Review

A meta-analysis of effectiveness of interventions to improve adherence in pregnant women receiving antiretroviral therapy in sub-Saharan Africa

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A R T I C L E   I N F O

A B S T R A C T

Objective: We evaluated the effectiveness of interventions aimed at improving antiretroviral therapy (ART) adherence during pregnancy in sub-Saharan Africa.
Methods: For this meta-analysis, the following databases were searched: MEDLINE Complete, Embase, Global Health, CINAHL Complete, and Google Scholar. Randomized and nonrandomized studies were considered for inclusion if they involved an intervention with the intent of improving medication adherence among pregnant women taking ART in sub-Saharan Africa. Databases were searched from inception to the end of August 2017. The primary outcome assessed was adherence to ART, defined as the proportion of women adherent to treatment in the control and intervention groups. Risk ratios and random effect meta-analysis were undertaken, and heterogeneity was examined with the I^2 statistic.
Results: The systematic search of databases yielded a total of 402 articles, of which 19 studies were selected for meta-analysis with a total of 27,974 participants. Nine types of interventions were identified in the 19 studies to improve ART adherence. The test for the subgroup differences showed that there was a statistically significant difference among the 9 subgroups of interventions, χ^2 (8) = 102.38; p = 0.00001. Collectively, in the meta-analysis, the various intervention types made a significant impact on improving medication adherence. The overall effect estimate with 95% CI was as follows: 1.25 (95% CI = 1.03, 1.52, p = 0.03). The following risk ratio results for meta-analysis were obtained for the three interventions that showed significant impact on adherence; namely social support and structural support, 1.58 (95% CI = 1.36, 1.84, p < 0.00001); education, social support and structural support = 2.60 (95% CI = 1.95, 3.45, p < 0.00001); and device reminder = 1.13 (95% CI = 1.05, 1.20, p = 0.0004). The proportion of women who were adherent to ART as a result of the interventions was 59.3% compared with 22.5% in the control groups.
Conclusion: The use of device reminder, a combination of social support and structural support, and education, social support and structural support has the potential to improve ART adherence during pregnancy. Good quality prospective observational studies and randomized control trials are needed in sub-Saharan Africa to determine the most effective interventions.

Contents

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Introduction

Living with human immunodeficiency virus (HIV) is a major health problem for pregnant women in sub-Saharan Africa. As of the end of 2015, approximately 90% of the 1.4 million pregnant women with HIV lived in sub-Saharan Africa with over 90% of pediatric HIV cases occurring as a result of mother-to-child transmission (MTCT) (UNICEF, 2016; UNAIDS, 2015). Geographically, sub-Saharan Africa comprises the African continent that lies south of the Saharan Desert and includes 49 countries.

A pooled analysis of outcomes of infants infected with HIV in sub-Saharan Africa showed that 35% and 52% of children living with HIV die by the age of one and two years respectively (Newell et al., 2004). Without antiretroviral therapy (ART), from 20 to 45% of infants born to mothers living with HIV will become infected (De Cock et al., 2000). ART refers to the use of 3 or more antiretroviral drugs that suppress HIV replication. Adherence using ART can lead to virtual elimination of pediatric HIV, reducing the risk of transfer to less than 2% (Cooper et al., 2002). A Global Plan aimed at eliminating new pediatric HIV infections and increasing maternal survival was launched in 2011 at a United Nations General Assembly High Level Meeting on AIDS, prioritizing 22 countries accounting for 90% of pregnant women living with HIV. The priority countries comprise 21 sub-Saharan African countries and India. According to the Joint United Nations Programme on HIV/AIDS (UNAIDS), in its final accountability report of the Global Plan released in 2016, a key goal was to decrease HIV infections among children resulting from MTCT by 90% in 2015 from the baseline level in 2009. This goal was not achieved but a significant 60% reduction in new HIV infections resulting from MTCT was obtained.

