Study Protocol

Efficacy of Therapeutic Plasma Exchange Adsorption Diafiltration(PEAF)
for Septic Shock With Multiple Organ Dysfunction Syndrome in intensive care unit：
A Multicenter,Open-Parallelled ,Randomized and Controlled Clinical Trial

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Principal Investigator Ming Wu MD PhD

Sponsor Shenzhen Second People's Hospital

Investigators and Institutional Review Board

Principal Investigator

Ming Wu MD PhD

Other Investigators

School of Public Health, Southern Medical University

Guangzhou, Guang Dong, China, 510515

Shengli Zhang, Ph.D

Institutional Review Board

The IRB

Background

Septic shock with multiple organ dysfunction syndrome (MODS) is a life-threatening clinical condition due to coagulant disorder immunoparalysis to infection. For this reason the extracorporeal therapies for the treatment of septic shock with MODS have become widespread in the ICU and, at the same time, new extracorporeal depurative techniques have been developed for the removal of inflammatory mediators. One of these techniques is therapeutic plasma exchange (TPE) that remove pathologically elevated cytokines and simultaneously to replace protective plasmatic factors. other techniques is CPFA (coupled plasma-filtration adsorption) that uses a sorbent once the separation between plasma and blood has been obtained with a plasma filter. The others is Plasma dialysis filtration(PDF) that can remove inflammatory mediators for patients with multiple organ dysfunction syndrome.

Aims and Goals

The current protocol is to evaluate the effect of Therapeutic Plasma Exchange Adsorption Diafiltration (PEAF) on Septic shock with multiple organ dysfunction syndrome (MODS).

Setting and design

This is a open-parallelled ,randomized and controlled clinical trial and the study is endorsed by Health and Family Planning Commission of Shenzhen Municipality and Shenzhen Second People's Hospital, and is approved by Medical ethics committee of Shenzhen No.2 People's Hospital.

According to the mortality rate of patients with sepsis combined with MODS in our hospital for about one year is about 40%. The literature reported that the OR of coupled plasma-filtration adsorption(CPFA)treatment group was 0.36 (according to α=0.05, unilateral, 1−β=0.8; n=152(76×2)), according to statistical principles，The sample size calculated by PASS11.0 requires at least 152 cases, an increase of 10% of shedding cases. the total number of cases is at least 168 subjects finally.

Power	Sample Size Grp 1 N1	Sample Size Grp 2 N2	Prop|H1 Grp 1 or Trtmnt P1	Prop Grp 2 or Control P2	O.R. if H0 OR0	O.R. if H1 OR1	Target Alpha	Actual Alpha	Beta
0.8041	76	76	0.1935	0.4000	1.000	0.360	0.0250	0.0259	0.1959

Methods:

The patients are considered registered once the informed consent form has been obtained by the patient or legal representative. The recruitment process ends with the patient center randomisation. Patients will be divided randomly into two arms (control and intervention).

The characteristics of the groups are: Control group: Treatment following the suggestions provided by the recent surviving sepsis guidelines, as well as standard care guidelines typically followed in China. HVHF, High volume hemofiltration for septic shock with MODS is permitted in Control group routinely（Blood pump: 200ml/min, replacement fluid pump 45ml/kg/min, dialysate pump 45ml/kg/min, waste pump 90ml/kg/min, and high-volume hemofiltration for 16 hours with ACF180™ AsahiKASEI or AV1000S™ Fresenius）

Intervention group: the patient is placed in the PEAF group, he/she will receive treatment with PEAF immediately after randomization. PEAF that is TPE (therapeutic plasma exchange 20ml/kg/d Fresh frozen plasma, Blood pump: 120ml/min, replacement pump 20ml/kg/min, dialysate pump 0ml/kg/min, waste pump 20ml/kg/min, plasma exchange 1 hour) plus PFA (Blood pump: 120ml/min, Plasma separation rate 25-30%, plasma-filtration adsorption with Mediasorb™ BELLCO ITALY

≥30ml/min) and HVPDF(High volume plasma diafiltration with ACF180™ AsahiKASEI or Ultraflux AV1000S™ Fresenius , Blood pump same as PFA , replacement fluid pump 2000ml/h, dialysate pump 2000ml/h, waste pump 4000ml/h),with PFA and HVPDF for 15 hours in the first 3 days. Same protocol with control group after 3days.

