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

Thesis

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By

Tarek AbdelSalam AbdelFattah Ibrahim

M.B.B.Ch.

Under supervision of

Professor.Ramzy Hamed El-Mawardy

Professor of Cardiology-Cardiology Department
Faculty of Medicine – Ain Shams University

Ass.Prof.Ahmed Shawky El-Serafy

Assistant Professor of Cardiology-Cardiology Department
Faculty of Medicine – Ain Shams University

Dr. Ehab Mohammed El-Fekky

Lecturer of Cardiology-Cardiology Department
Faculty of Medicine – Ain Shams University

Cardiology Department, Faculty of Medicine,
Ain Shams University, **2016**

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Tarek AbdelSalam Abdel Fattah Ibrahim

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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
H2O2	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-sytolic volume

List of Abbreviations cont...

Abb.	Full term
MI	Myocardial infarction
MR	Mitral regurgitation
MVD	Multivessel disease
NAC	N-acetylcysteine
NaCl	Sodium chloride
NAHCO3	Sodium bicarbonate
NO	nitric oxide
NSAIDs	Non-steroidal anti-inflammatory drugs
NYHA	New York Heart Association
O2_	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.