CARNITOR® levocarnitine injection 1 g/5 mL

Leadiant Biosciences

Carnitine Deficiency in Patients Undergoing Continuous Renal Replacement Therapy (CRRT)

Carnitine: An Intrinsic Component of Mitochondrial Metabolism[1]

- Helps transport long-chain fatty acids into the mitochondria
- Facilitates the production of cellular energy through β-oxidation
- Plays a pivotal role in protecting myocyte cell membranes from oxidative damage

Causes of Carnitine Deficiency

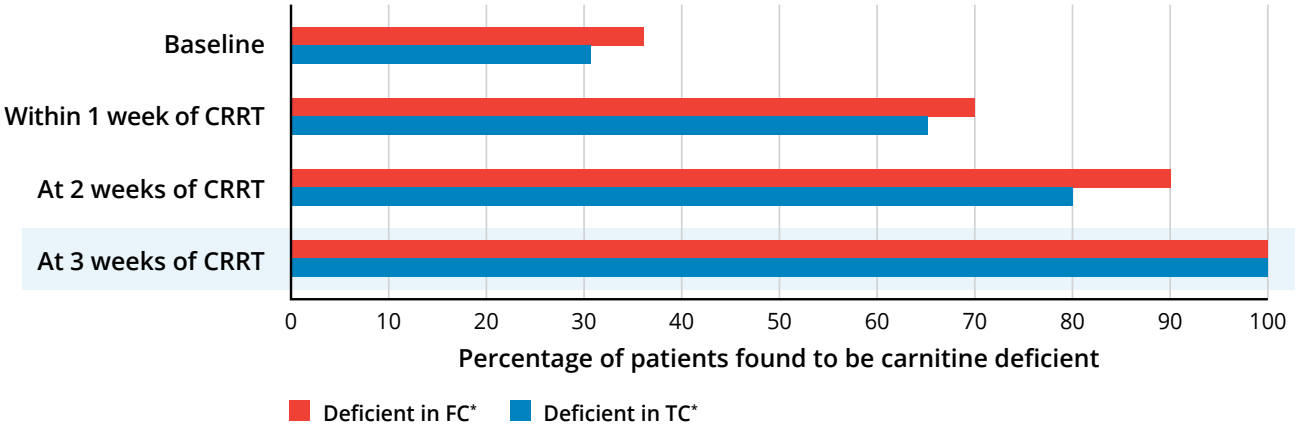
- Can occur as a primary disorder due to the deficiency of L-carnitine cellular transporters[2]
- More prevalent as secondary deficiency due to certain metabolic disorders or conditions such as insufficient intake, medical treatments promoting excretion, and excessive elimination by hemodialysis[2]

Carnitine deficiency in children receiving continuous renal replacement therapy

Kristen Sgambat & Asha Moudgil, *Hemodialysis International* 2016

- Retrospective review based of the records of 42 patients with a mean age of 7.9 ± 1.1 years (range 0-26 years) receiving CRRT at Children's National Health System between 2011 and 2014 due to acute kidney injury (AKI)[1]
- Examined the following parameters[1]:
  - Total carnitine (TC)
  - Free carnitine (FC)
  - Feeding modality
  - Severity of illness
  - Survival outcome

CARNITINE DEFICIENCY IN PEDIATRIC CRRT PATIENTS[1]



*Deficiency was determined by comparing levels to accepted age-based ranges for free and total carnitine.[1]

The percentage of patients with carnitine deficiency increased from 30% to 100% after 3 weeks of CRRT treatment.[1]*

Conclusion: Carnitine deficiency is common in ICU patients and is made profoundly worse with prolonged CRRT.[1]

INDICATION

CARNITOR® (levocarnitine) Injection is indicated for the prevention and treatment of carnitine deficiency in patients with end stage renal disease who are undergoing dialysis.

CARNITOR® (levocarnitine) Injection is also indicated for the acute and chronic treatment of patients with an inborn error of metabolism which results in secondary carnitine deficiency.

Please see Important Safety Information about CARNITOR® on reverse side.

