

Strategies to prevent HIV transmission to serodiscordant couples

Estratégias de prevenção da transmissão do HIV para casais sorodiscordantes

Ronaldo Campos Hallal^I, Juan Carlos Raxach^{II}, Nêmorea Tregnago Barcellos^{III}, Ivia Maksud^{IV}

ABSTRACT: *Introduction:* The use antiretroviral reduces the sexual transmission of HIV, expanding interventions for serodiscordant couples. *Objective:* This article aims to review the use of antiretroviral and other prevention interventions among serodiscordant couples and to analyze its use in Brazil. *Methods:* A retrospective review was performed through the MEDLINE database and bases included in the Biblioteca Virtual em Saúde. *Results:* The articles recovered exhibit four main strategies: (1) condom; (2) reduction of risks in sexual practices; (3) use of antiretrovirals, particularly early initiation of antiretroviral therapy (TASP) and pre-exposure prophylaxis (PrEP); (4) risk reduction in reproduction. *Discussion:* TASP is highly effective in reducing sexual transmission, PrEP was tested in serodiscordant couples and both reduce the sexual transmission risk in different sexual practices, enabling individualized prevention strategies. *Conclusions:* When used in combination, antiretrovirals and sexual practices with condoms offer greater efficacy than any single strategy. The combined use of new and old strategies allows us to build a prevention policy for all.

Keywords: Acquired immunodeficiency syndrome. Health care. Sexuality. HIV seropositivity. Health services. Health public policy.

^ISanta Casa de Porto Alegre – Porto Alegre (RS), Brasil.

^{II}Associação Brasileira Interdisciplinar de AIDS – Rio de Janeiro (RJ), Brasil.

^{III}Graduate Program in Public Health, Universidade do Vale do Rio dos Sinos; Hospital Sanatório Partenon; State Secretaria of Health – Porto Alegre (RS), Brasil.

^{IV}Instituto Fernandes Figueira, Fundação Oswaldo Cruz – Rio de Janeiro (RJ), Brasil.

Corresponding author: Ronaldo Campos Hallal. Avenida Mariland, 1043, casa 5, São João, CEP: 90040-191, Porto Alegre, RS, Brasil. E-mail: rcamposhallal@gmail.com

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RESUMO: *Introdução:* O emprego de antirretrovirais reduz a transmissão sexual do HIV, ampliando possibilidades de prevenção da sua transmissão em casais sorodiscordantes. *Objetivo:* Revisar a utilização de antirretrovirais combinados com outras estratégias na prevenção entre casais sorodiscordantes e analisar seu emprego no Brasil. *Métodos:* A revisão foi realizada na base de dados MEDLINE e nas bases incluídas na Biblioteca Virtual em Saúde. *Resultados:* Os artigos encontrados exibem quatro principais estratégias: (1) uso de preservativos; (2) hierarquização de riscos por exposição sexual; (3) emprego de antirretrovirais, especialmente o início precoce do tratamento (TASP) e profilaxia pré-exposição (PrEP); (4) redução de riscos na reprodução. *Discussão:* A TASP, com elevada eficácia na diminuição de transmissão sexual, e a PrEP, avaliada em casais sorodiscordantes, reduzem o risco de transmissão sexual do HIV em diferentes práticas sexuais, possibilitando individualizar as estratégias de prevenção. *Conclusões:* O uso combinado de novas e antigas estratégias possibilita construir uma política de prevenção para todos.

Palavras-chave: Síndrome de imunodeficiência adquirida. Atenção à saúde. Sexualidade. Soropositividade para HIV. Serviços de saúde. Políticas públicas de saúde.

INTRODUCTION

New studies about reducing the risks of sexual transmission of HIV by employing strategies combined with the use of antiretrovirals (ARV) extend possibilities of intervention for serodiscordant couples (partners with different serology for HIV). These relationships are becoming more frequent, given the improvement of the quality and expectancy of life of people living with HIV (PLHIV)¹.

In the situation of serodiscordance, social identities and sexual orientation can be flexible, with various possibilities of marital arrangements, in addition to monogamy. The notions of heterosexuality, homosexuality and bisexuality may vary according to the understanding of the subjects, their trajectory and temporality².

In 2010, the Ministry of Health (MOH) published ARV usage recommendations to prevent sexual transmission of HIV using sexual post-exposure prophylaxis (PEP) and antiretroviral therapy (ART) to reduce the risk of sexual transmission in the context of reproductive desire, strengthening the right to reproduction³.

The Joint United Nations Programme on HIV/ AIDS (UNAIDS) included, among its goals for 2010 – 2015, what was defined as “the political revolution and HIV prevention practices,” proposing to focus efforts on serodiscordant couples establishing new interventions that impact the transmission of HIV⁴.

