Timing of Live Attenuated Vaccination in Infants Exposed to Infliximab or Adalimumab *in Utero*: A Prospective Cohort Study in 107 Children

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Abstract

Background and Aims

For infants exposed *in utero* to anti-tumour necrosis factor-α [TNF] medications, it is advised that live-attenuated vaccinations be postponed until the drug is cleared, but little is known about time to clearance. To minimize delays before live-attenuated vaccination can be given, we aimed to develop a pharmacokinetic model to predict time-to-clearance in infants exposed during pregnancy.

Methods

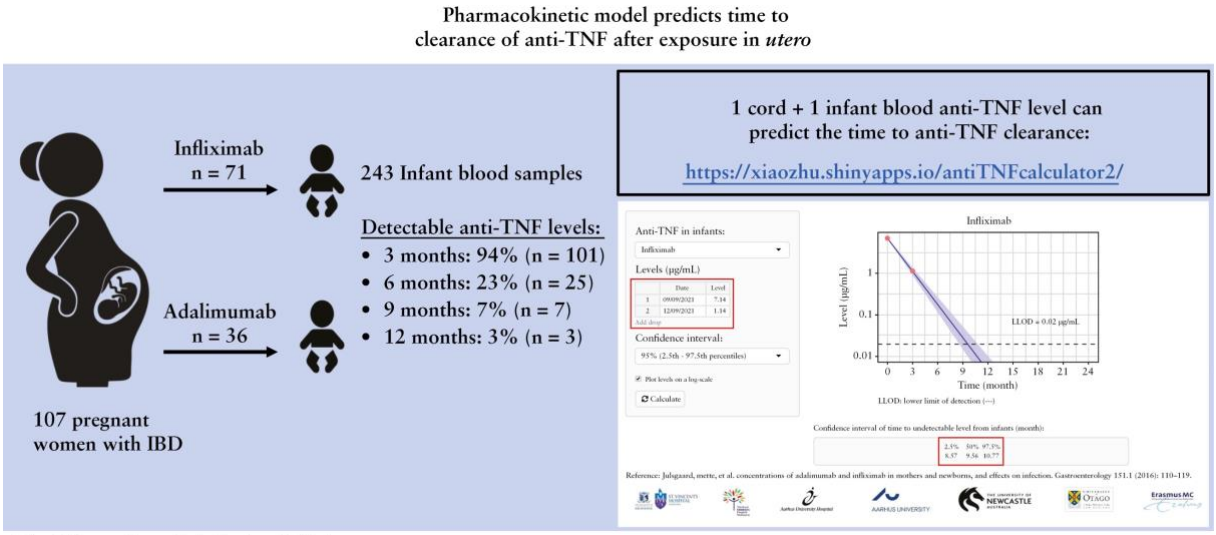
We prospectively followed *in utero* infliximab/adalimumab-exposed infants of mothers with inflammatory bowel disease across four countries between 2011 and 2018. Infants with a detectable anti-TNF umbilical-cord level and at least one other blood sample during the first year of life were included.

Results

Overall, 107 infants were enrolled, including 166 blood samples from 71 infliximab-exposed infants and 77 samples from 36 adalimumab-exposed infants. Anti-TNF was detectable in 23% [*n* = 25] of infants at 6 months. At 12 months, adalimumab was not detected but 4% [*n* = 3] had detectable infliximab. A Bayesian forecasting method was developed using a one-compartment pharmacokinetic model. Model validation showed that the predicted clearing time was in accordance with the measured observations. A clinician-friendly online calculator was developed for calculating full anti-TNF clearing time: https://xiaozhu.shinyapps.io/antiTNFcalculator2/.

Conclusions

Almost one-quarter of infants born to mothers receiving anti-TNF during pregnancy have detectable anti-TNF at 6 months. To limit the time to live-attenuated vaccination in infants of mothers receiving anti-TNF during pregnancy, the results of a cord drug level at birth and a second sample ≥ 1 month thereafter can be used to estimate the time for full anti-TNF clearance in these children.



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