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CORRESPONDENCE

To the Editor: I read with great interest the article by Hafkamp *et al.* (1) concerning the treatment of unconjugated hyperbilirubinemia of Crigler-Najjar disease with orlistat and I would like to make a comment about the method.

The authors found that orlistat treatment achieved an increase in fecal fat concentration and a decrease in fecal unconjugated bilirubin (UCB) concentration in all patients. However, neither fecal fat nor fecal UCB concentrations differed between orlistat responsive and nonresponsive patients. The only difference of responders was a tendency to have a lower dietary fat intake and lower body mass index. The authors acknowledged that orlistat caused gastrointestinal side effects such as diarrhea. However, they provided no data regarding the difference of frequency and severity of diarrhea between responders and nonresponders. Intestinal transit time has an impact on enterohepatic circulation of bilirubin (2). The longer the feces wait in intestinal lumen, the higher the UCB is absorbed by enterocytes. Thus, a reduction in intestinal transit time caused by diarrhea may result in a decrease in enterohepatic circulation of bilirubin. It would be interesting to see if there was any difference in intestinal transit time between responders and nonresponders.

Balahan Makay
Department of Pediatrics
Dokuz Eylül University Hospital
İzmir, Turkey

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2. Kotal P, Vítek L, Fevery J 1996 Fasting-related hyperbilirubinemia in rats: the effect of decreased intestinal motility. Gastroenterology 111:217–223

Response

To the Editor: We appreciate the comments of Makay related to our recent study in which orlistat treatment decreased unconjugated hyperbilirubinemia in Crigler-Najjar disease (1). Makay suggests that the mechanism may be related to a shortened intestinal transit time by orlistat treatment, which then decreases the enterohepatic circulation and plasma concentration of unconjugated bilirubin (UCB) and increases fecal excretion of UCB. We investigated whether support for this possibility exists, but literature on the effect of orlistat on gastrointestinal transit time is scarce. Guerciolini (2) reported that orlistat did not significantly disturb gastrointestinal transit time; however, actual data were not mentioned. Orlistat has been shown to accelerate gastric emptying, but these studies did not report the transit times through the whole intestine (3,4). In our trial, orlistat caused diarrhea in some patients. If the mechanism by which orlistat decreases plasma UCB concentrations would involve intestinal transit time, one would expect the most prominent decrease in plasma UCB concentration in the patients with diarrhea, *i.e.*, with a reduced intestinal transit time. However, this was not the case. Diarrhea was reported equally by responders (patients who had a $>10\%$ decrease in plasma UCB concentration during orlistat) and nonresponders. A number of patients occasionally had remarkably yellow-orange oily stools, but there was no significant difference between the groups. We do realize, however, that the study population was relatively small and that actual intestinal transit time was not measured. We, therefore, cannot conclusively exclude a relationship between intestinal transit time and the orlistat-induced decrease in plasma UCB concentration. A negative relationship between intestinal motility and plasma UCB concentrations was reported previously in Gunn rats (5). We, therefore, propose to study this relationship in more detail in Gunn rats on orlistat treatment.

Anja M. Hafkamp
Henkjan J. Verkade
Department of Pediatrics
University Medical Center Groningen
Groningen, The Netherlands

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