Self-monitoring and self-management of oral anticoagulation

This review should be cited as:

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ABSTRACT

BACKGROUND: The introduction of portable monitors (point-of-care devices) for the management of patients on oral anticoagulation allows self-testing by the patient at home. Patients who self-test can either adjust their medication according to a pre-determined dose-INR schedule (self-management) or they can call a clinic to be told the appropriate dose adjustment (self-monitoring). Several trials of self-monitoring of oral anticoagulant therapy suggest this may be equal to or better than standard monitoring.

OBJECTIVES: To evaluate the effects of self-monitoring or self-management of oral anticoagulant therapy compared to standard monitoring.

SEARCH STRATEGY: We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library* 2007, Issue 4), MEDLINE, EMBASE and CINAHL (to November 2007). We checked bibliographies and contacted manufacturers and authors of relevant studies. No language restrictions were applied.

SELECTION CRITERIA: Outcomes analysed were thromboembolic events, mortality, major haemorrhage, minor haemorrhage, tests in therapeutic range, frequency of testing, and feasibility of self-monitoring and self-management.

DATA COLLECTION AND ANALYSIS: The review authors independently extracted data. We used a fixed-effect model with the Mantzel-Haenzel method to calculate the pooled risk ratio (RR) and Peto's method to verify the results for uncommon outcomes. We examined heterogeneity amongst studies with the Chi^2 and I^2 statistics.

MAIN RESULTS: We identified 18 randomized trials (4723 participants). Pooled estimates showed significant reductions in both thromboembolic events (RR 0.50, 95% CI 0.36 to 0.69) and all-cause mortality (RR 0.64, 95% CI 0.46 to 0.89). This reduction in mortality remained significant after the removal of low-quality studies (RR 0.65, 95% CI 0.46 to 0.90). Trials of self-management alone showed significant reductions in thromboembolic events (RR 0.47, 95% CI 0.31 to 0.70) and all-cause mortality (RR 0.55, 95% CI 0.36 to 0.84); self-monitoring did not (thrombotic events RR 0.57, 95% CI 0.32 to 1.00; mortality RR 0.84, 95% CI 0.50 to 1.41). Self-monitoring significantly reduced major haemorrhages (RR 0.56, 95% CI 0.35 to 0.91) whilst self-management did not (RR 1.12, 95% CI 0.78 to 1.61). Twelve trials reported improvements in the percentage of mean INR measurements in the therapeutic range. No heterogeneity was identified in any of these comparisons.

AUTHORS' CONCLUSIONS: Compared to standard monitoring, patients who self-monitor or self-manage can improve the quality of their oral anticoagulation therapy. The number of thromboembolic events and mortality were decreased without increases in harms. However, self-monitoring or self-management were not feasible for up to half of the patients requiring anticoagulant therapy. Reasons included patient refusal, exclusion by their general practitioner, and inability to complete training.

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COMMENTS

Coumarins or vitamin K antagonists are oral anticoagulant drugs with wider use in daily medical practice. Because of their pharmacokinetic and pharmacodynamic characteristics, frequent laboratory monitoring is required, since inappropriate use can result in thrombotic or major and minor hemorrhagic complications. This laboratory monitoring is performed through measurement of the prothrombin time, expressed as the international normalized ratio (INR). It should be done monthly or every 45 days, among stable patients. Portable monitors, which make it possible for patients to self-test, are increasingly being used in developed countries. Therefore, it is important to evaluate the impact of INR monitoring using this equipment, with regard to the frequency of new thrombotic events and bleeding complications, in order to instill confidence among physicians and patients.

This review of 18 studies showed that there were significant reductions in thrombotic events and mortality through the use of portable monitors. Although there was a difference between self-management (self-adjustment of doses) and self-monitoring (self-testing and calling a clinic for the dose to be adjusted) regarding new thromboembolic events and major bleedings, it was possible to show that patients had a better quality of life under oral anticoagulant therapy. Nevertheless, self-testing could not be used by all patients. Moreover, even though several portable monitors are available, with different costs and sensitivities, the authors did not clarify which equipment was used or whether they observed differences between them. However, this review shows that using portable monitors to check the INR is a condition that can alter and improve the clinical evolution of patients under oral anticoagulant treatment. In addition, this review shows that new studies need to be developed in order to evaluate the differences in economic impact between the traditional INR method and portable monitors, and even between the several portable monitors.

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Antiretroviral therapy (ART) for treating HIV infection in ART-eligible pregnant women

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ABSTRACT

BACKGROUND: This systematic review focuses on antiretroviral therapy (ART) for treating human immunodeficiency virus (HIV) infection in ART-eligible pregnant women. Mother-to-child transmission (MTCT) is the primary means by which children worldwide acquire HIV infection. MTCT occurs during three major timepoints during pregnancy and the postpartum period: in utero, intrapartum, and during breastfeeding. Strategies to reduce MTCT focus on these periods of exposure and include maternal and infant use of ART, caesarean section before onset of labour or rupture of membranes, and complete avoidance of breastfeeding. Where these combined interventions are available, the risk of MTCT is as low as 1-2%. Thus, ART used among mothers who require treatment of HIV for their own health also plays a significant role in decreasing MTCT.

