Study Protocol Summary

Title

Low Dose Continuous Furosemide Effect on Cardiac Surgery Patients With Kidney Dysfunction

Main Researcher

dr. Prieta Adriane, SpAn., M.Kes.,KAKV

RS Jantung dan Pembuluh Darah Harapan Kita, Jakarta

Sponsor

none

Aims

1. 1. to Analyze trends in estimated glomerular filtration rate parameters from administration of low-dose furosemide continuous infusion in patients with mild-moderate renal dysfunction undergoing cardiac surgery.
2. 2. To analyze the need for a therapeutic dose of intravenous diuretic after low-dose continuous furosemide in patients with mild to moderate renal dysfunction undergoing cardiac surgery.
3. 3. To analyze the need to use renal replacement therapy as a marker of worsening renal function leading to acute renal failure after continuous administration of low-dose furosemide in patients with renal dysfunction undergoing cardiac surgery.

Ethical Issue(s) of the Protocol

1. Administration of fluids or drugs to patients that can affect patient outcomes
2. Taking blood samples from patients for laboratory examination
3. Evaluating the effects of drug administration
4. Patient condition follow up in study period
5. Inconvenience of patient or family for additional information needed in research involvement

Study Design

Clinical Study : *double blinded randomized controlled study*

Anticipated Outcome

Perioperative administration of low dose continuous furosemide infusion can gives protective effect in cardiac surgery patients with mild to moderate kidney, Measured by the improvement of post operative eGFR

Inclusion and exclusion criteria

Inclusion criteria:

1) 18-65 years old
2) Undergo elective heart surgery, types of surgery: coronary bypass (coronary artery bypass graft/CABG), single heart valve replacement surgery, one or two heart valve repair surgery, coronary bypass surgery with single heart valve repair/replacement.
3) Using cardiopulmonary bypass machine in surgical procedures
4) Patients with ejection fraction >40%
5) Patients with mild to moderate impaired renal function (eGFR 30-89 mL/min/1.73 m2 and have never had renal replacement therapy

Exclusion criteria:

1) Heart disease patients with ejection fraction < 40%

2) Patients with preoperative acute renal failure of any cause

3) Patients with stage 4-5 chronic renal failure and/or who require previous renal replacement therapy

4) Patients with emergency surgery or undergo redo operation heart surgery

5) Patients with complex heart disease, for example those requiring IABP insertion, replacement of more than 2 heart valves, coronary heart disease with severe valve abnormalities, patients with suspected severe pulmonary hypertension.

6) Congenital heart disease patients

7) Patients with major blood vessel (aorta) disorders and/or those affecting the renal artery supply directly

8) Patients who are following other studies that affect drug administration

9) Patients with hemodynamic compromise caused by bleeding, sepsis, anaphylactic or cardiogenic shock

10) Patients who refuse to be involved in the study

***Withdrawal or discontinuation* Criteria**

Kriteria withdrawal:

1) Hemodynamically unstable patient (with persistent hypotension, taking > 2 inotropic drugs/ > 2 vasoactive drugs, patient with IABP, patient with ECMO)
2) Patients in cardiogenic shock
3) Patients with long use of cardiopulmonary bypass machine (>140 minutes)
4) Patients with pulmonary hypertension crisis or severe pulmonary hypertension
5) Patients who have to undergo redo surgery for any reasons
6) Patients with postoperative bleeding requiring large amounts of transfusion
7) Patients given extra bolus furosemide or mannitol outside the established protocol
8) Patients with anaphylactic shock of any cause

Interventions

Ethical clearance for the study was approved by Institutional Review Board of National Cardiovascular Center Harapan Kita. Patients eligible for the study was recruited and written informed consent was obtained after clear explanation of the study. Allocation of furosemide and control group was done using simple computer randomization by staff who was not involved in the study. Furosemide infusion and normal saline was prepared by independent pharmacist blinded to the study. Furosemide solution was prepared to contain 40 mg of furosemide diluted with normal saline to a total volume of 40 cc (1 mg / 1 cc) and control solution was prepared to contain only 40 cc of normal saline. Both solution was packaged in 50-cc syringe and prepared in similar fashion. The solution was administered after induction of anesthesia with rate of 2 cc

per hour for 12 hours.

Metode Analisa*

The data obtained will be analyzed using the SPSS software program. Basic characteristic data will be displayed according to the specified variable type. Numerical variables with normal distribution will be displayed in the form of mean ± standard deviation or median (minimum-maximum) if the distribution is not normal. Categorical variables will be displayed as a percentage (amount). Data from the two groups were analyzed using x2 analysis (chi square) or Fisher's exact test, respectively. The level of statistical significance refers to the P value <0.05

Evaluation Criteria (Response/Outcome)

changes in glomerular filtration rate parameters after intervention in subjects will be evaluated, the need/indication for therapeutic diuretic therapy, and use of renal replacement therapy, length of stay in the ICU and incidence of mortality will be analyzed.

Safety Parameters Criteria (Toxicity)

Renal Function pre and post treatment

Blood gas analysis

Blood electrolyte

Abstract

Background:

Renal dysfunction is consistently an independent risk factor for the development of cardiovascular disease. Several studies have identified that renal dysfunction increases the risk of mortality in patients undergoing cardiac surgery and that the risk increases with the degree of renal dysfunction. Several strategies are used to prevent worsening of kidney function, such as the use of loop diuretics furosemide as prophylactic. Several recent studies have investigated the protective effect of furosemide in cardiac surgery in preventing worsening of renal function, but these studies mostly were conducted in patients with normal renal function. Patients with preoperative renal dysfunction are more in urgent need of effective renal protective strategies. Based on above, this study aimed to analyze the effect of continuous administration of low-dose furosemide on patients with mild to moderate renal dysfunction undergoing cardiac surgery.

Methods:

The study design was a double-blind randomized controlled trial. Subjects will be randomly divided into 2 groups; the furosemide group (n=43) and the control group (n=44). This study started since May 28, 2021; after obtaining an ethical clearance from the hospital ethics committee. Inclusion criteria included patients aged 18-65 years with left heart ejection fraction >40%, mild to moderate renal dysfunction category (eGFR 30-89 mL/min/1.73 m2) who underwent elective cardiac surgery; such as coronary artery bypass graft (CABG), replacement of one heart valve, repair of one or two heart valves, and using cardiopulmonary bypass machine. Exclusion criteria included heart disease patients with stage 4-5 chronic renal failure, on renal replacement therapy, cardiac ejection fraction <40%, emergency or repeat surgery, complex heart disease, congenital heart disease, aortic vascular surgery, massive bleeding, sepsis, and currently participating in other research. Continuous furosemide (2 mg/hour) or 0.9% NaCl (2 mL/hour) was given after the induction of anesthesia and continued until 12 hours of administration. After drug administration was completed (12 hours) the first blood sample was obtained to check blood urea nitrogen concentration, urea, creatinine serum and estimated glomerular filtration rate. Sampling was repeated again at the 24th hour, 48th hour and 120th hour since the drug was started. A decrease in GFR > 20% of the preoperative value is considered a decrease in renal function, and an increase of >20% of third sample value in the fourth sample is considered an improvement of renal function. Deterioration of renal function to severe renal dysfunction or requiring renal replacement therapy is considered an event of acute renal failure.

Keywords: Furosemide, Glomerulus Filtration Rate, Renal Dysfunction, Cardiac Surgery

Researcher,

_____ 24 Maret 2021

dr. Prieta Adriane, SpAn, M.Kes, KAKV