|  |
| --- |
| **Therapeutic drug monitoring for pulmonary tuberculosis and lung function outcomes** |
| S. Bailey1, D. Kocic2,3, R. Wong3, E. Pang2, S. Stocker2, S. Reuter Lange4, X. Hu1, A. Byrne1,3 |
| *1Department of Thoracic Medicine, St Vincents Hospital, NSW, Australia*  *2Department of Clinical Pharmacology,* Sydpath, *St Vincents Hospital, NSW, Australia*  3*Faculty of Medicine, University of New South Wales, NSW, Australia*  4*Department of Clinical Pharmacology, University of South Australia, SA, Australia* |
| **Introduction/Aim:** Mycobacterium tuberculosis(TB) medication doses are rarely individualised to patients’ pharmacokinetics and absorption. Sub-therapeutic plasma levels of TB medications have been associated with delayed culture conversion, however, their relationship with lung function outcomes is unknown and could be important in the aetiology of post tuberculosis lung disease (PTLD). We hypothesise that TB patients with lower serum drug concentrations of first line TB medications would have poorer lung function outcomes.  **Methods:** Multi-centre, prospective observational study of adults with laboratory confirmed pulmonary TB without rifampicin resistance. Blood was collected at 2, 4 and 6 weeks after TB treatment initiation and on each occasion at 0, 1, 3 and 6 hours post ingestion of rifampicin, isoniazid, ethambutol and pyrazinamide. High performance liquid-chromatography (HPLC) tandem-mass spectrometry was used to determine the maximal drug concentrations (*Cmax*) for each medication. Lung function including FEV1, FVC, TLC and DLCO were measured at TB treatment completion and Spearman’s correlation coefficient was used to compare the relationship between sub-therapeutic *Cmax* levels and abnormal lung function.  **Results:** Of 15 adults with a median age of 34 years (interquartile range 33.5), 47% (7/15) recorded sub-therapeutic levels of one or more anti-tuberculosis drug at least one time-point during therapy (53%, 8/15 were therapeutic throughout). More patients with therapeutic drug levels throughout had normal FEV1, TLC and DLCO at completion of treatment compared to those with sub-therapeutic levels (60% vs 40%; 67% vs 33% and 67% vs 33% respectively), although this did not reach statistical significance (p>0.05).  **Conclusion:**  Sub-therapeutic tuberculosis drug levels are common during the intensive phase of treatment of rifampicin susceptible pulmonary tuberculosis in our study and may be associated with abnormal lung function at TB treatment completion. Larger studies are needed to determine if obtaining therapeutic *Cmax* levels can prevent PTLD.  **Grant Support:** St Vincent’s Clinic Foundation - Research Grant Award |