PHARMACOGENOMICS-GUIDED STRATEGY FOR ERADICATION OF \textit{H. pylori}

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The current standard regimens for the eradication of \textit{H. pylori} consisted of a proton pump inhibitor (PPI), amoxicillin and clarithromycin. PPIs are mainly metabolized in the liver by the genetically determined enzyme, S-mephenytoin 4'-hydroxylase (CYP2C19). There are genetic differences in the activity of this enzyme. Plasma concentrations of PPIs and their ability to inhibit acid secretion differ to a significant extent among the different CYP2C19 genotype groups. \textit{H. pylori} eradication rates by a triple therapy with a proton pump inhibitor, amoxicillin and clarithromycin at standard doses depend on bacterial susceptibility to clarithromycin and patient CYP2C19 genotypes. We examined the usefulness of a personalized therapy for \textit{H. pylori} infection based on these factors as determined by genetic testing.

First, optimal lansoprazole dosing schedules that would achieve sufficient acid inhibition to allow \textit{H. pylori} eradication therapy in each of different CYP2C19 genotype groups were determined by a 24-hour intragastric pH monitoring. Next, 300 \textit{H. pylori}-positive patients were randomly assigned to the standard regimen group (lansoprazole 30 mg bid, clarithromycin 400 mg bid, and amoxicillin 750 mg bid for one week) or the tailored regimen group based on CYP2C19 status and bacterial susceptibility to clarithromycin assessed by genetic testing. Patients with failure of eradication underwent the second-line regimen. The per-patient cost required for successful eradication was calculated for each of the groups.

In the first-line therapy, the intention-to-treat eradication rate in the tailored regimen group was 96.0\% (95\%CI = 91.5\%-98.2\%, 144/150), significantly higher than that in the standard regimen group (70.0\%: 95\%CI = 62.2\%-77.2\%, 105/150) (P < 0.001). Final costs per successful eradication in the tailored and standard regimen groups were $377.1 and $376.9, respectively.

The pharmacogenomics-based tailored treatment for \textit{H. pylori} infection allowed a higher eradication rate by the initial treatment without an increase of the final per-patient cost for successful eradication. We also reported the usefulness of supplementation of famotidine in the rapid metabolizers of CYP2C19.

The roles of genotyping test in the \textit{H. pylori} eradication are to determine the rapid metabolizers of CYP2C19 who have the higher risk of eradication failure due to insufficient dose of a PPI with a standard regimen and to avoid the use of antibiotics to which \textit{H. pylori} is resistant. Patients underwent this genomics-guided therapy have greater chance of successful eradication of \textit{H. pylori} by the initial therapy and seem to be satisfied by this strategy because of a high eradication rate. The pharmacogenomics information is also useful for the development of strategy for patients who have failed in 2 or more regimens. Therefore, pharmacogenomics test is of great importance in the \textit{H. pylori} eradication therapy.

\textbf{References:}