Review Article

Pre- and post-sexual exposure prophylaxis of HIV: An update

Yogesh S. Marfatia, Sheethal K. Jose, Reema R. Baxi, Ruchi J. Shah
Department of Skin-VD, Baroda Medical College, Vadodara, Gujarat, India

Address for correspondence:
Dr. Sheethal K. Jose, Department of Skin-VD, SSG Hospital, Vadodara, Gujarat, India. E-mail: sheethaljos@gmail.com

Abstract

Pitfalls in current HIV prevention strategies include late HIV testing, vulnerability among youth and females; lack of emphasis on treatment, low acceptance of circumcision, and nonavailability of protective vaccines. Continuing high-risk sexual behavior, forceful sex, coercive and nonconsensual sex, rape, and unprotected sexual activities make women the most vulnerable to acquisition of sexually transmitted infection/HIV and necessitates a more radical approach of prevention in high-risk individuals who do not have HIV. Preexposure prophylaxis is defined as the administration of antiretroviral drugs to an uninfected person before potential HIV exposure to reduce the risk of infection and continued during risk. The rationale of this approach is to administer preventive dose of drug(s) before exposure to HIV so the moment virus enters the body, HIV replication is inhibited and HIV is not able to establish permanent infection. Postexposure prophylaxis (PEP) following potential sexual exposure is an important form of nonoccupational PEP which is an emergency intervention to abort HIV acquisition arising from exposure to HIV-infected blood or potentially infectious bodily fluids following sexual exposure.

Key words: Emtricitabine, HIV, postexposure prophylaxis following potential sexual exposure, preexposure prophylaxis, tenofovir

INTRODUCTION

With the advent of effective antiretroviral therapy (ART), HIV is no longer considered a terminal illness but a manageable long-term condition. Taking a leap further, it is now increasingly being used for prevention-both preexposure prophylaxis (PrEP) and postexposure prophylaxis (PEP). Pitfalls in current HIV prevention strategies include late HIV testing, low awareness of vulnerability among youth and females; lack of emphasis on treatment, low acceptance of circumcision, and nonavailability of protective vaccines. Continued high-risk sexual behavior, forceful sex, coercive and nonconsensual sex, rape, and unprotected sexual activities make women the most vulnerable to acquisition of sexually transmitted infection (STI)/HIV and necessitates a more radical approach of prevention in high-risk individuals who do not have HIV. Furthermore, there has been increasing HIV incidence among men who have sex with men (MSM) in the UK despite increased HIV testing and earlier initiation of ART.[1] Thus, pre- and post-sexual prophylaxis offers an additional safety net for all men and women at risk due to sexual behaviors.

Free HIV and virus-infected cells are present in blood, semen and in lesser quantities in vaginal and cervical secretions [Table 1].[2] Risks of HIV acquisition from sexual exposure is up to 1% as

Access this article online

Quick Response Code:

Website: www.ijstd.org

DOI: 10.4103/ijstd.IJSTD_26_17

How to cite this article: Marfatia YS, Jose SK, Baxi RR, Shah RJ. Pre- and post-sexual exposure prophylaxis of HIV: An update. Indian J Sex Transm Dis 2017;38:1-9.

compared to 92.5% with blood transfusion and 15%–30% with vertical transmission.[3]

PREEXPOSURE PROPHYLAXIS

PrEP is defined as the administration of antiretroviral drugs to an uninfected person before potential HIV exposure to reduce the risk of infection and continued during risk.[3] PrEP can be in the form of a pill taken by mouth or a gel applied to the vagina or rectum. The rationale of this approach is to administer a preventive dose of drug(s) before exposure to HIV, so the moment virus enters the body, HIV replication is inhibited and HIV is not able to establish permanent infection. For high-risk individuals who test HIV negative, offering PrEP is recommended in addition to the provision of free condoms, circumcision, education about risk reduction strategies, etc. Voluntary male medical circumcision has shown up to 60% reduction in transmission risk in circumcised heterosexual men.[4]

A drug named Truvada which is a combination of tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) has been approved by the U.S. Food and Drug Administration on July 16, 2012, for PrEP regimen in combination with safer sex practices to reduce the risk of sexually acquired HIV-1 in adults at high risk.[4] It has been recently approved in India for prevention of HIV costing about Rs. 2200 for a month.[5]

