

Recommendations of the Swiss Federal Commission for Sexual Health (FCSH) on pre-exposure prophylaxis (PrEP) for HIV prevention

Introduction

The HIV pre-exposure prophylaxis (PrEP) – an oral chemoprophylaxis – gives men and women at high risk of acquiring HIV temporarily the possibility to protect themselves against HIV infection by regular use of antiretroviral drugs. The medication needs to be taken daily, or at least for a sufficient length of time before and after at-risk sexual contacts. This pharmacological intervention offers substantial, but not complete protection against HIV infection. Nor does it protect against other sexually transmitted infections (STIs) or viral hepatitis. It should therefore be combined, if possible, with other preventive measures – in particular, condom use.

PrEP should be prescribed and monitored by physicians with experience both in the provision of sexual health advice and in the use of antiretroviral drugs.

In Switzerland, HIV drugs are not approved for prophylactic use. Physicians who prescribe oral chemoprophylaxis for HIV prevention do so on an off-label basis and are thus liable for any adverse effect that may occur. The drug costs are not reimbursable under compulsory health insurance.

Recommendation

The protective effects of oral chemoprophylaxis – with regard to HIV but not to other STIs – are comparable to those of condom use, although at a disproportionately higher price, and with potential long-term adverse effects not being fully known. The FCSH therefore recommends PrEP only for limited periods and only for a small group of persons at substantial risk of acquiring HIV, for whom consistent condom use is not a viable option, and where regular prophylactic use of antiretroviral drugs will enable them to engage in sexual activity without fear.

Target Group

In Switzerland, prescription of PrEP may be considered for HIV-negative persons at high risk of HIV infection. The risk depends on behavioural factors (high number of sexual partners, difficulties using condoms consistently for anal or vaginal sex) and on the prevalence of HIV in the

group concerned. High risk may be indicated by recently acquired infections such as syphilis or *lymphogranuloma venereum*, use of so-called chemsex drugs, or repeated use of HIV post-exposure prophylaxis. It may also be appropriate to prescribe PrEP for a limited period if the risk is temporarily increased (e.g. sex tourism/sex parties in countries/cities with high HIV prevalence). The FCSH believes that the cost-benefit ratio will only be favourable for a minority of men who have sex with men (MSM), i.e. in cases where the risk of HIV infection is substantially increased.

HIV-negative persons who have sex with a partner known to be HIV-positive and receiving effective antiretroviral therapy (ART) do not require PrEP. This is because, according to the official Swiss guidance issued in 2008 [1], the risk of sexual transmission is negligible in HIV-infected persons on effective ART (undetectable blood viral load for more than 6 months).

Drugs with proven prophylactic efficacy

At present, the efficacy of oral PrEP has only been demonstrated for the combination of tenofovir 245 mg and emtricitabine 200 mg (TDF/FTC). In Switzerland, this product is available under the name Truvada® for CHF 900 per month (packs containing 30 tablets). In most studies, efficacy was demonstrated with a daily dose [2, 3]. For MSM at high risk of HIV infection, while intermittent use has also been shown to be effective (two TDF/FTC tablets 2–24 hours before planned sexual contact, a third tablet 24 hours and a fourth 48 hours after the first drug intake), the frequency of PrEP use in the study concerned was very high (median: 15 tablets per month), and consequently the efficacy of just 2 tablets before and after a single contact cannot be demonstrated with certainty. The authors themselves point out that the favourable results of the study cannot be extrapolated to persons using the intermittent PrEP regimen less than four times a month [4].

At the same time, with intermittent use, a total of 7 tablets per week should not be exceeded. The efficacy of oral PrEP with tenofovir alone (245 mg, without emtricitabine) has only been demonstrated in studies involving heterosexual contacts. As with most medication – and condoms – HIV chemoprophylaxis is only effective if used correctly.

Prescribing

When PrEP is prescribed off-label, several points need to be taken into consideration. It is essential that the patient is confirmed to be (and remain) HIV-seronegative. The prescriber must be aware of the potential renal and bone toxicity and also inhibition of telomerase activity associated with chronic use of tenofovir [5-8]. The following precautions should therefore be observed: restriction of PrEP to persons with normal renal function, avoidance of concurrent administration of nephrotoxic drugs, regular monitoring of renal function (at least every 3–6 months) and optimal vitamin D intake. Prescriptions should be written for a maximum period of 3 months so as to ensure regular checks. If HIV seroconversion is clinically suspected or confirmed during prophylactic use of TDF/FTC, the medication must be discontinued immediately.