In April 2012, the World Health Organization (WHO) released prevention strategies for serodiscordant couples, recommending the increased supply of testing and counseling for couples and partners, and the provision of ART for HIV-positive partners, in order to prevent sexual transmission. In 2014 the MS published a recommendation to stimulate the earlier start of ART, in order to reduce risk of transmission, regardless of the LT-CD4+⁵.

Therefore we reflect on prevention from the ability to manage risks according to specific contexts, considering three plans that are intertwined:

1. the policy formulation and management plan;
2. the plan of the subjects;
3. the plan of the “operators” of prevention (health teams and activists). In this sense, we situate the debate on “risk management” within the vulnerability framework, considering its three levels: social, programmatic and individual^{6,7}.

The possibility of using antiretrovirals to prevent HIV transmission modifies the field of comprehensive care for couples, based almost exclusively on promoting the use of condoms. Strategies such as the use of pre-exposure prophylaxis (PrEP) can help change the model of care, through the need of following seronegative partners of PLHIV, as the current culture in the health system is following only PLHIV^{8,9}. The treatment of PLHIV to prevent sexual transmission (TASP) requires counseling and approach of continued sexuality.

This article aims to review the individualized use of ARVs for prevention among serodiscordant couples, combined with other prevention measures, analyzing scenarios and implications for its use in Brazil.

METHODOLOGY

The review was conducted through MEDLINE and the bases included in the Virtual Health Library (VHL/BVS). The latter includes Latin American publications and, more specifically, Brazilian ones, using information from LILACS, Spanish Bibliographic Index of Health Sciences (IBECS), MEDLINE and SciELO. The choice of these bases allowed the analysis of international, regional and local literature on the subject of this review.

In MEDLINE, initially the following descriptors were used: *hiv, acquired immunodeficiency syndrome, AIDS, transmission, prevention, control, serodiscordant couples* and *mixed status*. In a second search, the term *transmission* was removed. A limit was not established for period of publication or language.

The keywords used in the research of VHL included HIV, AIDS and serodiscordant couples, in an integrated manner. All attempts to limit the search, include terms in other languages or detail the descriptors, resulted in reducing the number of retrieved documents and were abandoned.

Retrieved documents were organized in tables. After an initial selection of articles based on their titles, those directly related to the review topic were maintained and categorized by subject. Based on the abstracts, those specifically with prevention strategies among serodiscordant couples that form the basis of this text were included. There were also documents published by non-governmental organizations (NGOs). Documents and international institutions documents, in addition to abstracts presented at congresses, seminars and conferences, and articles identified in the references of the read documents were also included in the review.

RESULTS

The total of findings of the databases based on the keywords are:

- MEDLINE: 1,501 articles (the first search resulted in 605 articles and the second in 1,381 articles, 485 being repeated articles). Among those identified, 64% were published from 2010 on, and 238 articles were selected to aggregate information for this review. Of these, 67 deal with reproduction including in vitro fertilization techniques, 28 studied PrEP, 18 address antiretroviral treatment as prevention, 8 evaluate the use of condoms, and the others address different aspects of prevention of HIV transmission;
- VHL: 26 documents were identified when the terms were searched in an integrated manner. Of these, after full reading, 18 articles remained. Three articles recovered in the databases were also located in MEDLINE. All these articles were considered in the review and 32 of them were actually included, along with 5 official documents and/or recommendations and 1 summary presented in congress. The articles found present four main strategies of prevention among serodiscordant couples: condoms, risk prioritization, use of ARVs and prevention measures in the context of conception.

USE OF CONDOMS

The use of condoms has been the main strategy for prevention and offers high efficiency to avoid HIV transmission and other sexually transmitted diseases (STDs) with favorable cost-benefit ratio. Among serodiscordant couples, the annual risk of HIV transmission can be reduced from 20 – 25% to 3 – 7% with the consistent use of male condoms¹. Moreover, the use of condoms may be low or irregular in different sexual practices of PLHIV^{2,7}. Serodiscordant couples have greater compliance than the general population, though it varies from 39.2% in serodiscordant couples in general⁶, reaching 78.5% in serodiscordant couples where the woman is seropositive⁹.

In most cases, the difficulties in condom use are associated with matters as gender, power relations, decreased pleasure, lack of confidence and advanced age^{3,8}. In some situations, the use of condoms is replaced by the risk prioritization with the choice of “lower risk” practices, such as oral sex⁴.

RISKS AND SEXUAL PRACTICES

The practice of unprotected anal sex is the main mode of HIV transmission; the lack of knowledge of serology represents an additional risk of 50% while engaging in unprotected sexual practices⁵.

A model developed for Peru and the United States showed that, among men who have sex with men (MSM), an average of 32 and 39% of transmissions occur between steady partners. Also unprotected anal sex was related to HIV status, disclosure of HIV status and stage of the disease¹⁰.

American MSM who are social network users have been adopting risk reduction strategies in anal intercourse without the use of condoms¹¹. Among couples, this practice reinforces the satisfaction, love, intimacy and trust of the relationship¹².

