بسم الله الرحمن الرحيم

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تم رفع هذه الرسالة بواسطة /صفاء محمود عبد الشافى

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

ملاحظات: لايوجد

Silymarin for the Prevention of Contrast Induced Nephropathy after Percutaneous Coronary Intervention in Patients with Acute ST Segment Elevation MI

Thesis

Submitted for Partial Fulfillment of Master's Degree of Cardiology

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2022

سورة البقرة الآية: ٣٢

Acknowledgment

First and foremost, I feel always indebted to ALLAH, *the Most Kind and Most Merciful.*

I'd like to express my respectful thanks and profound gratitude to **Prof. Dr./ Ahmed Mohamed El-Missiri,** *Professor of Cardiology - Faculty of Medicine- Ain Shams University for his keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.*

I am also delighted to express my deepest gratitude and thanks to **Dr / Abd El-Rahman Elsayed Attia,** *Lecturer of Cardiology, Faculty of Medicine, Ain Shams University, for his kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.*

I would like to express my hearty thanks to all my family for their support till this work was completed.

Last but not least my sincere thanks and appreciation to all patients who participated in this study.

Aya Malik Amin

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List of Abbreviations

Abb.	Full term
ACT	*Acetylcysteine for Contrast-induced nephropathy Trial*
AD	*Alzheimer's disease*
AKI	*Acute kidney injury*
ARF	*Acute renal failure*
BMI	*Body mass index*
bpm	*Beat per minute*
CIN	*Contrast induced nephropathy*
CKD	*Chronic kidney disease*
CM	*Contrast media*
eGFR	*Estimated glomerular filtration rate*
ET-1	*Endothelin*
GFR	*Glomerular filteration rate*
H2O2	*Hydrogen peroxide*
HF	*Heart failure*
HOCM	*High-osmolar contrast media*
HR	*Heart rate*
HS	*Highly significant*
LOCM	*Low-osmolar contrast media*
LVEF	*Left ventricular ejection fraction*
NS	*Non significant*
*O2_*	*Superoxide*
*OH_*	*Hydroxyl radical*
PCI	*Percutaneous coronary intervention*

List of Abbreviations

Abb.	Full term
PCI	*Percutaneous coronary intervention*
RBS	*Random blood sugar*
RI	*Renal impairment*
ROS	*Reactive oxygen species*
S	*Significant*
Scr	*Serum creatinine*

INTRODUCTION

Contrast induced nephropathy (CIN) is defined as acute renal injury that occurs within 24-72 hours of exposure to I.V. or intra-arterial iodinated contrast media that cannot be attributed to other causes. [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. [1]

The rise in serum creatinine usually peaks on the third to fifth day post-contrast exposure and returns 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 medium 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.[7]

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 due 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]

Aim of the Work

To study the role of a single dose of silymarin in the prevention of CIN in patients with acute ST elevation MI undergoing primary percutaneous coronary intervention.

Chapter 1
CONTRAST-INDUCED NEPHROPATHY

Contrast induced nephropathy (CIN) is a grave complication of angiographic procedures and arises from administration of iodinated contrast media (CM) [17]. CIN is the third most common cause of hospital acquired acute renal injury representing about 12% of the cases. The incidence of CIN varies from 0 to 24% depending on the patient's risk factors [18].

It is generally a transient and reversible state of acute renal injury [19]. However, the development of CIN is linked to a more prolonged hospital stay, an augmented morbidity and mortality and higher healthcare costs. [17]

Treatment of CIN is predominantly of supportive nature, consisting of calculated fluid and electrolyte management; however, dialysis may be required in some cases. [20]

Definition:

Clinical and experimental studies have used different laboratory parameters to define CIN. [21,22] Currently, CIN is most commonly defined when either of the following occur within 48 hours after contrast administration and persists for two to five days: [23-29]

- A 25% increase in serum creatinine (SCr) concentration from baseline value, Or

- An absolute increase in SCr of at least 0.5 mg/dL (44.2 µmol/L)

Epidemiology

CIN is one of the most significant causes of hospital-acquired acute kidney injury (AKI).[30]

The reported incidence of CIN following percutaneous coronary intervention (PCI). This depends on the associated risk factors, with the greatest incidence being reported after emergency PCI. [32-34]

The incidence of CIN is low in patients with normal renal function (0-5%). [35] However, several prospective controlled trials reported an incidence of 12-27% in patients having preexisting renal impairment. [36] Moreover, in one study, an incidence as high as 50% was found in patients with diabetic nephropathy undergoing coronary angiography despite the use of low-osmolar contrast medium (LOCM) and adequate hydration.

Sequelae:

Patients who develop CIN have greater complications, a worse prognosis, more serious long-term outcomes, and a longer hospital stay, which result in elevated medical costs.[37,38]

CIN may also be linked to an increased risk of death which is independent of other risk factors. [37] Hospital mortality rates in such patients have been reported as 36% and the two-year survival rate as only 19%. [38]

Patients who undergo a primary percutaneous intervention for acute myocardial infarction and the procedure complicates with CIN were reported to be significantly more likely to have major complications within hospital admission such as acute pulmonary edema, the need for pacemaker insertion, cardiogenic shock, and respiratory failure. [39] Patients with renal insufficiency are at a more significant risk of developing atherosclerosis. [40]

Pathophysiology

No definitive answer has been defined as regards the pathogenesis of CIN in the literature. The most commonly reported theory for the development of CIN following contrast administration relies upon the vasoconstriction of the vessels in the renal medulla leading to reduced oxygen delivery. [41]

Moreover, reduced oxygen delivery and prolonged vasoconstriction lead to enhanced production of oxygen-free radicals such as hydrogen peroxide and superoxide leading to increased damage. [42] Other suggested causes of this condition are elevated blood viscosity, reperfusion injury, direct toxic damage to the cells, and the release of dopamine, angiotensin II