TO COMPARIE IONIC VERSUS NONIONIC CONTRAST MEDIA IN RENAL ANGIOGRAPHY
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ABSTRACT

BACKGROUND
The adverse effects of ionic and nonionic contrast media, were compared in a group of 44 healthy renal donors undergoing renal angioigraphy as a screening procedure, for adverse reactions and change in renal function.

MATERIALS AND METHODS
44 healthy renal donors, with normal renal function and no associated co-morbid conditions, who underwent renal angioigraphy under DSA as a screening procedure for renal assessment were selected. Of them, 22 donors were randomly chosen to be given ionic contrast medium (Diatrizoate Sodium, Diatrizoate Meglumine) and 22 nonionic contrast medium (Iohexol and Iopamidol), in the dosage of 1 ml/kg body weight. They were assessed pre and 48 hours post procedure for vitals and laboratory assessment of blood (blood urea, serum creatinine), Urine (specific gravity, proteins, RBC etc.) and GFR by DTPA scan.

RESULTS
Only mild type of adverse reactions like injection site pain, feeling of warmth and nausea were noted in both the groups. No adverse reactions of moderate or severe type were noted in either group. No significant change in the renal function was noted in both the groups as assessed by blood analysis (blood urea & Serum creatinine), urine analysis and GFR by DTPA scan 48 hours post contrast administration.

CONCLUSION
These results suggest that in dosage of 1ml/kg body weight, which is adequate for good opacification and necessary clinical information, ionic contrast media are as safe as more expensive nonionic media in healthy patients with no co-morbid conditions.

KEYWORDS
Contrast Media, Contrast Induced Nephropathy, Adverse Reactions.

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In view of the nephrotoxicity and other systemic and life-threatening complications attributed to ionic or High Osmolar Contrast Media (HOCM), there have been quantum leaps in the CM technology to develop safer, less chemotoxic and more effective nonionic, Low Osmolar Contrast medium, LOCM (600-800 mOsm/kg) and Iso Osmolar Contrast Medium, IOCM (290 mOsm/kg) and safer methods of their delivery.

These made ways for intravascular interventional therapy, which in several cases replaced conventional surgery, permitting safe and selective demonstration of vascular anatomy and their supplied organs and even the cardiac chambers. These caused fewer renal, hemodynamic, systemic and ECG changes during angiography compared to conventional CM, making intravascular injection of contrast media for digital subtraction angiography (DSA) more safer and effective for visualization of the renal, cardiovascular and, neurovascular systems.

The discipline of vascular and interventional radiology is vibrant, dynamic and rapidly evolving with advances in interventional radiology procedures, there is need for increased dosage and hence the need for safer intravascular contrast media.

The development of LOCM or IOCM is one of the most important medical discoveries made at the end of the century. The American congressional records, while awarding Valentine Medal of the American Academy of Medicine on 16th May 1978 to Moses Swick, the real developer of the present day CM stated that "Swick’s work was one of the five major contributions of an individual to medicine".

**Aims and Objectives**

I. The study aimed to compare ionic with nonionic contrast media in renal angiography.

II. To determine the incidence of adverse reactions pertinent to-
   a. General and systemic effects
   b. Renal adverse effects

**MATERIALS AND METHODS**

This is a study from Jan 2001 to March 2005, wherein prospective renal donors who underwent renal angiography as a routine screening procedure prior to renal donation were studied. The cases were from the urology department of university recognized teaching hospital.

The donors were randomly assigned to receive either ionic contrast like Diatrizoate Sodium, Diatrizoate Meglumine (Trazograf 76% with 370 mgI/ml) and Diatrizoate Meglumine (Trazograf 60% with 282 mgI/ml) or non-ionic contrasts like Iohexol (300 mgI/I/ml), Iopamidol (300 mgI/I/ml). The total dose of contrast used was 1 ml/kg of body weight.

After obtaining detailed informed consent from donors for undergoing renal angiography and blood, urine examination and DTPA (Diethylene Triamine Pentacetate) scan for assessing renal function (GFR), post angiography, they were taken up as a case for the study.

**Subject Selection**

**Inclusion Criteria**

1. Renal donors with Normal kidney functions (Normal blood urea and serum creatinine).
2. Age between 25 years- 50 years.
3. Normal DTPA scan.
4. Willingness to consent and complete follow up requirements of study.

**Exclusion Criteria**

1. Raised serum creatine (> 1.5 mg/dl) and blood urea values (> 45 mg/dl)
2. Comorbid conditions (DM, HTN, TB, or hyperglycaemia (plasma glucose >140 mg/dl)
3. Coagulopathy or Hemoglobinopathies (e.g.: sickle cell disease)
4. History of bronchial asthma or any known allergy to drugs or food stuffs
5. Allergy to intravenous contrast media

**Equipment**

The renal angiography was carried out using a state-of-the-art Siemens Digital Subtraction Angiography machine of 1000 mAs (Polystar Top).