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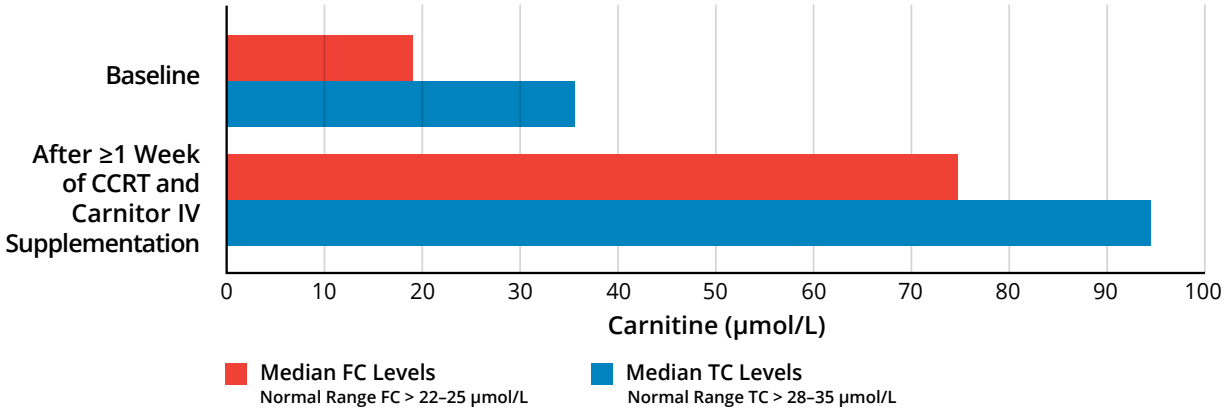
Role of Carnitine Supplementation in Patients Undergoing CRRT

In a subsequent study, the authors demonstrated that supplementation with IV Carnitor in a small cohort of selected pediatric CRRT patients resulted in plasma TC and FC well into the normal range.[3]

- Study of the effect of levocarnitine supplementation on carnitine deficiency in pediatric CRRT patients
- Examined children receiving CRRT due to AKI in an ICU setting

Treatment Cohort (n = 9)
Received 20 mg/kg/day IV carnitine supplementation added to TPN while on CRRT. TC and FC levels were measured at baseline and after ≥ 1 week of CRRT.

CARNITINE LEVELS WITH SUPPLEMENTATION IN PEDIATRIC CRRT PATIENTS[3]



Conclusion: Children undergoing CRRT are at high risk for carnitine deficiency. Carnitine supplementation prevents and treats carnitine deficiency.[3]

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Serious hypersensitivity reactions, including anaphylaxis, laryngeal edema, and bronchospasm have been reported following CARNITOR® administration, mostly in patients with end stage renal disease who are undergoing dialysis. Some reactions occurred within minutes after intravenous administration of CARNITOR®.

If a severe hypersensitivity reaction occurs, discontinue CARNITOR® treatment and initiate appropriate medical treatment. Consider the risks and benefits of readministering CARNITOR® to individual patients following a severe reaction. If the decision is made to re-administer the product, monitor patients for a reoccurrence of signs and symptoms of a severe hypersensitivity.

Drug Interactions

Reports of INR increase with the use of warfarin have been observed. It is recommended that INR levels be monitored in patients on warfarin therapy after the initiation of treatment with levocarnitine or after dose adjustments.

ADVERSE REACTIONS

Neurologic Reactions: Seizures have been reported to occur in patients, with or without pre-existing seizure activity, receiving either oral or intravenous levocarnitine. In patients with pre-existing seizure activity, an increase in seizure frequency and/or severity has been reported.

Gastrointestinal Reactions: Transient nausea and vomiting have been observed. Less frequent adverse reactions are body odor, nausea, and gastritis. An incidence for these reactions is difficult to estimate due to the confounding effects of the underlying pathology.

Hypersensitivity reactions: Anaphylaxis, laryngeal edema and bronchospasm (see WARNINGS AND PRECAUTIONS).

To report SUSPECTED ADVERSE REACTIONS, contact Leadiant Biosciences, Inc. at 1-888-393-4584 or by email at drugsafety@leadiant.com or contact the FDA at 1-800- FDA-1088 or www.fda.gov/safety/medwatch. Please refer to Carnitor Injection Full Prescribing Information provided herein.

References:
1. Sgambat K, Moudgil A. Carnitine deficiency in children receiving continuous renal replacement therapy. *Hemodial Int* 2016;20:63-67.
2. Oami T, Oshima T, Hattori N et al. L-carnitine in critically ill patients—a case series study. *Ren Replace Ther* 2018;4(13):1-8.
3. Sgambat K, Clauss S, Moudgil A. Effect of levocarnitine supplementation on myocardial strain in children with acute kidney injury receiving continuous kidney replacement therapy: a pilot study. *Pediatr Nephrol 2021*. Epub ahead of print.