DRUGS

Tenofovir disoproxil fumarate

- Oral prodrug of tenofovir, a nucleotide analog with activity against retroviruses, including HIV-1, HIV-2, and hepadnaviruses
- TDF is rapidly converted to tenofovir after absorption, which is metabolized to active tenofovir diphosphate, which is a competitive inhibitor of HIV-1reversetranscriptaseandterminates the growing DNA chain
- Long half-life of 17-h allowing once-daily dosing
- Drugs such as acyclovir, valacyclovir, cidofovir, aminoglycosides, high-dose or multiple nonsteroidal anti-inflammatory drugs or other drugs that reduce renal function or compete for active renal tubular secretion may increase serum concentrations of TDF.[6]

Emtricitabine

- An analog of cytidine
- Inhibits reverse transcriptase; helps to lower the viral load and indirectly increase the number of T-cells or CD4 T-cells.[6]

EMTRICITABINE TENOFOVIR COMBINATION

The drug is administered as a single daily oral dose in a formulation containing 300 mg of TDF and 200 mg of FTC. Important qualities that make this combination an ideal agent for PrEP include:

- Potent antiretroviral activity against all HIV subtypes
- Rapid onset of activity after ingestion
- Early action in HIV's life cycle, and
- Once-daily dosing with few drug interactions.[6]

Common adverse reactions reported in people who take the drug to prevent HIV infection include nausea, vomiting, diarrhea, headache, respiratory tract infections, arthralgia, and weight loss. Tenofovir has been linked to renal impairment and loss of bone mineral density.[7]

Indications Centers for Disease Control and Prevention guidelines [Table 2][4]

Clinical eligibility for preexposure prophylaxis [Table 3][4]

The time from initiation of daily oral doses of TDF/FTC to maximal protection against HIV infection is unknown. It has been shown that the

Table 1: Estimated per-act risk for acquisition of HIV by sexual exposure route[2]

Exposure route	Risk (%)
Sexual intercourse	
Receptive penile-vaginal intercourse	0.01-0.15
Insertive penile-vaginal intercourse	0.1-0.01
Receptive anal intercourse	0.05
Insertive anal intercourse	0.065
Receptive oral intercourse	0.01
Insertive oral intercourse	0.005

Table 2: Indications of preexposure prophylaxis- Centers for Disease Control and Prevention guidelines

Anyone who is in an ongoing sexual relationship with an HIV-infected partner
A gay or bisexual man who has had sex without a condom or has been diagnosed with a STI within the past 6 months, and is not in a mutually monogamous relationship with a partner who recently tested HIV-negative
A heterosexual man or woman who does not always use condoms when having sex with partners known to be at risk for HIV (e.g., injecting drug users or bisexual male partners of unknown HIV status), and is not in a mutually monogamous relationship with a partner who recently tested HIV-negative
Anyone who has, within the past 6 months, injected illicit drugs and shared equipment or been in a treatment program for injection drug use[4]

pharmacokinetics of TDF and FTC vary by tissue. Maximum intracellular concentrations of tenofovir diphosphate are reached in blood after approximately 20 days of daily oral dosing, in rectal tissue at approximately 7 days, and in cervicovaginal tissues at approximately 20 days.[8] However, there are no data available about intracellular drug concentrations in penile tissues to inform considerations of protection for male insertive sex partners. PrEP efficacy has been shown to be as high as 100% if taken daily as prescribed, even with occasional missed doses.

Follow-up visits

Done at least every 3 months to provide the following [Table 4].

Test for bacterial STI and renal function should also be done every 6 months.[4]

Issues

- Medication adherence - Adherence to treatment forms the crux of PrEP. Strict adherence to ART is essential for sustained HIV suppression in people living with HIV/AIDS patients, and this is also required for PrEP therapy.[6] PrEP trial initiative showed that participants who took the medication on 90% or more days had a 79% decrease in HIV incidence. They must be counseled to strictly adhere to medication along with specific behavioral and structural modifications such as limiting number of sexual partners and condom use with each sexual encounter. Monitoring for adverse outcomes and development of resistance are also important
- Start-up syndrome - Gastrointestinal symptoms in the 1st month consisting of primarily nausea, diarrhea, vomiting abdominal pain. Can be caused due to both drugs
- Risk compensation – The introduction of an intervention that reduces the perceived risk of the behavior or activity may cause a person to increase risky behavior is called "risk compensation."[8] PrEP implementation is highly likely to cause this effect. Behavioral disinhibition will only increase HIV transmission if the prevention strategy has low efficacy. Condoms protect against STIs not prevented by PrEP, thus regular monitoring and counseling regarding condom use are advised given recent data from PrEP use in regular clinical practice in San Francisco indicating a 40% drop-off rate in condom use among PrEP users
- Drug-resistance and resulting loss of treatment options.