**Pre-Procedure Assessment**

Ultrasonographic examination was carried out prior to renal angiography by GE (Logic 400 and 500), equipped with a 3.5 and 5 MHz abdominal probes to determine the size, position and cortico-medullary differentiation of kidneys.

**Laboratory Studies**

Complete haemogram with blood urea, serum creatinine, prothrombin time. Urine for specific gravity, proteins, sugars, RBC, ketones, and amino sugars and glomerular filtration rate (GFR) by DTPA.

**Vitals**

Temperature, pulse, blood pressure, and heart rate were recorded before, during and after the procedure.

**Medical and Treatment History**

Chronic illness like DM, HTN, TB, haemoglobinopathies (SCD) or any allergy were ruled out. Enquiries were made about treatment/drug history for antihypertensives, calcium antagonists, metformin, and nephrotoxic drugs like aminoglycosides, NSAIDs.

Detailed information about the procedure, immediate adverse effects of the CM that they were likely to face like the site pain, nausea, heat sensation and altered taste sensation.

They were admitted to hospital one day prior to procedure. Clear fluids were given after midnight and were kept nil orally 4 hours prior to procedure.
**Procedure**

Arterial access was gained via trans-femoral route using Seldinger technique of single/double wall puncture. Aortogram was obtained by placing Pig tail catheter in the aorta. Selective renal angiogram was obtained with RDC/Cobra catheter. Post angiography IVU film was obtained followed by removal of arterial sheath with compression of the puncture site.

**Patient Monitoring During the Procedure**

Heart rate, blood pressure, respiratory rate, SPO2 were maintained pre, intra and post procedure with a noninvasive monitor (Siemens SC 6002 XL).

**Post Procedure Management**

The arterial puncture site was compressed for 20 minutes. Patient was shifted to the ward and advised Bed rest for 12 hours with leg in extended position. IV. Life line was maintained. Oral fluids were resumed after 1 hour after, followed by light diet. Analgesics were advised for pain.

Vitals like temperature, pulse, B.P. and heart rate were monitored. Patient was watched for puncture site hematoma and distal pulses.

Delayed reactions like urticaria, hypotension, headache, bronchospasm, convulsion, cardiac dysrhythmias, cardiovascular collapse, and cardiac arrest were watched for.

Patient was discharged after 48 hours.

**Post Procedure Follow Up**

After 48 hours post procedure, the patients were screened for any complications and the following investigations were performed.

- Blood urea
- Serum creatinine
- Total leucocyte count
- Urine for SG, proteins, sugars, RBC, ketones
- GFR by DTPA

**Procedure Related Complications Looked for Like**

- Hematoma at the puncture site
- Thrombosis of vessels
- Distal emboli
- Pseudo aneurysm

**Contrast Media Related Complications**

Patients were observed upto 48 hrs after the administration of CM for adverse events which were graded as mild, moderate or severe as per the following table.6

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain at injection site</td>
<td>Severe Vomiting</td>
<td>Convulsion</td>
</tr>
<tr>
<td>Nausea</td>
<td>Extensive Urticaria</td>
<td>Unconsciousness</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Dyspnoea</td>
<td>Laryngeal Oedema</td>
</tr>
<tr>
<td>(retching)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flushing</td>
<td>Rigors</td>
<td>Bronchospasm</td>
</tr>
</tbody>
</table>

**RESULTS**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Ionic (n=22)</th>
<th>Non-ionic (n=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>28 yrs. - 40 yrs.</td>
<td>33.0</td>
<td>3.61</td>
</tr>
<tr>
<td>25 yrs. - 56 yrs.</td>
<td>28.73</td>
<td>4.10</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Weight (kg)</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>55 kg. – 70 kg.</td>
<td>63.8</td>
<td>4.78</td>
<td>25 kg. – 70 kg.</td>
</tr>
<tr>
<td>50 kg. – 70 kg.</td>
<td>62.45</td>
<td>6.38</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sex</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 (90.9)</td>
<td>20</td>
<td>02 (09.1)</td>
</tr>
<tr>
<td>15 (68.2)</td>
<td>02</td>
<td>07 (31.8)</td>
</tr>
</tbody>
</table>

