Loperamide and Ileostomy Output—Placebo-controlled Double-blind Crossover Study

Loperamide, *a* newly synthesized anti-diarrhoeal agent more potent than diphenoxylate (Lomotil)\(^1\) inhibits the peristalsis and the response to coxial stimulation and nicotine in the isolated guinea-pig ileum, probably through a direct effect on nerve endings or intramural ganglia, or both.\(^2\) The present study was designed to analyse this inhibitory activity on human small intestinal peristalsis in vivo.

Materials and Methods

Twenty volunteers, aged 25-73, with well-established ileostomies for ulcerative colitis (15 patients), Crohn's disease (4), colonic polyposis (2), and colonic adenocarcinoma (1), were asked to weigh their daily ileostomy output with a precision tubular balance, continuing their usual daily activities and diet. After a three-day drug-free period, they were allocated at random to either seven-day loperamide-seven-day placebo sequence or the reverse. Each patient was given a bottle with 2-mg loperamide capsules and a bottle with identical looking placebo capsules for each treatment period and was asked to take two capsules twice a day for the first four days and, if needed, to adapt the daily dose to six capsules for the remaining three days of each period. Non-parametric tests\(^2\) were used for statistical evaluation.

Results and Discussion

The median and range of the daily faecal weights were 645 (100-2620), 500 (80-2010), and 660 (100-2020) respectively during the drug-free, loperamide, and placebo period. Individual data are summarized in the fig. There were no appreciable daily variations.

![Graph](image)

Effect of loperamide and placebo on daily ileostomy output

Daily faecal outputs were significantly lower during the loperamide period than during drug-free or placebo periods (P<0.001). Median daily ileostomy output decreased by 22 % in the loperamide period, and increased by 2 % in the placebo period compared with the drug-free period. There was no correlation between the duration of the ileostomy and the faecal output. Sixteen of the 20 patients guessed the code correctly, whereas four were uncertain—though their faecal weights were obviously lower with loperamide. The total number of loperamide capsules taken during the last three days of the study period was much lower than the corresponding number of placebo capsules (median and range respectively 15, 5 (3-18), and 18 (9-18) (P<0.05). During loperamide therapy patients noticed an increased urinary production and experienced an improvement in their ileostomy care and soiling accidents. There were few adverse experiences and these were probably not drug-related, except for one patient who complained of nausea during the opening of his ileostomy because of increased stool consistency. Extensive laboratory tests showed no abnormal results.

We suggest that loperamide, by inhibiting small intestinal peristalsis, prolongs the intestinal transit time and thereby increases the waste and salt absorption. Because of its effectiveness, its low incidence of side effects, and its lack of toxicity, loperamide is a reliable adjunct in controlling excessive ileostomy losses of water and electrolytes and so is advantageous in ileostomy care.


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Diagnosis of Miliary Tuberculosis by Transbronchial Lung Biopsy

In the last 20 years there has been a striking change in the clinical pattern of miliary tuberculosis, with a decrease in frequency but an increase in the number of undiagnosed cases and the age of affected patients.\(^1\) Sputum smears and cultures are frequently negative, so that definitive diagnosis is delayed. We have recently seen a patient whose chest x-ray film showed a miliary pattern in whom miliary tuberculosis was diagnosed by transbronchial lung biopsy within 48 hours of admission. Effective chemotherapy produced a dramatic recovery.

Case History

A 71-year-old Negro was admitted to another hospital with a three weeks' history of lethargy. He had lost 30 lb (13.6 kg) weight over the preceding three months. His temperature was 38°C, pulse 108/min, respirations 24/min, and blood pressure 100/75 mm Hg. He was lethargic but oriented when aroused. Abnormal laboratory data included: leucocyte count 3.7 x 10⁹/l, serum sodium 112 mmol/l. Chest x-ray films showed a diffuse interstitial infiltrate with a miliary pattern. Zielh-Nielsen and auramine-rhodamine stains of the transtracheal aspirate were negative for acid-fast bacilli (A.F.B.). As the patient appeared septic, he was treated with broad-spectrum antibiotics pending culture results. He remained febrile and on the third day was transferred to Denver General Hospital with a temperature of 39°C-3°C. Miliary tuberculosis was now suspected with associated adenoid insufficiency or the syndrome of inappropriate secretion of antidiuretic hormone. Four hours after transfer he was given intravenous corticosteroids and started triple antituberculosis therapy. His fever abated and his confusion cleared within 12 hours. A fiberoptic bronchoscopy and a transbronchial biopsy were done on the third day. Tracheobronchial anatomy was normal; multiple bronchial brushings were obtained for stains, cultures, and cytologic evaluation. Four transbronchial lung biopsies were taken from the lower lobe for culture and histological evaluation. A.F.B. stains of this tissue showed multiple organisms. Smears from the bronchial brushes stained for A.F.B. were negative, though cultures of the brushes were positive.