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Efficacy of 6-MP in achieving mucosal healing in children and adolescents with Crohn's disease

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Background: 6-MP is an immunomodulatory medication frequently prescribed for the induction and maintenance of remission in patients with moderately to severely active Crohn's disease. Although symptomatic improvement has been shown in a proportion of patients with Crohn's disease taking 6-MP, there is a paucity of data confirming improvement in the degree of mucosal disease in patients receiving this medication. The aim of this study was to determine the degree of endoscopic mucosal healing in a group of pediatric patients treated for Crohn's disease with 6-MP without the use of a biologic agent.

Methods: A retrospective review of the medical records of pediatric patients started on 6-MP for Crohn's ileitis and/or colitis was performed. The Pediatric Crohn's Disease Activity Index (PCDAI) score and Simple Endoscopic Score for Crohn's Disease (SES-CD) were determined for all subjects at the time they initiated therapy with 6-MP and at least 6 months thereafter. Patients placed on 6-MP as a post-operative prophylactic agent were excluded.

Results: Thirteen children aged 8 to 16 years at the time of diagnosis, met inclusion criteria. The total daily dosage of 6-MP ranged from 1-1.5 mg/kg (mean=1.1 mg/kg), and the duration of therapy between their initial and surveillance colonoscopies ranged from 2 to 36 months (mean=12.4 months). Seven of the 13 patients (54%) discontinued usage of 6-MP due to perceived failure to respond to treatment. Interestingly, only 4 of these 7 patients experienced an increase in their PCDAI score while taking 6-MP and only 2 of these 7 showed an increase in their SES-CD. Of the 6 patients who continued on therapy following their surveillance endoscopic procedures, all experienced an improvement of their PCDAI score, while only 3 patients showed an improvement in their SES-CD.

Conclusions: In this small cohort of pediatric patients with moderate or severe Crohn's disease treated with 6-MP, more than half discontinued therapy within 3 years of treatment. The clinical symptoms and laboratory results that comprise the PCDAI score do not seem to correlate well with the SES-CD score. 6-MP may have been stopped prematurely in some patients.

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Role of gastric microbiota in clinical outcome of *Helicobacter pylori* infection

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The prevalence of *Helicobacter pylori* infection is higher in developing countries than in the industrialized world probably reflecting the critical influence of socio-economic factors. The prevalence among adults is over 80 percent in many developing countries as compared to 20 to 50 percent in industrialized countries. The outcome of infection with *H. pylori* varies widely, a large fraction of infected individuals remain asymptomatic, a small fraction develops peptic or duodenal ulcers, an even smaller fraction develop gastric adenocarcinoma and MALT-lymphoma. We are investigating whether there is any correlation between the composition of the gastric microbiota and clinical outcome of *H. pylori* infection in the Indian population. Gastric endoscopy samples were collected from individuals with different clinical symptoms ranging from asymptomatic to peptic and duodenal ulcers to gastric cancers. For each sample 16S rDNA libraries were created and next generation sequencing was performed. The relative abundance of different genera in the gastric microbiome of individuals with different clinical symptoms and asymptomatic individuals was compared. In general, the most abundant genera in the gastric microbiota of asymptomatic individuals without *H. pylori* infection or very low abundance of *H. pylori* (less than 1% of the gastric microbiota) were *Haemophilus*, *Streptococcus* and *Neisseria*. None of these genera were detected in patients with high abundance of *H. pylori* and severe gastric lesions instead a more diverse microbiota with almost equal abundance of *Pseudomonas*, *Flavobacterium*, *Corynebacterium* and *Rothia* was observed. Furthermore, the effect of the normal gastric microbiota on growth and expression of virulence genes in *H. pylori* has been examined.

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