**Table 1. Demographic Data of Patients**

@By student ‘t’ Test #Chi-square Test

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ionic</td>
<td>Non-Ionic</td>
</tr>
<tr>
<td>Systolic B.P. (mm Hg)</td>
<td>117.0 ± 5.71</td>
</tr>
<tr>
<td>Diastolic B.P. (mm Hg)</td>
<td>70.0 ± 0</td>
</tr>
<tr>
<td>Pulse rate</td>
<td>70.1 ± 1.02</td>
</tr>
</tbody>
</table>

**Table 2. Profile of Physical Examination in Both the Groups (N=44)**

@By student ‘t’ Test P>0.05 Not significant

<table>
<thead>
<tr>
<th>Period</th>
<th>Mean BUN (mg/dl) (X ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ionic</td>
<td>Non-Ionic</td>
</tr>
<tr>
<td>Pre-Angiography</td>
<td>32.68 ± 2.73</td>
</tr>
<tr>
<td>Post-Angiography</td>
<td>32.45 ± 3.13</td>
</tr>
</tbody>
</table>

**Table 3. Comparison of Changes in Average Blood Urea Nitrogen (Bun) between the Two Groups Before and After Renal Angiography (n=44)**

@By student ‘t’ Test P>0.05 Not significant

<table>
<thead>
<tr>
<th>Period</th>
<th>Mean Serum creatinine (mg/dl) (X ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ionic</td>
<td>Non-Ionic</td>
</tr>
<tr>
<td>Pre-Angiography</td>
<td>1.16 ± 0.14</td>
</tr>
<tr>
<td>Post-Angiography</td>
<td>1.15 ± 0.17</td>
</tr>
</tbody>
</table>

**Table 4. Comparison of Changes in Average Serum Creatinine between the Two Groups Before and After Renal Angiography (n=44)**

By Student’s ‘t’ Test P>0.05 Not Significant.
Serum creatinine levels did not show any significant change in both the groups.

By student ‘t’ Test’  \( P>0.05 \) Not Significant.

Average specific gravity (SG) did not show any significant change in both the groups.

<table>
<thead>
<tr>
<th>Period</th>
<th>Mean SG (X ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ionic</td>
</tr>
<tr>
<td>Pre-Angiography</td>
<td>1012.32 ± 0.72</td>
</tr>
<tr>
<td>Post-Angiography</td>
<td>1013.15 ± 0.93</td>
</tr>
</tbody>
</table>

*Table 5. Comparison of Changes In Average Specific Gravity (Sg) Of Urine between the Two Groups Before and After Renal Angiography (n=44)*

Total urinary proteins/24 hrs did not show any significant change in both the groups.

By student ‘t’ Test’  \( P>0.05 \) Not Significant.

<table>
<thead>
<tr>
<th>Period</th>
<th>Mean Proteins gm/24 hrs (X ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ionic</td>
</tr>
<tr>
<td>Pre-Angiography</td>
<td>0.26 ± 0.07</td>
</tr>
<tr>
<td>Post-Angiography</td>
<td>0.25 ± 0.06</td>
</tr>
</tbody>
</table>

*Table 6. Comparison of Changes in Urinary Proteins /24 Hrs between the Two Groups Before and After Renal Angiography (n=44)*

By student ‘t’ Test’  \( P>0.05 \) Not Significant.

Total urinary volume /24hrs did not show any significant change in both the groups.

By student ‘t’ Test’  \( P>0.05 \) Not Significant.

<table>
<thead>
<tr>
<th>Period</th>
<th>Urine Volume / 24 hrs. (ml) (X ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ionic</td>
</tr>
<tr>
<td>Pre-Angiography</td>
<td>3075 ± 892.59</td>
</tr>
<tr>
<td>Post-Angiography</td>
<td>3000.0 ± 891.13</td>
</tr>
</tbody>
</table>

*Table 7. Comparison of Changes in Urine Volume /24 hrs between the Two Groups Before and After Renal Angiography (n=44)*

By student ‘t’ Test’  \( P>0.05 \) Not Significant.

Comments: In this study total urine volume /24hrs did not show any significant change in both the groups.

By student ‘t’ Test’  \( P>0.05 \) Not Significant.

Average GFR (measured by DTPA scan) did not show any significant change in both the groups.

By student ‘t’ Test’  \( P>0.05 \) Not Significant.

