Tacrolimus exposure in human milk: case series from the UmbrelLACT study – A contribution from the ConcePTION project

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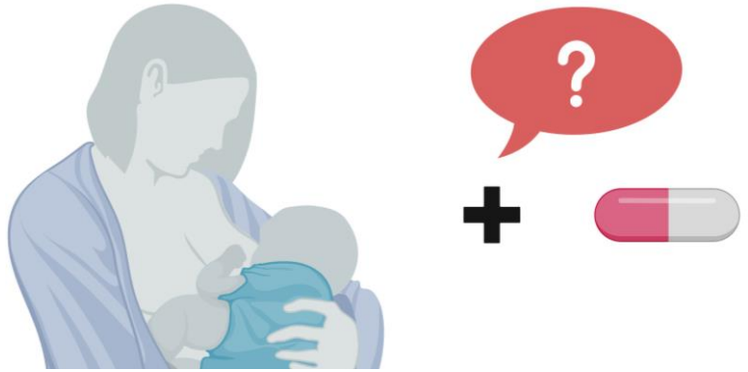
Introduction



Medicine use and safety during breastfeeding is understudied. Tacrolimus intake during breastfeeding is generally considered safe, but uncertainty exists for higher doses.

The pharmacokinetic data and exposure of women using tacrolimus (≥0.2 mg/kg/day) while breastfeeding were studied in the UmbrelLACT study[1].

Methods

Steady-state milk samples were collected at **14 days (patient 1; 0.5-0.6 mg/kg/day)** and **2 months postpartum (patient 2; 0.2 mg/kg/day)**. Blood concentrations were extracted from the medical files of patient 1, while patient 2 donated 2 blood samples.

Tacrolimus concentrations in human milk and blood samples were determined using liquid chromatography with tandem mass spectrometry to subsequently assess **milk-to-blood (M/B) ratio and estimated infant exposure through human milk**.

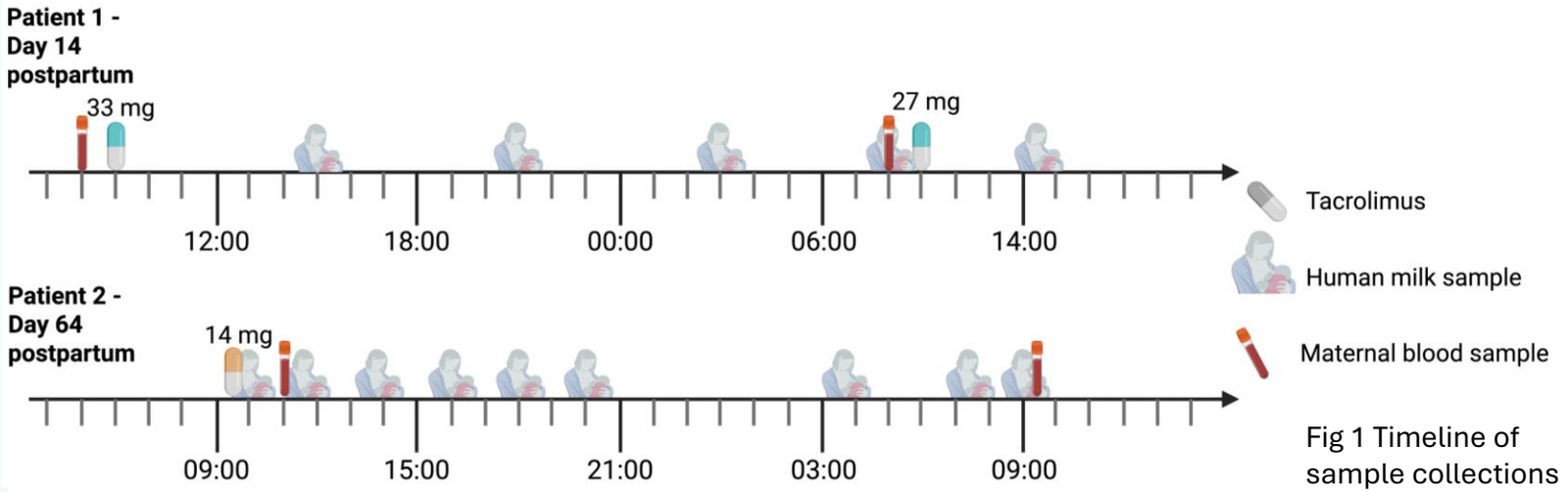


Fig 1 Timeline of sample collections

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Results

Tacrolimus concentrations in human milk ranged **from 0.41 to 2.36 ng/mL**, resulting in average steady-state concentrations of 1.41 ng/mL and 0.75 ng/mL.

