Methods and Approaches to HIV Prevention

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Key words: *HIV, prevention, prophylaxis*

HIV is a sexually transmitted infection (STI) that emerged as a global pandemic in the 1980s (Vermund, 2013). Since its emergence, this past decade marks the first time that there have been slight declines in infection rates throughout the world (Joint United Nations Programme on HIV/AIDS [UNAIDS], 2012; World Health Organization [WHO], 2012). While HIV remains a life-threatening illness, with proper treatment the life expectancy of an individual with HIV can be comparable to the general population of their given countries (UNAIDS, 2012).

In 2012, global estimates suggested approximately 35.3 million people were living with HIV infection around the world (WHO, UNAIDS, & UNAIDS/WHO Working Group on Global HIV/AIDS and STI Surveillance, 2013). HIV prevalence rates have been reported to range from 1 in 10 in the general adult population to as high as 1 in 2 in certain age/gender groups such as men who have sex with men (MSM) and female sex workers (UNAIDS, 2012; National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, & Division of HIV/AIDS Prevention, 2012). In addition, 95% to 97% of HIV-infected people live in low- and middle-income countries (LMIC; WHO, 2013).

In the United States, the economic collapse that began in 2008 has heightened public awareness of the expenses associated with health care. With national incidence of HIV infection estimated at 1.1 million persons (National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention & Division of HIV/AIDS Prevention, 2012), the costs associated specifically with HIV-related illness, disability, and death are high (Schwartländer et al., 2011). In the United States, treatment of STIs has been estimated to cost $16 billion annually. Because HIV is a life-long illness, it is one of the costliest (National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, 2013a). Advanced HIV infection gradually destroys the immune system, resulting in AIDS (UNAIDS & United Nations, 2012; Vermund, 2013; WHO, 2012). According to the Centers for Disease Control and Prevention (CDC), an individual with HIV is diagnosed as having AIDS when s/he is severely immune suppressed, having a CD4+ T lymphocyte count lower than 200 cells/mm^3 (Castro et al., 1993).

HIV Prevention

Behavioral Prevention Strategies

HIV infection rates remain high and have been rising in certain sub-populations throughout the world (CDC, 2013; UNAIDS & United Nations, 2012). There is no evidence to suggest that the HIV pandemic is self-limiting or will resolve without intervention (UNAIDS & United Nations, 2012; WHO, 2012). HIV mutates rapidly (Streeck, D'Souza, Littman, & Crotty, 2013) and any one individual can be co-infected with several strains, each of which may carry drug resistances. Furthermore, when different strains infect the same cell, the virus can swap or incorporate new resistant genes into the

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JOURNAL OF THE ASSOCIATION OF NURSES IN AIDS CARE, Vol. 28, No. 1, January/February 2017, 19-24
http://dx.doi.org/10.1016/j.jana.2016.09.005
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daughter virions. The current state of science suggests that a vaccine against this malady will not be available in the near future as the range of genetic variants of HIV makes therapy and the development of a generalizable vaccine more challenging (WHO, 2015). Therefore, other prevention modalities have been recommended and widely used around the world. These strategies are briefly reviewed.

Barrier protection. Numerous prevention measures have been encouraged by public health and infection control authorities around the world; these techniques demonstrate varying levels of efficacy. For example, the use of latex condoms in conjunction with lubricants, also known as barrier protection, has been highly effective in preventing the transmission of HIV (McCormack et al., 2016). However, barrier protection must be used appropriately and consistently for greatest risk reduction. Research has found that the use of barrier protection tends to be inconsistent (McCormack et al., 2016). For instance, a study of 732 MSM in San Francisco, California, found that only 28% of study participants used condoms regularly (McFarland et al., 2012).

Circumcision. Circumcision is another prevention strategy encouraged by some public health and infection control authorities. Some men resist circumcision because of concerns that male circumcision impairs penile function and leads to sexual dysfunction (CDC, 2012). However, circumcised men have a 57% to 61% decreased risk of HIV transmission during heterosexual intercourse (CDC, National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, & Division of HIV/AIDS Prevention, 2012). Despite the demonstrated benefits of circumcision in HIV prevention, there is concern that the benefits of circumcision may be offset by high-risk behaviors. For example, some men, believing that circumcision has provided adequate protection for HIV and other STIs, respond by dispensing with latex condom use altogether (Lagarde, Dirk, Puren, Reathe, & Bertran, 2003). Although there has been a demonstrated reduced risk for HIV transmission in penile-vaginal intercourse for men who are circumcised, there is little evidence that these same benefits exist in penile-anal intercourse. Given that the predominant mode of HIV transmission in the United States is among MSM, the CDC does not presently have recommendations on male circumcision for HIV prevention in the United States. The CDC does, however, encourage that uncircumcised adolescent and adult males, as well as parents and guardians of infant males, be counseled on the risks and potential benefits of male circumcision of reducing risk of acquiring HIV (CDC, 2008).

