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INTERMITTENT ANTIRETROVIRAL PROPHYLAXIS WITH TENOFOVIR AND EMTRICITABINE PROTECTS MACAQUES AGAINST REPEATED RECTAL SHIV EXPOSURES

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BACKGROUND: Antiretroviral pre-exposure prophylaxis (PrEP) is a promising new biomedical strategy to prevent the transmission of HIV. We recently showed that daily PrEP with tenofovir (TFV) and emtricitabine (FTC) fully protected macaques from rectal SHIV transmission. TFV and FTC have long intracellular half-lives and can potentially achieve extended prophylactic activity when given intermittently. We assessed if PrEP given around the time of virus exposure can be as protective as daily PrEP.

METHODS: Two different intermittent PrEP modalities with FTC (20 mg/kg) and TFV (22 mg/kg) were given subcutaneously to rhesus macaques. One group ($n=6$) received FTC/TFV 2 h before and 24 h after virus exposure; the other group ($n=6$) received FTC/TFV only 2 h before virus exposure. Protection was compared to that previously seen with daily FTC/TFV PrEP. An additional 21 macaques (nine real-time and 12 historical controls) did not receive any drug treatment. All animals were exposed rectally once weekly for up to 14 weeks with a low dose of SHIV_{SF162p3} (10 TCID₅₀ or 7.6×10^5 vRNA copies) that expresses an R5 tropic HIV-1 envelope. Infection was monitored by serology and PCR amplification of SHIV sequences from plasma and PBMCs. Animals were considered protected if they were seronegative and PCR negative during PrEP and up to 70 days thereafter.

RESULTS: Twenty of the 21 untreated macaques became infected after a median of 2.5 rectal exposures. The majority of the animals (16/21 or 76%) were infected during the first four challenges (median=2.1), four (19%) were infected between exposures 8 and 12 (median=10.5), and only one (4.8%) remained uninfected after 14 exposures. All the animals receiving daily PrEP, or PrEP before and after virus exposure were protected. Available data from 10 challenges in macaques receiving single-dose PrEP showed one of six animals infected at exposure 8.

CONCLUSIONS: Two-dose PrEP given before and 24 h after virus exposure can be as effective as daily PrEP. Single-dose PrEP is highly effective but not sufficient to achieve full protection, suggesting that the extended antiviral activity in the second 24 h dose also contributes to protection. These data highlight the importance of effectively blocking the early stages of virus replication and show the promise of intermittent PrEP as a strategy for HIV prevention.

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