Table 3: Clinical eligibility for preexposure prophylaxis

Guidelines
Documented negative HIV test
No signs/symptoms of acute HIV infection
Normal renal function; creatinine clearance must be ≥60 mL/min
No contraindicated medications such as acyclovir, valacyclovir, cidofovir, aminoglycosides, high-dose, or multiple NSAIDs
Documented hepatitis B virus infection and vaccination status - patients susceptible to HBV infection (especially MSM, IVDU) should be vaccinated. Both TDF and FTC are active against HBV[4]
Screen/test for pregnancy, and assess whether women are planning to become pregnant and if any are breastfeeding

NSAIDs=Nonsteroidal anti-inflammatory drugs; MSM=Men who have Sex with men; IVDU=Intravenous injection drug use; TDF=Tenofovir disoproxil fumarate; FTC=Emtricitabine

Table 4: Follow-up visits

Guidelines
HIV test
Medication adherence counseling
Behavioral risk reduction support, side-effect assessment
STI symptom assessment
Renal function test

STI=Sexually transmitted infection

Patients who had an acute infection when PrEP was initiated have the highest risk of developing drug resistance. The acute infection can only be excluded if HIV testing follows a period of no potential exposure to HIV, which is not practical in people who have sex often and a delay in initiation of PrEP carries the greater risk of an HIV infection that could be avoided:

- Sexual orientation or gender identity of patients are not routinely asked or discussed
- High cost of PrEP and unappreciated drug toxicity
- Development of drug resistance
- Lack of information about PrEP among potential providers
- Lack of substantial health service infrastructure and staffing for PrEP implementation and community education for MSM.

Discontinuation of preexposure prophylaxis

Patients discontinue PrEP due to personal choice, intolerable toxicities, chronic nonadherence to the prescribed dosing regimen, or acquisition of HIV infection. On discontinuation for any reason, HIV status at the time of discontinuation, reason for PrEP discontinuation, recent medication adherence, and reported sexual risk behavior should be documented.

If the patient is HIV positive, estimation of viral load, CD4 count and resistance testing should be done and if HIV negative, linkage to risk reduction support should be done.[4]

PREEXPOSURE PROPHYLAXIS FOR SERODISCORDANCE

Approximately, 45% of HIV-infected individuals have an HIV-negative partner. The use of ART and PrEP reduces the transmission risk to 0.5% among adherent HIV-uninfected individuals who are serodiscordant couples.[9] The option of early ART in combination with PrEP while the index member of the couple has a detectable viral load should be considered among HIV serodiscordant monogamous couples.[7]

PREGNANCY OR BREASTFEEDING WHILE ON PREEXPOSURE PROPHYLAXIS MEDICATION

Women without HIV in serodiscordant couples are at substantial risk of HIV acquisition during attempts to conceive, and there is also an increased risk of HIV acquisition during pregnancy. PrEP use periconceptionally and during pregnancy by the uninfected partner may offer an additional tool to reduce this risk. Data directly related to the safety of PrEP use during pregnancy and lactation are very limited but indicate no increase in the prevalence of birth defects due to first trimester exposure to either FTC or TDF among HIV-infected pregnant women. A single small study of periconception use of TDF in uninfected women in HIV-discordant couples found no ill effects on the pregnancy and no HIV infections. However, a recent study, maternal tenofovir use for at least 8 weeks in the third trimester in HIV-positive women was associated with a 12% reduction in neonatal bone mineral content at 0–4 weeks postpartum; even though its clinical significance is not yet known.[8] There is also limited drug exposure to infants through breast milk. The World Health Organization has recommended the use of TDF/FTC or lamivudine (3TC)/efavirenz for all pregnant and breastfeeding women for the prevention of perinatal and postpartum mother-to-child transmission of HIV. Providers should educate HIV-discordant couples who wish to become pregnant about the potential risks and benefits of all available alternatives for safer conception and if indicated make referrals for assisted reproduction therapies.

