INNOVATION PARTNERSHIPS
UNIVERSITY OF MICHIGAN

Markers of L-Carnitine Drug Response in Patients with Sepsis

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Diagnostics
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OVERVIEW

Novel predictive and pharmacodynamic serum biomarkers for patients with sepsis

- Identifies sepsis patients most likely to respond to treatment with L-carnitine
- Provides point of care diagnostics to permit personalized medicine in sepsis

BACKGROUND

Sepsis represents the body's response to infection and has become an increasingly common health-care problem that is responsible for 250,000 deaths every year. Despite advancements in sepsis treatment, its management is complicated by a lack of proper diagnostic tools and effective therapies. The development of novel methods for detection and treatments for sepsis has been inhibited by a limited understanding of proper patient selection as well as an imprecise knowledge of medication titration and dosing.

Although pharmacogenomics has been employed to predict drug response in sepsis patients, the results of this approach have yielded only intermittent success. Sepsis is characterized by metabolic disturbances, and preliminary data suggests a relative L-carnitine, a branched non-essential amino acid, deficiency may contribute to metabolic dysfunction. Clinical studies show that traditional phenotyping (e.g., sequential organ failure score (SOFA)) alone is not sufficient to identify carnitine responsive sepsis patients. Thus, there is a growing need for biomarkers that can indicate both the utility of L-carnitine and titration of the dosage.

INNOVATION

Researchers at the University of Michigan have utilized metabolomics to successfully differentiate sepsis patients as either "carnitine responders" or "carnitine non-responders" as a marker for potential treatment response. The blood metabolites used in the approach pioneered by these investigators include detection of ketone bodies, acetylcarnitine (AC), and carnitine (C) as well as a calculation of the AC:C ratio. Clinicians can leverage this data to deliver L-carnatine therapy to appropriate patients early in their clinical course when the intervention has a better chance to provide a favorable response. In general, "low ketone" L-carnitine-treated patients have significantly better survival than "high ketone" L-carnitine-treated patients. Additionally, metabolites of L-carnitine that change over time can identified and may be used to monitor the drug's effectiveness and any signs of adverse drug reactions.