A recent study addressing the construction of vulnerability dimensions between serodiscordant couples reveals that some couples who can not use condom, as an alternative, use ARV associated with a change in practices, such as avoiding anal sex and “withdrawal”¹³.

A US multicenter cohort identified 60 seroconversions among 2,189 MSM followed up for 18 months; unprotected anal sex, having more than one HIV-positive partner and condom breakage or slippage were associated with transmission. The estimated infectivity by sexual act in receptive anal intercourse without condoms, with HIV-positive partner, was 0.82%, with a confidence interval of 95% (95%CI) 0.24 – 2.76; and 0.18% (95%CI 0.10 – 0.28) in protected receptive anal intercourse with HIV-positive partner or unknown HIV status. Infectivity in protected anal insertion with seropositive partner or with unknown status was 0.04% (95%CI 0.01 – 0.11) and 0.06% (95%CI 0.02 – 0.19), when the relation was unprotected. In receptive oral practice with ejaculation, infectivity was 0.04% (95%CI 0.01 – 0.28)¹⁴.

A systematic review of the probability of HIV transmission, with or without ARTs, in annals practices, analyzed studies published up to 2010. Studies describing infectivity by sex (4 studies) and partnership (12 studies) were included. The population of these studies involved homosexual couples (12 studies), heterosexual (3 studies) or both (1 study) who had reported at least 50% of anal penetrations where the partner was known to be HIV positive. Considering only those with detailed methodological description, two estimates involving homosexual couples and two involving heterosexual couples were included, identifying risk of transmission by sexual act of 1.8% (95%CI 0.3 – 3.2) for unprotected receptive anal sex, between heterosexual and homosexual couples ($p = 0.674$). The risk of transmission was 1.38% (95%CI 0.0 - 3.38) when the HIV-positive was in the asymptomatic period and 18.35% (95%CI 2.08 – 34.6) when there was a diagnosis of AIDS. Given the heterogeneity of the analytical method, the probability of transmission per sexual act in unprotected insertive anal intercourse could range from 0.0002 to 0.013%; and in unprotected receptive anal intercourse from 0.0011 to 0.061%¹⁵.

An African cohort analyzed for 24 months 3,297 serodiscordant heterosexual couples (67% HIV-positive women) performing successive viral load measures to assess the factors associated with transmissibility¹⁶. The seropositive partner monthly informed the number of sexual intercourse and condom use, reported in 93% of sexual contacts. The median of protected and unprotected sex was three and zero, respectively. There were 86 transmissions

genetically related to the partner; in three of them (3.5%), the positive partner reported that there was no sexual relationship in the period preceding the transmission. The transmission rate for unprotected sex was 0.0019 (95%CI 0.0010 – 0.0037) in men-women and 0.0010 (95%CI 0.0006 – 0.0017) in women-man, and a relative risk (RR) of 1.03 ($p = 0.93$) was found when adjusted for viral load (VL), indicating that the increased risk in men-women was due to higher VL ($4.1 \log_{10}$ $3.8 \log_{10}$). The use of condoms reduced infectivity by 78% (RR = 0.22; 95%CI 0.11 – 0.42), regardless of the sex of the positive partner. Median sex dropped from 4.0 on the inclusion to 2.5 in the 24th follow-up month¹⁶.

PREVENTION THROUGH THE USE OF ANTIRETROVIRALS

Among serodiscordant couples, there are three prevention strategies with ARV use that can be considered:

- a) the initiation of antiretroviral therapy in PLHIV;
- b) PrEP; and
- c) nPEP. The discussion will focus on the results of TASP and PrEP studies among serodiscordant couples.

Antiretroviral treatment and reduction of HIV transmission

In 2000, an observational study of serodiscordant couples in Uganda showed that the VL average was higher in couples in which partners were infected. A multivariate analysis showed that the increase of 1 logarithm to VL was associated with the incidence rate of HIV transmission in the range of 2.45 (95%CI 1.85 – 3.26); when VL was less than 1,500 copies/mm³, no transmission occurred¹⁷.

A meta-analysis published in 2009 with 5,021 serodiscordant heterosexual couples of 11 cohort studies identified 461 transmissions, a rate of 0.46/100 person/follow-up year (95%CI 0.19 – 1.09) when the positive partner was in treatment, representing a 92% reduction in sexual risk transmission¹⁸.