Needle and syringe exchange. Although HIV is classified as an STI, it can be transmitted by contaminated blood as well as through sexual intercourse. The most common exposure to blood is through shared needles and syringes via intravenous drug use (National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, & Division of HIV/AIDS Prevention, 2012). Programs that supply sterile needles and syringes to intravenous drug users have been effective in reducing HIV transmission rates throughout the world (WHO, 2012). In Australia, for example, HIV infection rates in intravenous drug users have been maintained at about 1% over the course of this pandemic. This is related to the wide use of needle and syringe exchange programs (Topp, Day, Iversen, Wand, & Maher, 2011). Despite proven effectiveness, there are challenges with establishing sufficient numbers of needle and syringe exchange programs to effectively control this form of HIV transmission (Mathers et al., 2010), particularly in LMIC where cost is prohibitive (UNAIDS & United Nations, 2012).

Biomedical HIV Prevention Strategies

Antiretroviral (ARV) drugs can be used for primary prevention of, as well as for treatment of, HIV infection (Cohen, Muessig, Smith, Powers, & Kashuba, 2012). These agents can be used prior to exposure for preexposure prophylaxis (PrEP), after exposure for postexposure prophylaxis (PEP), and after seroconversion as HIV treatment for prevention (TasP; Cohen & Gay, 2010; Linden, 2011; Mayer & Venkatesh, 2010).

PrEP. There are a number of approaches to the use of PrEP, having various degrees of efficacy. One such example is the use of ARVs as

microbicides, which, thus far, is a promising approach to reducing the spread of HIV (McCormack et al., 2016; National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, 2013b).

The use of intravaginal tenofovir gel prior to sexual intercourse demonstrated a reduced rate in HIV transmission up to 54% in sexually active adult women who were not pregnant or planning to become pregnant (Karim et al., 2010; WHO, 2012). Oral preparations of PrEP also exist and have demonstrated efficacy in the prevention of HIV. The use of daily oral tenofovir-emtricitabine by MSM in England resulted in an 86% reduction in HIV acquisition (McCormack et al., 2016). However, PrEP is effective only when taken as prescribed (Haberer et al., 2015). Adherence to intravaginal PrEP appears to be consistently low; higher adherence rates have been noted with oral PrEP in some populations (McCormack et al., 2016), but this has not always been the case. A study conducted in reproductive-age women in South Africa, Uganda, and Zimbabwe found no reduction in HIV contraction rates with either oral or intravaginal PrEP secondary to poor adherence (Marrazzo et al., 2015).

Despite research suggesting the potential benefits, the use of ARVs as PrEP is controversial. Varying levels of adherence to PrEP have caused concern for the risk of creating drug resistance (Cáceres, O'Reilly, Mayer, & Baggaley, 2015). Additionally, the use of PrEP has come under criticism for being an unethical use of limited resources (Macklin & Cowan, 2012). A number of ethical principles are in conflict with each other when it comes to treatment versus prevention of HIV with ARVs (Macklin & Cowan, 2012). Some argue that, where ARVs are limited, the focus should be on using all available resources to provide treatment to those who already have HIV and will die without treatment. Macklin and Cowan (2012) suggested that it was unethical to allow individuals who were the sickest to worsen and die so that a portion of the available ARV resources could be allocated to prevent HIV infections in those who were uninfected, even if they were at risk for becoming infected. Others argued that the focus should be on preventing the most possible number of deaths from HIV by decreasing the risk of new infections in those at greatest risk for contracting HIV with the use of PrEP (Singh, 2013). They have suggested that not allocating resources for PrEP for those at highest risk for contracting HIV would be a violation of human rights (Singh, 2013). Singh (2013) argued that there was a duty to protect the interest of all people and, therefore, the most ethical approach would be to allocate resources for HIV treatment as well as for HIV prevention.

Despite these controversies, in July 2012 the U.S. Food and Drug Administration approved a combination antiretroviral therapy (cART) regimen for use as PrEP, in conjunction with other prevention modalities, in high-risk populations in the United States (National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention, 2013b). At the same time, WHO published recommendations for the use of PrEP for individuals at substantial risk of HIV infection (WHO, 2015).

