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Treatment with isoniazid or rifampin for latent tuberculosis infection: population-based study of hepatotoxicity, completion and costs

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The use of 4 months rifampin (4R) instead of 9 months of isoniazid (9H) for treatment of latent tuberculosis infection is supported by our findings of lower risk of severe hepatotoxicity, better completion and lower adjusted direct costs with 4R <http://bit.ly/3agWLh9>

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ABSTRACT Clinical trials suggest less hepatotoxicity and better adherence with 4 months rifampin (4R) *versus* 9 months isoniazid (9H) for treating latent tuberculosis infection (LTBI). Our objectives were to compare frequencies of severe hepatic adverse events and treatment completion, and direct health system costs of LTBI regimens 4R and 9H, in the general population of the province of Quebec, Canada, using provincial health administrative data.

Our retrospective cohort included all patients starting rifampin or isoniazid regimens between 2003 and 2007. We estimated hepatotoxicity from hospitalisation records, treatment completion from community pharmacy records and direct costs from billing records and fee schedules. We compared rifampin to isoniazid using logistic (hepatotoxicity), log-binomial (completion), and gamma (costs) regression, with adjustment for age, co-morbidities and other confounders.

10 559 individuals started LTBI treatment (9684 isoniazid; 875 rifampin). Rifampin patients were older with more baseline co-morbidities. Severe hepatotoxicity risk was higher with isoniazid (n=15) than rifampin (n=1), adjusted OR=2.3 (95% CI: 0.3–16.1); there were two liver transplants and one death with isoniazid and none with rifampin. Overall, patients without co-morbidities had lower hepatotoxicity risk (0.1% *versus* 1.0%). 4R completion (53.5%) was higher than 9H (36.9%), adjusted RR=1.5 (95% CI: 1.3–1.7). Mean costs per patient were lower for rifampin than isoniazid: adjusted cost ratio=0.7 (95% CI: 0.5–0.9).

Risk of severe hepatotoxicity and direct costs were lower, and completion was higher, for 4R than 9H, after adjustment for age and co-morbidities. Severe hepatotoxicity resulted in death or liver transplant in three patients receiving 9H, compared with no patients receiving 4R.