

The role of Trimetazidine in the Prevention of Contrast-Induced Nephropathy After Coronary Angiography Procedures

Thesis

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

لَسْبَدَّ اُنْكَ لَا عِلْمَ لَنَا
إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْعَظِيمُ

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List of Abbreviations

Abb.	Full term
ACE.....	Angiotensin converting enzyme
AKI.....	Acute kidney injury
ARB.....	Angiotensin receptor blocker
ARF.....	Acute renal failure
AS.....	Aortic stenosis
ATP.....	Adenosine triphosphate
BP.....	Blood pressure
CABG.....	Coronary artery bypass grafting
CAD.....	Coronary artery disease
CHF.....	Congestive heart failure
CI-AKI.....	Contrast induced acute kidney injury
CIN.....	Contrast induced nephropathy
CM.....	Contrast media
COX.....	Cyclooxygenase
CT.....	Computed tomography
CTGF.....	Connective tissue growth factor
CVS.....	Cerebrovascular stroke
DM.....	Diabetes mellitus
ECG.....	Electrocardiography
eGFR.....	Estimated glomerular filtration rate
ET-1.....	Endothelin 1
H ₂ O ₂	Hydrogen peroxide
HF.....	Heart failure
HOCM.....	High-osmolar contrast media
HR.....	Heart rate
IV.....	Intravenous
LAD.....	Left anterior descending artery
LCX.....	Left circumflex artery
LM.....	Left main trunk
LOCM.....	Low-osmolar contrast media
LVEDV.....	Left ventricular end-diastolic volume
LVEF.....	Left ventricular ejection fraction
LVESV.....	Left ventricular end-systolic volume

List of Abbreviations cont...

Abb.	Full term
MI.....	Myocardial infarction
MR.....	Mitral regurgitation
MVD.....	Multivessel disease
NAC.....	N-acetylcysteine
NaCl.....	Sodium chloride
NAHCO ₃	Sodium bicarbonate
NO.....	nitric oxide
NSAIDs	Non-steroidal anti-inflammatory drugs
NYHA.....	New York Heart Association
O ₂	Superoxide radical
OH-.....	Hydroxyl radical
OM	Obtuse marginal
PCI	Percutaneous coronary intervention
PVD.....	Peripheral vascular disease
RCA.....	Right coronary artery
RCTs	Randomized controlled trials
ROS.....	Reactive oxygen species
RR	Relative risk
SCr	Serum creatinine
SFA	Superficial femoral artery
TMZ.....	Trimetazidine
TR.....	Tricuspid regurgitation
TRT	Targeted renal therapy
Vs	Versus

Abstract

The reported incidence of CIN following percutaneous coronary intervention lies between 0 and 24%. This depends on the associated risk factors, with the greatest incidence being reported after emergency PCI.

Patients who develop CIN have greater complications, a worse prognosis, more serious long-term outcomes, and longer duration of hospital stay. Hospital mortality rates in such patients have been reported as 36% and the two-year survival rate as only 19%. Following PCI, CIN is linked to higher incidence of cardiogenic shock, pulmonary edema and need for target vessel revascularization after one year.

The pathophysiology of CIN encompasses multiple interacting mechanisms. They include induced vasospasm of the renal vessels where the medulla is already relatively hypoxic, direct cytotoxic effects on renal cells and indirect damage through the generation of oxygen free radicals.

Keywords: Aortic stenosis- Coronary artery disease- Cyclooxygenase- Cerebrovascular stroke- Electrocardiography- N-acetylcysteine

INTRODUCTION

Contrast induced nephropathy (CIN) may be defined as Acute renal failure (ARF) that occurs within 24-72 hours of exposure to I.V. or intra-arterial iodinated contrast media that cannot be attributed to other causes. In most cases it is a non-oliguric ARF with an asymptomatic transient decline in renal function. ^[1]

The renal function impairment is mirrored by an absolute increase by 0.5 mg/dl (or greater) or relative increase by 25% (or greater) of serum creatinine from baseline or better by a decrease in urine output to 30-60ml/min.

The rise in serum creatinine is peaking on the third to fifth day post-contrast exposure returning to baseline within 10-14 days. ^[2]

CIN occurs in up to 5% of hospitalized patients with normal renal function prior to injection of contrast media. ^[3]

It occurs more frequently in patients with renal impairment particularly if associated with diabetic nephropathy. ^[4]

Among all procedures utilizing contrast agents for either diagnostic or therapeutic purposes, coronary angiography and percutaneous coronary interventions are associated with the highest rates of CIN. ^[5]

This is mainly related to:

- Intra-arterial injection.
- High dose of contrast used.
- Type of patients who are usually in advanced age with one or more comorbid conditions such as advanced vascular disease, severe long standing hypertension, diabetes and some renal function impairment.^[6]

It has been demonstrated that the use of low-osmolar contrast media (LOCM) rather than high-osmolar contrast media (HOCM) is beneficial in reducing the incidence of CIN in patients with pre-existing renal failure.

Adverse reactions to contrast media with occurrence of CIN range from 5% to 12% for HOCM and for 1-3% for LOCM.^[7-10]

The European Society of Urogenital Radiology has stated that the real risk of CIN are represented by the presence of pre-existing renal impairment particularly when secondary to diabetic nephropathy, but also to salt depletion and dehydration, congestive heart failure, an age greater than 79 years and concurrent use of nephrotoxic drugs.^[11-12]

It is necessary to use precautions to prevent contrast media induced nephrotoxicity.^[13-16]

The first precaution is to monitor renal function by measuring serum creatinine before and daily for 5 days after contrast injection. ^[17]

The second precaution is to discontinue the nephrotoxic drugs (aminoglycosides, vancomycin, amphotericin B, metformin & non-steroidal anti-inflammatory) drugs before the procedure. ^[18]

The third precaution is adequate hydration of the patient. ^[19-20]

IV infusion of 0.9% saline at a rate of about 1ml/kg body weight per hour beginning 6-12 hours before the procedure and continuing for 12-24 hours after the procedure. ^[17]

The fourth precaution is choosing LOCM to be the contrast of choice. ^[21]

The fifth precaution is the use of anti-oxidants as N-acetyl cysteine ^[22], ascorbic acid ^[23] and statins. ^[24]

Recently, Trimetazidine has been described as a cellular anti-ischemic agent. ^[25]

Previous studies demonstrated that Trimetazidine prevents the deleterious effects of ischemia-reperfusion at both the cellular and mitochondrial levels and exerts an anti-oxidant effect. ^[26]

It inhibits excess release of oxygen free radicals, limits cellular acidosis, protects ATP stores, reduces membrane lipid peroxidation and inhibits neutrophil infiltration. ^[27]

The administration of Trimetazidine (35 mg twice daily) is an effective way for preventing transient renal dysfunction due to radio-contrast agents.