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The Impact of Hydration and Other Strategies in prevention of Contrast-Induced Nephropathy

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Abstract

Introduction and purpose

Contrast-induced nephropathy (CIN) remains a significant concern in clinical practice, particularly among patients undergoing contrast-enhanced imaging or interventional procedures. Characterized by an acute decline in renal function following exposure to contrast media, CIN not only poses substantial morbidity and mortality risks but also presents

challenges in patient management and healthcare resource utilization. Despite extensive research efforts, the precise pathophysiology of CIN remains incompletely understood, with multifactorial mechanisms involving renal ischemia, oxidative stress, and direct tubular toxicity implicated in its development. This review explores the impact of hydration and other prophylactic strategies on the prevention of CIN. Numerous studies have demonstrated the effectiveness of various hydration protocols, including isotonic saline and bicarbonate solutions, in reducing the incidence of CIN. Additionally, the review evaluates the efficacy of pharmacological agents such as N-acetylcysteine, statins, and ascorbic acid, as well as emerging techniques like remote ischemic preconditioning.

Material and method

There was a comprehensive review of the literature available in the "Pubmed" and Google Schoolar databases. The primary focus was on identifying high-risk patients and exploring possibilities for decreasing the risk of developing CIN.

Summary

Our review managed to present the current understanding of risk factors and prevention strategies for contrast-induced nephropathy (CIN), encompassing key aspects such as etiology, risk-factors and preventative interventions. Through the synthesis of diverse research findings, we explore the multifaceted nature of CIN development, including the influence of patient-related factors like renal function, comorbidities, and medication usage, as well as procedural variables such as contrast volume and type. By analyzing various studies and meta-analyses, we aim to elucidate the complex interplay of these factors and provide clinicians with evidence-based insights into risk stratification and preventive measures.

Keywords: Contrast-induced nephropathy, hydration, CIN, risk factors, prevention, contrast media, acute kidney injury, renal dysfunction

Introduction

With the ever-increasing utilization of contrast media in diagnostic and interventional procedures, the occurrence of contrast-induced nephropathy (CIN) has also been on the rise. CIN is a form of acute kidney injury occurring after administering contrast media for diagnostic imaging procedures. It is estimated to be the third most common cause of hospital-acquired renal failure and is associated with significant morbidity and mortality. (1) Even a minor CIN may increase the risk of adverse outcomes and have a long-term impact on patient. (2)

Contrast agents play a significant role in modern medical imaging as they enhance the visibility of blood vessels and organs, allowing for better diagnosis and evaluation of various medical conditions. They are commonly used in diagnostic procedures such as computed tomography scans, angiography, and cardiac catheterization. With the use of contrast media becoming more prevalent, it is important to understand the risk factors for developing CIN and how to prevent its occurrence.

Defining Contrast-Induced Nephropathy

Contrast-Induced Nephropathy (CIN), also known as contrast-induced acute kidney injury (CI-AKI), is significant complication characterized by sudden decline in kidney function following the administration of contrast media during medical imaging procedures. It typically manifests with a range of symptoms and clinical signs, which can vary in severity depending on factors such as the individual's renal function, the type and amount of contrast media used, and the presence of other comorbidities. CIN may manifest as oliguria, which is decreased urine output (less than 400 mL/day), or anuria (less than 100 mL/day). As kidney function declines, the body may retain excess fluid, leading to edema, electrolyte imbalance and nausea.

Present definition of CIN, suggested by European Society of Urogenital Radiology (ESUR) is increase of serum creatinine level by ≥25% or an absolute increase of ≥44 μmol/L (0.5 mg/dL) within 72 hours after administration of contrast media, with excluding other potential causes of acute kidney injury. (3)

