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# Medication shows promise for patients with severe chronic constipation

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A new medication appears to offer significant relief to patients with severe chronic constipation while minimizing the likelihood of cardiac-related side effects, according to results of a study published this week in the *New England Journal of Medicine*.

The trial involved 38 medical centers and was led by Michael Camilleri, M.D., a Mayo Clinic gastroenterologist. Patients who met the study criteria were randomly assigned to receive either of two dosage levels of prucalopride, a medication that stimulates protein receptors involved in contraction of the colon, or a placebo.

“Many more of the patients taking prucalopride were able to have spontaneous bowel movements without having enemas or taking laxatives, as compared to those who were given placebo,” says Dr. Camilleri. “The time it took to have a first bowel movement was much shorter, and quality of life and other abdominal symptoms also were improved for those taking the study drug.”

Constipation is a common medical problem, affecting about 15 percent of Americans who spend several billion dollars each year on laxatives and other treatments. Prevalence is higher among women and African-Americans and is particularly increased in the elderly. This study involved patients with an extreme but common version of constipation called severe chronic constipation. To participate, patients had to have at least six months of constipation, defined as an average of fewer than three bowel movements a week.

Those who had more than four bowel movements during the two-week "run-in" period before treatment began were not eligible.

"The normal range of bowel movements is anywhere from three per day to three per week," explains Dr. Camilleri. "The 620 patients studied in this trial were severely constipated, averaging only one bowel movement during the two weeks before entering treatment, and most had struggled with the problem for several years, not merely months."

The 2 milligram (mg) and 4 mg doses of prucalopride appeared roughly equal in benefit, with about 30 percent of patients averaging three bowel movements per week during the 12-week study. Only 12 percent of patients on placebo averaged three bowel movements per week. Nearly half (47.3 and 46.6 percent, respectively) of the patients taking prucalopride increased their bowel movements by at least one per week, while about a quarter (25.8 percent) of those on placebo had a similar improvement.

The most common adverse effect from the drug was diarrhea, which tended to occur in the early stages of treatment, but most patients later settled into a more normal routine of bowel movements. Increased bowel movements and diarrhea are expected effects of the drug. Only 1.5 percent and 4.4 percent of patients treated with 2 mg and 4 mg of prucalopride, respectively, stopped the drug due to diarrhea. "This suggests that the diarrhea was less bothersome than the constipation had been," Dr. Camilleri says. Headaches were a less frequent side effect.

Dr. Camilleri says the cardiac risk issues that have been raised about related drugs for constipation including tegaserod, appear to be less of a concern for prucalopride. "Prucalopride is highly selective in its effect, and doesn't interact significantly with other protein receptors, such as those involved in regulating heart rhythm," he explains. "We conducted electrocardiogram testing during the study and did not find heart rhythm

issues, although two of the three patients who withdrew from the study did have symptoms, palpitations and dizziness that may have been attributable to an effect on the cardiovascular system."

Source: Mayo Clinic