<table>
<thead>
<tr>
<th>Period</th>
<th>AVERAGE GFR (X ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ionic</td>
</tr>
<tr>
<td>Pre-Angiography</td>
<td>114.72 ± 18.28</td>
</tr>
<tr>
<td>Post-Angiography</td>
<td>117.87 ± 19.80</td>
</tr>
</tbody>
</table>

*Table 8. Comparison of Changes in Average Glomerular Filtration Rate (GFR) between the Two Groups Before and After Renal Angiography (n=44)*

By Chi-square test’  \( P< 0.05 \) Significant

**Adverse Events**

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>Ionic</th>
<th>Non-Ionic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>07 31.8</td>
<td>04 18.2</td>
</tr>
<tr>
<td>Pain at injection site</td>
<td>15 68.2</td>
<td>08 36.4</td>
</tr>
</tbody>
</table>

*Table 9. Profile of Adverse Events Experienced by Patients in Both Groups after the Administration of Contrast Media (n=44)*

By student ‘t’ Test’  \( P>0.05 \) Not Significant.
891.13 respectively and nonionic group 3045 ± 851.92 & 3000 ± 848.53 respectively. The P value >0.05, suggested that the differences were statistically insignificant, and levels did not show any significant change in both groups.

Average GFR (by DTPA scan) Pre & post contrast in the ionic group in the range of 114.72 ± 18.28 & 117.87 ± 19.80 respectively and nonionic group 112.22 ± 19.20 & 117.31 ± 24.03 respectively. The P value >0.05, suggested that the differences were statistically insignificant and GFR did not show any significant change in both groups.

Adverse events in the Ionic group were noted in 15 (67%) patients, injection site pain in 8 (36%) and nausea in 7 (31%) patients. In the Nonionic group these were noted in only in 09(40.9%) patients, Injection site pain in 5 (36%) and nausea in 04 (18.2%) donors. The donors in ionic group experienced more discomfort than the nonionic group. Since p <0.05, it suggested that the difference was significant.

DISCUSSION
In our study 44 healthy prospective renal donors with normal renal function (normal levels of blood urea, serum creatinine and GFR by DTPA), who underwent renal angiography as a screening procedure, were randomly given ionic or nonionic CM with an aim to compare both groups for their general systemic effect and renal effects.

Dosage of Contrast Followed
In our study the dosage of contrast was 1 ml/kg body weight which is sufficient for good opacification and necessary clinical information.

Renal Handling of Contrast Media
After intravascular administration, CM particles move across capillary membranes (except an intact blood-brain barrier) into the extracellular interstitial space followed by reversal of movement back into the intravascular compartment, reaching a state equilibrium within 2 hrs. In patients with normal renal function, 99% of CM elimination is through glomeruli and <1% through extrarenal routes, 50% of CM is eliminated within 2 hrs, 75% within 4 hrs and 98% within 24 hrs post administration. In cases with normal renal function, concentration of CM decreases in a monoexponentially way in 150 mins post contrast. But in patients with impaired renal function, this phase is delayed. CM particles exert an osmotic force, causing reduced reabsorption and increased excretion of H₂O and Na⁺ from the tubules. This natriuresis stimulates TGF (Tubulo-glomerular-feedback response) and the diuresis increases intratubular-pressure, thus reducing the GFR.

Adverse Reactions to Contrast Media
A. Systemic adverse reactions
B. Nephrotoxic adverse reactions

A. Systemic Adverse Reactions
Pathogenesis of systemic adverse reactions involves direct cellular effects, enzyme induction, activation of complement, fibrinolytic, kinin and other systems. The Systemic adverse reactions to CM are further classified as Idiosyncratic and Non- idiosyncratic.

Idiosyncratic Reactions
Typically begin within 20 mins of CM injection, independent of the dose administered, even without prior sensitization, with no predictable pattern of recurrence. Despite the similarity in manifestation, they are not true hypersensitivity reactions as IgE antibodies are not involved.

Based on the Severity of Symptom the Reactions can be Classified As-
1. Mild Reactions
2. Moderate Reactions
3. Severe Reactions

Mild Reactions
The symptoms are scattered urticaria, pruritus, rhinorhoea, nausea, brief retching or vomiting, coughing and dizziness. These do not require any treatment only reassurance and observation for the progression or evolution of more severe reactions.

Moderate Reactions
The symptoms are headache, facial or laryngeal oedema, mild bronchospasm, dyspnœa, tachycardia, bradycardia, hypertension, palpitations, abdominal cramps, persistent vomiting and diffuse urticaria.

Severe Reactions
The symptoms are life-threatening arrhythmias like ventricular tachycardia, hypotension, bronchospasm, laryngeal or pulmonary oedema, seizures, syncope, and death. These reactions require urgent measures and prompt management.

Non-Idiosyncratic Reactions
Bradycardia is due to CM induced heightened systemic parasympathetic activity.

Untreated, these can lead to cardiovascular collapse.

Systemic hypotension is due to peripheral vasodilatation.

Autonomic manifestations include nausea, vomiting, diaphoresis, sphincter dysfunction, and mental status changes.

