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A Mathematical Modelling Framework to Assess the Impact of Antiviral Strategies on HIV Transmission

Stopping the AIDS epidemic constitutes a major challenge to mankind. Up to now, HIV infected individuals cannot be cured. However, one possible way of stopping the epidemic is to disrupt its transmission. In 2009, approximately 370,000 infants became infected with HIV during pregnancy, delivery and breastfeeding [1]. A single dose of nevirapine (NVP) can reduce HIV transmission by half, when administered to the mothers before birth and to their newborns shortly after birth. This simple and cost-efficient method is widely applied in resource-constrained settings.

Based on a ugandan program for the prevention of mother-to-child transmission, we assessed the pharmacokinetics of NVP in HIV infected pregnant women and their newborns. The derived pharmacokinetic parameters were used in a stochastic model of HIV dynamics and -transmission. Subsequently, we used the model to predict HIV transmission rates during the first two years after birth with different alterations of the basic NVP scheme. The model predictions were in excellent agreement with data from seven independent HIV prevention trials. We found that the maternal NVP constitutes a major risk for resistance development and subsequent treatment success in the HIV infected mother [2]. However, maternal NVP decreases HIV transmission to the newborn substantially. Our model revealed a perplexing mechanism: Maternal NVP does not reduce the number of viral particles that come into contact with the child during birth. Instead, maternal NVP reduces HIV transmission by providing NVP trans-placental to the child, so that protective NVP levels are available at the moment of viral contact during delivery. Our model also revealed, that extended newborn NVP administration can protect the infant from acquiring HIV during the breastfeeding period without further risk of resistance selection.

Extended newborn NVP, as well as single-dose maternal NVP protect the newborn from HIV acquisition by a mechanism, which could best be termed 'pre-exposure prophylaxis' (PrEP). In view of the predictive power of our model, we are encouraged that a very similar modeling framework may be useful to study the impact of PrEP on sexual transmission of HIV, which could become a central tool to curb the HIV epidemic in the near future [3].

References

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