STUDIES ON PREEXPOSURE PROPHYLAXIS

PROUD open-label

In October 2014, the British PROUD open-label oral TDF/FTC PrEP demonstration determined that MSM assigned to receive PrEP had an 86% decrease in their risk of becoming HIV-infected compared to no treatment.[10,11]

iPrEx study

A retrospective analysis of drug levels found that individuals who took the medication at a frequency of approximately four times/week had a comparable level of protection to those who took the medication on a daily basis.[11,12]

iPERGAY

A study conducted in France and Quebec, iPERGAY, a placebo-controlled trial evaluating pericoital oral TDF/FTC prophylaxis found that MSM assigned to receive active medication were 86% less likely to become HIV-infected than those assigned to the placebo condition. However, more data are required in pericoital oral PrEP.[12,13]

Partners preexposure prophylaxis

A randomized trial of oral ART was conducted for use as PrEP among HIV-1 – serodiscordant heterosexual couples from Kenya and Uganda. The HIV-1 – seronegative partner in each couple was randomly assigned to one of three study regimens – once-daily tenofovir (TDF), combination tenofovir (TDF)–FTC, or matching placebo – and followed monthly for up to 36 months. A relative reduction of 67% in the incidence of HIV-1 in serodiscordant partner with TDF and 75% with TDF–FTC group. Both study medications significantly reduced the HIV-1 incidence among both men and women.[14]

OTHER DRUGS FOR PREEXPOSURE PROPHYLAXIS

1. No antiretroviral regimens other than a daily oral dose of TDF/FTC have been approved for PrEP. Bangkok Tenofovir Study demonstrated significantly reduced risk of HIV in intravascular ultrasound on daily oral tenofovir and suggested that TDF alone can be considered as an alternative in these groups.[15] While partners PrEP trial has demonstrated efficacy of tenofovir alone as a PrEP regimen[14]
2. Vaginal and rectal tenofovir gel (1%) - In July 2010, the Centre for the AIDS Programme of Research in South Africa-004 trial established that PrEP with intravaginal TDF gel could reduce the risk of HIV acquisition among at-risk African women. Even, rectal TDF gel (1%) has been tried in MSM as a topical PrEP with questionable efficacy

Advantages of topical PrEP include higher rate of adherence and increased intravaginal tissue concentrations of tenofovir[16]

3. Raltegravir (RAL) (integrase strand transfer inhibitor) and Maraviroc (CCR5 inhibitor), have been tested on humanized RAG-hu mice and results show that oral administration of either of these drugs prevents vaginal HIV-1 infection.[16]

POSTSEXUAL EXPOSURE PROPHYLAXIS

PEP is an emergency intervention to abort HIV acquisition arising from occupational (i.e., needle stick or mucous membrane splash) or nonoccupational (i.e., sexual or injecting drug use) exposure to HIV-infected blood or potentially infectious bodily fluids. It is a comprehensive management which includes first aid, counseling, risk assessment, relevant laboratory investigations based on informed consent of the source and exposed person; depending on the risk assessment, provision of short-term of ART, follow-up and support.

An important form of nonoccupational PEP is PEP following potential sexual exposure (PEPSE) which could be due to unprotected sexual exposure, sexual exposure involving a broken or slipped condom, sexual assault, etc.[17] It is not feasible on ethical grounds to conduct randomized, placebo-controlled clinical trials for PEPSE. However, data relevant to PEPSE guidelines are available from animal transmission models, perinatal clinical trials, observational studies of health-care workers receiving prophylaxis after occupational exposures, and observational and case studies of PEPSE use. Two observational PEPSE studies undertaken in Brazil: one among MSM and another among women following sexual assault demonstrated that fewer HIV seroconversions occurred among individuals taking PEPSE compared with those who did not.[1] Cost-effectiveness analyses have suggested that PEPSE is cost-effective in high-risk exposures such as receptive anal sex with an HIV-infected partner or a partner of unknown HIV status.[18]

BASELINE ASSESSMENTS OF THE EXPOSED [TABLE 5]

Concurrent acquisition of hepatitis C virus (HCV) and HIV infection might lead to delayed HIV seroconversion. Therefore, for those with HCV antibody test is negative at baseline but positive at 4–6 weeks after the exposure, HIV antibody tests should be conducted at 3 and 6 months to rule out delayed seroconversion.

