Pre-Exposure Prophylaxis in Teenagers: Prevent or Facilitate?

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Human immunodeficiency virus (HIV) epidemics

It is estimated that, worldwide, 75 million people have been infected since the HIV epidemic started.[1] In 2017, 1.8 million new cases were reported, 30% of these were in people 15 to 25 years of age.[1]

In Portugal, 1,068 new cases of HIV infection were reported in 2017, which corresponds to a rate of 10.3 cases/10^5.[2] The rate of new cases was 3.4 cases/10^5 in people between 15 to 19 years, rising to 18.4 cases/10^5 in the group of 20 to 24 years of age.[2] It can be speculated that some of these infections may have occurred at a pediatric age (< 18 years).

Viral suppression significantly reduces the risk of transmission.[3] This strategy of treatment as prevention has been adopted in campaigns all around the world, together with the implementation of voluntary free HIV-tests, education on safe sex practices (including the use of condoms), and post-exposure prophylaxis.[3] Nonetheless, there is still a rise of new HIV cases, especially in risk groups, namely men who have sex with men and migrants.[2]

Concept and evolution of pre-exposure prophylaxis (PrEP)

The use of antiretroviral drugs in post-exposure prophylaxis and prevention of mother-to-child transmission has led to the concept of PrEP, the use of antiretroviral drugs by non-infected people to prevent sexual transmission of HIV.[4] Several clinical trials have emphasized its efficacy, with rates of 44% to 75% risk reduction, although it depends on the adhesion rates.[4-6] In 2014, the World Health Organization has recommended the introduction of PrEP as a means of preventing new HIV cases.[7]

In 2016, based on the PartnersPrEP[5] and iPrEx clinical trials,[6] the European Medicines Agency (EMA) approved Truvada®, a combination of tenofovir and emtricitabine (TDF/FTC),[8] for PrEP in adult risk populations.

In the pediatric age, the studies are limited, but the evidence of efficacy in adults and the known safety profile of TDF/FTC led EMA to approve Truvada® for PrEP in children aged 12 or more and a weight of 35 kg or more, without known renal disease, pointing to the necessity of a global HIV prevention strategy, including other measures such as regular and correct use of condoms, knowledge of one's serological HIV status, and regular screening of sexually transmitted diseases.

And in Portugal

In 2017, the Directorate-General of Health (DGS) published a norm establishing that people with a high risk of contracting HIV infection should be referred to a hospital clinic.[10] This high risk includes, among others, people who, in the last six months, had unprotected sex with partners with unknown serological status or a previous diagnosis of sexually transmitted diseases, had sexual intercourse under the influence of psychoactive substances, use intravenous drugs or had a relationship with a viral non-suppressed HIV-infected partner.[10] Clinical evaluation and institution of other preventive measures should occur before prescribing a PrEP regime.[10] A trimestral screening of other sexually transmitted diseases and PrEP side effects should also be performed.[10]

Maybe teenagers were not regarded in the norm since it was published in 2017 and EMA only approved TDF/FTC for PrEP in the pediatric age in February 2018. In addition, at that time, data regarding efficacy, safety, and implementation of PrEP in this population was limited.

Is there a point in considering PrEP as a risk reducing strategy in teenagers?

PrEP in teenagers?

Because of their psychological and behavior characteristics, teenagers are considered as a risk

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group for contracting HIV. This fact is addressed in the Portuguese legislation,[11] which refers to adolescents as a priority intervention group in matters of reproductive health and the prevention of sexually transmitted diseases.

In Portugal, 27%-29% of the adolescents begin their sexual activity around the age of 15.5 years.[12] At their first sexual encounter, 91.8% use condoms, but this rate decreases to 80% with time.[12] The fact that about 9% of these teenagers assume having had sexual intercourse under the effect of alcohol or other psychoactive drugs is worrisome.[12]

The risk is not the same throughout life, and PrEP does not need to be continued throughout life. The notion of protection during risk periods may help the adhesion rates.

Implementing PrEP regimes in teenagers raises important practical issues. The efficacy is directly related to adhesion. In the few studies conducted in this population, the adhesion rates are considerably lower than in adult populations. One of the greatest challenges in PrEP will be to find strategies that improve this adhesion, which will necessarily include regular appointments in an adequate environment, regular warnings about medication, finding strategies to minimize social stigma and continued health education.

Pre-exposure prophylaxis must only be used in individuals without an HIV infection, and this status must be reconfirmed at regular intervals. TDF/FTC, *per se*, does not constitute an adequate treatment of HIV and, therefore, there is a potential risk of developing resistances. In the presence of symptoms suggestive of an acute HIV infection, PrEP should be postponed at least a month, and a negative serological status should be confirmed.

Implementing PrEP regimens is, naturally, associated with an immediate increase in health costs. Nonetheless, its potential for reducing HIV infection rates and the limitation of utilization of periods of higher risk will probably lead to a reduction of long-term costs associated with antiretroviral therapy throughout life.

Other questions regarding PrEP in teenagers

The main side effects of TDF/FTC are its potential renal and osseous toxicity associated with long-term exposure. The utilization of PrEP in shorter periods of time (risk periods) and regular screening of renal function may minimize this risk.

The concept of risk compensation is one of the more controversial aspects of PrEP. It regards the potential engagement in riskier sexual behaviors because of a notion of complete protection while using PrEP. There are, now, no clinical studies that address this specific notion, and it can be speculated that behavior and educational interventions conducted during regular appointments may minimize this potential worrisome effect.

The potential side effects in implementing PrEP regimen in teenagers must necessarily be counterweighed with the potential beneficial effects which include:

- Possibility of preventing sexually acquired HIV infections;
- Early diagnosis of other sexually transmitted diseases (a pressing problem in teenagers);
- Opportunity of the optimal monitoring of various aspects of sexual health;
- Opportunity of intervention in terms of health education and reduction of long-term risks.

Final remarks

Besides sexual abstinence, measures for the prevention of HIV sexual transmission include only the use of condoms. In Portugal, the highest rate of new HIV infection is among young adults. Developing strategies that enable the reduction of new cases is a priority.

In our opinion, PrEP under the current scientific knowledge is an important weapon to prevent new HIV cases, especially in teenagers. The change in society's sexual standards means that teenagers are engaging in risk behaviors earlier in life. Every teenager considered of high risk, including those with unsafe sex practices, multiple partners, or previous diagnosis of sexually transmitted diseases should be evaluated at a hospital visit by an experienced medical professional and, if under the inclusion criteria, should be offered inclusion in a PrEP regime. Although PrEP does not replace the need of other strategies (use of condoms, avoiding recreational intravenous drug use or safe sexual practices), it is, undoubtedly, a tool with great potential in order to allow our young people to have a responsible, rewarding, and safe experience of their sexuality.

Keywords: Adolescent; Anti-HIV Agents/therapeutic use; Emtricitabine, Tenofovir Disoproxil Fumarate Drug Combination/therapeutic use; HIV Infections/epidemiology; HIV Infections/prevention & control; Portugal; Pre-Exposure Prophylaxis

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Confidentiality of data

The authors declare that they have followed the protocols of their work center on the publication of patient data.

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