Pharmacokinetic characteristics of first-line anti-tuberculous drugs in gastrectomized patients

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Background
Gastrectomy can influence pharmacokinetics of various drugs by altering gastrointestinal (GI) conditions such as gastric acidity and gastric emptying time. The purpose of this study is to evaluate the effect of gastrectomy on the pharmacokinetics of first-line anti-tuberculous (TB) drugs.

Methods
Thirty-four patients with active tuberculosis receiving standard first-line anti-TB drug regimen (isoniazid, rifampicin, pyrazinamide and ethambutol) participated in this study. Half of the patients had received gastrectomy due to gastric cancer (gastrectomy group) and the other half had not received any gastrointestinal surgery (control group). At least one month after the initiation of anti-TB treatment, serial plasma samples were collected at pre-dose and 1, 2, 4, 6, and 8 hours post-dose for noncompartmental analysis. Mann-Whitney U test and Kruskal-Wallis Test were used to compare the data between the groups.

Results
The demographic characteristics were similar between the gastrectomy and control group: 60 vs. 53 years (age), 1.66 vs. 1.65 m (height), and 54.7 vs. 57.7 kg (body weight) respectively (p > 0.05). The plasma concentrations of isoniazid and rifampicin were significantly lower in the gastrectomy group than in the control group: mean ± standard deviation (SD) of the area under the concentration-time curve from time 0 to last measurable time point (AUCₙₚₙₜ) for isoniazid were 5.47 ± 4.54 and 10.76 ± 7.25 (mg·h/L); and mean ± SD of AUCₙₚₙₜ for rifampicin were 28.46 ± 15.89 vs. 64.89 ± 28.44 (mg·h/L) for the gastrectomy and control group, respectively. The median time to reach maximal plasma concentration (Tₘₐₓ) of rifampicin was prolonged in the gastrectomy group (4 and 2 hours for the gastrectomy and control group, respectively). There were no significant differences in the pharmacokinetics of pyrazinamide and ethambutol between the groups.

Conclusions
Gastrectomized patients with active TB exhibited lower systemic exposure to isoniazid and rifampicin and delayed oral absorption of rifampicin, compared with active TB patients without history of GI surgery. This information should be considered for the successful treatment of TB in gastrectomized patients.