PEP. PEP is most effective when initiated within 72 hours of HIV exposure (Chan, Gough, Yoong, Dimeo, & Tan, 2013) and is most frequently prescribed as a 28-day, three-drug course of ARVs (Foster et al., 2015). While PEP is well tolerated and has demonstrated success in preventing HIV transmission (Chan et al., 2013), a major drawback is that people are often unaware that they have been exposed to the virus before the 72-hour timeframe has expired. This means that individuals who are potentially at greatest risk (i.e., MSM and female sex workers) may not seek treatment before this window has closed. Another major drawback is suboptimal adherence (Foster et al., 2015); treatment failure with PEP has been linked to poor adherence and early discontinuation of therapy (Ford et al., 2014). Completion rates appear to be highest for MSM and lowest for victims of sexual assault (Malinverni, Libois, Gennotte, La Morté, & Mols, 2016). Data have suggested that PEP completion rates could improve with the use of a single-tablet treatment for those exposed to HIV (Foster et al., 2015).

A study conducted in Austria found a 0% HIV seroconversion rate for 450 people who began PEP within 72 hours of HIV exposure via routes including unprotected homosexual and heterosexual contact with an HIV-infected partner, needle-stick injuries, rape, and intravenous drug use for both males and females (Schreiner, Stingl, Rieger, & Jalili, 2013). With

comparable findings in the United States, the CDC recommends that clinicians promptly initiate cART for individuals who seek care within 72 hours of exposure to HIV (Smith et al., 2005). WHO has also developed recommendations for PEP irrespective of exposure source (Ford & Mayer, 2015).

TasP. TasP involves effectively treating those who are already infected with HIV with early cART so as to decrease the likelihood that they will spread HIV to others. Early cART refers to regimens that are begun when CD4+ T lymphocyte counts are above 350 cells/mm^3, whereas late cART refers to therapy initiated after CD4+ T lymphocyte counts have declined below 250 cells/mm^3. The aim is to suppress the HIV viral load to an undetectable level while at the same time maintaining adequate immune function. The initiation of early cART has been found to decrease HIV transmission rates by 96% among heterosexual, monogamous, serodiscordant couples (Cohen et al., 2011). Similar to PrEP and PEP, reduction in HIV transmission rates is contingent on strict adherence to cART regimens. Product availability is a major consideration when initiating life-long therapies.

There is concern regarding the cost-effectiveness and feasibility of TasP, particularly for LMIC (Walensky et al., 2013), where the resources tend to be more limited but the disease burden is higher (WHO, 2013). To help address this reservation, the HIV Prevention Trials Network investigators collaborated with others to project potential future outcomes in two LMIC, India and South Africa (Walensky et al., 2013). A micro-simulation model of HIV disease, treatment, and transmission was used to conduct a model-based analysis to evaluate projected costs associated with early and late cART. Study results demonstrated that over a lifetime, the longer lifespan associated with early cART was also associated with greater per-person costs when compared to delayed cART. However, when taking into account the associated reduction in HIV transmission rates (Eaton et al., 2012), early cART actually saved costs over a 5-year period (Walensky et al., 2013). WHO now recommends initiating cART in all adults living with HIV irrespective of clinical staging or CD4+ T lymphocyte count (WHO, 2015).

Discussion

Although there have been promising research findings (Chan et al., 2013; Foster et al., 2015; Karim et al., 2010; McCormack et al., 2016; Schreiner et al., 2013), it is unlikely that any one prevention modality will be sufficient to reverse the global progression of the HIV pandemic (Mansergh, Herbst, Mimiaga, & Holman, 2015). HIV testing and the appropriate and consistent use of latex condoms will remain central to HIV prevention efforts worldwide (McCormack et al., 2016). However, a combination of biomedical and behavioral prevention strategies remains necessary to effectively reduce HIV infection rates (Kurth, Celum, Baeten, Vermund, & Wasserheit, 2011), as none of these strategies can be effective without appropriate participation and adequate adherence. A study conducted in Switzerland found that people infected with HIV were most likely to transmit the infection to others during their first year of infection as well as during cART interruptions in chronic illness (Marzel et al., 2016). This brings to light the need for improved HIV testing efforts as well as action plans to improve treatment adherence. Further research is needed to identify methods to improve cooperation with currently available HIV treatment and prevention strategies by those at greatest risk for contracting this infection as well as for those already infected (Toledo, McLellan-Lemal, Henderson, & Kebaabetswe, 2015).

Disclosures

The author reports no real or perceived vested interests that relate to this article that could be construed as a conflict of interest.

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