ASSESSMENT OF SOURCE [TABLE 6][2]

Time of postexposure prophylaxis

PEP should be started ideally within 2 h but certainly within 72 h and continued for 28 days. Animal studies have shown initiating PEP within 12, 24, or 36 h of exposure was more effective than initiating PEP 48 h or 72 h following exposure.[20,22] During follow-up, HIV status should be reassessed at 4–6 weeks, 3 months, and 6 months after exposure, although shorter serologic follow-up (e.g., at 3 or 4 months) may be possible if using a fourth-generation assay. Persons who repeatedly seek PEP should be considered for PrEP, as daily PrEP may be more protective than repeated episodes of PEP.[20]

RISK ASSESSMENT

1. Evaluation of exposure-type and severity of the exposure, quantity of body substance involved, depth of injury and the recency of exposure

Table 5: Baseline investigations of the exposed

HIV - antibody testing - ideally, a combination of antibody and antigen tests should be done within 3 days to establish infection status at the time of exposure, with pre- and post-test counseling. Testing is repeated at 4-6 weeks and 3 months after exposure[19]
Screening for STIs such as syphilis, gonorrhea, and chlamydia. Baseline VDRL testing should also be done
Pregnancy testing in women of childbearing potential
Hepatitis B and C serology
Baseline complete blood count with differential and platelet count
Liver function tests
Blood urea or serum creatinine

STIs=Sexually transmitted infections; VDRL=Venereal disease research laboratory

Table 6: Assessment of source

Source with unknown HIV status[20]
Clinical evaluation should be done that includes HIV testing using a fourth-generation combined Ag/Ab test
Due to short window period available, if the risk associated with the exposure is high, PEPSE can be initiated first and then source be tested for his/her HIV status. Drug can then be discontinued if source is seronegative
When the source is PLHA on ART[20,21]
Most recent viral load and history of antiretroviral drug resistance should be enquired. This will help to avoid prescribing medications to which the source virus is likely to be resistant
Plasma HIV RNA testing of the source person is recommended
If the source person's HIV screening result is negative, but there has been a risk for HIV exposure in the previous 6 weeks
If the source person's HIV screening result is positive but confirmatory antibody differentiation assay is nonreactive or indeterminate

PLHA=People living with HIV/AIDS; ART=Antiretroviral therapy

2. Plasma HIV viral load high load in the source increase the risk. Due to high HIV viral load, the probability of transmission when the source person is in the acute and early stage of HIV infection (first 6 months) has been shown to be 8- to almost 12-fold higher than exposures that take place after the viral set point[23,24]
3. Viral loads in genital tract-correlate with plasma viral loads[23]
4. Breaches in mucosal barrier such as mouth or genital ulcer disease and trauma following sexual assault or first intercourse may increase the risk of HIV acquisition[25]
5. Menstruation or other bleeding-facilitate transmission[26]
6. STIs-enhance HIV transmission and increase HIV shedding from the genital tract. However, this may not occur in individuals on effective ART[25]
7. Ejaculation-increases risk of HIV transmission
8. Circumcision significantly reduces risk of HIV acquisition among heterosexual men in high prevalence countries[27,28]
9. Cervical ectopy[26]
10. ART-transmission risk is decreased if source persons are on effective ART.[29]

WORLD HEALTH ORGANIZATION 2014 GUIDELINES FOR POSTEXPOSURE PROPHYLAXIS (GIVEN FOR 28 DAYS) [TABLE 7][30]

NACO guidelines 2014 for postexposure prophylaxis[31]

- Tenofovir (300 mg) + 3TC (300 mg) + efavirenz (600 mg) once daily for 28 days
- In case of intolerance to efavirenz, regimen containing protease inhibitor (atazanavir/r or LPI/r) can be used.

Centers for Disease Control and Prevention (CDC) 2016 guidelines for PEP (28-day course of three drug regimen) [Table 8].[32]

THREE DRUG REGIMEN FOR POSTEXPOSURE PROPHYLAXIS

The recommendation for a 3-drug antiretroviral regimen is based on data that combination of ≥3 antiretroviral drugs provides maximal suppression of viral replication. Furthermore, protection against acquiring resistant virus would be greater with a 3-drug regimen compared with a 2-drug regimen.[23] Recommending a 3-drug regimen for all patients who receive PEPSE will increase the likelihood of successful prophylaxis in light of potential exposure to virus with resistance mutation(s) and will provide consistency across PEP guidelines for both PEPSE and occupational PEP.[21,34] In addition, if infection occurs despite PEPSE, a 3-drug regimen will more likely limit the emergence of resistance than a 2-drug regimen.

Zidovudine is no longer recommended in the preferred PEP regimen because it is believed to have no clear advantage in efficacy over tenofovir while having significantly higher rates of treatment-limiting side effects.

