Rifampin dosing and pharmacokinetics from an international TDM service, 2022

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Rifampin (RIF) is a key part of the standard RIPE regimen for TB. We analyzed therapeutic drug monitoring (TDM) data from our clinical lab, January 1 to December 31, 2022. 1699 samples were sent by 151 locations, including 1242 paired samples at roughly 2 and 6 hours post dose (73%). For the 606 paired sample patients with demographic data, 61% were male, median age 50 (range <1-94) years. Median dose 600 mg (range 50-2400); most were dosed 5-7 days per week (595, or 98%). Median “2 hour” concentration was 6.47 mcg/ml (range 0.00 to 45.16). Peak values were highly correlated with dose ($p<0.0001$). Median values (mcg/ml) are shown (delayed 6h>2h):

600 mg dose, N = 356, 2h = 8.78 (max 39.54), 6h = 5.04 (max 22.1), 30% delayed

750 mg dose, N = 17, 2h = 14.66 (max 25.24), 6h = 6.47 (max 20.18), 18% delayed

900 mg dose, N = 81, 2h = 12.10 (max 51.70), 6h = 8.44 (max 34.49), 33% delayed

1200 mg dose, N = 90, 2h = 12.45 (max 42.72), 6h = 12.07 (max 33.67), 48% delayed

1500 mg dose, N = 11, 2h = 7.72 (max 38.44), 6h = 19.66 (max 26.77), 73% delayed

1800 mg dose, N = 5, 2h = 5.70 (max 36.32), 6h = 20.46 (max 30.06), 80% delayed

2100 mg dose, N = 2, 2h = 24.42 (max 35.59), 6h = 31.30 (max 45.16), 50% delayed

2400 mg dose, N = 1, 2h = 4.15, 6h = 35.45

Delayed absorption was common, especially with higher doses, suggesting that single 2 hour samples are not adequate. Once again, the 600 mg dose of RIF has been proven to be “the minimally effective dose of rifampicin” [Denis Mitchison, 2002]. Higher doses of RIF (through 2100 mg) have been proven to be more effective and no more toxic. RIF 1200 mg would be a reasonable next step in routine dosing across all patients, working towards higher doses.