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Review article

Can we rely on the antiretroviral treatment as the only means for human immunodeficiency virus prevention? A Public Health perspective

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ABSTRACT

The evidence that supports the preventive effect of combination antiretroviral treatment (cART) in HIV sexual transmission suggested the so-called 'treatment as prevention' (TAP) strategy as a promising tool for slowing down HIV transmission. As the messages and attitudes towards condom use in the context of TAP appear to be somehow confusing, the aim here is to assess whether relying on cART alone to prevent HIV transmission can currently be recommended from the Public Health perspective.

A review is made of the literature on the effects of TAP strategy on HIV transmission and the epidemiology of other sexual transmitted infections (STIs) in the cART era, and recommendations from Public Health institutions on the TAP as of February 2014. The evolution of HIV and other STIs in Barcelona from 2007 to 2012 has also been analysed.

Given that the widespread use of cART has coincided with an increasing incidence of HIV and other STIs, mainly amongst men who have sex with men, a combination and diversified prevention methods should always be considered and recommended in counselling. An informed decision on whether to stop using condoms should only be made by partners within stable couples, and after receiving all the up-to-date information regarding TAP.

From the public health perspective, primary prevention should be a priority; therefore relying on cART alone is not a sufficient strategy to prevent new HIV and other STIs.

¿Podemos confiar en el tratamiento antirretroviral como único método para la prevención del virus de la inmunodeficiencia humana? Una perspectiva de Salud Pública

Palabras clave:
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RESUMEN

La efectividad del tratamiento antirretroviral (TAR) combinado en la reducción de la transmisión del VIH ha impulsado la estrategia «tratamiento como prevención» (TcP) como herramienta prometedora para controlar la epidemia del VIH. Debido a que los mensajes y actitudes respecto al uso del preservativo en el contexto del TcP pueden parecer confusos, en este trabajo se evaluó si usar únicamente TAR como estrategia de prevención puede ser recomendado desde una perspectiva de Salud Pública.

Se hizo una revisión de la literatura sobre la efectividad del TAR en la transmisión del VIH y epidemiológica de otras infecciones de transmisión sexual (ITS). También se realizó una revisión de las recomendaciones vigentes (febrero 2014) sobre TcP desde diferentes instituciones de Salud Pública. Asimismo, se analizó la evolución del VIH y otras ITS en Barcelona durante el periodo 2007–2012.

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Dado que el amplio uso del TAR ha coincidido con un aumento en la incidencia del VIH y otras ITS, especialmente entre hombres que tienen sexo con hombres, en el consejo asistido se contempla la utilización combinada de diferentes métodos de prevención. La decisión sobre el uso del preservativo se debe tomar en el seno de las parejas estables serodiscordantes, con pleno conocimiento de los riesgos y limitaciones del TAR cuando se utiliza como único medio de prevención. Desde la perspectiva de la Salud Pública, la prevención primaria debe ser una prioridad. Confiar en el TAR solamente como una estrategia de prevención de nuevas infecciones por el VIH y otras ITS no sería suficiente, ya que el éxito del TcP depende no solo de diagnosticar y tratar adecuadamente, sino también de mantener conductas de sexo seguro para evitar la transmisión de ITS, de realizar controles clínicos adecuados y de tener acceso continuado al TAR.

Background and rationale

Antiretroviral therapy in post-exposure prophylaxis (PEP) and in pre-exposure prophylaxis (PrEP) is effective,[1] and a Cochrane review of 25 clinical trials documented the benefits of the combination antiretroviral treatment (cART) in limiting the risk of mother-to-child transmission of HIV infection.[2] These findings have served as a basis for recommendations regarding prevention of vertical HIV transmission and helped to formulate algorithms for PEP protocols and approved PrEP use for certain high-risk groups.[3] An observational study published in 2010[4] and a clinical trial[5] demonstrated also the role of cART in the prevention of HIV transmission from HIV-infected persons to their sexual partners.

