

Intra-patient variability in adalimumab drug levels within and between cycles in Crohn's disease

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SUMMARY

Background

Whether therapeutic drug monitoring for adalimumab needs to be performed at trough has not been defined.

Aim

To determine intra-patient adalimumab drug-level variation and to identify modulating patient and disease factors.

Methods

In this prospective observational study, adult patients with Crohn's disease established on maintenance adalimumab had drug levels measured repeatedly according to pre-defined schedules (visit 1: day 4–6, visit 2: day 7–9, trough: day 13–14) across two consecutive fortnightly cycles. Disease activity was assessed using Harvey–Bradshaw Index, C-reactive protein and faecal calprotectin. For this analysis, trough levels ≥ 4.9 $\mu\text{g/mL}$ were considered therapeutic.

Results

Nineteen patients underwent 111 evaluations. Mean intra-patient drug levels from paired visits between cycles did not differ (visit1 cycle1: 4.81, cycle2: 5.21 $\mu\text{g/mL}$, $P = 0.24$, visit2 cycle1: 4.86, cycle2: 4.82, $P = 0.91$ and trough cycle1: 3.95, cycle2: 3.95, $P = 0.99$), irrespective of disease activity. Drug levels were stable over the first 9 days (visit 1–2), but declined to trough by a mean 1.06 and 0.89 $\mu\text{g/mL}$ between visit 1 or 2, respectively ($P < 0.001$). Models using nontemporal factors (smoking, syringe delivery device) and levels at earlier visits accounted for 66–80% of the variance in trough levels. On receiver-operating curve analysis, thresholds identified in the first 9 days that predicted a therapeutic trough level were similar to the trough threshold itself, with high sensitivity but modest specificity.

Conclusion

While therapeutic drug monitoring should be performed at trough, a drug level ≥ 4.9 $\mu\text{g/mL}$ obtained during the first 9 days predicts a therapeutic trough drug level with reasonable confidence.