

**N-acetylsysteine versus Prostaglandin E1 as a Renal
Protective Strategy in Infra Renal Aortic CrossClamping Surgery;**

A comparative study

Protocol of Thesis

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"وقل ربي زدني علما"

Aknowledgement

Aknowledgement

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Abstract

Abstract

Objectives:

Our aim is to compare between the effects of intraoperative intravenous N-acetylsysteine infusion to intravenous prostaglandin E1 infusion for prevention of renal injury in patients undergoing abdominal aortic surgery with infrarenal aortic cross clamping.

Patients & Methods:

After approval of our Departmental Ethics and Research Committee, written informed consents were obtained from patients. Thirty patients were enrolled in the controlled randomized study. There were 26 male and 4 female patients with a mean age of 52.056 ± 9.40 years scheduled for abdominal aortic surgery with infrarenal aortic cross-clamping with normal preoperative serum creatinine level (<1.5 mg/dl.), patients were randomly assigned into three equal groups each containing 10 patients as follows:

Control group in which patients were received saline infusion at a rate of 2 ml/Kg/h after skin incision till 30 min after aortic de-clamping, NAC group in which patients were received N-acetylcysteine(FLUIMUCIL® 5g/25ml,Zambon)after skin incision at a dose of 150mg/kg infused in 20 min, followed by an infusion of 20 mg/kg/h till 30 min after aortic de-clamping, and PGE1 group in which patients were received PGE1 (PROSTIN*VR, 0.5mg/mL, Pfizer) after skin incision at a dose of 20 ng/Kg/min till 30 min after aortic de-clamping.

Demographic data including patient's age, weight, gender, ASA score, co-morbidities and indication for surgery were recorded.

Patients' vital signs were monitored before induction of anesthesia as a baseline till 72h postoperatively and it were recorded for this study at the baseline, 5 min after induction, 5 min after starting study drug infusion, 5 min after aortic cross clamp, 5 after removal of the clamp, 5 min before discontinuation of inhaled anesthetics, 12h, 24h, 48h and 72h thereafter postoperatively.

Abstract

These vital signs included heart rate, invasive mean arterial blood pressure, CVP, SpO₂.

The total duration of surgery (started from skin incision till skin closure) and the total duration of infra-aortic cross clamping were also measured. Total amount of fluids and blood products given during surgery were also recorded.

The amount of urine output intraoperatively and the amount of urine output every 12 h during the 1st 72 h postoperatively was collected and measured. Any diuretic use and its dose during the 1st 72 h postoperatively were also recorded.

Blood samples for measurement of plasma creatinine were taken preoperatively then it was repeated at 6h, 24h, 48h and 72h postoperatively. Cystatin C and urinary albumin/creatinine ratio were measured before aortic clamping as a baseline the repeated at 24 h postoperatively.

Serum creatinine based monograms and urine creatinine and urinary albumin were analyzed using routine laboratory methods. Cystatin C was measured using an automated system. The primary endpoint in this study was acute kidney injury as indicated by presence of any of the following:

Fulfilling one or more of RIFLE criteria namely; doubling of serum creatinine, reduction in urine output < 0.5 ml/h over 12 h, reduction in glomerular filtration rate >50% which is calculated using Cockcroft-Gault formula every 24 h for the 1st 72 h postoperatively. Or elevated serum cystatin C level over 1.4 mg/litre. Or elevated urinary albumin creatinine ratio (as an indicator of glomerular injury) >300 mg albumin/g creatinine.

Secondary endpoints were: ICU mortality, ICU length of stay (LOS) and possible postoperative complications including abdominal re-exploration during the 1st 72h after surgery for bleeding or for lower limb ischemia and percent of patients needed vasopressors or inotropes.

Results:

There were no significant statistical differences between the three studied groups as regarding renal protection in that type of patients.

Abstract

Conclusion:

Acute renal injury is a reported complication following abdominal aortic surgery with infra-renal aortic cross-clamping. Although the mentioned role of N-acetylcysteine and prostaglandin E1 in prevention of renal injury, we could not find an evidence of that role in our study population. The principal measure for prevention of acute kidney injury in these patient remained adequate hydration with maintenance of a good perfusion pressure and avoidance of nephrotoxic agents. It is recommended that, to repeat the study on large scale patients with extending the study drugs' infusion time to reach 24 h. Also, it is recommended to repeat the study on patient who required supra-renal clamping of the aorta as the incidence of renal injury in these patients is higher than those with infra-renal clamping.

Key words:

Abdominal aortic surgery – Abdominal aortic aneurysm – Aoro-occlusive disease – Infrarenal aortic cross clamping – Acute kidney injury – Renal protection – N-acetyl cysteine – Prostaglandin E1.

