Comparison of the Efficacy and Safety of Dopamine, Norepinephrine and Epinephrine in the Treatment of Pulmonary Hypertensive Crisis under Hemodynamic Monitoring

Study Protocol

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(1) Randomization: Patients who meet the inclusion criteria will be randomly divided into three groups: dopamine, norepinephrine and epinephrine. The randomization method is block randomization, and the ratio of dopamine, norepinephrine and epinephrine in each group is 1:1:1. Each hospital assign the case number from the initial case number to the end of the case enrollment according to the order of the enrolled cases. If an enrolled case is withdrawn for any reason, the case number will be invalidated, and new cases will be assigned by the data management group. If a hospital withdraw from the trial for any reason during the course of the trial, the hospital and patient numbers used by the hospitals that had withdrawn from the trial will be invalid, and the hospital and patient numbers used by the re-enrolled hospitals and patient numbers will be new. The data management group is responsible for number assignment.

(2) Study drug preservation and management scheme:

The study drugs will be purchased by the pharmacy department and be stored according to the conditions required by the instructions. After randomization, clinical orders will be issued by the treating physician and followed by the nurse according to the randomization protocol.

(3) Vasopressor medication regimen:

After starting the study, blood pressure and heart rate will be monitored every 10 minutes during the initial phase, and the clinician will adjust the drug dose according to hemodynamic parameters, blood pressure, and heart rate, with a target mean arterial pressure of ≥65mmHg.

Dopamine group: the initial dose of dopamine is 2ug/kg/min, the dose of dopamine is increased or decreased by 2ug/kg/min, and the maximum dose of dopamine is 20ug/kg/min.

Norepinephrine group: the initial dose of norepinephrine is 0.02ug/kg/min, the dose of up or down regulation is 0.02ug/kg/min, and the maximum dose of norepinephrine is 0.2ug/kg/min;

Epinephrine group: the initial dose of epinephrine is 0.02ug/kg/min, and the dose of epinephrine is 0.02ug/kg/min up or down, and the maximum dose of epinephrine is 0.2ug/kg/min.

When the circulation is stable, the drug dose can be adjusted by monitoring blood pressure and heart rate every 30 minutes. The target mean arterial pressure is 65mmHg or higher, and vasopressors could be discontinued when the patient do not require vasopressors and has been hemodynamically stable for 24 hours, but if MAP is less than 65mmHg again during this period, the study drug can be reintroduced.

Patients are switched to open treatment if they have reached the maximum clinical dose of the study drug during treatment but still have hemodynamic instability, or if they have progressed to SCAI stage D or E, or if they have severe arrhythmias (ventricular tachycardia, ventricular fibrillation, or atrial fibrillation), severe vomiting, or severe tissue necrosis. Transition to open vasopressor therapy is at the discretion of the study physician.

All other treatments - including supplemental oxygen, diuretics, other pulmonary hypertension-targeting agents, and cardiotonic agents (milrinone, levosimendan, and dobutamine) - are left to the discretion of the clinician.

To prevent infection and thrombosis, the floating catheter will be left in place for no more than 72 hours. The maximum duration of the study is 28 days, and patients who are readmitted to the hospital within 28 days of randomization will be assigned to continue the study drug they have previously received to ensure maximum exposure to the study drug. For patients who are hospitalized for more than 28 days, the use of vasopressors will be left to clinician discretion.

(4) Evaluation indicators of drug treatment:

① **Hemodynamic parameters:** hemodynamic parameters at H0, H6, H24, H48, and H72

② **Changes of vital signs (blood pressure, heart rate, respiratory rate)**

are recorded at H0, H2, H4, H6, H12, H24, H48, H72, and then every 24 hours until the day of discharge

③ **Arterial blood gas analysis (lactic acid, PaO2, PaCO2, SaO2)** : H0, H6, H24, H48, H72, day 7, day 14, day 21, day 28 (if the hospitalization time is between 7 and 28 days, the examination on the day of discharge is required)

④ **BNP or NT-proBN**P: H0, H24, H48, H72, day 7, day 14, day 21, day 28 (if the hospital stay is between 7 and 28 days, the test on the day of discharge is required)

⑤ **Echocardiography:** H0, H24, H48, H72, day 7, day 14, day 21, day 28 (if the hospitalization time is between 7 and 28 days, the examination on the day of discharge is required)

⑥ Daily intake and output: intake and output (urine volume must be recorded, drainage volume should be recorded if there is ascites drainage, and diarrhea should be recorded if there is diarrhea, etc.)

(5) The daily cumulative dose and maximum dose of the study drug during the study period will be recorded

(6) The side effects related to the study drug and the dosage of the drug when they occurred will be recorded

Drug-related side effects are as follows:

Dopamine: chest pain, palpitations, arrhythmias (especially at high doses), headache, vomiting, pain in the hands and feet, local necrosis or gangrene, allergies."

Norepinephrine: local tissue necrosis, acute renal failure associated with the study drug, skin whitening along the venous route, injection site skin ulceration, allergy, rash, arrhythmia, headache, and palpitations."

Adrenaline: palpitations, headaches, increased blood pressure, tremors, vomiting, arrhythmias."

(7) Other drug treatment during the study period: including diuretics, targeted drugs for pulmonary hypertension, inotropic drugs (milrinone, levosimendan, dobutamine)