일반연제 4

Effect of Rifampin on the Pharmacokinetics of Rosiglitazone in Healthy Subjects

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Background and Objective: Rifampin (INN, rifampicin) caused several drug interactions with co-administered antidiabetic drugs. Rosiglitazone is a novel thiazolinedione anti-diabetic drug but little is known about the drug interaction between rifampin and rosiglitazone. Our objective was to investigate the effect of rifampin on the pharmacokinetics of rosiglitazone in humans.

Method: In an open-label, randomized two-way crossover study, 10 healthy Korean male subjects were treated once daily for six days with 600 mg rifampin or with placebo. On day 7, a single dose of 8 mg rosiglitazone was administered orally. Plasma rosiglitazone concentrations were measured.

Results: Rifampin significantly decreased the mean area under the plasma concentrationtime curve for rosiglitazone by 65% (2947.9 versus 991.5 ng · hr/ml; $P<0.001$) and the mean elimination half-life from 3.9 to 1.5 hours ($P<0.001$). The peak plasma concentration of rosiglitazone was significantly decreased by rifampin (537.7 versus 362.3 ng/ml; $P<0.01$). The apparent oral clearance of rosiglitazone increased about three-fold after rifampin treatment (2.8 versus 8.5 L/h; $P<0.001$).

Conclusion: This study showed that rifampin affected the disposition of rosiglitazone in humans, probably by the induction of CYP2C8 and to a lesser extent CYP2C9. Therefore, caution should be exercised during the co-administration of rifampin and rosiglitazone.

Key Words: Pharmacokinetics, Rifampin, Rosiglitazone, Cytochrome P450 2C8 (CYP2C8)