Pharmacokinetics of L-carnitine in patients with end-stage renal disease undergoing long-term hemodialysis.

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Abstract

OBJECTIVE:

L-Carnitine is an endogenous molecule involved in fatty acid metabolism. Secondary carnitine deficiency may develop in patients with end-stage renal disease undergoing long-term hemodialysis because of dialytic loss. In these patients L-carnitine can be administered to restore plasma and tissue levels. The objective of this study was to evaluate the pharmacokinetics of intravenous L-carnitine in patients undergoing long-term hemodialysis.

METHODS:

Twelve patients undergoing three dialysis sessions/week received L-carnitine intravenously (20 mg x kg(-1)) at the end of each dialysis session for 9 weeks. Plasma samples were analyzed for L-carnitine, acetyl-L-carnitine, and total carnitine by HPLC.

RESULTS:

Under baseline conditions, the mean +/- SD predialysis plasma concentration of L-carnitine was 19.5 +/- 5.6 micromol/L, decreasing to 5.6 +/- 1.9 micromol/L at the end of the dialysis session. These concentrations were substantially lower than endogenous levels in healthy human beings. Under baseline conditions the extraction ratios of L-carnitine and acetyl-L-carnitine by the dialyser were 0.74 +/- 0.07 and 0.71 +/- 0.11, respectively. During repeated dosing, there was accumulation of L-carnitine in plasma, and after 9 weeks of dosing, the predialysis and postdialysis plasma levels were 191 +/- 54.1 and 41.8 +/- 13.0 micromol/L, respectively. The predialysis and postdialysis plasma levels of L-carnitine decreased once dosing was ceased but had not returned to pretreatment levels after 6 weeks.

CONCLUSION:

The study demonstrated that removal of L-carnitine by hemodialysis is extremely efficient and that patients undergoing hemodialysis had plasma concentrations that were substantially lower than normal, particularly during dialysis. During repeated administration of L-carnitine, the predialysis and postdialysis concentrations of the

compound increased steadily, reaching an apparent steady state after about 8 weeks. It is proposed that this accumulation arose from the distribution of L-carnitine into a deep tissue pool that includes skeletal muscle.