Hong Kong J. Dermatol. Venereol. (2013) **21**, 69-71

Views and Practice

HIV treatment as prevention

KH Wong 黃加慶 and KCW Chan 陳志偉

Using antiretrovirals to prevent HIV is nothing new. Even in the early 1990s when there were only the "first generation" anti-HIV drugs, biomedical means was conceptualised for the prevention of mother-to-child transmission (MTCT) of HIV and put into clinical trials. The landmark ACTG 076 study published in 1994 showed that zidovudine reduced MTCT from 25.5% to 8.3%.[1] Given the scientific advances thereafter, the risk of perinatal transmission has been reduced nowadays to about 1% with early maternal diagnosis and prophylactic intervention.[2] The risk of occupational HIV transmission after percutaneous exposure in health care setting can also be lowered with post-exposure prophylaxis.[3]

How about sexual contact, the main mode of transmission worldwide and in Hong Kong? Again, a long time ago plasma HIV-1 viral load was found to be associated with the risk of infecting partner in HIV sero-discordant heterosexual couples.[4] Ecological studies in western countries also suggested the role of highly active antiretroviral therapy (HAART) in averting an HIV epidemic. For example, new cases of HIV decreased from 1996 to 1999 when HAART was scaled up in British Columbia, Canada.[5] The drop in cases stabilised when the growth of HAART coverage in British Columbia slowed but experienced a further drop in new diagnoses when treatment coverage increased again from 2004 to 2009. In San Francisco, US, from 2004 to 2008, when more patients on HAART achieved full viral suppression leading to a lower community viral load, there was a corresponding drop in new diagnoses and HIV incidence in the same period.[6] Notwithstanding, these findings were limited by the study designs of not being able to demonstrate a causal relationship.

Nevertheless, the game changer on treating HIV infection: to prevent or reduce HIV transmission – HPTN 052 study - was published in August 2011, so much so that the Science magazine elected "HIV treatment as prevention" to be "The Breakthrough of the Year". Being a multi-centre randomised controlled trial with over half of the study subjects recruited from Africa, HPTN 052 found a 96% reduction of linked HIV transmission in stable HIV serodiscordant couples who were prescribed early HAART when the CD4 count was 350-550/μl vs. delayed therapy when the CD4 count fell to <250/μl.[7] Moreover, patients in the early HAART group had less clinical events, largely due to a lower incidence of extra-pulmonary tuberculosis. Of note, all study participants were given ongoing counselling on risk behaviour reduction, condom use, together with screening and treatment of sexually transmitted infections.

Special Preventive Programme, Centre for Health Protection, Department of Health, Hong Kong

KH Wong, MBBS, FHKAM(Medicine)
KCW Chan, MBBS, FHKAM(Medicine)

Correspondence to: Dr. KH Wong

Special Preventive Programme, Centre for Health Protection, Department of Health, 3/F, Wang Tau Hom Jockey Club Clinic, 200 Junction Road East, Kowloon

In April 2012, the World Health Organisation issued its *Guidance on couples HIV testing and counselling - including antiretroviral therapy for treatment and prevention in serodiscordant couples*. This supported the use of HAART for HIV prevention in serodiscordant couple as a public health approach.[8] Clearly, it is challenging to achieve this theoretical benefit in real practice. Studies in Mozambique[9] and US[10] have concluded less than 5% of cases diagnosed positive and <30% of infected cases respectively achieved the target of undetectable viral load. Programmes to maximise the diagnosis of infected cases, linkage to care, counselling for HAART initiation, clinic retention and support for drug adherence are all indispensable components of the new strategy.

The other concept of using anti-retrovirals in HIV negative cases as a preventative measure to reduce acquisition of HIV became widely discussed in 2010 after the publication of two randomised, controlled studies on pre-exposure prophylaxis (PrEP). The CAPRISA 004 study[11] showed a 40% reduction in the risk of HIV acquisition by using peri-coital tenofovir gel in females, while the iPrEx study[12] found a 44% reduction in HIV incidence in men who have sex with men who were given daily emtricitabine and tenofovir disoproxil fumarate. Protection correlated strongly with adherence to the drugs in both trials. In contrast, the FEM-PrEP trial showed no efficacy of oral emtricitabine and tenofovir disoproxil fumarate[13] and the VOICE (Vaginal and Oral Interventions to Control the Epidemic) study have already failed with daily oral tenofovir or tenofovir gel.[14,15]

Scientists are still grappling with the discrepancies of PrEP studies and have so far postulated both adherence and differential pharmacokinetics as possible factors.[16,17] If so, PrEP could be more complicated than initially thought. A one-size-fit-all strategy might not be possible and, in all likelihood, prescription of such potentially toxic medications to healthy subjects on a long term basis will have to be individualised and carefully followed. Other concerns including behavioural risk compensation, breakthrough infections, resistant viral strains, selection criteria, cost affordability, cost effectiveness and opportunity cost have also been raised. Interim guidance issued by the US CDC[18] illustrates the complexities involved.

