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Combination Treatment Increases Remission of Inflammatory Bowel Diseases in Children

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Children with inflammatory bowel diseases (IBD) who were originally treated with thiopurines alone had improved remission rates and decreased steroid use after low-dose thiopurines were combined with allopurinol, according to a recent study led by physician-researchers at Nationwide Children's Hospital.

The review, published in the *Journal of Pediatric Gastroenterology and Nutrition*, appears to be the largest of its kind assessing pediatric outcomes for the combination therapy.

Patient-to-patient variation in thiopurine metabolism impacts the success of the single therapy, says Brendan Boyle, MD ([/find-a-doctor/profiles/brendan-m-boyle](#)), a member of the Division of Pediatric Gastroenterology, Hepatology, and Nutrition ([/specialties/gastroenterology-hepatology-and-nutrition](#)) at Nationwide Children's and senior author of the study.

"The thiopurines have been used for decades for the treatment of both adults and children with IBD," says Dr. Boyle. "Some children are not able to tolerate its use because of individual variation in the way the medication is metabolized. This can result in liver

irritation or sub-optimal response to the therapy. Adding allopurinol creates a more favorable breakdown of the medication that allows the thiopurines to be used more effectively and without causing the side effects.”

The retrospective chart review included data from 52 patients aged 2-21 years with a diagnosis of Crohn’s disease, ulcerative colitis, or indeterminate colitis treated with the combination of thiopurine (azathiopurine or 6-mercaptopurine) and allopurinol at Nationwide Children’s from 2008 to 2015. The mean duration of thiopurine monotherapy before initiation of the combination therapy was 13.1 months.

After beginning a reduced thiopurine dose (25-33% of the original dose) with allopurinol, the therapeutic metabolite 6-thioguanine (6-TG) level doubled in patients remaining in the study at both 6 and 12 months. Importantly, this increase was also associated with increased remission rates and improved rates of liver toxicity.

These results are consistent with previous studies in adults demonstrating that allopurinol with a low thiopurine dose can increase 6-TG and decrease 6-MMP levels to allow continued use of the medication. Additionally, patients at both time points also saw large reductions in the need for steroid treatment.

The combination therapy appeared safe, and no patients discontinued the treatment due to leucopenia or malignancy. However, approximately 40 percent of patients required a change in therapy: 11 patients by 6 months and 9 patients by 12 months. This finding was consistent with the known variable effectiveness of thiopurines. Seventeen of the original 52 patients (33%) had switched to anti-TNF therapy by the end of the study.

“The field of IBD is moving toward the use of newer medications including biologic and anti-TNF therapies, and thiopurines are being used less frequently than in the past,” says Dr. Boyle, who is also an associate professor of Pediatrics at The Ohio State University College of Medicine. “However, there is a population of patients that for various reasons may need to keep using thiopurines. Adding allopurinol can be an effective way to allow these patients to remain on thiopurines, to optimize their dosing to achieve target drug levels, and to stay in remission without having to switch their medication.”

Reference:

Serpico MR, Maltz R, Crandall W, Bricker J, Dotson JL, Kim SC, Boyle B. Thiopurine optimization through combination with allopurinol in children with inflammatory bowel diseases (<https://www.ncbi.nlm.nih.gov/pubmed/29601433>). *Journal of Pediatric Gastroenterology and Nutrition*. 2018 Mar 29. [Epub ahead of print]

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