Persons evaluated for PEPSE should also be provided any indicated prevention, treatment, or supportive

Table 7: WHO 2014 guidelines for postexposure prophylaxis (given for 28 days)

Exposed	Guidelines
Adults and adolescents	TDF+3TC (or FTC), LPV/r or ATV/r is recommended as the preferred third drug RAL, DRV/r or EFV can be considered as alternative options
Children <10 years	AZT+3TC, ABC+3TC or TDF+3TC (or FTC) can be considered as alternative regimen LPV/r- preferred third drug

TDF=Tenofovir disoproxil fumarate; 3TC=Lamivudine; LPV=Lopinavir; ATV=Atazanavir; RAL=Raltegravir; DRV=Darunavir; EFV=Efavirenz; ABC=Abacavir; FTC=Emtricitabine

Table 8: Centers for Disease Control and Prevention 2016 guidelines for postexposure prophylaxis (28-day course of 3-drug regimen)[32]

Exposed	Regimen
Healthy adults and adolescents	Preferred regimen TDF (300 mg) FTC (200 mg) once daily RAL 400 mg twice daily or DTG 50 mg daily Alternative regimen TDF (300 mg) FTC (200 mg) once daily DRV (800 mg) and RTV (100 mg) once daily
Adults and adolescents aged ≥13 years with renal dysfunction (creatinine clearance ≤59 mL/min)	Zidovudin and 3TC, with both doses adjusted to degree of renal functionRAL 400 mg twice daily or DTG 50 mg once daily
Children aged 2-12 years	TDF (8 mg/kg) FTC (6 mg/kg once daily) RAL (dose according to age and weight)
Children aged 4 weeks to <2 years	Zidovudine oral solution 3TC oral solution RAL or LTC/ritonavir oral solution, with each drug dosed to age and weight

DRV=Darunavir; RTV=Ritonavir; TDF=Tenofovir disoproxil fumarate; RAL=Raltegravir; DTG=Dolutegravir; 3TC=Lamivudine; LTC=Lopinavir; FTC=Emtricitabine

care for other exposure-associated health risks and conditions (e.g., bacterial STIs, traumatic injuries, hepatitis B virus and HCV infection, or pregnancy). Individuals at risk for frequently recurring HIV exposures (e.g., injection drug use, or sex without condoms) or who report receipt of ≥1 course of PEPSE in the past year should be given risk-reduction counseling and intervention services, including consideration of PrEP.

ISSUES

- False sense of protection and therefore reduction in primary preventive measure and further increase in high-risk behavior
- Despite its short duration, completion rates for PEP are low. Therefore, counseling and other adherence support measures are recommended
- Cost of care, payment for medications and feasibility of implementation of guidelines the risks and benefits of prophylactic ART
- Transmissions may occur in few cases despite being on PEP. This may be attributed to delayed initiation of PEP, presence of resistant virus in the source, different penetration of drugs into tissue compartments, poor/nonadherence, and further high-risk sexual exposures[21]
- Compartmentalization of HIV, in particular within the genital tract, may result in differential virus evolution or evolution of resistance, which may have implications for transmission
- Individuals may present in a state of acute anxiety following possible exposure to HIV but the decision to administer PEP should be based on the risk of HIV acquisition[35,36] and the potential adverse effects of ART. When the risk of HIV acquisition is low individuals should be reassured and referred for psychological support if required.

