Effects of rifampin on the pharmacokinetics and pharmacodynamics of gliclazide, a sulfonylurea antidiabetic drug.

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Objective: Our objective was to investigate the effect of rifampin on the pharmacokinetics and pharmacodynamics of gliclazide, a sulfonylurea antidiabetic drug metabolized by CYP2C9.

Method: In a randomized, two-phase crossover study, 9 healthy subjects were treated for 6 days with 600 mg rifampin or placebo once daily. On day 7, a single oral dose of 80 mg gliclazide was administered. Plasma gliclazide, blood glucose concentrations, serum insulin were measured.

Results: Rifampin decreased the mean area under the plasma concentration-time curve of gliclazide by 70% ($p<.001$) and the mean elimination half-life from 9.5 to 3.3 hours ($p<.05$). The systemic clearance of gliclazide increased about 4-fold after rifampin treatment ($p<.001$). Significant difference in the blood glucose response to gliclazide was observed between placebo and rifampin phase ($p<.01$).

Conclusion: The effects of rifampin on the pharmacokinetics of gliclazide suggest that rifampin induced the CYP2C9-catalyzed metabolism of gliclazide. Concomitant use of rifampin with gliclazide can lead to a considerably reduced glucose-lowering effect of gliclazide.