Abbreviations

µg:	microgram
A- type:	atrial type
A.F:	atrial fibrillation
AAA:	abdominal aortic aneurysm
ABG:	arterial blood gases
ACEIs:	angiotensin converting enzyme inhibitors
ACLI:	acute lower limb ischemia
ACR:	albumin/creatinine ratio
ADH:	anti-diuretic hormone
ADQI:	the Acute Dialysis Quality Initiative
AKI:	acute kidney injury
AKIN:	Acute Kidney Injury Network criteria
ALT:	Alanine transaminase
ANP:	atrial natriuritic peptide
AOD:	aortic occlusive disease

Abbreviations

ARF:acute renal failure

ASA:American society of anesthesiologists

AST:aspartate aminotransferase

ATN: acute tubular necrosis

ATP: adenosine tri-phosphate

AVP: arginine vasopressin

AXC:aortic cross clamping

BUN:blood urea nitrogen

BUN:blood urea nitrogen

C3, C4: complement 3, 4

Ca²⁺: calcium

CBC: complete blood count

cc/kg/ hour:cubic centimeter per kilogram per hour

C_{CR}: creatinine clearance

CI-AKI: contrast induced acute kidney injury

CIN:contrast induced nephropathy

CKD: chronic kidney disease

Cl:chloride

CLI:chronic limb ischemia

cm: centimeter

cmH₂O:centimeter water

CO:cardiac output

COX- 1: cyclo-oxygenase-1

Abbreviations

COX-2:cyclo-oxygenase-2

CPB:cardio-pulmonary bypass

CRF: chronic renal failure

CT: computed tomography

CVP:central venous pressure

CXR:chest x-ray

DA1 and DA2:dopaminergic receptors 1 and 2

Dg/gram: dalton gram per gram

ECG:electrocardiography

EDTA:Ethylenediaminetetraacetic acid

EDTA: ethylene diamine tetra acetate

eNOS: endothelial nitric oxide synthase

ESRD: end-stage renal disease

ET: endothelin

EVAR: endovascular aneurysm repair

FE: fractional excretion of sodium

FFP:fresh frozen plasma

GFR: glomerular filtration rate

GGT: gamma glutamyl transferase

gm: gram

GSH/GSSG ratio:reduced glutathione to oxidized glutathione ratio

GSH: glutathione in its reduced form

GST: α -glutathione S-transferase

Abbreviations

- H₂O₂**: hydrogen peroxide
- Hb**:hemoglobin
- Hct**:hematocrit
- HELLP**:*hemolysis, elevated liver enzymes and low platelets*
- HES**:hydroxyl ethyl starch
- I cells**:intercalated cells
- I/R**: ischemia reperfusion
- IABP**:intra-aortic aortic balloon pump
- ICAM-1**:intercellular adhesion molecule-1
- ICU**: intensive care unit
- IHD**:ischemic heart disease
- IL**:intreleukin
- IL-18**: interleukin 18
- IPC**: ischemic preconditioning
- kD**: kilo dalton
- KIM-1**: kidney injury molecule-1
- L**: Litre
- LD**: lactate dehydrogenase
- LOS**:length of ICU stay
- M:F**:male to female ratio
- m²** :square meter
- MAP**:mean arterial pressure
- mcg/kg/min**:microgram per kilogram per minute

Abbreviations

MDRD:	the Modification of Diet in Renal Disease study equations
mEq/L:	milli-equivelant per litre
mg/d:	milligram per day
mg/dl:	milligram per decilitre
mg:	milligram
MI:	myocardial ischemia
ml/hour:	milliliter per hour
mL:	millilitre
mmHg:	millimeter mercury
mmol:	millimol
mOsm:	milliosmol
n:	number
Na+:	sodium
NAC:	N-acetyl cysteine
NaCl:	sodium cholride
NAG:	urinary N-Acetyl- β -D-glucosaminidase
ng/kg/min:	nanogram per kilogram per minute
NGAL:	neutrophil gelatinase-associated lipocalin
NHE3:	sodium-hydrogen exchanger 3
NO:	nitric oxide
NORF:	non oliguric renal failure
NSAID:	non steroidal anti-inflammatory drugs
O.R:	operation room

Abbreviations

OH: hydroxyl radicals

P cells: principal cells

p:p value

PACU:postoperative care unit

PaO₂:arterial oxygen tension

PC:prothrombin concentration

P_{CR}: plasma creatinine

PEEP: positive end-expiratory pressure

PENIA:particle-enhanced nephelometric immunoassay

PG: prostaglandin

pH:power of hydrogen

PRCs:packed red blood cells

proANP[1-98]: proatrial natriuretic peptide (1-98)

PT:prothrombin time

RBF: renal blood flow

RBS:random blood sugar

RCIN:radiocontrast induced nephropathy

RIFLE: R, risk; I, injury; F, failure L, loss; E, end-stage

RIPC: remote ischemic preconditioning

ROS: reactive oxygen species

RPF: renal plasma flow

RR:respiratory rate

S_{Cr}: serum creatinine

Abbreviations

SD:standard deviation

SIRS:systemic inflammatory response syndrome

SPO₂: arterial oxygen saturation

SVR: systemic vascular resistance

T12-L1: 12th thoracic to 1st lumbar vertebrae

T12-L3: 12th thoracic to 3rd lumbar vertebrae

TAAA: thoraco-abdominal aortic aneurysm

TNF- α :tumor necrosis factor alpha

U/S:ultrasound

U: P_{OSM}: urine-to-plasma osmolar ratio

U_{CR}:urinary creatinine

UOP:urine output

Urinary b-NAG: urinary beta-N-acetyl glucosaminidase

V: urinary flow rate

X clamp: aortic cross-clamping

α_1 : alpha-1 sympathetic receptors

β_1 : beta-1 sympathetic receptors

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