Infant Postnatal Prophylaxis (PNP) following maternal viraemia during breastfeeding

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Background:
Increasingly, women living with HIV in resource-rich settings are choosing to breastfeed but experience in managing maternal viraemia is limited.

Methods:
Case series from the Paediatric Virtual Clinic (PVC).

Results:
Case 1:
Born at term, to a mother taking tenofovir disoproxil/emtricitabine, darunavir/ritonavir. Maternal HIV viral load (VL)<50 copies/mL less than 4 weeks prior to delivery, the infant received 4 weeks zidovudine (AZT) monotherapy. Infant and maternal VL at 0 and 6 weeks were undetectable. At 3 months, maternal VL 310 copies/mL, repeat sampling 2 days later 760 copies/mL. Breastfeeding ceased (supported with cabergoline), and the infant started PNP at neonatal dosing (AZT 4mg/kg BD, lamivudine(3TC)2mg/kg BD and nevirapine (NVP)4mg/kg OD). Following PVC discussion, PNP was changed to treatment dosing; dolutegravir (DTG 5mg OD dispersible), 3TC(5mg/kg BD) and AZT(12mg/kg BD) for one month.

Case 2:
Born at term, to a mother with fully suppressed HIV throughout pregnancy on DTG + abacavir + 3TC. Infant received 2 weeks AZT post-delivery. Maternal VL at 1 month 451 copies/mL, prompting cessation of breastfeeding (supported with cabergoline) and infant PNP (dosing as above) advised. DTG dispersible tablets(DT) and raltegravir granules were not available, so half a dissolved 10mg DTG film-coated tablet (FCT) was commenced. Increased to full 10mg DTG FCT following PVC discussion whilst dispersible DTG was obtained.

Case 3:
A three-year old child exclusively breastfed for 6 months, with ongoing nocturnal breastfeeds, during which their mother was newly diagnosed with HIV after a prolonged febrile illness; VL 126,381 copies/mL, prior antenatal serology was negative. Child’s VL was undetectable and serology negative. Breastfeeding was discontinued acutely but with difficulty; the mother was prescribed cabergoline and the family given behavioural support. PNP commenced: DTG(25mgOD dispersible), 3TC(5mg/kg/BD) and AZT(9mg/kg/BD) for one month.

All children were confirmed HIV uninfected 12 weeks post-PNP.

Conclusions:
These cases highlight challenges surrounding PNP in infancy and early childhood following maternal viraemia during breastfeeding and the need for national guidelines.

Case 1 shows the importance of establishing the correct drug regime. Neonatal PNP dosing is not appropriate after 4 weeks of age and dolutegravir is a more appropriate third agent from this time (now licenced for children ≥3kg / ≥4 weeks of age).

Case 2 highlights the difference in bioavailability between dispersible and film coated tablet DTG formulations; with dosing ratio of ~1:1.6 respectively. Although barrier to resistance of DTG is high, treatment failure is reported with suboptimal drug levels.

Case 3 highlights the difficulty of prompt cessation of established breastfeeding despite pharmacological and family support, and consideration of the risk of transmission in an older child - maternal seroconversion during breast feeding causes up to 50% of mother-to-infant transmissions worldwide.

Learnings:
- Cabergoline dosing differs for day 1 post-partum vs established breastfeeding.
- International guidelines on PNP for breastfeeding infants are needed!