Pathophysiology

The exact pathophysiology of contrast-induced nephropathy is not fully understood, but it is believed to be multifactorial. Several mechanisms have been proposed, including direct toxic effects of the contrast media on renal tubular cells, interplay of hemodynamic, inflammatory mechanisms, oxygenation, and the release of vasoactive substances leading to renal vasoconstriction. Following the administration of iodinated contrast media, there is a reduction in renal blood flow due to vasoconstriction of the afferent arterioles, primarily mediated by the release of endothelin and adenosine. This reduction in blood flow, particularly in patients with pre-existing renal impairment or underlying cardiovascular disease, leads to ischemic injury to the renal tubular cells. Additionally, the contrast agents themselves can directly induce toxicity within the renal tubules, causing cellular injury and dysfunction. The generation of reactive oxygen species (ROS) and the activation of inflammatory pathways further exacerbate renal injury by promoting oxidative stress and inflammation. These cascades of events ultimately result in impaired renal function, manifested as a decrease in glomerular filtration rate and potentially leading to contrast-induced nephropathy. Understanding the intricate pathophysiological mechanisms underlying CIN is essential for developing preventive strategies and targeted interventions to mitigate the risk of renal injury in susceptible individuals undergoing contrast-enhanced procedures. (4)

Identifying High-Risk Patients

In medical practice, it is important to recognize high-risk patients in clinical settings to prevent contrast-induced nephropathy. This can be achieved by implementing preventive strategies and ensuring optimal patient care. Numerous risk factors for the development of CIN have been identified in the literature. Reviewing the patient's history will help identify most risk factors and should be the first step in patient evaluation.

Risk factors of CIN

It is wise to evaluate all possible risks before using contrast, as the likelihood of CIN appears to increase significantly with the number of risk factors present. Standard procedure for determining the risk of patients undergoing computer tomography diagnostic or interventional radiologic procedures is based on eGFR (estimated glomerular filtration rate), which is one of the most essential predictors for the possibility of developing CIN. (5) There have been developed scoring systems, often used in risk evaluation for critically ill patients needing emergent percutaneous coronary intervention (PCI). These scoring systems consider factors

such as age, blood pressure, diabetes, Intra-aortic balloon pump, congestive heart failure, anemia, and contrast volume.(6)

Chronic Kidney Disease

One significant risk factor for developing contrast-induced nephropathy is preexisting renal dysfunction. Patients with chronic kidney disease, particularly those in advanced stages, are at a higher risk of developing CIN. This risk is determined based on the estimated glomerular filtration rate (eGFR) or estimated creatinine clearance and must be carefully evaluated before any contrast media administration. Guidelines about evaluating risk based on GFR vary depending on country, but we can generally consider a GFR of less than 60 mL/min/1.73m2 to represent a high risk for developing CIN for intra-arterial contrast media administration, and less than 45 mL/min/1.73m2 for intravenous contrast media administration. (7)

Diabetes

Diabetes is considered a significant risk factor for developing CIN when associated with renal insufficiency, but it does not increase the risk compared to nondiabetic patients when accompanied by proper renal function. (8) It is important to note, patients supplementing metformin should temporarily discontinue its use before contrast administration, it does not increase the risk of CIN, but its may induce lactic acidosis, which may be lethal in rare cases. (9)

Medications

The use of nephrotoxic medications can increase the risk of developing contrast-induced nephropathy. These medications include nonsteroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, aminoglycosides, vancomycin, amphotericin B, immunosuppressive drugs and loop diuretics. To minimize the nephrotoxic effects of these medications, they should be withheld for 24 to 48 hours before contrast administration and then continued for another 24 to 48 hours after the procedure, if possible. (10)

Type of Contrast

Contrast agents, commonly iodinated compounds, are categorized into two main types: ionic and non-ionic. Ionic contrast agents, characterized by higher osmolality, were associated with

a higher risk of CIN due to their greater nephrotoxic potential. However, advancements in medical technology have led to the widespread adoption of non-ionic contrast agents, which have lower osmolality and are consequently less nephrotoxic. This shift has significantly contributed to the reduction of CIN incidence. (11–13)

Other Factors

Other conditions that may increase a patient's risk of developing CIN include hypotension, cardiovascular disease, sepsis, and cirrhosis. These diseases can lead to renal hypoperfusion, increasing the risk of contrast-induced nephropathy. Additionally, older age can result in decreased renal function, reduced renal mass, and diminished renal reserve, which can contribute to an increased risk of developing CIN.

