# Hubungan Kadar Rifampisin Dan Isoniazid Darah Dengan Konversi Sputum Pasien TB Paru Di Akhir Fase Intensif = Association Between Blood Rifampicin And Isoniazid Concentration With Sputum Conversion Among Pulmonary TB Patients At The End Of Intensive Phase

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Abstrak

Pendahuluan: Kadar obat yang rendah dalam darah pasien TB paru diduga berhubungan dengan respon pengobatan yang buruk seperti kegagalan konversi sputum mikroskopis, yang merupakan risiko terjadinya kegagalan pengobatan. Namun berbagai penelitian
menunjukan hasil kontroversial, sebagian menunjukan terdapat hubungan antara kadar obat dengan konversi sputum akhir intensif, sebagian lagi menunjukan respon terapi yang
sama baiknya untuk kadar normal maupun kadar rendah. Faktor yang diduga menyebabkan perbedaan hasil ini adalah perbedaan MIC rifampisin dan isoniazid terhadap Mycobacterium tuberculosis (MTB) pada pasien-pasien TB di setiap wilayah.
Penelitian ini bertujuan mengetahui hubungan kadar rifampisin dan isoniazid darah dengan konversi, serta hubungan rasio kadar puncak rifampisin dan isoniazid darah
terhadap MIC (Cmax/MIC) dengan konversi sputum pasien TB paru di akhir fase intensif.
Metode: Desain penelitian adalah kasus kontrol dengan jumlah sampel sebanyak 40 orang, yang terbagi dalam kelompok kasus (tidak konversi, n=20) dan kelompok kontrol (konversi, n=20). Kadar rifampisin dan isoniazid darah diukur pada dua jam setelah
minum obat yang merupakan perkiraan kadar puncak rifampisin dan isoniazid, menggunakan metode LC/MS-MS. Data MIC diambil dari 20 isolat kultur MTB sputum pasien TB paru kasus baru di RSP dr. H.A Rotinsulu Bandung menggunakan metode MGIT.
Hasil: Dari 40 pasien didapatkan rerata kadar rifampisin 5,58±2,41 mg/L dengan 36 pasien (90%) diantaranya memiliki kadar puncak di bawah normal. Untuk isoniazid
didapatkan median kadar 1,46 (0,40-6,10) mg/L dengan 32 pasien (80%) diantaranya memiliki kadar puncak isoniazid di bawah normal. Pada penelitian ini didapatkan MIC
rifampisin 0,25 mg/L dan MIC isoniazid 0,05 mg/L, lebih rendah dibanding kadar kritis masing-masing obat.
.....Introduction: Low plasma drug concentration in pulmonary TB patients are thought to be associated with poor treatment outcomes such as microscopic sputum conversion failure, which is a risk of treatment failure. However, various studies showed controversial results, some showed that there was an association between drug concentration with sputum conversion at the end of intensive phase, while others showed the same good outcome for normal and low concentrations. Factors thought to cause these controversial in results are the differences in the MIC of rifampicin and isoniazid against Mycobacterium tuberculosis in TB patients in each region. This study aims to determine the association between blood rifampicin and isoniazid concentratiom with sputum conversion, as well as the association between the ratio of peak blood concentration of rifampicin and isoniazid to MIC (Cmax/MIC) with sputum conversion of pulmonary TB

patients at the end of the intensive phase.
Methods: The study design was a case-control study with a sample size of 40 subjects, which were divided into a case group (non-conversion, n=20) and a control group (conversion, n=20). The blood concentration of rifampicin and isoniazid were measured two hours after taking the drug which is an estimate of the peak concentrations of rifampicin and isoniazid, using the LC/MS-MS method. MIC data were taken from 20 MTB sputum culture isolates from new cases of pulmonary TB patients at RSP dr. H.A Rotinsulu Bandung using the MGIT method.
Results: Of the 40 patients, the mean concentration of rifampicin was 5.58 ± 2.41 mg/L with 36 patients (90%) of whom had peak concentrations below normal. For isoniazid, the median concentration was 1.46 (0.40-6.10) mg/L with 32 patients (80%) of whom had peak concentration of isoniazid below normal. In this study, the MIC of rifampicin 0.25 mg/L and MIC of isoniazid 0.05 mg/L were lower than the critical concentration of each drug.
There was no association between blood rifampicin concentration (OR: 11.18; 95% CI: 0.20-223.00, p= 0.106), blood isoniazid concentration (OR: 3.86; 95% CI: 0.67-22 .22, p= 0.235), and the Cmax/MIC ratio of rifampicin (OR: 0.474; 95% CI: 0.039-5.688, p=1.00) with intensive final sputum conversion. However, there was an association between low concentration of both drugs simultaneously (OR: 6.00; 95% CI: 1.08-33.27, p = 0.028), and the Cmax/MIC ratio of isoniazid (OR: 4.333; 95% CI: 1.150). -16,323, p= 0.027) with sputum conversion at the end of the intensive phase.
Conclusion: There was no association between blood rifampicin concentration, blood isoniazid concentration, and the Cmax/MIC ratio of rifampicin with microscopic sputum conversion at the end of the intensive phase. However, there was an association between low concentration of both drugs and the Cmax/MIC ratio of isoniazid and sputum conversion at the end of the intensive phase.