture /PCR	Not recommended	Not recommended	Not recommended	Not recommended	Include the sample according to the patient's sexual practices. Same indications as for the urethral sample.

[1] Follow the procedure indicated in Table **2** and add a urine sample for the urine culture.

[2] The following materials are required for the indicated sample protocol: 2 dry Dacron swabs with Stuart-Amies transport medium or similar medium. If direct seeding of the shoot is possible, blood agar, chocolate agar, Saboraud-Chloramphenicol agar, and a selective agar should be used for gonococcal isolation (GC-LECT agar or similar medium) in case ofendocervical intake. The culture plates should be maintained at 37°C, and the chocolate agar and GC-LECT agar should also be maintained at 37°C in an atmosphere with 5% CO2. For the cultivation of trichomonas, a Roiron or Diamond medium was inoculated with one of the intakes.

[3] If endocervical sampling is not to be performed, the inclusion of a Dacron swab with the UTM medium is acceptable for the detection of *C. trachomatis* using a nucleic acid detection test.

[4] The following materials are required for the indicated sample protocol: 2 dry Dacron endocervical swabs, including Stuart-Amies medium or similar medium and another with the UTM medium. An endocervical sample should be obtained from the cervix of the remnants of vaginal discharge,after previous cleaning, with the aid of gauze and forceps. When possible, direct seeding of the shoot should be performed on selective agar for gonococcal isolation (GC-LECT agar or similar medium). The culture plates should be maintained at 37°C in an atmosphere with 5% CO2.

[5] It is preferable to obtain a urethral sample with a swab than a urine sample due to the greater sensitivity. Instead, its use is relegated to: 1) population screening studies; 2) locations without laboratories that can care for the samples with minimum guarantees of quality for proper processing; and 3) cases where the patient cannot tolerate the sample study due to its invasive nature. However, it should be noted that in urine samples, only the indication of infection by *N. gonorrhoeae* and *C. trachomatis* is supported by a nucleic acid detection test.

For most STIs, there are effective treatment methods (Table **4**) [34] and, in some cases, prophylaxis. Drug resistance, particularly the antibiotic resistance of gonorrhea, has markedly increased in recent years and consequently limited the treatment options. Although rare, antimicrobial resistance has been noted for other STIs as well. Therefore, early prevention and treatment are crucial [34].

Table 4. Considerations and treatment of sexually transmitted infections (STI).

STI	Treatment	Alternative regimens
Nongonococcal sexual transmitted infection	Azithromycin 1 g, orally, in a single dose Doxycycline 100 mg, orally, twice a day for 7 days	Erythromycin base 500 mg, orally, 4 times a day for 7 days Erythromycin ethyl succinate 800 mg, orally, 4 times a day for 7 days Ofloxacin 300 mg, orally, twice a day for 7 days Levofloxacin 500 mg, orally, once a day for 7 days
Gonococcal sexual transmitted infection (uncomplicated)	[A]Ceftriaxone 250 mg, IM, in a single dose, plus [B] Azithromycin 1 g, orally, in a single dose	Cefixime 400 mg, orally, in a single dose, plus [B] Azithromycin 2 g, orally, in a single dose
Gonococcal sexual transmitted Infection (complicated)	Ceftriaxone 1 g, IV, every 24 hours	Ceftriaxone 1 g, IV, every 24 hours; Cefotaxime 1 g, IV, every 8 hours; Ceftriaxone 1 g, IV, every 24 hours; or Cefotaxime 1 g, IV, every 8 hours
Trichomoniasis	Metronidazole[1] 2 g, orally, in a single dose, or Tinidazole 2 g, orally, in a single dose	Metronidazole 500 mg, orally, twice a day for 7 days
[C]Bacterial vaginosis	Metronidazole[1] 500 mg, orally, twice a day for 7 days, or Metronidazole gel, 0.75%, one full applicator (5 g) intravaginally, once a day for 5 days, or Clindamycin cream, 2%, one full applicator (5 g) intravaginally	Tinidazole 2 g, orally, once daily for 2 days, or Tinidazole 1 g, orally, daily for 5 days, or [4]Clindamycin 300 mg, orally, twice a day for 7 days, or Clindamycin ovules 100 mg, intravaginally, at bedtime for 3 days

(Table 4) contd.....

