Therapeutic drug monitoring for Rifampin, Isoniazid and Pyrazinamide among Newly Diagnosed Tuberculosis in Shenzhen, China

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Background and Research Hypothesis

- High TB burden in China
- TB relapse and the emergence of MDR-TB. Long duration to launch a new drug
- Optimize the doses of the first-line drugs may maximize their bactericidal and sterilizing activities
- Therapeutic drug monitoring (TDM)

------- a technique using plasma drug concentrations to determine dosage.

Background and Research Hypothesis

- TDM for Cmax of the first-line drugs are well below the proposed target Cmax concentrations in a substantial fraction of patients.
- Estimation of Cmax based on one 2-h post-dose sample may not have the necessary accuracy.
- Cmax based on a 2-h and a 6-h sample allow the clinician to distinguish between delayed absorption and malabsorption in TB treatment.
- Very limited TDM data from Chinese TB patients.

Objective

- To estimate Cmax of INH, RMF, PZA based on a 2-h and a 6-h sample in Chinese patients.

Methods

- A retrospective analysis was performed of 148 new active TB patients ,In whom early TDM at a 2-h post-dose sample and a 6-h post-dose sample were completed after more than 1 week standard four-drug treatment from 30/10/2016 to 30/10/2017.

- High performance liquid chromatography (HPLC) was used for TDM testing.

Inclusion Criteria

- Age 18-65 year
- Diagnosed active TB
- Receiving oral administration of standard four-drug TB treatment
- No other medicine taken together （Except insulin for glucose control)

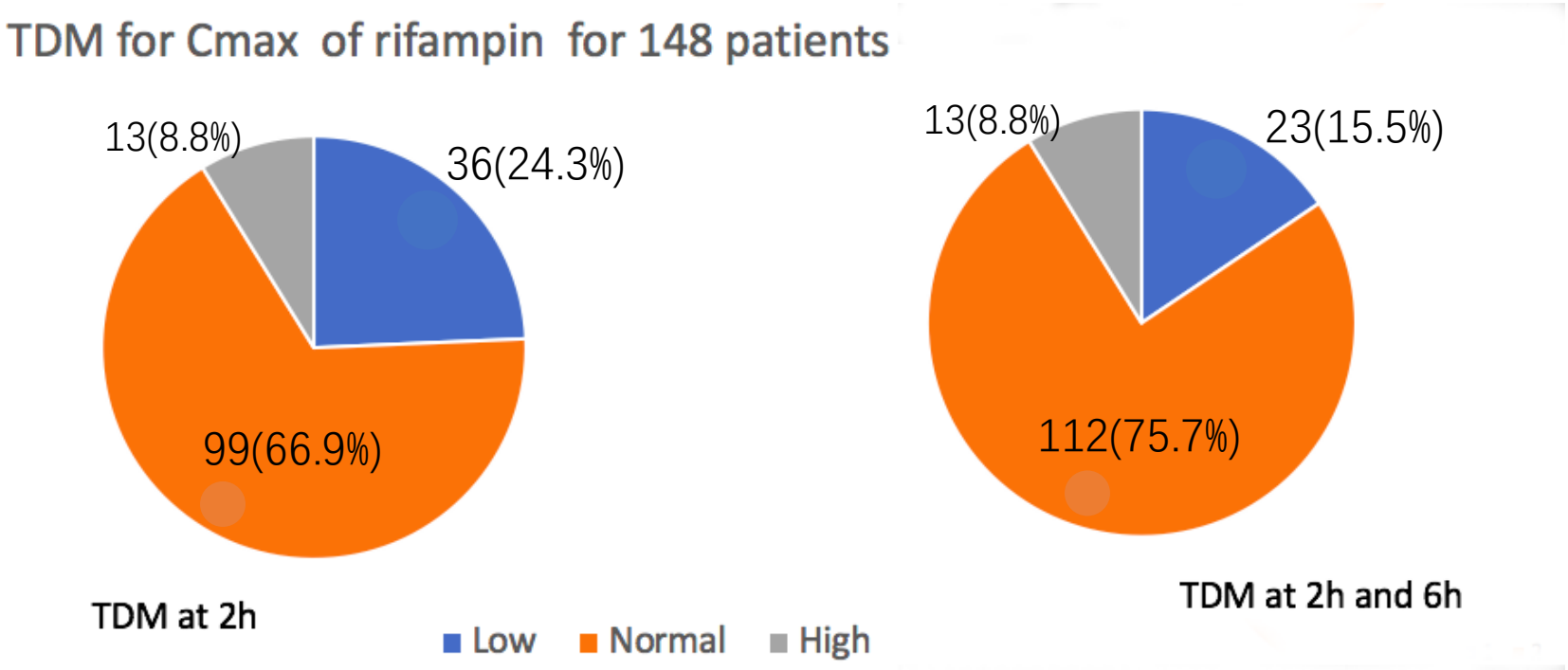
Exclusion Criteria

- Do not receiving standard four-drug TB treatment
- TB treatment in vein
- Dialysis
- HIV ,HBV,HCV coinfection
- Tuberculous meningitis

Statistic Analysis

- Estimate the proportion of Low Cmax, Normal Cmax, and High Cmax in TB patients.
- Compare the proportion of malabsorption between DM patients and non-DM patients with x^2 test.
- SPSS（version18.0） for analysis.