Adherence to ART constitutes a challenge for people living with HIV, especially in pregnant women (Palmer, 2004). Many pregnant women experience "morning sickness" in the early stages of their pregnancy and this may contribute to lower medication adherence during this period (ACOG, 2004). Nearly 70–85% of pregnant women experience nausea and vomiting and these symptoms may be worsened by gastrointestinal side effects of ART, such as zidovudine and tenofovir (Nachega et al., 2012; Joseph et al., 2016). Heartburn is also commonly associated with pregnancy and may adversely affect the medication-taking behavior of pregnant women (Nachega et al., 2012). Reduction in pediatric HIV infections resulting from MTCT is largely dependent on ART adherence among HIV positive pregnant women, therefore failure to adhere to ART during pregnancy can lead to suboptimal viral load suppression, with increased risk of the mother passing on HIV to the unborn child (Hayman, 2009; Haubrich et al., 1999; Bangsberg et al., 2000; Welles et al., 2000; Johnson et al., 2001). Optimal adherence to prescribed ART is therefore crucial to accomplish maximal viral load suppression required to prevent MTCT (Igwegbe et al., 2010).

Knowledge of intervention types that improve ART adherence during pregnancy can play a crucial role in virtually eliminating MTCT. Previous research in sub-Saharan countries, such as Zambia, South Africa and Nigeria, has identified low adherence to ART as a major barrier to MTCT (Clouse et al., 2013; Phillips et al., 2014;

Ngoma et al., 2015; Omonaiye and Agu, 2016). Despite well-established evidence demonstrating that a high adherence level of 95% or greater is required to achieve consistent viral load suppression in persons living with HIV (Murphy et al., 2000; Corey et al., 2007; Ferradin et al., 2006), a 2012 systematic review on medication adherence during and after pregnancy in high, middle and low income countries reported sub-optimal adherence levels. This review reported that the overall proportion of pregnant women who had greater than 80% adherence to ART was 73.5% (Nachega et al., 2012). To date, there is no published review involving synthesis of interventions aimed at improving ART adherence during pregnancy in sub-Saharan Africa. The aim of this meta-analysis is to evaluate the effectiveness of interventions at improving ART adherence during pregnancy in sub-Saharan Africa.

Methods

Search strategy and selection criteria

The preferred reporting items for systematic review and meta-analysis (PRISMA) was used to guide the meta-analysis process (PRISMA, 2015). Databases searched included: MEDLINE Complete, Embase, Global Health and CINAHL Complete, and Google Scholar. Various combinations of keywords and Medical Subject Headings (MeSH) were used, including human immunodeficiency virus, pregnant women, mother to child transmission of HIV, pregnancy, adherence, antiretroviral therapy, vertical transmission of HIV, and interventions to improve adherence. Articles retrieved from these searches were imported into EndNote (X7 version) and duplicates were removed. Databases were searched from inception to the end of August 2017.

Studies were considered for inclusion if they involved an intervention with the intent of improving medication adherence among pregnant women taking ART in sub-Saharan Africa. No restrictions were placed on language and publication date. Studies on adherence amongst exposed babies born to HIV positive mothers and HIV positive postpartum mothers were excluded. Articles involving reviews, editorials, commentaries or letters were also excluded. One author (O.O.) screened identified abstracts after the search. Of articles that were potentially relevant, full-text versions were independently examined by four authors (O.O., P.N., S.K. and E.M.) to determine whether they met the inclusion criteria. If there was uncertainty or disagreement about whether certain studies met the inclusion criteria, the authors discussed and negotiated agreement on eligible studies.

Once the study selection process was completed, one of the authors (O.O.) used a data extraction form to document information from the selected studies. This data extraction form comprised the study design, population studied, setting, participants, sample size, data collection methods used to assess adherence, threshold of adherence and the type of interventions used to improve ART adherence. Independent review of data abstraction process was conducted by the remaining three authors (E.M., S.K. and P.N.) and discrepancies found were resolved by discussion.

We assessed the methodological quality of the included studies using the Downs and Black checklist (Downs and Black, 1998). The