In summary, treating infected partners of serodiscordant couples appears promising as part of the public health strategies in HIV control while more data is needed for PrEP before a consensus can be reached. In any case, these biomedical preventative approaches are best viewed as supplemental to rather than a replacement of basic modalities of prevention, including condom use for safer sex which remains the time-tested gold standard.

References

1. Connor EM, Sperling RS, Gelber R, Kiselev P, Scott G, O'Sullivan MJ, et al; Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. N Engl J Med 1994;331: 1173-80.
2. Townsend CL, Cortina-Borja M, Peckham CS, de Ruiter A, Lyall H, Tookey PA. Low rates of mother-to-child transmission of HIV following effective pregnancy interventions in the United Kingdom and Ireland, 2000-2006. AIDS 2008;22:973-81.
3. Cardo DM, Culver DH, Ciesielski CA, Srivastava PU, Marcus R, Abiteboul D, et al. A case-control study of HIV seroconversion in health care workers after percutaneous exposure. Centers for Disease Control and Prevention Needlestick Surveillance Group. N Engl J Med 1997;337:1485-90.
4. 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.
5. Montaner JS, Lima VD, Barrios R, Yip B, Wood E, Kerr T, et al. Association of highly active antiretroviral therapy coverage, population viral load, and yearly new HIV diagnoses in British Columbia, Canada: a population-based study. Lancet 2010;376:532.
6. Das M, Chu PL, Santos GM, Scheer S, Vittinghoff E, McFarland W, et al. Decreases in community viral load are accompanied by reductions in new HIV infections in San Francisco. PLoS One 2010;5:e11068.

7. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al; HPTN 052 Study Team. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med 2011;365:493-505.
8. World Health Organisation. Guidance on coupes HIV-testing and counseling including antiretroviral therapy for treatment and prevention in serodiscordant couples: recommendations for a public health approach, April 2012. Available at http://apps.who.int/iris/bitstream/10665/44646/1/9789241501972_eng.pdf.
9. Micek MA, Gimbel-Sherr K, Baptista AJ, Matediana E, Montoya P, Pfeiffer J, et al. Loss to follow-up of adults in public HIV care systems in central Mozambique: identifying obstacles to treatment. J Acquir Immune Defic Syndr 2009;52:397-405.
10. Centers for Disease Control and Prevention (CDC). Vital signs: HIV prevention through care and treatment-United States. MMWR Morb Mortal Wkly Rep 2011; 60:1618-23.
11. Abdool Karim Q, Abdool Karim SS, Frohlich JA, et al; CAPRISA 004 Trial Group. Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. Science 2010; 329:1168-74.
12. Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L; iPrEx Study Team. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med 2010;363:2587-99.
13. FHI statement on the FEM-PrEP HIV prevention study [press release]. Durham, NC: Family Health International; April 18, 2011. Available at http://minilicious.wordpress.com/2011/04/18/fhi-statement-on-the-fem-prep-hiv-prevention-study/.
14. NIH modifies "VOICE" HIV prevention study in women [press release]. Bethesda, MD: National Institute of Allergy and Infectious Diseases; September 28, 2011. Available at http://nih.gov/news/health/sep2011/niaid-28.htm.
15. MTN statement on decision to discontinue use of tenofovir gel in VICE, a major HIV prevention study in women [press release]. Pittsburgh, PA: Microbicide Trials Network; November 25, 2011. Available at http://www.mtnstopshiv.org/node/3619.
16. Patterson KB, Prince HA, Kraft E, Jenkins AJ, Shaheen NJ, Rooney JF, et al. Penetration of tenofovir and emtricitabine in mucosal tissues: implications for prevention of HIV-1 transmission. Sci Transl Med 2011; 3:112re4.
17. Kashuba AD, Patterson KB, Dumond JB, Cohen MS. Pre-exposure prophylaxis for HIV prevention: how to predict success. Lancet 2012;379(9835):2409-11. [DOI:10.1016/S0140-6736(11)61852-7].
18. US CDC. Interim guidance: preexposure prophylaxis for the prevention of HIV infection in men who have sex with men. MMWR 2011;60:65-8.