Efficacy

In 2010, it was shown that daily use of TDF/FTC in MSM leads to a 44% relative reduction in the incidence of HIV infection (95% confidence interval: 15%–63%). Put differently, 100 persons needed to be treated for 1 year in order to prevent a single HIV infection (iPrEx, [9]). The main reason for this modest efficacy was the fact that tablets were not taken regularly. When the drug was used correctly, efficacy was over 90%. It is thus crucial that drug treatment adherence should be ensured by means of regular discussions, starting before treatment is initiated. Two recent studies in England (PROUD, [2]) and France (IPERGAY, [4]) showed – after a treatment period of 12 and 13 months respectively – relative reductions of 86% (90% confidence

Procedure in practice

Information to be provided for the patient:

- Costs and potential adverse effects of PrEP (bone, renal, see text)
- If primary HIV infection is clinically suspected, immediate diagnostic measures (fourth-generation HIV test) and suspension of PrEP.

Before PrEP is prescribed

- Assessment and discussion of the indication. The patient must have a substantially increased risk of HIV infection.
- Confirmed negative HIV serology at least 6 weeks after the most recent risk situation
- Normal renal function (safety of TDF/FTC not established for eGFR below 50 mL/mi)
- Exclusion of hepatitis B infection based on HBsAg and ALT: in patients with active hepatitis B infection, consider continuation of hepatitis B therapy after discontinuation of PrEP
- Additional laboratory investigations: serology tests for hepatitis A, B and C, and syphilis
- Hepatitis A and B vaccination if the patient is not immune
- Anal, oral and urethral (vaginal) smears for *C. trachomatis* and *N. gonorrhoeae*
- Optimization of vitamin D intake

Every 3 months

- Assessment and discussion of ongoing indication.
- HIV serology (fourth-generation HIV test)
- Syphilis serology
- Examination for symptoms of STIs (anal and genital inspection)
- Anal, oral and urethral (vaginal) smears for *C. trachomatis* and *N. gonorrhoeae*
- Evaluation and promotion of drug treatment adherence
- Evaluation of adverse effects and potential interactions

Every 6 months

- Hepatitis C serology, transaminases
- Assessment of renal function (in patients with normal renal function and no nephrotoxic co-medication or other renal risk factors; otherwise, every 3 months)

interval: 58–96) and 82% (intention-to-treat analysis, 95% confidence interval: 36–97). The main difference from the iPrEx study was the highly selective enrolment (IPERGAY participants, in a third of cases, had experience in the use of post-exposure prophylaxis (PEP), reported a median of 8 partners in the past 2 months; and, in almost half of all cases, reported recent use of chemsex drugs; the risk profile of the PROUD participants was very similar). In the IPERGAY study, the number needed to treat for 1 year to prevent an HIV infection was 18, compared to 13 in the PROUD study. The IPERGAY study is of particular interest because TDF/FTC was no less effective than in the PROUD study, even though it was only used intermittently (see above). However, pharmacokinetic studies also suggest that PrEP should be started in MSM about 1 week before it is required [10].

In the light of these studies, the WHO recommends that oral PrEP containing TDF should be offered to persons at substantial risk of HIV infection [11]. The WHO explicitly does not recommend PrEP for all MSM, but as an additional HIV prevention option for specific periods when individuals feel at a higher risk of infection [12]. The European AIDS Clinical Society (EACS) recommends PrEP for adults at high risk of acquiring HIV infection, and in particular for MSM and transgender individuals who are not consistent in their use of condoms [13]. Both organisations underline the need for clinical monitoring of PrEP.

The WHO defines a substantial risk of infection as an HIV incidence of about 3 per 100 person-years or higher [14]. In Switzerland, the annual rate of new HIV diagnoses for MSM is currently around 0.3 per 100 person-years (FOPH). This comparison indicates that, in Switzerland, PrEP is not appropriate for all MSM.

Cost-effectiveness

Within Europe, calculations of the cost-effectiveness of PrEP are only available from a UK study. This suggests that Truvada® would be cost-effective if prescribed specifically for MSM who have engaged in condomless anal intercourse with five or more casual partners in the past three months, or if the current price (Truvada® is somewhat cheaper in the UK) were reduced by 80% [15].

According to the above definition, less than 1000 persons across Switzerland would be eligible for PrEP, which, with daily use, would lead to yearly drug costs of approx. CHF 10 million [16].

Conclusions

The FCSH takes the view that, over the long term, financial resources for HIV prevention are best deployed if the number of infectious individuals continues to be effectively reduced –

by consistent compliance with the “safer sex” rules, by early diagnosis and treatment, and by timely interruption of chains of transmission in the early stages of HIV infection [17, 18]. Prescription of PrEP may well be indicated in certain cases. The FCSH recommends that experience with the use of antiretrovirals for HIV prevention in Switzerland should be monitored, documented and evaluated using an appropriate system.

Literature

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