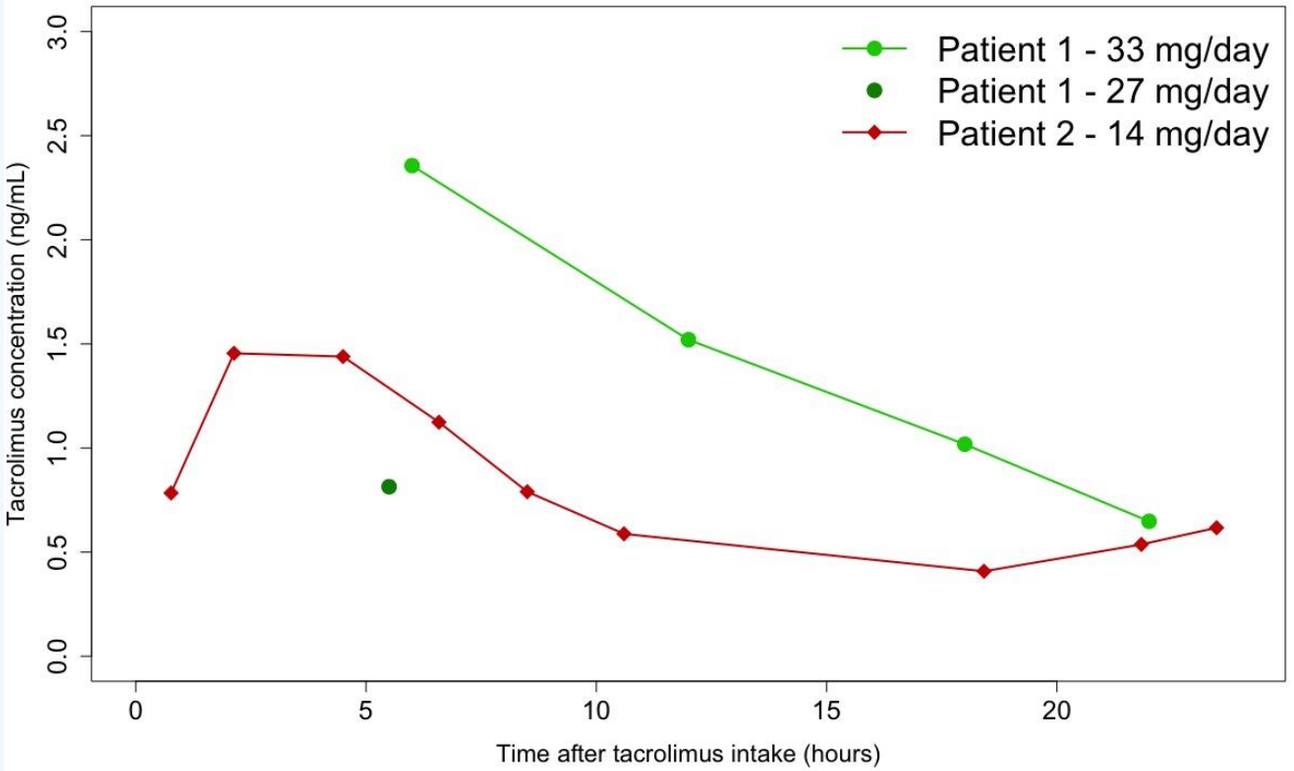

Fig 2 Tacrolimus concentrations in human milk over 24 hours after tacrolimus intake.

Infant exposure was calculated using the daily infant dosage (DID; ng/kg/day) and relative infant dose (RID; %) and a human milk intake of 150 mL/kg/day and 200 mL/kg/day.

$$DID\ (ng/kg/day) = average\ concentration\ (ng/mL) * human\ milk\ intake\ (mL/kg/day)$$

$$RID\ (\%) = \frac{DID\ (\mu g/kg/day)}{daily\ maternal\ dosage\ (\mu g/day)/maternal\ weight\ (kg)}$$

Table 1: The daily infant dosage (DID; ng/kg/day) and relative infant dose (RID; %) of tacrolimus in patient 1 and 2 using 150 (200) mL/kg/day.

	DID	RID
Patient 1 (33 mg)	212 (282)	0.04 (0.05)
Patient 2 (14 mg)	113 (150)	0.06 (0.08)

The **single time-point M/B ratio** was 0.1 for patient 1, and 0.03 and 0.09 for patient 2.

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Conclusion

- ✓ **Tacrolimus levels** in human milk were **generally low** in both patients (0.41 to 2.36 ng/mL).
- ✓ These tacrolimus concentrations resulted in **low infant exposure estimations** (RID 0.04-0.08).
- ✓ Despite the higher daily dose of tacrolimus (0.2-0.6 mg/kg/day) in these patients, the estimated **infant exposure is similar to other published cases** (human milk concentrations: 0.0038 – 3.219 ng/mL; RID: 0.059 - 0.9%).[2]
- ✓ **Further research** leading to additional safety data regarding immunological or nephrotoxic adverse events in infants is warranted.
- ✓ Similarly, data on **infant exposure to maternal tacrolimus use during breastfeeding** should be studied.

References

(1) Van Neste M, *et al*. BMJ Paediatr Open (2024).

(2) Le HL, *et al*. Ther Drug Monit (2020).

Acknowledgements

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Figures on slide 1 were created with BioRender.com

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