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Standard vaccines increase HIV-1 transcription during antiretroviral therapy.

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Abstract

OBJECTIVES: Curative strategies using agents to perturb the HIV reservoir have demonstrated only modest activity, whereas increases in viremia after standard vaccination have been described. We investigated whether vaccination against non-HIV pathogens can induce HIV transcription and thereby play a role in future eradication strategies.

DESIGN: A randomized controlled trial (<u>NCT00329251</u>) was performed to compare the effects of clinical vaccines with placebo on HIV transcription and immune activation.

METHODS: Twenty-six HIV-infected individuals on suppressive antiretroviral therapy were randomized to receive a vaccination schedule (n=13) or placebo (n=13). Cell-associated RNA and DNA were extracted from peripheral blood mononuclear cells, and HIV was quantified by droplet digital PCR using primers for gag and 2-LTR (for HIV DNA), unspliced gag RNA (gag usRNA), multispliced tat-rev RNA (tat-rev msRNA) and polyA mRNA.

RESULTS: Significant increases in gag usRNA after influenza/hepatitis B vaccination (P=0.02) and in gag usRNA (P=0.04) and polyA mRNA (P=0.04) after pneumococcus/hepatitis B vaccination were seen in vaccinees but not controls. HIV DNA and plasma HIV RNA did not change in either group. Increases in CD4 and CD8 T-cell activation markers (P=0.08 and P<0.001, respectively) and HIV-specific CD8 responses (P=0.04 for p24 gag, P=0.01 for p17 gag and P=0.04 for total gag) were seen in vaccinees but not controls.

CONCLUSION: In this study, vaccination was associated with increases in HIV cell-associated RNA and HIV-specific responses during antiretroviral therapy. Using standard vaccines to stimulate HIV transcription may therefore be a useful component of future eradication strategies.

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