OBJECTIVE: Our objective was to assess the current literature regarding the treatment of HIV infection in pregnant women who are clinically or immunologically eligible for ART. This review includes an evaluation of the optimal time to start therapy in relation to the woman's laboratory parameters and/or gestational age. It also includes an analysis of which specific antiretroviral medications to start in women who are not yet on ART and which agents to continue in women who are already on ART.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW: In June 2009, electronic searches were undertaken in these databases: Cochrane's "CENTRAL," EMBASE, PubMed, LILACS, and Web of Science/Web of Social Science. Hand searches were performed of the reference lists of all pertinent reviews and studies identified. Abstracts from relevant conferences were searched. Experts in the field were contacted to locate additional studies. The search strategy was iterative.

SELECTION CRITERIA: We selected randomized controlled trials and observational studies that evaluated pregnant women with HIV infection who were eligible for ART according to criteria defined by the WHO guideline review committee. Studies were included in the systematic review when a comparison group was clearly defined and where the intervention comprised triple ART. For a study to be considered, each medication in the ART regimen needed to be clearly described.

DATA COLLECTION AND ANALYSIS: Two authors independently assessed the selected studies for relevance and inclusion. Relevant data was then extracted from included studies, and the risk of bias assessed. In each included study, the relative risk (RR) for the intervention versus the comparison group was calculated for each outcome, as appropriate, with 95% confidence intervals (CIs).

MAIN RESULTS: To our knowledge, there are no randomized controlled trials or observational studies that address the optimal time to start antiretroviral drugs in ART-eligible pregnant women in relation to the woman's laboratory parameters and/or gestational age. The medications to continue in ART-eligible pregnant women who are already receiving ART also have not been evaluated systematically in the current literature. The long-term mortality of HIV-positive pregnant women on ART for their own health, and the long-term virologic or clinical efficacy of ART in treating them, has not been evaluated in randomized clinical trials. In this review, surrogate outcomes for long-term mortality and virologic and clinical efficacy (e.g. MTCT and infant HIV transmission or death) were evaluated to determine the efficacy of specific antiretroviral regimens to start in women who are not yet on ART. In June 2009, electronic searches were undertaken in these databases: Cochrane's "CENTRAL," EMBASE, PubMed, LILACS, and Web of Science/Web of Social Science. Hand searches were performed of the reference lists of all pertinent reviews and studies identified. Abstracts from relevant conferences were searched. Experts in the field were contacted to locate additional studies. The search strategy was iterative.

AUTHORS' CONCLUSIONS: In ART-eligible pregnant women with HIV infection, ART is a safe and effective means of providing maternal virologic suppression, decreasing infant mortality, and reducing MTCT. Specifically, AZT/3TC/NVP, AZT/3TC/LPV-r, and AZT/3TC/ABC have been shown to decrease MTCT. More research is needed regarding the use of specific regimens and their maternal and infant side-effect profiles.

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COMMENTS

Without any intervention, the risk of mother-to-child transmission (MTCT) of HIV is around 25.5%. MTCT occurring at the time of partum and during labor accounts for 65% of such transmission, while occurrences in uterus account for 35%. Breastfeeding by HIV-positive mothers accounts for around 7 to 22% of HIV transmission to children. Several studies have demonstrated reductions in MTCT of between 0 and 22%, through the following interventions: reduction of the viral load to less than 1000 copies/ml at the end of pregnancy; caesarean section before the onset of labor or rupture of membranes; and prophylactic administration of antiretroviral therapy (ART) for pregnant women, newborns and during breastfeeding, using AZT.

In 1994, the results from Protocol 076 (Pediatric AIDS Clinical Trial Group; PACTG) were published in New Engl J Med. 1994:331(18):1173-1180. This randomized, placebo-controlled, double blind trial demonstrated that for pregnant women with CD4 cell counts of more than 200 cells/mm^3, AZT administration before labor and during delivery and for newborns during the first six weeks of life reduced MTCT of HIV by 67.5%.

Protease inhibitors were introduced in 1997, in association with other forms of ART for HIV treatment. Through this, it was possible to reduce the viral load to undetectable levels, i.e. below the threshold of laboratory methods at that time. Morbidity and mortality were greatly reduced. Furthermore, the use of ART consisting of a combination of three drugs was capable of achieving important reductions in viral load and MTCT, down to levels close to 0%.

The WHO guidelines and the Brazilian STD/AIDS program consider that patients are eligible to start ART if they present CD4 cell counts lower than 350/mm^3. In the 1994 study mentioned above, pregnant women were included only if their counts were more than 200 cells/mm^3, and therefore both eligible women and non-eligible women (CD4 counts of more than 350 cells/mm^3) were included in the study. Nowadays, all HIV-positive pregnant women should receive ART, whether their CD4 cell count is more than or less than 350 cells/mm^3, in order to prevent MTCT. Pregnant women who started treatment with counts of more than 350 cells/mm^3 can stop ART under medical discretion until such time that their cell counts go down to the established threshold, according to the guidelines.

The lack of randomized studies on the issues mentioned in this review does not decrease the importance of testing all pregnant women for HIV. Women who test positive should receive ART or prophylaxis for HIV, in order to avoid MTCT and preserve their health. It seems unnecessary to perform randomized studies to evaluate the optimal time to start ART among eligible pregnant woman, given that there is so much good evidence regarding the benefits of ART starting when the CD4 cell count is below 350 cells/mm^3, both among pregnant and among non-pregnant women. With regard to the treatment regimens mentioned, it should be borne in mind that nevirapine produces liver toxicity in women with CD4 cell counts of more than 250 cells/mm^3.

In clinical practice, this review does not modify the established approaches relating to pregnant women, and the studies suggested in the review will only add better knowledge of the evolution of HIV infection in women, which is already the subject of studies among non-pregnant women.

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