CONCLUSION

Although effective ART is now accessible, high-risk sexual behavior is continued as reflected by the occurrence of new cases. Vulnerable population like victims of nonconsensual high-risk sexual activities are in need of aggressive preventive approach in terms of pre- and post-sexual exposure prophylaxis. Potential disadvantages of this approach include misuse of such drugs as a substitute of safe behavior, drug toxicities, and drug resistance.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Benn P, Fisher M, Kulasegaram R; BASHH; PEPSE Guidelines Writing Group Clinical Effectiveness Group. UK guideline for the use of post-exposure prophylaxis for HIV following sexual exposure (2011). Int J STD AIDS 2011;22:695-708.
2. Training modules for medical officers on HIV Care and treatment (Including ART); NACO: Ministry of Health and Family Welfare. 2007. p. 159-75.
3. Naswa S, Marfatia YS. Pre-exposure prophylaxis of HIV. Indian J Sex Transm Dis 2011;32:1-8.
4. US Public Health Service. Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2014 Clinical Practice Guideline. Available from: http://www.cdc.gov/hiv/pdf/PrEPguidelines2014.pdf. [Last cited on 2014 Oct 05].
5. The Hindu: Pre- Exposure Prophylaxis in Gay Men; 13 September, 2015. Available from: http://www.thehindu.com/sci-tech/health/preexposure-prophylaxis-prevents-hiv-infection-in-gay-men/article7645530.ece. [Last accessed on 2017 Jan 10].
6. Ferrell KW, Woodard LM, Woodard TJ. Role of medication therapy management in preexposure prophylaxis therapy for HIV prevention. J Pharm Pract 2015;28:10-2.
7. Steinbrook R. Preexposure Prophylaxis for HIV Infection; 2017.
8. Kelesidis T, Landovitz RJ. Preexposure prophylaxis for HIV prevention. Curr HIV/AIDS Rep 2011;8:94-103.
9. McMahon JM, Myers JE, Kurth AE, Cohen SE, Mannheimer SB, Simmons J, *et al.* Oral pre-exposure prophylaxis (PrEP) for prevention of HIV in serodiscordant heterosexual couples in the United States: Opportunities and challenges. AIDS Patient Care STDS 2014;28:462-74.
10. Mayer KH, Hosek S, Cohen S, Liu A, Pickett J, Warren M, *et al.* Antiretroviral pre-exposure prophylaxis implementation in the United States: A work in progress. J Int AIDS Soc 2015;18 4 Suppl 3:19980.
11. PROUD: PROUD Study Key Messages Q & A and Further PrEP Trial Information; December, 2015. Available from: http://www.proud.mrc.ac.uk/default.aspx. [Last accessed on 2017 Feb 20].
12. Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, *et al.* Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med 2010;363:2587-99.
13. AVAC Global Advocacy for HIV Prevention: IPERGAY; AVAC; October, 2014. Available from: http://www.avac.org/trial/ipergay. [Last accessed on 2017 Feb 06].
14. Baeten JM, Donnell D, Ndase P, Mugo NR, Campbell JD, Wangisi J, *et al.* Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. N Engl J Med 2012;367:399-410.
15. Choopanya K, Martin M, Suntharasamai P, Sangkum U, Mock PA, Leethochawalit M, *et al.* Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): A randomised, double-blind, placebo-controlled phase 3 trial. Lancet 2013;381:2083-90.
16. Abraham BK, Gulick R. Next-generation oral preexposure prophylaxis: Beyond tenofovir. Curr Opin HIV AIDS 2012;7:600-6.
17. Jain S, Mayer KH. Practical guidance for nonoccupational postexposure prophylaxis to prevent HIV infection: An editorial review. AIDS 2014;28:1545-54.
18. Schechter M, do Lago RF, Mendelsohn AB, Moreira RI, Moulton LH, Harrison LH; Praca Onze Study Team. Behavioral impact, acceptability, and HIV incidence among homosexual men with access to postexposure chemoprophylaxis for HIV. J Acquir Immune Defic Syndr 2004;35:519-25.
19. Mackie NE, Coker RJ. Post-exposure prophylaxis following non-occupational exposure to HIV: Risks, uncertainties, and ethics. Int J STD AIDS 2000;11:424-7.
20. Cresswell F, Waters L, Briggs E, Fox J, Harbottle J, Hawkins D,

