Rifabutin for the Treatment of Tuberculosis in Patients Intolerant to Rifampicin

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Purpose
Rifabutin and Rifampicin both belong to the rifamycin group. Rifabutin containing regimen was as effective as the rifampicin containing regimen for the treatment of tuberculosis in HIV or non-HIV TB patients proved by the Cochrane review: Rifabutin for treating tuberculosis published in 2008. Rifabutin was also well tolerated by the HIV and non-HIV TB patients. However, the side effect of rifabutin was little and similar but not the same with rifampicin. Many experts recommended to use rifabutin if rifampicin intolerable. But the success rate had not ever been reported. So we review data of rifampicin intolerable TB patients in Chest Hospital to evaluate the success rate of launching rifabutin-containing regimen for the rifampicin intolerant patients with pulmonary tuberculosis.

Materials and methods
This study was done between 2006 March and 2009 January. If the patient was intolerant to rifampicin, rifabutin-containing regimen was tried except patient had severe thrombocytopenia, shock, Steven-Johnson syndrome or total bilirubin over 10 mg/dl. We divided the patients into three group according to major adverse effect: skin rash group, hepatitis group and GI upset group. Every patient was required to rechallenge rifampicin once to ensure the major side effect caused by rifampicin. Drug induced hepatitis was defined as 3 times over upper normal limit of ALT with symptoms or 5 times without symptoms. Intolerable skin rash and GI upset was defined as side effect intolerated by patient even treated with the adjvant therapy like antihistamine, prednisolone, antacid and other symptom-relieved drugs. We define success if patient could continue rifabutin to complete full course of treatment and cure was declared. Failure was defined as patient should be stopped rifabutin due to the same or other side effect during the course of treatment. Patient will drop-out for analysis if the result cannot be determined like default or transfer out or rifabutin discontinued without definite cause.

Results
There were 125 patients had ever been treated with rifabutin in this period. There were 23 patients used rifabutin for MDR-TB(15), XDR-TB(1), Rif-resistant TB(3), AIDS-TB coinfection(2) and MAC infection(2). There were 102 patients used rifabutin for rifampicin intolerable adverse effect including 31 patients for drug allergy with skin rush (31.6%), 35 patients for hepatitis (35.7%), 25 patients for GI upset like nausea, vomiting, poor appetite (25.5%) and 7 case for other causes like flu-like syndrome(1), jaundenia(1), red-eye(1) and unknown cause (3). (Figure 1)

There were 15 cases failed due to the same side effect in skin rash group (31 cases), so the cross-adverse effect rate of skin rash between Rifampicin and Rifabutin was 48%. There were 4 cases failed due to the same side effect in hepatitis group (31 cases), so the cross-adverse effect rate of hepatitis between Rifabutin and Rifampicin was 13%. There were 2 cases failed due to the same side effect in GI upset group (21 cases), so the cross-adverse effect rate of GI upset between Rifabutin and Rifampicin was 9.5%. The mean time of failure outcome was 57.26 days (range 1-579 days, median is 12 days) and success outcome was 514 days, median is 203.5 days. (Figure 2)

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Conclusions
More than half of rifampicin intolerable TB patient could tolerate rifabutin-containing regimen used in. The rifabutin-containing regimen is as effective as the rifampicin-containing regimen in rifampicin intolerable patients. In order to increase the cure rate and shorten the treatment course, we suggest rifabutin-containing regimen should be tried for all patients of pulmonary tuberculosis if the rifampicin-containing regimen was intolerable.

Key word: Tuberculosis, Rifampicin, Rifabutin, adverse drug effects