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Hepatocellular transport and gastrointestinal absorption of lanthanum in chronic renal failure

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Lanthanum carbonate is a new phosphate binder that is poorly absorbed from the gastrointestinal tract and eliminated largely by the liver. After oral treatment, we and others had noticed 2–3 fold higher lanthanum levels in the livers of rats with chronic renal failure compared to rats with normal renal function. Here we studied the kinetics and tissue distribution, absorption, and subcellular localization of lanthanum in the liver using transmission electron microscopy, electron energy loss spectrometry, and X-ray fluorescence. We found that in the liver lanthanum was located in lysosomes and in the biliary canal but not in any other cellular organelles. This suggests that lanthanum is transported and eliminated by the liver via a transcellular, endosomal-lysosomal-biliary canicular transport route. Feeding rats with chronic renal failure orally with lanthanum resulted in a doubling of the liver levels compared to rats with normal renal function, but

resulted in a doubling of the liver levels compared to rats with normal renal function, but the serum levels were similar in both animal groups. These levels plateaued after 6 weeks at a concentration below $3 \times 10^{-4} \text{g/g}$ in both groups. When lanthanum was administered intravenously, thereby bypassing the gastrointestinal tract-portal vein pathway, no difference in liver levels was found between rats with and without renal failure. This suggests that there is an increased gastrointestinal permeability or absorption of oral lanthanum in uremia. Lanthanum levels in the brain and heart fluctuated near its detection limit with long-term treatment (20 weeks) having no effect on organ weight, liver enzyme activities, or liver histology. We suggest that the kinetics of lanthanum in the liver are consistent with a transcellular transport pathway, with higher levels in the liver of uremic rats due to higher intestinal absorption.



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Keywords

lanthanum; liver; phosphate binder; renal failure

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