A mathematical model presented in 2006 predicted that providing cART to every HIV-positive person in the world would stop the HIV epidemic within 50 years.[6] Since then, extensive efforts have been made in the province of British Columbia, Canada, to support the test-and-treat strategy, including expanding HIV testing by implementing the programme of routine testing in emergency departments for individuals with no prior risk factors or indications for HIV testing, and promoting earlier access to cART. As a result, the proportion of HIV-infected people with undetectable viral load increased and that has been accompanied by substantial reduction in new diagnoses of HIV in this province.[7] Several attempts to analyse the cost-effectiveness of the treatment as prevention (TAP) strategy strongly indicated cost-saving effect of early initiation of cART over time.[8,9]

However, other studies indicate that even in the communities where a high proportion of HIV-infected persons receive cART and have undetectable viral loads, the incidence of HIV is similar to estimates reported from developed country settings in the pre-cART era.[10] Furthermore, the changing perception of the risk of transmission from HIV-positive persons on cART may influence the frequency of high-risk sexual behaviour.[11]

The aim of this paper is to assess whether relying on cART alone is a sufficient strategy in preventing HIV in the community and individual level, based in existing evidence and recommendations from national and international public health institutions; and reviewing the evolution of HIV and other STIs during the period 2007–2012 using surveillance data from a large city (Barcelona) where cART is universally provided. For the literature review, we searched PubMed electronic database for original articles and reviews published in English and Spanish from 2008–2013 on cART in the context of prevention of sexual HIV transmission, challenges of HIV prevention strategies based on condom and reemerging STI since the introduction of cART. As well, we have identified important relevant publications published before 2008 using the snowball method by checking the references of selected papers, and finally included most recent publications as of June 2014.

Impact of cART on sexual HIV transmission – current evidence

The idea that cART might decrease the spread of the HIV infection by reducing the infectivity of treated HIV-positive persons has been considered since the late 1990s. A clear association between the plasma viral load and the risk of onwards transmission of HIV was identified already in 2000, indicating that transmission is rare among persons with less than 1500 copies of HIV-1 RNA per millilitre.[12]

Several independent systematic reviews of the observational studies and randomised control trials conducted among heterosexual serodiscordant couples have been published recently. In three studies where the virologic suppression by cART was documented, the rate of transmission was 0 per 100 person-years with a 95% confidence interval (CI): 0 to 0.05.[13] The Cochrane review in 2013[14] and the review conducted by Attia and colleagues in 2009 similarly suggested that the risk of sexual transmission for heterosexual serodiscordant couples when the HIV-positive partner was on suppressive treatment was minimal.[15]

The strongest evidence gained in a clinical trial regarding the protective effect of the cART on HIV transmission in serodiscordant couples came from the HPTN-052 study.[5] It included 1763 serodiscordant couples divided into two groups based on the timing of the cART initiation: receiving cART either immediately (early therapy) or after a decline in the CD4 count or the onset of HIV-1-related symptoms (delayed therapy). Importantly, all couples received counselling on every visit and were provided with free condoms. Overall 39 HIV-1 transmissions were observed (incidence rate: 1.2 per 100 person-years; CI: 0.9 to 1.7). Of these, 28 were virologically linked to the infected partner (incidence rate: 0.9 per 100 person-years, CI: 0.6 to 1.3). Only one of the 28 linked transmissions was reported in the early-therapy group (hazard ratio: 0.04; CI: 0.01 to 0.27; $p < 0.001$). Based on these findings, the authors concluded that early initiation of cART reduced linked transmissions by 96%. The only genetically confirmed transmission from an HIV-positive participant on cART happened at the early stage of the treatment; before achievement of an undetectable viral load.

Concerns have been raised about the external validity the results of the HPTN-052 trial among those engaging in anal intercourse, including MSM and transgendered persons (among its 1763 serodiscordant couples, only 37 were MSM) as the rate of transmission per-act associated with anal intercourse in persons who are not on suppressive cART is greater than the rate associated with penile-vaginal intercourse.[16] However, interim results of an ongoing observational study among serodiscordant MSM couples, presented in March 2014, suggested that cART may substantially reduce the risk of HIV transmission also during anal sex.[17]

In the same time, many investigators have pointed on the fact that still there is not enough scientific evidence to state that the risk of the HIV transmission from the person on effective cART is practically zero, because there is evidence that plasma viral load