et al. UK guideline for the use of HIV post-exposure prophylaxis following sexual exposure, 2015. Int J STD AIDS 2016;27:713-38.
21. Leynaert B, Downs AM, de Vincenzi I. Heterosexual transmission of human immunodeficiency virus: Variability of infectivity throughout the course of infection. European Study Group on Heterosexual Transmission of HIV. Am J Epidemiol 1998;148:88-96.
22. New York State Department of Health AIDS Institute. Update: HIV Prophylaxis Following Non-Occupational Exposure; 2013. Available from: http://www.hivguidelines.org/clinicalguidelines/postexposure-prophylaxis/hiv-prophylaxis-following-nonoccupational-exposure/. [Last accessed on 2013 Jul 22].
23. Rothenberg RB, Scarlett M, del Rio C, Reznik D, O'Daniels C. Oral transmission of HIV. AIDS 1998;12:2095-105.
24. Quinn TC, Wawer MJ, Sewankambo N, Serwadda D, Li C, Wabwire-Mangen F, *et al*. Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. N Engl J Med 2000;342:921-9.
25. Sadiq ST, Taylor S, Kaye S, Bennett J, Johnstone R, Byrne P, *et al.* The effects of antiretroviral therapy on HIV-1 RNA loads in seminal plasma in HIV-positive patients with and without urethritis. AIDS 2002;16:219-25.
26. Gitau RW, Graham SM, Masese LN, Overbaugh J, Chohan V, Peshu N, *et al.* Effect of acquisition and treatment of cervical infections on HIV-1 shedding in women on antiretroviral therapy. AIDS 2010;24:2733-7.
27. Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, Puren A. Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: The ANRS 1265 Trial. PLoS Med 2005;2:e298.
28. Templeton DJ. Male circumcision to reduce sexual transmission of HIV. Curr Opin HIV AIDS 2010;5:344-9.
29. Tsai CC, Emau P, Follis KE, Beck TW, Benveniste RE, Bischofberger N, *et al*. Effectiveness of post-inoculation PMPA treatment for prevention of persistent SIV infection depends critically on timing of initiation and duration of treatment. J Virol 1998;72:4265–73
30. World Health Organisation: Guidelines on Post exposure Prophylaxis for HIV and Use of Cotrimoxazole Prophylaxis for Prevention of HIV Related Infections Among Adults, Adolescents and Children – A Public HEALTH Approach. Geneva: WHO; December, 2014. Available from: http://apps.who.int/iris/bitstream/10665/145719/1/9789241508193_eng.pdf?ua=1.
31. National Aids Control Organisation (NACO): Revised Guidelines for Post Exposure Prophylaxis for HIV; New Delhi; NACO; December, 2014. Available from: http://www.naco.gov.in/sites/default/files/RevisedGuidelinesforPostExposureProphylaxis (PEP) forHIV.pdf.
32. Centers for Disease Control and Prevention, US Department of Health and Human Services: Updated Guidelines on Anti-Retroviral Prophylaxis after Sexual, Injection Drug Use or Other Non-Occupational Exposure to HIV; United States; 2016. Available from: https://www.cdc.gov/hiv/pdf/programresources/cdc-hiv-npep-guidelines.pdf.
33. Quirino T, Niero F, Ricci E, Pusterla L, Carradori S, Gabbuti A, *et al.* HAART tolerability: Post-exposure prophylaxis in healthcare workers versus treatment in HIV-infected patients. Antivir Ther 2000;5:195-7.
34. Ibáñez A, Puig T, Elias J, Clotet B, Ruiz L, Martínez MA. Quantification of integrated and total HIV-1 DNA after long-term highly active antiretroviral therapy in HIV-1-infected patients. AIDS 1999;13:1045-9.
35. Gray RH, Wawer MJ, Brookmeyer R, Sewankambo NK, Serwadda D, Wabwire-Mangen F, *et al.* Probability of HIV-1 transmission per coital act in monogamous, heterosexual, HIV-1-discordant couples in Rakai, Uganda. Lancet 2001;357:1149-53.
36. Jin F, Jansson J, Law M, Prestage GP, Zablotska I, Imrie JC, *et al.* Per-contact probability of HIV transmission in homosexual men in Sydney in the era of HAART. AIDS 2010;24:907-13.

MCQ

1. The risk of acquiring HIV in a female from an unknown source through vaginal intercourse is:
   a. 0.1%–0.2%
   b. 1%–2%
   c. 0.15%–0.20%
   d. 0.01%–0.15

2. TDF and FTC are used for PrEP in dose of:
   a. 100 mg FTC 300 mg TDF
   b. 200 mg TDF 200 mg FTC
   c. 300 mg TDF 200 mg FTC
   d. 300 mg FTC 200 mg TDF

3. One of the following is not clinically eligible for PrEP:
   a. Having HIV and on ART
   b. Having hepatitis B infection
   c. Not having pregnancy/breastfeeding
   d. Creatinine clearance >60 ml/min

4. PEP should be started ideally:
   a. Within 1 h
   b. Within 1/2 h
   c. Within 2 h
   d. None of the above

5. The following is recommended by CDC for PEP:
   a. TDF (300 mg), FTC (200 mg) once daily, RAL 400 mg twice daily or dolutegravir (DTG) 50 mg daily
   b. TDF 200 mg, FTC (300 mg) once daily, RAL 200 mg twice daily or DTG 50 mg daily
   c. FTC (200 mg) once daily, RAL 400 mg twice daily or DTG 50 mg daily
   d. Tenofovir TDF (300 mg), RAL 400 mg twice daily or DTG 50 mg once daily

Answers

1. d
2. c
3. a
4. c
5. a