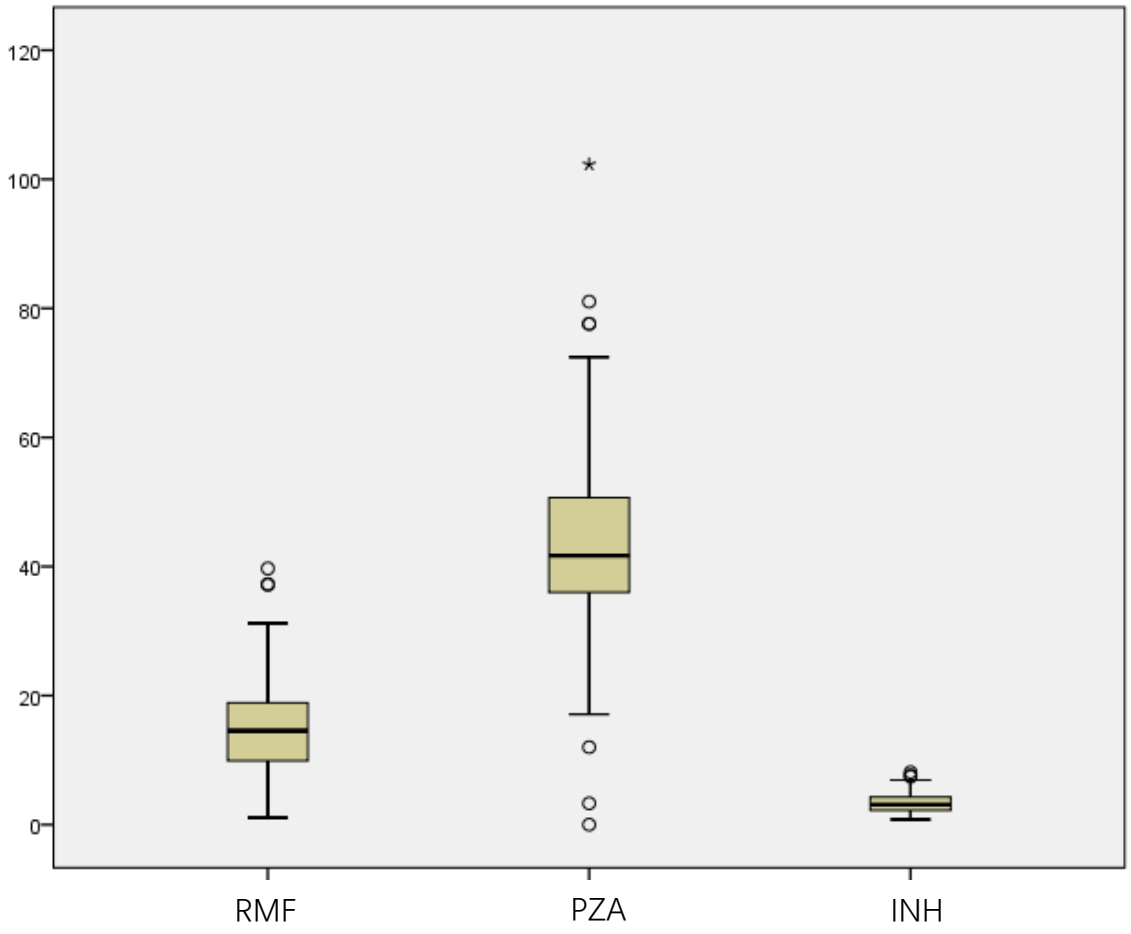
Key results



13 of 36 (36.1%) reached standard Cmax（8-24ug/ml）at a 6-hour post-dose samples

Key results

TDM results of three tuberculosis drugs of 148 patients



Key results

TDM results of three tuberculosis drugs of 148 patients

TDM （Therapeutic drug monitoring）	low	Normal	High
RMF（8-24ug/ml）	23(15.5%)	112(75.7%)	13(8.8%)
INH（3-6ug/ml）	70(47.3%)	71(48%)	7(4.7%)
PZA（35-60ug/ml）	17(11.5%)	112(75.7%)	19(12.8%)

unexpected findings

The proportion of low Cmax has no difference between diabetes and non-diabetes.

TDM （Therapeutic drug monitoring）	TB-DM	TB	Statistics
RMF(<8ug/ml)	2/30	21/118	x^2 =2.26,*P*=0.166
INH(<3ug/ml)	17/30	51/118	x^2 =1.74,*P*=0.221
PZA(<35ug/ml)	6/30	11/118	x^2 =2.68,*P*=0.114

Conclusion

- 2-h and 6-h post-dose samples should be collected for TDM to estimate for Cmax of RMF.
- A 2-h post-dose TDM is mostly enough for estimation of Cmax for INH and PZA.
- Low Cmax is more commonly seen in INH than RMF and PZA.
- no difference of Cmax of INH and RMF and PZA between diabetes and non-diabetes.

Weakness

- Only once TDM for the patients. No dosage adjustment after TDM.
- The relation of the serum concentration of isoniazid and NAT2 gene was not set up.
- Treatment outcome and relapse rate were not mentioned in this study.
- No Cmax:MIC was discussed.

Ackownledgment

- *Thank you!*