Indian J Med Res 143, February 2016, pp 125-128
DOI:10.4103/0971-5916.180194

Editorial

Antiretroviral pre-exposure prophylaxis: A new opportunity to slow HIV spread in India

Since the first case of HIV was diagnosed in Chennai in 1986, there have been close to three million Indians who have become infected with HIV and approximately 2.4 million currently living with the virus[1]. Although this represents the third largest HIV epidemic in the world (after South Africa and Nigeria), the current number of infected Indians actually reflects the success of the National AIDS Control Organization's prevention programmes with HIV incidence decreasing in many districts[2]. The prevalence of HIV in antenatal clinics was 0.35 per cent, and over the past decade, the number of districts where HIV prevalence exceeded 1 per cent decreased from 140 to 80[3]. Part of the containment of the epidemic may be due to increased awareness and community education, but increased uptake of antiretroviral medications may also play a role, given that more than one million Indians have been prescribed highly active antiretroviral therapy (HAART), which could attenuate HIV spread[3]. However, the epidemic continues to be highly concentrated in key populations, ranging from injecting drug users (IDUs) in the northeast with overall rates of HIV ranging from 7 to 9 per cent in large sentinel surveillance studies, to men who have sex with men (MSM) in many cities with rates between 4 and 6 per cent (and even higher rates in transgender women), and female sex workers (FSWs) with rates generally exceeding 5 per cent[1,2].

Although recent studies have shown that early initiation of antiretroviral therapy will decrease HIV transmission[3], the majority of Indians living with HIV have not yet initiated HAART. HIV intervention for them and groups at risk for HIV (MSM, FSW, IDUs, HIV sero-discordant heterosexual couples) has primarily focused on counselling, condom use, harm reduction, HIV/STI (sexually transmitted infection) testing and HIV awareness campaigns. It will take years before the majority of people living with HIV are on virally-suppressive therapy, making it likely that HIV transmission will continue in the foreseeable future, unless other primary prevention modalities are optimized.

In recent years, emphasis on preventive treatment as intervention for those at risk has gained momentum as a possible HIV prevention strategy. There have been several randomized controlled clinical trials looking at either oral or topical tenofovir-based regimens for chemoprophylaxis, referred to as PrEP (pre-exposure prophylaxis). In most of these studies oral PrEP was found to be highly efficacious[4-9]. These studies included heterosexual HIV discordant couples, MSM, transgender women, and IDUs. Three oral or topical PrEP studies of young women in sub-Saharan Africa did not demonstrate efficacy[10-12]. The primary reason for the lack of PrEP efficacy in these studies was suboptimal medication adherence. Subsequent studies of open-label access to tenofovir-emtricitabine PrEP demonstrated higher efficacy rates when individuals consistently used the medication[13]. PrEP demonstration projects are underway in Thailand, South Africa, Brazil, Australia, many sites in the U.S. and several are planned for European countries[14]. The initial findings of PrEP demonstration projects suggest that PrEP can be implemented successfully in high risk populations. The public health effectiveness of PrEP, however, may vary in diverse settings calling for locally-tailored PrEP evaluations, given that the social and structural reasons why HIV spreads in different parts of the world is mediated by distinct cultural dynamics.

Currently, there is one Indian PrEP demonstration project focusing on female sex workers, led by The Sonagachi Project in Kolkata[15]. Since that trial is designed to assess PrEP feasibility in one population, the study will not provide sufficient evidence to recommend that PrEP be made routinely available by the National or State AIDS Control Programmes for high risk individuals. Thus, other Indian demonstration projects are needed to provide sufficient evidence to support wider implementation. Prior socio-behavioural studies have found that Indian women and MSM indicated a willingness to use oral or topical PrEP, if proven to be effective[16-22], but now the challenge is to determine feasibility and impact in all key populations.

There have been concerns raised by critics that providing generic antiretroviral therapy to large numbers of HIV-uninfected people may neither be cost-effective nor easily sustainable. However, in a recent study conducted in British genitourinary medicine clinics[8], it was found that because of the high HIV incidence in MSM who were not assigned to receive PrEP immediately, the ratio of people needed to be offered PrEP to prevent infections was 13 to 1. Offering PrEP to high risk people can be highly cost-effective, since PrEP can be stopped when risk decreases, while treating HIV is lifelong. For PrEP to be cost-effective in India, the key will be to identify those at substantial risk for HIV infection. Concerns have also been with regard to the use of PrEP in promoting antiretroviral resistance. However, increase in resistance has not been reported in PrEP studies till date[23].

While there are concerns, there are also multiple advantages of PrEP if included as part of a comprehensive health package for individuals at highest risk for HIV. Since PrEP medication requires ongoing clinical monitoring, individuals who might not otherwise be seeking health services would be expected to come to clinics on at least a quarterly basis[24]. These visits could facilitate provision of quality care and support services including psychosocial counselling, screening for sexually transmitted infections and other referral services. The recent study in the developed world suggests that people who use PrEP may have substantial risk for non-HIV STIs, but the argument can be made that it is better to diagnose these infections earlier before these individuals transmit these infections to new partners[25]. It is also extremely important to note that for PrEP to be optimally effective in decreasing HIV incidence in socially marginalized populations, the drivers of HIV risk taking, ranging from stigma and personal violence[26-28], to depression[29,30], and substance use[31] must also be effectively addressed as part of a comprehensive HIV prevention package.

In summary, PrEP today using tenofovir-emtricitabine is "PrEP 1.0," in that it offers a new modality for HIV prevention, but it is a bio-behavioural intervention that needs to be carefully implemented. Given that Indian society is diverse, a next logical step for PrEP implementation should be the expansion of demonstration projects in diverse parts of the country to provide PrEP and clinical monitoring for individuals who are at highest risk for HIV. These would include heterosexual HIV discordant couples who want to have children, MSM, transgender women, female sex workers, and injecting drug users, based on local epidemiological patterns. If these demonstration projects prove to be successful, acceptable and feasible with at-risk individuals demonstrating an interest in accessing PrEP and a willingness to adhere to the medication, then it would make sense to expand PrEP access nationally for key populations. There are other approaches being investigated for antiretroviral chemoprophylaxis such as the use of vaginal rings, other types of gels, and injectable medications[14]. The advantage of some of these approaches may be that these can allow for the medication to be given less frequently (in the case of injections), or that the medication may be used topically around the time of coitus (*e.g.* rings or gels). Thus, over the next few years, public health officials and clinicians may be able to offer individuals a menu of prevention modalities, analogous to the varieties of family planning options that are currently available. However, since only daily oral tenofovir-emtricitabine has been approved by the WHO for the use as PrEP in high risk populations, it is important for Indian federal and State governmental authorities to initiate more feasibility studies and demonstration projects, using implementation science research to determine how this preventive approach can be best used in the Indian context.

Acknowledgment

The assistance of Mary Childs in the preparation of this manuscript is acknowledged.

***Conflicts of Interest*:** None of the authors have a direct conflict of interest. The first author (KHM) has conducted research funded by Gilead Sciences, the

manufacturer of tenofovir-emtricitabine, but has never received personal support from the company.

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