The multicenter cohort *Partners in Prevention HSV/HIV Transmission Study* gathered 3,381 serodiscordant heterosexual couples from 7 African countries that were followed up for 24 months with HAART, started when the HIV-positive person reached the indication criteria established in the guidelines of each country (usually LT-CD4 200 and 250 cells/mm³). During this period, 349 participants (10%) initiated HAART, with an LT-CD4 median count of 192 cells/mm³. 103 episodes of transmission genetically related to the index partner were identified (incidence of 2.13 in 100 person/year), and only one among couples in which PLHIV was treated, with a 92% reduction risk of HIV sexual transmission by the use HAART (5.64 to 0.46 transmissions in 100 person/year). The proportion of unprotected sex reports decreased from 6.2 to 3.7% among those

who started HAART, presenting no alterations in the number of sex relations/month. Among the 94 transmissions of the partner that was not on HAART, 70% occurred with VL > 50,000 copies. During the study there were 39 transmissions that were not genetically related, representing an incidence of 0.81 in 100 person/follow-up year¹⁹.

The *HIV Prevention Trials Network 052* study (HPTN052) was the first clinical trial with sexual transmission as the outcome. It was conducted in 13 centers in 9 countries and randomized 1,763 serodiscordant couples (97% heterosexual) with LT-CD4 between 350 and 550 cells/mm³ for immediate start of HAART, or clinical follow-up until the LT-CD4 count reached values ≤ 250 cells/mm³, when HAART was started. The follow-up median was 1.7 years, and in that period, 39 HIV transmissions were observed (incidence rate of 1.2/100 person/year, 95%CI 0.9 – 1.7). Four transmissions occurred in the early-onset group (incidence rate of 0.3/100 person/year – (95%CI 0.1 – 0.6), and 35 in the delayed treatment group (2.2/100 person/year; 95%CI 1.6 – 3.1). Among transmissions, 28 were genetically related to the virus of the index partner (incidence rate of 0.9/100 person/year, 95%CI 0.6 – 1.3); wherein the transmission in the immediate treatment group occurred in the first three months of HAART (incidence rate of 0.1/100 person/year; 95%CI 0.0 – 0.4) while in the delayed treatment group transmissions occurred before starting HAART (incidence rate of 1.7/100 person/year, 95%CI 1.1 – 2.5), 67% being in woman-man relations. There was no significant difference in estimates of STDs in the reported use of condoms and adherence rate to 95% of ARV doses. The study showed that the immediate start of HAART in people with LT-CD4 between 350 and 550 cells/mm³ reduced the risk of sexual acquisition of HIV of the seropositive partner in 96%, among serodiscordant heterosexual couples, compared with the delayed group²⁰.

The 2 year follow-up of the same study demonstrated that the probability of a primary clinical event (death, stage 4 of WHO, tuberculosis, severe cardiovascular, vascular, renal or hepatic diseases, diabetes mellitus or neoplasm not related to AIDS) was 4.8% (95%CI 3.6 – 6.5) in the group with immediate treatment (CD4 between 350 and 550), and 7.9% (95%CI 6.2 – 10.1) in the group with delayed treatment. The relative risk ratio (delayed treatment versus early treatment) of a primary event was 0.73 (95%CI 0.52 – 1.03; p = 0.074)²¹.

A retrospective analysis of the Chinese national database between 2003 and 2011 identified 56,726 PLHIV who reported having seronegative partner. Excluding those with incomplete information and those who had been treated in the past, there were 38,862 (68.5%) serodiscordant couples, 24,057 of them in treatment and 14,085 without treatment. Those who were in treatment had predominantly blood transfer transmission, LT-CD4 median of 168 cells/mm³ and 2.4 years follow-up, while the virgin treatment group had predominantly sexual transmission, 1.2 years follow-up and LT-CD4 median score of 441 cells/mm³. In this study, 1,631 transmissions were identified which indicates an incidence rate of 1.61/100 person/year (95%CI 1.5 – 1.7). The rates observed in those who were on and off HAART were 1.3/100 person/year (95%CI 1.2 – 1.3) and 2.6/100 person/year (95%CI 2.4 – 2.8), respectively, representing a 26% reduction

of HIV transmission with hazards ratio adjusted to 0.74 (95%CI 0.65 – 0.84) in the treated group. On the other hand, the protection of transmission only occurred in the first year, and there was no reduction of transmissions associated with HAART when PLHIV was infected by injecting drug use or male partner of the same sex. The most common way of transmission was woman-man partnerships, although presenting no statistic significance²².

Results of the PARTNER study, published in the proceedings of the 21th Conference on Retrovirus and Opportunistic Infections (CROI), included participants reporting unprotected sex with no use of PrEP or PEP and VL of seropositive partner < 200 copies/mL. During two years, no HIV transmission genetically related to index partner occurred among 1,100 serodiscordant couples in HAART, 440 of which formed by MSM²³.

A systematic review of HIV transmission among serodiscordant heterosexual couples analyzed studies published up to December 2012. The primary endpoint was the incidence of HIV in seronegative partnership of seropositive individual using HAART and with undetectable VL. Including studies of HIV transmission and detectable VL, the pooled incidence rate was 0.14/100 person/year (95%CI 0.04 – 0.31). In sensitivity analysis, excluding the transmissions that occurred with detectable VL, the transmission rate was 0/100 person/year (95%CI 0.00 – 0.01). These results did not include data on sexual practices, STDs or frequency of condom use, among other variables²⁴.

