Development of a Traumatic Brain Injury Assessment Score Using Novel Biomarkers Discovered Through Autoimmune Profiling

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Introduction: At present, there is no effective method to objectively assess mild traumatic brain injury (mTBI). The underlying hypothesis for this investigation was that brain-specific autoantibodies can be used to identify proteins that will serve as circulating biomarkers for the assessment of mTBI. The goals of this research were to identify novel brain proteins targeted by TBI-induced autoantibodies and to determine if these proteins contribute to a circulating biomarker signature useful in the diagnosis and assessment of mTBI.

Methods: Patient blood samples were from 2 separate ongoing studies (cohort 1: mild to moderate; cohort 2: moderate to severe). Subjects were adults admitted to an emergency room with a diagnosis of head injury. Admission plasma samples were obtained from cohort 1 (n = 154) and 2 to 7 days postinjury. Cohort 2 (n = 106) had plasma samples obtained at admission, 6, 12, and 24 hours postinjury. Immunosorbtent electrochemiluminescent assays were developed for 2 of the novel biomarker proteins (peroxiredoxin 6, cyclin-dependent kinase 5) and 6 established neuropathology biomarkers. Study samples were interrogated against the newly established panel of biomarkers.

Results: The mean plasma values of 5 of the candidate TBI biomarker proteins in cohort 1 (mild/mod) were significantly (p = <0.03 to <0.0001) elevated at both admission and 2 to 7 days postinjury compared with controls. The mean plasma values of 5 of the candidate TBI biomarker proteins in cohort 2 (moderate/severe) were significantly (p = <0.01 to <0.001) elevated at admission, 6, and 12 hours postinjury compared with controls. The summation of the fold-changes observed in the plasma levels of 5 biomarkers differentiated control samples from both the mild to moderate cohort and the moderate to severe, with scores of 5, 17, and 32, respectfully.

Conclusions: This research has 2 major outcomes that are medically relevant in the mTBI research. First, it demonstrates that autoimmune profiling can be used to identify novel biomarkers for TBI. Second, this investigation demonstrates for the first time that a profile of biomarker responses can form the basis for a diagnostic assessment score that is sensitive for the detection of mTBI and can be standardized across clinical settings.

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Effects of the ResQPod on Maximum Concentration and Time to Maximum Concentration of Epinephrine in a Porcine Cardiac Arrest Model

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Introduction: The ResQPod, an impedance threshold device (ITD), was developed to augment cardiac output during cardiopulmonary resuscitation (CPR). If an ITD used with CPR does increase venous return and cardiac output, then the use of such a device should increase the maximum concentration (Cmax) of epinephrine in the plasma and decrease the time to maximum concentration (Tmax). The purpose of this study was to determine the effect of the ResQPod on kinetics of epinephrine in swine undergoing CPR for cardiac arrest.

Methods: This was a prospective, experimental design. Twelve swine were randomly assigned to 1 of 2 groups: CPR with the ResQPod and CPR without the use of the ResQPod. Pigs were administered potassium chloride by intravenous (IV) route to achieve cardiac arrest. Pigs were allowed to stay in arrest for 2 minutes. After 2 minutes of CPR, epinephrine was administered by IV push. Blood samples were collected at 0, 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 7.5, and 10 minutes after the injection of epinephrine. The analysis of epinephrine in the plasma was performed by the high performance liquid chromatography.

Results: A multivariate analysis of variance indicated that there were no significant differences in the 2 groups relative to the preintervention data (heart rate, arterial blood pressure, cardiac output, stroke volume, size, and mean arterial pressure) (p > 0.05) indicating the groups were equivalent on those parameters. The Cmax with the ResQPod group was less compared with the group without the ResQPod. However, there were no statistically significant differences between the groups relative to either Cmax and/or Tmax (p=0.276).

Conclusions: If the ResQPod enhanced delivery of epinephrine to the central circulatory system during CPR, the device would increase venous return and cardiac output. This in turn would decrease the time to maximum plasma concentration of the circulating epinephrine. It should enhance delivery of drug from the periphery more effectively and increase plasma concentrations. However, enhanced cardiac output would also increase distribution resulting in lower plasma concentrations. Also, it would increase liver blood flow, thereby increasing metabolism resulting in lower plasma levels of the parent drug.

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