

Expert Opinion on CRRT Application in Treatment of Novel Coronavirus

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National Medical Quality Control Center for Kidney Diseases, Blood Purification and Engineering Technology Branch of CPAM, Academic Committee of Blood Purification of PLA

The prevention and control of novel coronavirus has entered a crucial stage, and the treatment of critically ill patients is the key to reduce mortality. Current clinical research show that the incidence of acute kidney injury in novel coronavirus infected patients is 3% ~10%, and the application rate of continuous renal replacement therapy (CRRT) is 9% ~ 23%. In addition, severely infected patients have serious systemic inflammatory response syndrome (SIRS), which is often accompanied by life-threatening complications such as multiple organ dysfunction syndrome. *The Novel Coronavirus Diagnosis and Treatment Plan (Trial Version 5)* issued by the National Health Commission on February 3 suggests that critically ill patients with high inflammatory reactions may consider blood purification therapy.

The advantages of CRRT in treatment of novel coronavirus include: ①correcting the disorders of water electrolyte and acid-base imbalance, maintain the homeostasis and provide life support; ②removing toxic substances and metabolites; ③effective reducing fluid overload; ④ effective control of hyperthermia; ⑤ improve inflammatory state, endothelial function and immunity. Therefore, the rational application of CRRT is conducive to a better outcome of severe patients and decreasing mortality.

On the basis of summarizing the experience of CRRT applied to atypical pneumonia (SARS) and acute respiratory distress syndrome (ARDS), this expert opinion aims to provide guidance for the rational application of CRRT in the treatment process of novel coronavirus.

I. Indication of CRRT for 2019-nCoV infection

1. Patients with multiple organ dysfunction syndrome, sepsis or septic shock, ARDS and other inflammatory reactions;
2. Severe fluid load, lactic acidosis and other serious electrolyte and acid-base metabolic disorders;
3. Acute kidney injury requires blood purification;
4. Maintenance hemodialysis patients infected with novel coronavirus;
5. Others morbidities like severe pancreatitis, chronic heart failure, etc. complicated with novel coronavirus infection.

II. Contraindications to CRRT for 2019-nCoV infection

There is no absolute contraindication, but caution should be exercised when:

1. Difficult to establish proper vascular access.
2. Refractory hypotension.

III. Timing of start CRRT for 2019-nCoV infection

On the basis of evaluating indications and contraindications of CRRT, nephrologists or intensivists, together with patients and their families jointly decide to adopt and start CRRT. CRRT is recommended in the following situations:

1. Water electrolyte and acid-base balance difficult to correct by drugs;
2. Combined lactic acidosis
3. Combined with acute kidney injury;
4. Maintenance hemodialysis patients infected with 2019-nCoV missed hemodialysis for more than 2 days;
5. CRRT should implement as soon as possible for patients with acute pulmonary edema, ARDS or SIRS, heart failure and severe pancreatitis.

IV. Mode selection of CRRT for 2019-nCoV infection

1. It is suggested to adopt continuous venovenous hemofiltration (CVVH) by post-dilution of 20 ~ 25 ml/(kg.h). If pre-dilution is adopted, the dose should be increased by 5% ~ 10%.
2. For the treatment of severe electrolyte and acid-base imbalance, CVVH or continuous venovenous hemodiafiltration (CVVHDF) can be used, and the dose can be appropriately increased according to the degree of illness and treatment results.
3. For the treatment of severe fluid overload, slow continuous ultrafiltration (SCUF) can be used. The ultrafiltration rate is generally set at 2 ~ 5ml/min, which can be adjusted according to the actual clinical situation. In principle, the total amount of ultrafiltrate at one session should not exceed 4L.
4. CVVH is recommended for the purpose of improving inflammatory state with a dose of ≥ 35 mL/(KGH) of post-dilution; or/and continuous plasma filtration adsorption (CPFA), or hemoperfusion as required.
5. In the treatment of severe ARDS, extracorporeal membrane oxygenation (ECMO) can be used in combination.
6. For maintenance hemodialysis patients infected with novel coronavirus, CVVH or CVVHDF can be used. Recommended schedule can be 6 ~ 8h every other day.