Pre-exposure prophylaxis

PrEP is defined as the use of ART for HIV-negative people to reduce the risk of sexual HIV acquisition. The most studied diagrams are daily use of Tenofovir (TDF) or a combination of TDF with Emtricitabine (FTC).

PARTNERS PrEP analyzed serodiscordant heterosexual couples in Kenya and Uganda (n = 4,747). In this study, seronegative partners of PLHIV were randomized to receive TDF (n = 1,584), TDF-FTC (n = 1,579) or placebo (n = 1,584). Of 82 transmissions, 17 occurred in the TDF group, 13 in the TDF-FTC and 52 in the placebo group, indicating a relative reduction in the incidence of 67% (95%CI 44 – 81) for TDF, and 75% for the use of TDF-FTC (95%CI 55 – 87)²⁵.

A systematic review of PrEP studies, published in 2012, which included 6 randomized and controlled trials and a total of 9,849 participants, showed that TDF+FTC and TDF alone were more effective than placebo in both sexes, and more effective in men than women, although this difference was not statistically significant. The occurrence of adverse events was rare, and it was concluded that the PrEP studies had adequate methodological quality and moderate quality of evidence for preventing HIV transmission²⁶.

In 2011, the center for Disease Control and Prevention (CDC) recommended the use of PrEP for MSM at high risk practices, and the following year the TDF-FTC combination was registered in the Food and Drug Administration (FDA) for PrEP,

boosting its adoption in cities with large-magnitude epidemics. In 2012 CDC included heterosexual in PrEP indication and, in 2014, drug users and serodiscordant couples in the context of reproduction²⁷. Viral resistance may occur and should be considered when there is an infection before the beginning of the treatment²⁸.

RISK REDUCTION IN REPRODUCTION

Some countries have developed support guidelines to reproduction among serodiscordant couples, based on studies published in the past years²⁹⁻³¹. Under these guidelines, the approach of reproduction may involve the use of high technological density strategies, such as sperm washing with intrauterine insemination or in vitro fertilization. The employment of strategies with less technological density consists of HAART for PLHIV, in order to suppress viral replication, scheduling unprotected sexual intercourse in the fertile period in the absence of STD and good compliance to HAART³².

The planning includes counseling related to reproduction among serodiscordant couples with the approach of potential risks of each strategy, review of sexual health by ensuring the absence of STD and fertility evaluation of the couple to avoid repeated exposure. Two scenarios are possible, and different strategies are indicated:

1. When the man is HIV positive: sperm washing with intrauterine insemination or in vitro fertilization is the strategy that offers the lowest transmission risk³³. The disadvantages are high cost and low availability in most public health services. In situations in which the male partner remains with undetectable VL for a long period, natural conception with scheduled intercourse for the fertile period may be considered. The use of PrEP by the female partner can further reduce the risk²⁹.
2. When the woman is HIV positive: self-insemination eliminates the risk of transmission to the seronegative partner, since it avoids contact with genital fluids of the partner. The use of ARV by HIV-negative partner, in situations where the positive partner has undetectable VL for a prolonged period is also a possible strategy to be used, in case the option is unprotected sexual intercourse in the fertile period. The treatment and undetectable VL of the positive partner are also determinants for preventing vertical HIV transmission^{30,31}.

DISCUSSION

The use of ART expands the list of strategies and provides individualization of measures to prevent sexual transmission of HIV in serodiscordant couples. Its combination with other methods, such as condom use and risk prioritization, increases the effectiveness of prevention, promotes greater security for planning reproduction and can help people

who have emotional or sexual repercussions for fear of transmitting HIV to their HIV-negative partners.

Some serodiscordant couples do not want or can not use condoms. In these cases, counseling should include information about the transmission risk associated with sexual practices for the couple negotiation. Receptive anal intercourses present higher risks than the insertive anal practices, and the lowest risk occurs in oral sex, especially without ejaculation in the oral cavity^{14,15}.

The suppression of viral replication reduces the risk of sexual transmission; its combination with the practice of withdrawal in vaginal and anal intercourse enhances the risk reduction among heterosexual or homosexual couples.

Since 2012, the WHO recommends demonstrating projects of effectiveness, safety, applicability and sustainability of the use of PrEP among serodiscordant couples³⁴. Considering its implementation, it is necessary that some strategies are enhanced, as the measure of adherence to ARV, evaluation and monitoring of risk, and the estimated long-term toxicity among patients with comorbidities that may enhance the adverse effects of medications.

The use of PrEP should be considered for seronegative partnership when PLHIV is not in use or HAART, or when presenting detectable VL. There are no models of care to seronegative partnerships implemented in Brazil. Testing and counseling centers (TCC) advise on and address sexuality, necessary elements in the context of serodiscordance. However, in general, there are no doctors in their teams and no experience or training in the management of ARVs.