The scheme of the trial is displayed in figure 1 and figure 2

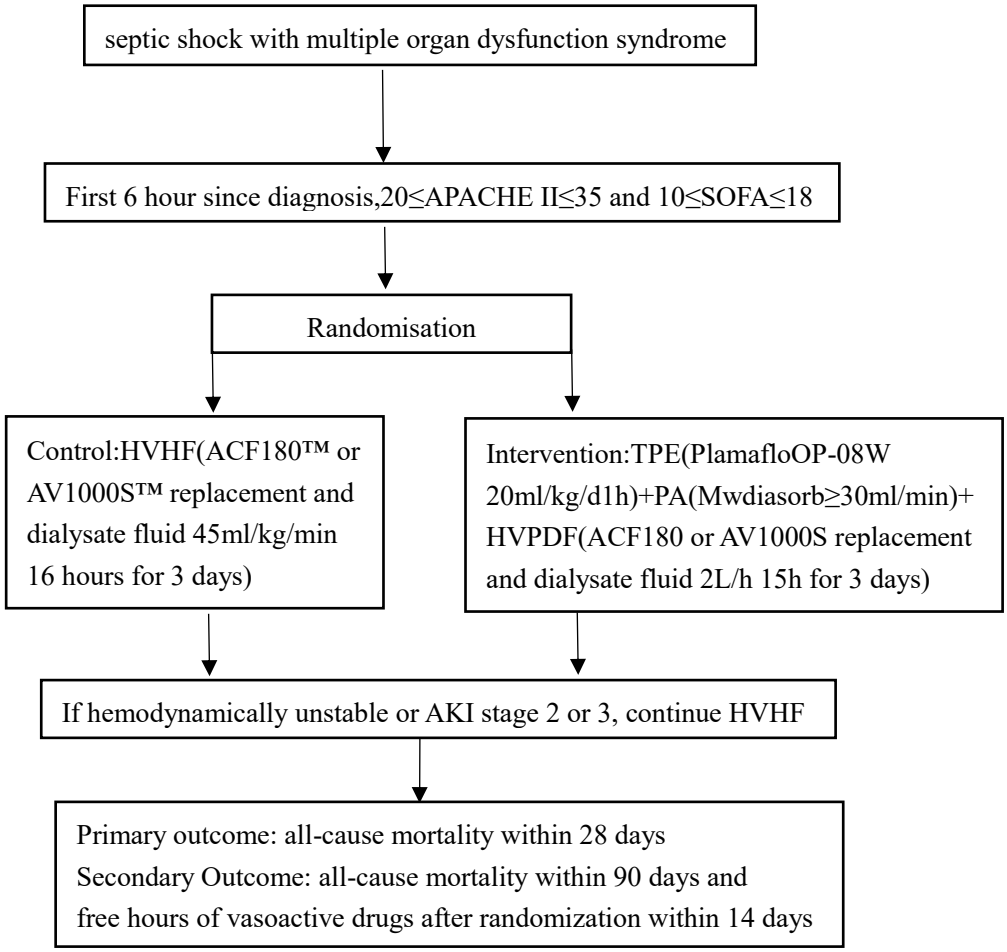

Figure 1: Study diagram

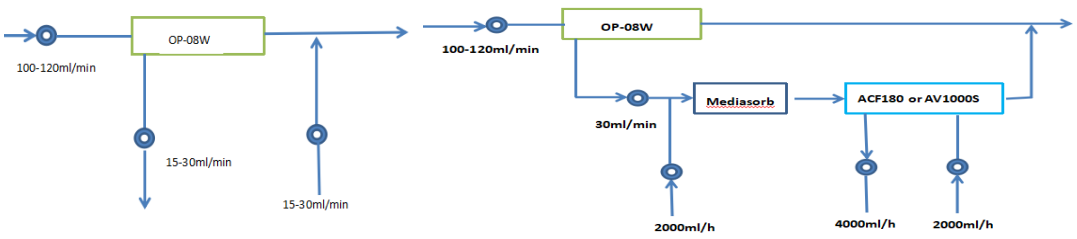

Figure 2: Pipeline connection

Variables and measurements

The primary outcome is all-cause mortality assessed at 28 days from the recruitment of the patient.

Moreover, at the descriptive level and in order to check the homogeneity of both groups, the following variables will be collected at the time of recruitment: birth year, gender, height, dry weight, body temperature, heart rate, blood pressure, count blood cell, glucose level, plasma creatinine, bilirubinaemia, plasma C reactive protein, procalcitonin level, blood gas analysis, lactate, urinary output(mL/kg/hours), arterial oxygen tension/fractional inspired oxygen ratio, International Normalized Ratio(INR),Prothrombin time(second),activated partial thromboplastin time(second),Fibrinogen(g/L),D-Dimer(mg/L),Organ function(Acute Physiology and Chronic Health Evaluation II，Sequential Organ Failure Assessment，The Confusion Assessment Method for The Intensive Care Unit).

Secondary Outcome: all-cause mortality within 90 days from randomization ,free hours of vasoactive drugs after randomization within 14 days.

Finally, for all patients enrolled in the study, 10 ml of whole blood was taken from 8 am to 10 am every day, After centrifugation, the plasma was stored in a negative 80-degree refrigerator for subsequent follow-up testing.