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RADIOGRAPHIC CONTRAST MEDIA INDUCED NEPHROPATHY IN PCI: A REVIEW

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INTRODUCTION

Percutaneous coronary intervention (PCI) is one of the two coronary revascularization techniques which are in use today for the treatment of coronary heart disease, the other one is coronary artery bypass grafting (CABG). PCI is a non surgical procedure for the revascularization of the coronary artery using a balloon catheter.[1] In India an exponential increase is seen in the rate of coronary interventions each year and the study reports shows that a total of 152332 PCI were done per year.[2] Various types of contrast-medias have been developed for use in PCI.[3] The main side effect associated is contrast induced nephropathy (CIN). In the general population the estimated incidence of contrast induced nephropathy was found to be 1-6% but in some patient sub-groups the risk may be as high as 50%. Even a small increase in serum creatinine level results in prolonged hospital stay, excess cost and dialysis is required for less than 1% patients.[4] Because of the high prevalence of acute kidney injury (AKI) seen in patients undergoing PCI, defining strategies to minimize the risk of AKI and to improve the safety and efficacy of the procedure is beneficial.[5]

Percutaneous Coronary Intervention

Percutaneous means "through unbroken skin". Percutaneous coronary intervention is performed by inserting a catheter through the skin in the groin or arm into an artery.[6] PCI involves both coronary angiography (CAG) and percutaneous transluminal coronary angioplasty (PTCA).[7] CAG is the "gold standard" for evaluating and defining coronary

artery disease.[8] It is used to identify the exact location and severity of CAD.[7] Coronary angioplasty is a non-surgical procedure that uses a catheter to place a small structure called a stent to open up blood vessels in the heart that have been narrowed by plaque buildup, a condition known as atherosclerosis.[9] When coronary angioplasty is carried out as an emergency after a heart attack, then it is called a primary PTCA, and has been advocated for treatment of acute myocardial infarction for over 15 years.[10]

Radiographic Contrast Media Used In PCI

Contrast agents are used as diagnostic molecules for the visualization of the vascular system. Radiographic contrast agents, or contrast media, are injected during PCI to render the intravascular structures visible.[11] Some of the common radiographic contrast media used in PCI are iodixenol, iohexol, sodium meglumine diatrizoate, iopamidol, ioxaglate etc.[12] One of the main factor contributing to high cost of PCI is the hike in the cost of contrast media. In angiogram procedure about 30 – 50 ml and in angioplasty about 150 – 250 ml of contrast dye is used. The price of contrast dye is nearly in the range of Rs. 500- 1000.[13] The different agents can be classified based upon three properties includes; The charge of the iodinated molecule (ionic or nonionic), The molecular structure (monomeric or dimeric) and The osmolality of the injected preparation (hyperosmolal, low osmolal and iso-osmolal relative to normal serum osmolality).[11]

Contrast Induced Nephropathy

Contrast-induced nephropathy is a serious complication of angiographic procedures resulting from the administration of contrast media (CM).[14] Nowadays, high-osmolar contrast media have been replaced by low-osmolar and iso-osmolar contrast media because of better tolerability, lower side effects, and, importantly, a lower incidence of CIN.[15] Contrast induced nephropathy, also known as 'contrast induced acute kidney injury' affects up to 15.3% of all hospitalized patients. Acute kidney injury -defined as Acute Kidney Injury Network (AKIN) stage 1 or greater or a new requirement for dialysis following PCI.

1. Stage 1 is defined as an absolute increase of ≥ 0.3 mg/dL or a relative increase of 50% in serum creatinine (S.Cr).
2. Stage 2 is defined as an increase in serum Cr to more than 200% to 300% (>2-to 3- fold) from baseline,

3. Stage 3 is defined as increase in serum Cr to more than 300% (>3-fold) from baseline (or serum Cr of more than or equal to 4.0 mg/dl with an acute increase of at least 0.5 mg/dl.[16]

As per Contrast Media Safety Committee of the European Society of Urogenital Radiology (ESUR), CIN is defined as an increase in serum creatinine of at least 25% or ≥0.5 mg/dl (44μmol/L) from baseline within 48 h after excluding other factors that may cause nephropathy, such as nephrotoxins, hypotension, urinary obstruction, or atheromatous emboli. Serum creatinine is the standard marker to detect CIN.

Pathophysiology

Although the definite mechanism of CIN is not well-understood, several mechanisms have been proposed.

- Renal medullary hypoxia due to either a decrease in vasodilators (nitric oxide or prostaglandins), or an increase in vasoconstrictors (adenosine and endothelin).
- Direct toxicity of CM which could be related to harmful effects of free radicals and oxidative stress.
- In addition, apoptosis may also play a role in the development of CIN.[17]

Two significant processes are known to be involved in the pathophysiology of CIN-vasoconstriction resulting in medullary hypoxia and direct toxicity caused by the contrast media to renal tubular cells. The mechanisms that have been implicated in these processes are dehydration, decreased prostaglandin and nitric oxide induced vasodilatation, impaired endothelial function, increase in renal adenosine concentration, increase in oxygen free radicals in response to hyper-osmotic load, increased intratubular pressure owing to contrast induced diuresis, increased urinary viscosity and obstruction of the tubules.[18]

Patient Related Risk Factors

The patient related risk factors are Older Age, Gender, Pre-existing Renal Disease, Diabetes Mellitus, Congestive Heart Failure and Reduced Left Ventricular Ejection Fraction, Hypertension, Angiotensin-Converting Enzyme (ACE) Inhibitors, Nephrotoxic Drugs, Multiple Myeloma, Metformin, Hypovolemia, Hypotension.[19]

Risk Scoring and Stratifications

Contrast-induced nephropathy is a possible complication of coronary diagnostic and interventional procedures.[20] Several risk stratification scoring systems have been developed to assess the risk of developing CIN. Mehran risk score, the most widely used and classic model for CIN.[21,22]

Treatment and Prevention Strategies

There is no definitive treatment available for established CIN. Several pharmacological and non-pharmacological approaches have been evaluated for the prevention of CIN. The prevention strategies are most important in patients at high risk for CIN, such as those with AKI or preexisting chronic kidney disease (CKD).

Non pharmacological approach	Pharmacological approach
• Minimizing the volume of CM • Preventing volume depletion • Avoiding activation of renal vasoconstriction • Avoid concomitant use of diuretics or nephrotoxic drugs (NSAIDs and aminoglycosides). • Avoid repetitive studies that are closely placed • Hemodialysis to remove CM from the circulation • Hemofiltration	• Volume expansion: dilution of contrast media by more fluid • Sodium bicarbonate: reduce free radical formation • Antioxidants (NAC and ascorbic acid): scavenging oxygen-derived free radical • Dopamine: increase renal blood flow and GFR.[14]

CONCLUSION

PCI is the main reperfusion technique used for the re-vacsularisation of the occluded coronary arteries. Contrast agents are used as diagnostic molecules for the visualization of the vascular system. Radiographic contrast agents, or contrast media, are injected during PCI to render the intravascular structures visible The usage of contrast media results in Contrast Induced Nephropathy, the main side effect of PCI. In an average about 15% of the patients undergoing PCI had got affected with CIN. In post- PTCA patients, a proper monitoring of the serum creatinine level and possible risk factors are necessary. Clinical pharmacists can play an important role in the detection and prophylatic management of CIN in high risk patients.

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