On the other hand, the Specialized Assistance Services for HIV and AIDS (SAE) perform the management of ARV since its implementation at the end of the 1980 decade. Among the main difficulties for these services to follow up seronegative partnerships are their predominantly biomedical approach and the great current demand for services to PLHIV, as their structures did not expand to the same extent as the number of people in clinical follow-up.

In some areas, about 30% of HIV transmissions are related to fixed partnerships³⁵, suggesting that the PLHIV treatment may have an impact on the reduction of incidence. In the decision to initiate HAART, particularly when the main objective is to reduce the transmission to sexual partners, the motivation of PLHIV in protecting their partnership should be carefully considered. Also, the possibility of future loss of motivation should be discussed, among other reasons, because of the dissolution of the relationship. The PLHIV must be informed of the potential clinical benefits of early treatment and the implications of stopping treatment. In this sense, HAART reduced the occurrence of clinical events in people with LT-CD4 < 550 cells²¹. Its use in prevention in serodiscordant relationships is still a recent intervention that imposes the need for dissemination and awareness among health professionals.

The available studies have not identified HIV transmission when the seropositive partner uses HAART with suppression of viral replication. However, these studies do

not provide detailed data on sexual activity, making it difficult to understand the risk associated with sexual intercourse, practices and sexual partnership, important elements for individualized advice. The presentation of results in incidence rate per 100 person/follow-up year makes it difficult to implement it in the context of counseling.

The variations present in studies may be related to differences in the distribution of risk factors in the analyzed populations, sexual behavior, duration and frequency of unprotected exposure, or presence of cofactors for transmission. The duration of studies (usually up to two years) limits the risk assessment throughout the life of serodiscordant couples.

In studies that genetically analyzed new infections in a previously negative partner, 20 to 38% of them did not relate to a stable partnership, but had been acquired out of the preferential relationship^{19,20,36}. When considering all infections, the effectiveness of TASP was 89%, showing that for some couples this strategy is insufficient^{10,20}. The lack of protection of seronegative partners in exposures with other people must be part of counseling, aiming the adoption of condoms. Available data on sexual transmission between same-sex couples on HAART and suppressed viral replication involved small samples, and detailed description is not yet available in the literature²³. The lack of information about HIV transmission in this population with use of TARV²⁴ limits the extrapolation of the studies results involving mostly heterosexual couples. Although the risk of transmission through insertive anal intercourse is similar between same-sex and heterosexual couples, the largest frequency of exposure increases the risk for same-sex couples.

Among 86 genetically related transmissions, 56 (65%) occurred in the period when the HIV positive partner reported unprotected sex, also indicating the existence of limitations in the studies that address transmissibility by sexual act¹⁶. The relative risk of sexual transmission changes depending on the viral load: each 10-fold increase in plasma viral load corresponds to a 2.9-fold increase in the risk of transmission at each sexual relationship¹⁶.

For optimizing TASP it is necessary to have an early diagnosis, ongoing counseling and approach to PLHIV sexuality, a dimension rarely considered in the reality of SAE.

Adherence and retention actions to treatment over time are insufficiently introduced in network services, even for populations with a higher risk of disease progression and death. In USA, only 45 to 55% of those who initiate HAART remain at clinical follow-up after 1 year³⁷. The Ministry of Health estimates that there are 718,000 PLHIV in Brazil; 574,000 diagnosed, 436,000 performing monitoring tests, 313,000 on HAART and 236,000 with undetectable VL³⁸, which shows the need to expand access to diagnosis, care and treatment. Actions to maintain care over time should be intensified, with consensual approach, alerts for poor compliance and establishing a network that includes managers, teams of SAE, the Family Health Strategy, civil society organizations and community initiatives. Access to exams and VL results is still limited, and often does not allow the identification of viral replication in time to prevent it.

The awareness of health teams to approach the desire of having kids is essential in the management of couples, given the demand for advice on issues related to reproductive planning. In general, the guidelines recommend high technological density approaches, little available in our segment. Such strategies are particularly important when the man is HIV positive. Risk reduction measures, with the use of PrEP, TASP and nPEP are currently recommended in Brazil in planning reproduction.

CONCLUSIONS

Several studies have drawn attention to the importance of providing different alternatives for PLHIV prevention and serodiscordant pairs¹³. The use of a single measure, such as TASP, may not be enough to prevent sexual transmission to seronegative partners, as an expressive part of them occurs in external sexual relations.

When used in combination, HAART, condoms and/or risk prioritization are more effective than any single strategy. For serodiscordant couples who do not want to or cannot use condoms, PLHIV treatment with viral suppression monitoring by the couple, combined with the choice of lower-risk sexual practices, including the withdrawal, optimize the reduction of transmission risk. It is important that health professionals include these interventions in counseling and in the “prevention speech”.

