Metabolomic Characterization of the Effects of CytoSorb® in a Cohort of Patients Suffering from Multiple Organ Dysfunction Syndrome (MODS): a Study Protocol

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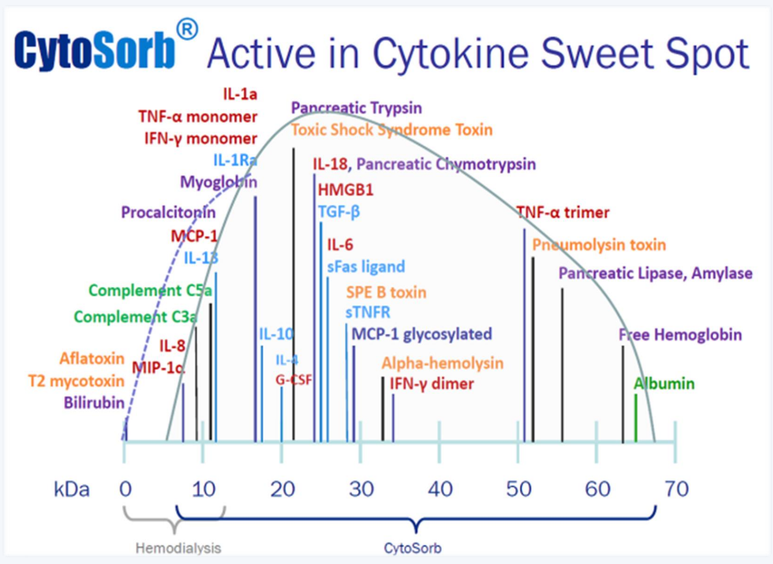
Background

Cytosorb® technology is an extracorporeal blood purification therapy which rapidly reduces the blood levels of inflammatory mediators and medium molecules. By interrupting the inflammatory storm, Cytosorb therapy is associated with hemodynamic and organ damage improvement.

Many studies showed the efficiency of Cytosorb® in the adsorption of pro-inflammatory cytokines, but little is known about the whole metabolic modifications induced by this treatment.

Aim of the study

Aims of our study protocol are: to describe whole metabolic effects of Cytosorb® through metabolomic analyses; to elaborate a mathematic model correlating significant modification to traditional outcomes, such as ICU-mortality, 30-days mortality, improvement of hemodynamics and hepatic and renal damage.



Material and Methods

The design of the study is prospective, observational.

Predicted sample size is 40 patients, receiving at least 1 cycle of Cytosorb®, suffering from MODS, defined as the development of progressive and potentially reversible physiologic dysfunction in 2 or more organs or organ systems: pulmonary, renal, hepatic, central neurologic, cardiovascular, and hematologic systems.

Blood samples will be collected at T0, before starting treatment, and T1=3h, T2=12h and T3=24 hours after Cytosorb® implementation.

Patients' clinical, laboratory and hemodynamic data will be collected at the same time intervals. Blood will be collected in heparin tubes, centrifuged for 10 min to obtain plasma aliquoted in 1.5 mL Eppendorf Safe-lock tubes. We will mark with permanent marker the sample code on each tube and record it on an Excel file. Then, we will store the samples at -80 °C as soon as possible until analysis. For the analysis of metabolomics data, the Excel data matrix containing patients data versus metabolites will be processed using homemade routines Matlab and R based, the integrated web-based platform MetaboAnalyst 4.0 and the SIMCAP+13, the Umetrics Software.

Results

All the groups of samples from patients affected by different response to the MODS perturbation and Cytosorb therapy will be tested as phenotypes of interest and then used to classify unknown sample before the start of treatment. Metabolites involved will be revealed, and they will be classified as "finger print" of these phenotypes. Biochemical links between the metabolites will be highlighted and "similarity" of each sample to the phenotypes will be measured in the metabolomics space.

Canonical pathways and perturbation-related networks will be analysed. All the biochemical links involving cytokines and other molecules will be analysed. Specific metabolomic profiles related to an optimal outcome of patient will be described and proper pre-treatment therapy would be suggested to "prepare" the patients to improve the perturbation response.

Conclusions

Cytosorb indications are expanding. A complete characterization of its performance in modifying the metaboloma could be useful iin predicting the subset of patients one can expect the maximum benefit.