V. Anti-coagulation of CRRT for 2019-nCoV infection

CRRT anticoagulant therapy should be implemented on the basis of fully evaluating the coagulation status of patients and whether contraindication exists.

1. Combined arterial oxygen partial pressure < 60mmHg and/or tissue perfusion insufficiency (serum lactic acid > 4 mmol/L), metabolic alkalosis, hypernatremia and severe liver dysfunction are contraindications to citric acid local anticoagulation.
2. Combined with severe liver dysfunction is a contraindication to argatroban.
3. Heparin drug allergy or heparin-induced thrombocytopenia (HIT) were the contraindications to heparin and low molecular weight heparin.
4. Heparin or low molecular weight heparin is recommended for patients with no active hemorrhage and normal or hyperfunction of coagulation.

(1) Usage of heparin:

For pre-dilution, the load dose is 15-20 mg intravenous injection, and the additional dose is 5-10 mg/h continuous intravenous infusion. For post-dilution, 20 ~ 30 mg intravenous load, and the additional 8 ~ 15 mg/h continuous intravenous infusion. The addition stops 30 ~ 60 min before the end of therapy. The dosage of anticoagulants is adjusted individually according to the coagulation state of patients. The longer the treatment lasts, the more reduction of additional dose should be.

(2) Usage of low molecular weight heparin:

The load dose is 60 ~ 80IU/kg intravenous injection, and the additional dose is 30 ~ 40IU/kg intravenous injection every 4 ~ 6h. The longer the treatment time is, the additional dose should be gradually reduced.

5. Patients with active bleeding or high risk of bleeding:

(1) Anticoagulant drugs may not be used for patients with international normalized ratio (INR) ≥ 1.5 before treatment.

(2) Patients with INR < 1.5 before treatment:

A. If no contraindication to citric acid, it is recommended to use standard citric acid anticoagulation: 4% sodium citrate solution is continuously administered in front of the filter at a dose of 1.3 times of blood flow (ml/min), with free calcium after the filter maintained at 0.25-0.35 mmol/L while in venous blood at 1.0-1.35 mmol/L, until CRRT is completed. It is not recommended to adopt an modified citric acid anticoagulation with calcium-free replacement or dialysis solutions.

B. Patients who are contraindicated to citric acid but no contraindication to argatroban can use argatroban anticoagulation: 1 ~ 2 μ g/(kg.min) for continuous pre-filter administration, or give a certain load dose (about 250 μ g/kg) to control the activated partial thromboplastin time (APTT) or INR < 1.5 times of the basic value with blood samples collected from peripheral vein or arterial terminal of CRRT pipeline, while APTT or INR 1.5 ~ 2.5 times of the basic value of blood samples collected from vein terminal of CRRT

pipeline.

C. For patients complicated with disseminated intravascular coagulation (DIC), anticoagulants will not be used if $\text{INR} \geq 1.5$ after basic anticoagulation with heparin plus transfusion of coagulation factors. If $\text{INR} < 1.5$ the dosage of heparin can appropriately increase.

VI. Indications and Timing of cessation of CRRT for 2019-nCoV infection

1. The patient's vital signs are stable, hemodynamics are normal, functions of vital organs such as heart and lung are restored, disorders of water, electrolyte and acid-base balance are corrected, and daily diuretic-free urine output is ≥ 1000 mL;
2. Patients with recovered renal function but sustained novel coronavirus pneumonia can be treated intermittently for 6 ~ 8 hours every other day.
3. Patients with recovered novel coronavirus pneumonia but impaired renal function may undergo hemodialysis or peritoneal dialysis until the restore of renal function, or the dialysis be maintained.

It should be noted that the treatment experience of CRRT in novel coronavirus is not sufficient at present. With the deepening of understanding of the 2019-nCoV and the accumulation of diagnosis and treatment experience, this expert opinion will be revised and updated later. May this expert opinion help to win the war against the novel coronavirus epidemic and reduce the death rate.