STI	Treatment	Alternative regimens
[C]Vulvovaginal candidiasis	Orally: Fluconazole 150 mg, orally, in a single dose Intravaginally Butoconazole 2% cream (single dose, bioadhesive product), 5 g, intravaginally, for 1 day, or Clotrimazole 2% cream 5 g, intravaginally, daily for 3 days OR Miconazle 2% cream 5 g, intravaginally, daily for 7 days, or Miconazle 1,200 mg vaginal suppository, one suppository for 1 day [A]Terconazole 0.4% cream 5 g, intravaginally, for 7 days, or Terconazole 0.8% cream 5 g, intravaginally, for 3 days Terconazole 80 mg vaginal suppository, daily, for 3 days,	
[2]Genital herpes	Acyclovir 400 mg, orally, 3 times a day for 7–10 days OR Acyclovir 200 mg, orally, 5 times a day for 7–10 days OR Valacyclovir 1 g, orally, twice a day for 7–10 days OR Famciclovir 250 mg, orally, 3 times a day for 7–10 days	
[3]Primary syphilis infection	Benzathine penicillin G 2.4 million units, IM, as a single dose If allergic to penicillin, consider desensitization, particularly if the patient is pregnant Recommended regimen for infants and children Benzathine penicillin G 50,000 units/kg, IM, up to the adult dose of 2.4 million units in a single dose	Doxycycline 100 mg, orally, twice a day for 28 days Tetracycline 500 mg, orally, 4 times a day for 28 days
Chancroid	First episode: Azithromycin 1 g, orally, in a single dose, or Ceftriaxone 250 mg, IM, in a single dose, or Ciprofloxacin 500 mg, orally, twice a day for 3 days., or Erythromycin base 500 mg, orally, 3 times a day for 7 days	Recurrence: Acyclovir 800 mg, orally, twice a day for 5 days, or Acyclovir 800 mg, orally, 3 times a day for 2 days, or Valacyclovir 500 mg, orally, twice a day for 3 days, or Valacyclovir 1 g, orally, once a day for 5 days, or Famciclovir 125 mg, orally, twice daily for 5 days, or Famciclovir 1 gram, orally, twice daily for 1 day
Lymphogranuloma venereum	Doxycycline 100 mg, orally, twice a day for 21 days	[A]Erythromycin base 500 mg, orally, 4 times a day for 21 days
[4]Genital warts (external)	Imiquimod 5% cream applied to warts, once daily at bedtime, for 3 times a week up to 16 weeks Sinecatechins 15% ointment applied to warts, 3 times a day for up to 16 weeks Podophyllinresin 10%–25%, trichloroacetic acid or bichloroacetic acid 80%–90% Cryotherapy	Intralesional interferon Podofilox 0.5% solution or gel applied to visible warts twice a day for 3 days, followed by no therapy for 4 days. Repeat up to 4 cycles Laser surgery

IM: intramuscular; IV: intravenous.

[A]Recommended treatment in pregnancy.

[B]As dual therapy, ceftriaxone and azithromycin must be administered together at the same time and day, and under direct observation.

[1]Although metronidazole crosses the placenta, data suggest that it poses a low risk to pregnant women. Recently studies have demonstrated that women can be treated with 2 g metronidazole in a single dose at any stage of pregnancy.

[C] Uncomplicated VVC and bacterial vaginosis is not usually acquired through sexual intercourse; hence, data do not support the treatment of sex partners.

[2]Treatment can be extended if disease is active after 10 days of therapy.

[3]Persons with HIV infection who have primary syphilis should be treated as those without HIV infection.

[3]Pregnant women with syphilis at any stage, who report penicillin allergy should be desensitized and treated with penicillin.

[4]Podofilox (podophyllotoxin), podophyllin, and sinecatechins use is not permitted during pregnancy. Imiquimod appears to pose a low risk but further investigation of its use in pregnancy is required.

Of note, the consultation and monitoring of the sexual health for transsexual and transvestite patients should be tailored according to the proposed sex-specific indications, and both their transgender status and sexual orientation should be taken into consideration [35].

If an STI is detected, patients should be instructed to abstain from sexual activity for at least 7 days following the initiation of treatment, regardless of the duration of treatment. The patient should also communicate to their recent

sexual contacts the potential for infection, and the doctor or other health professional in-charge should ensure that these steps are completed (either at the initial stage or subsequently at an agreed time). Partner notification and presumptive treatment of risk partners should also be performed if follow-up is not guaranteed [36].

CONCLUSION

In conclusion, STIs are frequently encountered in the primary care setting. Hence, FP will be primarily responsible for the outcome of such cases, and thus influence the improvement of public health. Therefore, it is vital that FP should remain alert and familiar with the signs and symptoms of STIs, as well as the different treatment options available.

One major concern regarding broad implementation of this strategy is the possible impact on high-risk sexual behaviors (risk compensation), which can result in increased transmission of STIs other than HIV. Although the data are still limited, this effect has not been observed in those taking PrEP. However, it should be kept in mind that the study conditions may not reflect usual practices. In the study environment, pharmacological therapy was accompanied by educational strategies, behavioral reinforcement, and a free supply of condoms to the patient. This reinforces the importance of a multifaceted approach to prevention, so that the implementation of a particular strategy does not result in lax adherence to other preventative strategies.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

No Animals/Humans were used for studies that are base of this research.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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