Preparing our health system for these interventions in serodiscordant couples involves modifying the current model of prevention, structuring the longitudinal follow-up of seronegative partners of PLHIV, providing inputs, ongoing counseling, regular HIV testing, routine evaluation of sexual health, STD treatment and individualized HAART indication. It is also necessary to qualify the reception and listening of health teams to reproductive planning with training, removal of access barriers to new prevention measures and reproduction procedures, including those of high technological density when the man is HIV positive.

The use of HAART to prevent sexual transmission among serodiscordant couples promotes quality of life, if it is based on the principle of individualization. The autonomous decision — therefore informative — of PLHIV in performing the treatment must be ensured in the implementation of the strategy, advancing the achievement of individual rights, such as sexual and reproductive rights, the right to prevention and universal access to treatment.

Finally, it is essential to establish an interdisciplinary dialogue on the various prevention strategies, considering contexts and situations to indicate each tool or technology, allowing us to build a prevention policy for everyone.

REFERENCES

- Dunkle KL, Stephenson R, Karita E, Chomba E, Kayitenkore K, Vwalika C, et al. New heterosexually transmitted HIV infections in married or cohabiting couples in urban Zambia and Rwanda: an analysis of survey and clinical data. *Lancet* 2008; 371(9631): 2183-91.
- van der Straten A, Gómez CA, Saul J, Quan J, Padian N. Sexual risk behaviors among heterosexual HIV serodiscordant couples in the era of post-exposure prevention and viral suppressive therapy. *AIDS* 2000; 14(4): F47-54.
- Reis RK, Gir E. Convivendo com a diferença: o impacto da sorodiscordância na vida afetivo-sexual de portadores do HIV/AIDS. *Rev Esc Enferm USP* 2010; 44(3): 759-65.
- Monteiro S. Perspectivas sócio-históricas na saúde: concepções sobre prevenção - prevenção ao HIV/AIDS: lições e dilemas. In: Fiocruz, editor. *O Clássico e o Novo: tendências, objetos e abordagens em ciências sociais e saúde*. Rio de Janeiro: Fiocruz; 2003. 444 p.
- Coates TJ. What is to be done? *AIDS* 2008; 22(9): 1079-80.
- Cunha GH, Galvão MTG. Métodos contraceptivos e de prevenção da transmissão/reinfecção do vírus entre portadores de HIV/aids. *Rev Rene* 2011; 12(4): 699-708.
- Hanif H, Bastos FI, Malta M, Bertoni N, Winch PJ, Kerrigan D. Where does treatment optimism fit in? Examining factors associated with consistent condom use among people receiving antiretroviral treatment in Rio de Janeiro, Brazil. *AIDS Behav* 2014; 18(10): 1945-54.
- Paiva V, Venturi G, França-Júnior I, Lopes F. Uso de preservativos: pesquisa Nacional MS / IBOPE, Brasil 2003. Disponível em: http://www.ip.usp.br/portal/images/stories/Nepaids/Relatrios/uso_de_preservativos.pdf (Acessado em 08 de dezembro de 2014).
- Santos NJS, Buchalla CM, Fillipe EV, Bugamelli L, Garcia S, Paiva V. Mulheres HIV positivas, reprodução e sexualidade. *Rev Saúde Pública* 2002; 36(4 Suppl 0): 12-23.
- Goodreau SM, Carnegie NB, Vittinghoff E, Lama JR, Sanchez J, Grinsztejn B, et al. What drives the US and Peruvian HIV epidemics in men who have sex with men (MSM)? *PLoS One* 2012; 7(11): e50522.
- Mitchell JW. HIV-negative and HIV-discordant gay male couples' use of HIV risk-reduction strategies: differences by partner type and couples' HIV-status. *AIDS Behav* 2013; 17(4): 1557-69.
- Greene GJ, Andrews R, Kuper L, Mustanski B. Intimacy, monogamy, and condom problems drive unprotected sex among young men in serious relationships with other men: a mixed methods dyadic study. *Arch Sex Behav* 2014; 43(1): 73-87.
- Fernandes NM. Vulnerabilidade ao HIV/AIDS entre casais sorodiscordantes acompanhados no Instituto de Pesquisa Clínica Evandro Chagas/Fiocruz. Rio de Janeiro: FIOCRUZ; 2013.
- Vittinghoff E, Douglas J, Judson F, McKirnan D, MacQueen K, Buchbinder SP. Per-contact risk of human immunodeficiency virus transmission between male sexual partners. *Am J Epidemiol* 1999; 150(3): 306-11.
- Baggaley RF, White RG, Boily MC. HIV transmission risk through anal intercourse: systematic review, meta-analysis and implications for HIV prevention. *Int J Epidemiol* 2010; 39(4): 1048-63.
- Hughes JP, Baeten JM, Lingappa JR, Magaret AS, Wald A, de Bruyn G, et al. Determinants of per-coital-act HIV-1 infectivity among African HIV-1-serodiscordant couples. *J Infect Dis* 2012; 205(3): 358-65.
- 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(13): 921-9.
- Attia S, Egger M, Müller M, Zwahlen M, Low N. Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis. *AIDS* 2009; 23(11): 1397-404.
- Donnell D, Baeten JM, Kiarie J, Thomas KK, Stevens W, Cohen CR, et al. Heterosexual HIV-1 transmission after initiation of antiretroviral therapy: a prospective cohort analysis. *Lancet* 2010; 375(9731): 2092-8.
- Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 2011; 365(6): 493-505.
- Grinsztejn B, Hosseinipour MC, Ribaudo HJ, Swindells S, Eron J, Chen YQ, et al. Effects of early versus delayed initiation of antiretroviral treatment on clinical outcomes of HIV-1 infection: results from the phase 3 HPTN 052 randomised controlled trial. *Lancet Infect Dis* 2014; 14(4): 281-90.
- Jia Z, Mao Y, Zhang F, Ruan Y, Ma Y, Li J, et al. Antiretroviral therapy to prevent HIV transmission in serodiscordant couples in China (2003-11): a national observational cohort study. *Lancet* 2013; 382(9899): 1195-203.

