LETTER TO THE EDITORS

Severe hypertension after initiation of rifapentine/isoniazid for latent tuberculosis in renal transplant candidates

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Dear Editors,

Latent tuberculosis infection (LTBI) is not uncommon among renal transplant candidates (RTC) [1]. Rifapentine/isoniazid (RPT/INH) administered for 12 weeks is one of the first-line treatments for LTBI [1], and we have recently showed that it is associated with higher completion rates than INH monotherapy for 9 months [2].

One theoretical concern in RTC is that RPT can decrease the efficacy of certain antihypertensive drugs (AHD) through the induction of cytochrome P (CYP) 3A4—CYP2C9 [3]. Namely, RPT can accelerate the metabolism of beta- and/or alpha-blockers, calcium channel blockers, and angiotensin receptor blockers [3,4].

To explore the impact of RPT on blood pressure (BP) control, we retrospectively reviewed medical records on 37 adult RTC with baseline BP of <140/90 mmHg who were started on RPT/INH for LTBI between March 2012 and February 2015. Only patients who were on AHD that could interact with RPT were included. All the patients were diagnosed by a positive QuantiFERON-TB gold in-tube test. Patients received weekly RPT 900 mg (if weight >50 kg) and INH 15 mg/kg (900 mg max) and daily pyridoxine for 12 weeks. Potential drug–drug interactions (DDI) between RPT and AHD were identified by Lexicomp®Lexi-Interact™ Online software [4]. We evaluated the incidence and onset of severe hypertension (≥180/110 mmHg) after starting RPT/INH. Patients had their BP monitored at home and dialysis, and they were also asked about their BP control in each clinic visit. All patients had at least one follow-up visit.

Table 1. Severe hypertension after initiation of rifapentine/isoniazid latent tuberculosis infection.

Patient	Baseline AHD	Elevation of BP (mmHg)	Onset (week)	Therapeutic interventions
1	**AMLO**, **LABE**, FUR	SBP 180s–190s	12th	None*
2	**NIFE**, LIS	180s/120s	4th	RPT/INH treatment discontinued†
3	**AMLO**, **LOS**, FUR, HDZ	SBP 220	1st	AMLO stopped and started on NIFE 60 mg BID
4	**CVD**	SBP 200s	5th	CVD ↑ from 3.125 mg BID to 6.5 mg BID
5	**CVD**	150s/110s	10th	AMLO was added
6	**METO**	200/110	5nd	METO ↑ from 25 mg BID to 50 mg BID, and LIS was added
7	**LOS**, **CVD**, HDZ	SBP 180s	11th	CVD ↑ from 3.125 mg BID to 6.5 mg BID
8	**LOS**, **AMLO**	170s/120s	2nd	HDZ 25 mg TID and LAB 100 mg BID (1 week later) were added

AHD, antihypertensive drug; BP, blood pressure; SBP, systolic blood pressure; AMLO, amlodipine; LABE, labetalol; FUR, furosemide; NIFE, nifedipine; LIS, lisinopril; LOS, losartan; HDZ, hydralazine; CVD, carvedilol; METO, metoprolol; BID, twice a day.

AHD that can interact with RPT appears in bold.

*No adjustment in AHD because the patient had completed the INH/RPT treatment at the time of BP elevation.

†RPT/INH discontinued because of severe anemia which was attributed to RPT.

doi:10.1111/tri.12881

A total of 37 RTC were evaluated. Twenty-nine (78%) were male and 18 (49%) were African American; the mean age was 56 ± 14 years. All patients had stage 5 chronic kidney disease (CKD) on dialysis except for three patients. Among those on dialysis, 31 (91%) were on hemodialysis and three (9%) on peritoneal dialysis. Twenty-four (65%) patients were on one AHD class, 10 (27%) on two, and three (8%) patients on three AHD classes that interact with RPT. Eight (22%) RTC developed severe hypertension after starting RPT/INH, most of them during the first 6 weeks of treatment (Table 1). All the patients that developed severe hypertension reported being adherent to AHD. Severe hypertension did not result in cerebrovascular accident or myocardial infarction in any patient. Thirty-five (95%) RTC completed the LTBI treatment. One patient discontinued it at 8 weeks due to vomiting, and regimen was discontinued in another patient due to severe anemia.

The occurrence of severe hypertension in this cohort was likely due to predictable DDI between RPT and AHD. We were unable to completely exclude the influence of other factors such as volume overload, sympathetic hyperactivity or erythropoietin treatment, which can cause uncontrolled hypertension in patients with CKD [5–7]. Our study is limited by the small number of cases, retrospective design, and lack of control group. Completion rates with RPT/INH are excellent [2], and this regimen remains an appealing alternative to INH in selected patients. Our data suggest that close BP monitoring is warranted in RTC receiving RPT/INH for treatment of LTBI. Future studies in this area are needed.

Funding

None.

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