Influence of Clarithromycin on the Pharmacokinetics / Pharmacodynamics of Lansoprazole in Relation to S-mephenytoin Oxidation Polymorphism

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We investigated the influence of clarithromycin on the lansoprazole metabolic disposition and plasma gastrin level after lansoprazole administration in two different phenotypic groups of S-mephenytoin hydroxylation polymorphism. Sixteen(8 extensive metabolizers: EMs : 8 poor metabolizer: PMs) healthy Korean subjects were given 500 mg of clarithromycin orally twice a day for 7 days. At the 8th day, they were given 30 mg lansoprazole orally and plasma was sampled serially. There were statistically significant (p <0.01 to 0.001) interphenotypic differences between the two groups in the mean kinetic parameters of lansoprazole and its metabolites except for AUC of lansoprazole sulfone.

	LAN		OH-LAN		LAN sulfone	
	EMs	PMs	EMs	PMs	EMs	PMs
C_{max}(ng/ml)	1151	2980	113	16	72	51
$t_{1/2}$ (hr)	2.5	8.1	3.3	7.1	9.9	7.3
AUC (ug/ml/hr)	2.97	12.34	0.29	0.13	0.48	0.48
CL_o (l/hr)	10.1	2.5				

After the lansoprazole dose, the AUC of gastrin does not significantly correlated with AUC of lansoprazole in plasma. These results suggest that inhibited CYP3A4 by clraithromycin decrease lansoprazole sulfone level and can affect lansoprazole pharmacodynamics in a Korean subjects.