23. Rogers A. HIV transmission risk through condomless sex if HIV+ partner on suppressive ART: PARTNER Study. In: 21st Conference on Retroviruses and Opportunistic Infections. Boston: CROI; 2014.
24. Loutfy MR, Wu W, Letchumanan M, Bondy L, Antoniou T, Margolese S, et al. Systematic review of HIV transmission between heterosexual serodiscordant couples where the HIV-positive partner is fully suppressed on antiretroviral therapy. *PLoS One* 2013; 8(2): e55747.
25. Baeten JM, Donnell D, Ndase P, Mugo NR, Campbell JD, Wangisi J, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *N Engl J Med* 2012; 367(5): 399-410.
26. Okwundu CI, Uthman OA, Okoromah CA. Antiretroviral pre-exposure prophylaxis (PrEP) for preventing HIV in high-risk individuals. *Cochrane Database Syst Rev* 2012; 7: CD007189.
27. US Public Health Service. Centers for Disease Control and Prevention (CDC). Preexposure prophylaxis for the prevention of HIV infection in the United States - 2014: a clinical practice guideline. Atlanta: CDC; 2014. 67 p.
28. Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med* 2010; 363(27): 2587-99.
29. National Institutes of Health (NIH). Public Health Service Task Force. Recommendations for use of antiretroviral drugs in pregnant HIV-1-infected women for maternal health and interventions to reduce perinatal HIV-1 transmission in the United States. Maryland: NIH; 2014. 64 p.
30. Fakoya A, Lamba H, Mackie N, Nandwani R, Brown A, Bernard E, et al. British HIV Association, BASHH and FSRH guidelines for the management of the sexual and reproductive health of people living with HIV infection 2008. *HIV Med* 2008; 9(9): 681-720.
31. Brasil. Recomendações para a terapia antiretroviral em adultos infectados pelo HIV – Suplemento III: tratamento e prevenção. Brasília: Ministério da Saúde; 2010.
32. Chadwick RJ, Mantell JE, Moodley J, Harries J, Zweigenthal V, Cooper D. Safer conception interventions for HIV-affected couples: implications for resource-constrained settings. *Top Antivir Med* 2011; 19(4): 148-55.
33. Semprini AE, Macaluso M, Hollander L, Vucetich A, Duerr A, Mor G, et al. Safe conception for HIV-discordant couples: insemination with processed semen from the HIV-infected partner. *Am J Obstet Gynecol* 2013; 208(5): 402.e1-9.
34. World Health Organization (WHO). Guidance on pre-exposure oral prophylaxis (PrEP) for serodiscordant couples, men and transgender women who have sex with men at high risk of HIV: recommendations for use in the context of demonstration projects. Geneva: WHO; 2012. 19 p.
35. van den Boom W, Konings R, Davidovich U, Sandfort T, Prins M, Stolte IG. Is serosorting effective in reducing the risk of HIV infection among men who have sex with men with casual sex partners? *J Acquir Immune Defic Syndr* 2014; 65(3): 375-9.
36. Eshleman SH, Hudelson SE, Redd AD, Wang L, Debes R, Chen YQ, et al. Analysis of genetic linkage of HIV from couples enrolled in the HIV Prevention Trials Network 052 trial. *J Infect Dis* 2011; 204(12): 1918-26.
37. Gardner EM, McLees MP, Steiner JF, Del Rio C, Burman WJ. The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clin Infect Dis* 2011; 52(6): 793-800.
38. Brasil. Ministério da Saúde. Boletim Epidemiológico: AIDS e DST. Brasília: Ministério da Saúde; 2013.

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