Preventative Strategies

Numerous research has been conducted on different substances for kidney protection, but the only proven strategies to lower contrast-induced nephropathy risk are the use of low or isoosmolar contrast agents and intravenous hydration with normal saline or sodium bicarbonate. Despite its popularity, the effectiveness of N-acetylcysteine remains unverified.

Hydration

One of the cornerstone strategies for preventing CIN is intravenous hydration with normal saline. This helps to maintain adequate renal perfusion and prevent contrast-induced renal vasoconstriction. It is cost efficient and also low-risk procedure. It is used to patients of all risk categories, but especially to patients with GFR <60 mL/min/1.73 m² or those with other risk factors for developing CIN (14) , in particular studies shown that female patients, diabetic patients, patients receiving more than 250ml of contrast and patients undergoing interventional cardiovascular procedures are the most beneficial to receive intravenous fluid therapy. (15,16)

N-acetylcysteine

The use of N-acetylcysteine as a preventative strategy for CIN is still debated. By boosting antioxidant defenses, NAC reduces the oxidative stress involved in CIN development, mainly

caused by reactive oxygen species produced by contrast media. Moreover, NAC's vasodilatory effects improve renal blood flow and may help alleviate ischemic injury. Some studies have shown a potential benefit in reducing the risk of CIN when N-acetylcysteine is administered before contrast exposure. However, other studies have not found a significant protective effect. Therefore, the use of N-acetylcysteine as a preventive measure for CIN is not currently widely recommended or accepted. (17,18)

Sodium Bicarbonate

Using sodium bicarbonate in the prevention of contrast induced nephropathy has been a subject of considerable interest in medical research. Sodium bicarbonate's theoretical benefit lies in its ability to alkalinize the urine, reducing the formation of reactive oxygen species and decreasing inflammation. This may help prevent contrast-induced tubular injury, thus preserving renal function. There is still controversy about the use of sodium bicarbonate in preventing CIN, many meta-analyses suggest positive effects in reducing the risk of CIN compared to hydration with normal saline. However, several analyzed studies were nonblinded and small in size. Therefore, more research is needed to determine the true efficacy of sodium bicarbonate in preventing CIN. (19–21)

Ascorbic acid

Ascorbic acid, also known as vitamin C, has shown some promise in preventing contrast-induced nephropathy. Studies have suggested that the antioxidant properties of ascorbic acid may help protect the kidneys from the oxidative stress induced by contrast media. Additionally, it is relatively inexpensive and has a favorable safety profile. Further research is necessary to fully establish the effectiveness of ascorbic acid in preventing CIN, but preliminary evidence is encouraging. (22,23)

Statins

Recent research has also investigated the potential role of statins in preventing contrast-induced nephropathy. Statins are known for their ability to improve endothelial function, reduce inflammation, and stabilize atherosclerotic plaques. These pleiotropic effects have led to speculation that statin therapy may have a protective effect on the kidneys in the setting of contrast media exposure. Some studies have shown a potential benefit of statin therapy in reducing the incidence of CIN, particularly in patients undergoing coronary angiography or

percutaneous coronary interventions. However, further large-scale clinical trials are needed to fully establish the role of statins in preventing CIN and to determine the optimal dosing and timing of statin administration in this context. (24,25)

Trimetazidine

Trimetazidine, a metabolic modulator that improves energy metabolism and exerts anti-ischemic effects, has been studied for its potential in preventing contrast-induced nephropathy. By enhancing cellular energy production and reducing oxidative stress, trimetazidine may protect the kidneys from the harmful effects of contrast media. Early research suggests that trimetazidine may have a role in mitigating the risk of CIN, particularly in high-risk patients undergoing procedures involving the use of contrast media. Further investigation is needed to determine the efficacy and safety of trimetazidine as a preventative strategy for CIN. Additional large-scale clinical trials are warranted to assess the optimal dose and administration protocol for trimetazidine in the context of contrast media exposure. (26)

