Loperamide and oro-caecal transit delay

Dr M. Van Wyk and colleagues in a recent paper published in this Journal (1985) concluded that loperamide, unlike diphenoxylate, does not significantly influence oro-caecal transit. This is in contrast with our experience. We studied the effect of intravenous (Basilisco *et al.*, 1985) and oral (data submitted for publication) naloxone on oro-caecal transit time after loperamide in 17 healthy volunteers (ten males, seven females; median age 25 years, range 23–35; median weight 68 kg, range 48–85). The subjects received placebo and loperamide in randomized sequences, and oro-caecal transit time was determined by the lactulose hydrogen breath test. Loperamide (4 × 2 mg tablets in the 14 subjects weighing more than 50 kg and 3 × 2 mg in the others) or identical placebo tablets were given 11.5 and 1 h before ingestion of lactulose. The results for individual subjects are reported in Figure 1; mean (s.d.) transit time was 141.8 (40.0) min after loperamide and 83.5 (33.7) min after placebo ($t = 5.75$, $P < 0.0001$, Student's *t*-test for paired data).

Our results agree with studies in patients with irritable bowel syndrome (Corbett *et al.*, 1981; Cann *et al.*, 1984) where a significant delay in oro-caecal transit was induced by loperamide. It is possible that the difference between our conclusion and that of Van Wyk *et al.* (1985) was due to the different dose and/or schedule of loperamide administration. These authors administered 2 × 2 mg tablets of loperamide 1.5 h before lactulose administration and it should be noted that although the loperamide plasma concentrations do not necessarily correlate with agonistic activity on the gut, the peak plasma concentrations occurs 4 h after intake and the elimination half-life varies from 7 to 15 h (Ooms *et al.*, 1984). Furthermore, in Van Wyk *et al.*'s (1985) study it appears that the drug indeed slowed gastrointestinal transit in five of the

Figure 1 Oro-caecal transit time in 17 subjects after placebo and loperamide.

seven subjects suggesting that statistical significance was not reached due to the small number of subjects tested.

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The influence of loperamide on oro-caecal transit time

We thank Dr Basilisco *et al.* (1986) for their comments on our recently published short report in this Journal (Van Wyk *et al.*, 1985). Indeed, some aspects of their comments as to why our study did not show a statistically significant delay in oro-caecal transit after loperamide pretreatment, are valid. However, as stated in our report, there was a linear relationship between the effects of loperamide and diphenoxylate (Pearson correlation coefficient $r = 0.89$; P values < 0.01). As the number of subjects used in our study was small this may well have influenced the statistical interpretation.

The discrepancy between our results and those of previous studies may possibly be ascribed to the different loperamide dosages and dosage schedules. The results of Cann *et al.* (1984) and Corbett *et al.* (1981) which showed a significant

delaying influence of loperamide on oro-caecal transit time only reflect those of patients with irritable bowel syndrome. These would obviously differ from those of normal volunteers. Therefore, the only comparable studies are those of Basilisco *et al.* (1985) and van Wyk *et al.* (1985).

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