Biomarker Circadian Rhythm Profiles in Critically Ill Mechanically Ventilated Patients

Annually, over 2 million Americans are treated in an intensive care unit (ICU) and experience the emotional and physiologic stress related to this health care milieu. Researchers have reported circadian rhythm disruptions in critically ill patients. Mechanically ventilated ICU patients are among the most critically ill and they comprise about half of the national ICU patient population, yet little is known about their circadian rhythm profiles.

Data from prospective, observational ICU studies have suggested an association between circadian rhythm biomarker recovery and physical recovery; however, these studies have been limited by either short study duration (e.g., 24 hours) or infrequent biomarker sampling (e.g., 12 hours). No reports were found that describe the natural trajectory of circadian rhythms in mechanically ventilated ICU patients. Data from our porcine adult ICU laboratory suggested that 24-hour circadian rhythms return in mechanically ventilated pigs experiencing prolonged acute ICU stress. Because the central pacemaker, which synchronizes individual biologic timing processes, cannot yet be directly observed in clinical studies, core body temperature, cortisol, and melatonin profiles are used as biomarkers for pacemaker function. The mechanism proposed from these findings and the literature is derived from developmental biologists who have found that timing of processes occurring during cellular proliferation and maturation are important to cellular function and, thus, synchronization may lead to optimal physiologic functioning and improved health status.

In this clinical study, we propose to collect urine samples every hour, blood samples every 2 hours, and core body temperature (CBT) readings every minute for up to 7 days or until mechanical ventilation is discontinued in mechanically ventilated ICU patients. Urinary free cortisol (UFC) and 6-sulfatoxymelatonin (6-SMT) levels will be assayed using HPLC. Bladder or rectal CBT will be recorded from the ICU monitor. We hypothesize that circadian cycles in CBT, UFC and 6-SMT biomarker profiles will return in mechanically ventilated ICU patients over time. The aims of this study are to: (1) Describe the cosinor parameters of CBT, UFC, and 6-SMT using an extended, multi-harmonic cosinor model for up to 7 days in mechanically ventilated ICU patients; (2) Compare the rate and time to entrainment of the CBT, UFC, and 6-SMT rhythm profiles; and (3) Measure environmental fluctuations of ambient light, sound, temperature and relative humidity to determine if these factors might explain biomarker profile entrainment.

The objective of this research is to identify predictable biomarker circadian rhythm profiles for guiding future environmental care protocols in the ICU; such protocols can be designed, tested and individualized to improve ICU patient outcomes.