Prostaglandins

Prostaglandins have been studied as a potential preventative strategy for contrast-induced nephropathy. Prostaglandins play a role in regulating renal blood flow and have vasodilatory effects on the renal vasculature. Clinical studies have shown that the use of prostaglandins may help to counteract the vasoconstrictive effects of contrast media on the kidneys, thereby potentially reducing the risk of CIN. However, further research is needed to establish the efficacy and safety of prostaglandin administration in preventing CIN. (27)

Nephrotoxic Medications

The management of contrast-induced nephropathy involves careful consideration of nephrotoxic medications, which can exacerbate renal injury when administered concurrently with contrast media. Agents such as nonsteroidal anti-inflammatory drugs, aminoglycoside antibiotics, and certain diuretics pose a heightened risk due to their potential to induce renal vasoconstriction or impair renal perfusion. If it is possible, these medications should be withheld from 24 to 48 hours before the procedure and should be restarted at least 48 hours after. (28)

Hemodialysis

Hemodialysis performed immediately after contrast administration is ineffective in preventing developing of CIN and has no role in it's management, despite removing a large portion of contrast media from the blood circulation. This is probably because contrast-induced injury develops quickly after the administration of contrast, it is decreasing circulating volume, and hemodialysis may also have nephrotoxic effects by triggering inflammatory pathways. (29) Patients suffering from advanced renal failure undergoing chronic hemodialysis do not require any protection before receiving contrast. Nonetheless, the need for earlier dialysis may arise due to volume expansion and increased serum osmolarity resulting from contrast administration. However, patients undergoing temporary hemodialysis should be considered as the highest risk of developing CIN.(30)

Hemofiltration

Hemofiltration is another technique that has been evaluated for the prevention of CIN. Unlike hemodialysis, is a form of continuous renal replacement therapy where there is no significant change in intravascular volume. Some research suggests that for individuals with long-term kidney failure undergoing percutaneous coronary interventions, administering hemofiltration in an ICU environment during the procedure may help prevent declines in renal function caused by contrast agent-induced nephropathy. This approach is also linked to better short-term and extended outcomes. (31) Despite the promising findings, hemofiltration is expensive, requires ICU facilities, and comes with its own set of risks. Due to a lack of substantial evidence and the high cost involved, hemofiltration has not been widely used, despite the potential for future use in patients at significant risk.

Contrast

Safely administering contrast media and reducing the risk of CIN depend on various factors, such as the type, volume, and route of administration. High-osmolar contrast, higher doses, and intraarterial administration have been linked to a greater risk of CIN compared to low-osmolar contrast, lower doses, and intravenous administration. (32,33)

Conclusion

Contrast-induced nephropathy is a significant problem in patients undergoing procedures that require contrast administration. The major risk factor for developing CIN is preexisting renal dysfunction, particularly in association with diabetes.Appropriate risk stratification, intravenous hydration with normal saline or sodium bicarbonate, withholding nephrotoxic medications, and using low or iso-osmolar contrast media are standard preventive measures for CIN. The primary focus should be on utilizing alternative imaging tests when feasible or reducing the utilization of contrast. Although the administration of NAC is widely practiced, its efficacy has not been definitively established. Clinicians should have a good understanding of preventive measures and the diagnosis of CIN in order to reduce its clinical consequences.

Disclosure

Author's contribution

Conceptualization: Kacper Reguła and Kamil Waloch; Methodology: Joanna Wojtania; Software: Kacper Reguła; Check: Kacper Płeska and Michał Łepik; Formal analysis: Andrzej Czajka and Bartłomiej Szymański; Investigation: Michał Łepik and Szymon Piaszczyński; Resources: Andrzej Czajka; Data curation: Zofia Uszok; Writing - rough preparation: Kacper Płeska and Zofia Uszok; Writing - review and editing: Krzysztof Rosiak and Kamil Waloch; Supervision: Szymon Piaszczyński; Project administration: Krzysztof Rosiak and Bartłomiej Szymański; Receiving funding - no specific funding.

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