Effectiveness of non-nucleoside reverse-transcriptase inhibitor-based antiretroviral therapy in women previously exposed to a single intrapartum dose of nevirapine: a multi-country, prospective cohort study.

Stringer JS, McConnell MS, Kiarie J, Bolu O, Anekthananon T, Jariyasethpong T, Potter D, Mutsotso W, Borkowf CB, Mbori-Ngacha D, Muiruri P, Ong'ech JO, Zulu I, Njobvu L, Jetsawang B, Pathak S, Bulterys M, Shaffer N, Weidle PJ.

Abstract

BACKGROUND:

Intrapartum and neonatal single-dose nevirapine (NVP) reduces the risk of mother-to-child HIV transmission but also induces viral resistance to non-nucleoside reverse transcriptase inhibitor (NNRTI) drugs. This drug resistance largely fades over time. We hypothesized that women with a prior single-dose NVP exposure would have no more than a 10% higher cumulative prevalence of failure of their NNRTI-containing antiretroviral therapy (ART) over the first 48 wk of therapy than would women without a prior exposure.

METHODS AND FINDINGS:

We enrolled 355 NVP-exposed and 523 NVP-unexposed women at two sites in Zambia, one site in Kenya, and two sites in Thailand into a prospective, non-inferiority cohort study and followed them for 48 wk on ART. Those who died, discontinued NNRTI-containing ART, or had a plasma viral load >or=400 copies/ml at either the 24 wk or 48 wk study visits and confirmed on repeat testing were characterized as having failed therapy. Overall, 114 of 355 NVP-exposed women (32.1%) and 132 of 523 NVP-unexposed women (25.2%) met criteria for treatment failure. The difference in failure rates between the exposure groups was 6.9% (95% confidence interval [CI] 0.8%-13.0%). The failure rates of women stratified by our predefined exposure interval categories were as follows: 47 of 116 women in whom less than 6 mo elapsed between exposure and starting ART failed therapy (40%; p<0.001 compared to unexposed women); 25 of 67 women in whom 7-12 mo elapsed between exposure and starting ART failed therapy (37%; p = 0.04 compared to unexposed women); and 42 of 172 women in whom more than 12 mo elapsed between exposure and starting ART failed therapy (24%; p = 0.82 compared to unexposed women). Locally weighted regression analysis also indicated a clear inverse relationship between virologic failure and the exposure interval.

CONCLUSIONS:

Prior exposure to single-dose NVP was associated with an increased risk of treatment failure; however, this risk seems largely confined to women with a more recent exposure. Women requiring ART within 12 mo of NVP exposure should not be prescribed an NNRTI-containing regimen as first-line therapy.