Abstract

Introduction

Co-trimoxazole prophylaxis is used to reduce morbidity and mortality in people with HIV. We systematically reviewed three topics related to co-trimoxazole prophylaxis to update WHO guidelines: initiation, discontinuation, and dose.

Methods

We searched PubMed, Embase, WHO Global Index Medicus, and clinical trial registries in November, 2013, for randomised controlled trials and observational studies including co-trimoxazole prophylaxis and a comparator group. Studies were eligible if they reported death, WHO clinical stage 3 or 4 events, admittance to hospital, severe bacterial infections, tuberculosis, pneumonia, diarrhoea, malaria, or treatment-limiting adverse events. Infant mortality, low birthweight, and placental malaria were additional outcomes for the comparison of co-trimoxazole prophylaxis and intermittent preventive treatment for malaria in pregnant women (IPTp). We compared a dose of 480 mg co-trimoxazole once a day with one of 960 mg co-trimoxazole once a day. We used a 10% margin for non-inferiority and equivalence analyses. We used random-effects models for all meta-analyses. This study is registered with PROSPERO, number CRD42014007163.

Findings

19 articles, published from 1995 to 2014 and including 35,328 participants, met the inclusion criteria. Co-trimoxazole prophylaxis reduced rates of death (hazard ratio [HR] 0·40, 95% CI 0·26ï 0·64) when started at CD4 counts of 350 cells per ε L or lower with antiretroviral therapy (ART) worldwide. Co-trimoxazole prophylaxis started at higher than 350 cells per ε L without ART reduced rates of death (0·50, 0·30ï 0·83) and malaria (0·25, 0·10ï 0·57) in Africa. Co-trimoxazole prophylaxis was non-inferior to IPTp with respect to infant mortality (risk difference [RD] ī 0·05, 95% CI ī 0·12 to 0·02), low birthweight (0·00, ī 0·07 to 0·07), and placental malaria (0·00, ī 0·10 to 0·10). Co-trimoxazole prophylaxis continuation after ART-induced recovery with CD4 counts higher than 350 cells per ε L reduced admittances to hospital (HR 0·42, 95% CI 0·22ï 0·80), pneumonia (0·73, 0·61ï 0·88), malaria (0·03, 0·01ï 0·10), and diarrhoea (0·61, 0·48ï 0·78) in Africa. A dose of 480 mg co-trimoxazole prophylaxis once a day did not reduce treatment-limiting adverse events compared with 960 mg once a day (RD ī 0·07, 95% CI ī 0·52 to 0·39).

Interpretation

Co-trimoxazole prophylaxis should be given with ART in people with CD4 counts of 350 cells per ε L or lower in low-income and middle-income countries. Co-trimoxazole prophylaxis should be provided irrespective of CD4 count in settings with a high burden of infectious diseases. Pregnant women with HIV in Africa should use co-trimoxazole rather than IPTp to prevent malaria complications in infants. Further research is needed to inform dose optimisation and co-trimoxazole use in the context of expanded ART in different epidemiological settings.