Vasovagal reactions are probably the result of coexisting circumstances such as emotion, apprehension, pain rather than CM

Other reactions are neuropathy, cardiovascular reactions, delayed reactions or subjective reactions like sensation of warmth, a metallic taste in the mouth, nausea and vomiting.

Physical Factors Responsible For Adverse Reactions
Physical factors like Osmolality, Ionicity and Viscosity play a major role in adverse effects due to CM (Table on opposite page)
of additional structures in the CM solution determine its osmolality. Increasing the iodine content enhances the contrast effect at the cost of increased osmolality and toxicity, hence the need for Low or Iso-Osmolar Contrast Media. Ionicity has direct tubulotoxic effects. Nonionic CM are less tubulotoxic than ionic CM with less toxicity and hence are preferred in patients with preexisting renal disease. Viscosity is responsible for discomfort/pain felt during intravenous administration of CM and cytotoxic effects like vacoulation of CM by proximal tubular cells.

In our study, only transient mild grade reactions like pain at injection site and nausea shortly after CM administration were reported, requiring no therapy but only assurance and close observation for progression to severe symptoms requiring urgent treatment.

Mild adverse events like nausea and injection site pain were noted in 15 (68.2%) in the ionic and 09 (40.9%) in the nonionic group. Injection site pain in the ionic and nonionic groups were noted in 15(36%) and 8(36.4%) cases respectively. Whereas, nausea was felt in 08(36.4%) and 07(31%) cases respectively. The P value <0.05, thus the difference was significant.

Our study found Mild grade reactions like injection site pain, heat sensation and nausea to be the most common reactions attributable to HOCM. Similar findings were also noted in studies by Katayama et al,7 Barret et al,10 Rasmussen et al,11Schwab et al,12 Moore et al,13 and Palmer et al who have implicated HOCM for these reactions. The findings suggested nonionic LOCM and IOCM better patient tolerance, less patient discomfort and less adverse reactions with compared to HOCM.

**Moderate and Severe Grade Reactions**

No reactions of moderate and severe grade were noted in our study as the cases under study were renal donors with normal renal function and no co morbidity. Such patients are considered low risk cases for adverse reactions even with ionic HOCM within therapeutic doses.

Moderate and severe grade reactions are more likely to occur in the debilitated or patients with co morbidity as shown in studies by Palmer et al,14 Schwab et al,12 Katayama et al,7 Moore et al,13 Barret,10 and Thrall et al15

**Nephrotoxic Effects or Contrast Induced Nephropathy (CIN)**

CIN (Contrast Induced Nephropathy) is defined differently in various studies. The most accepted definition is 'impairment in renal function (increase in S creatinine by more than 25% within 3 days of CM administration) in the absence of any other aetiology. Barret et al16 Rudnick et al,17 Idlee, et al18 and Porter et al.19

Ideally, S. creatinine level should be monitored beyond 48 hours, as it tend to peak 3-5 days after CM administration and return to baseline in 1-3 weeks.13,17,20,21,23

Incidence of CIN shows wide variation in reported incidence, due to differences in patient selection, differences in radiological procedures and definition of renal impairment by varying parameters in different studies. Katzberg et al8 and Rudnick et al.17

The incidence of CIN is low (0% -10%) in people with normal renal function.16,22 in patients with pre-existing renal impairment the incidence ranges from 12% - 27%, incidence as high as 50% reported in patients with diabetic nephropathy in studies by Manske et al23 in spite of using LOCM and adequate hydration.

Clinical Features of CIN There is peaking of S. creatinine levels within 3–4 days of administration of CM along with reduced creatinine clearance, reflecting in a reduction in GFR. Most patients are non-oliguric with mild proteinuria and occasional oliguria which are self-limiting, resolving within 1-2 wks. It needs to be differentiated from Syndrome of ateroembolism (catherter induced trauma) precipitating in cholesterol emboli manifesting as acute renal failure.24

Mechanism of CIN Acute renal functional changes can be induced by the CM by inducing the following - Increased Renal vascular resistance (RVR) - Increased urine flow - Reduced GFR and Na+ reabsorption. Three main mechanisms have been proposed25

A. Renal Ischemia B. Direct Tubular Toxicity C. Tubular Obstruction.

Renal ischemia is due to reduced renal perfusion caused by direct effect of CM on the kidney. It involves two responses. - RTVR -Renal Vascular Resistance response - TGF -Tubulo Glomerular Feedback response HOCMs produce marked natriuresis and diuresis activating the TGF response, leading to constriction of glomerular afferent arterioles causing reduction in GFR and increase in RTVR. There is a transient increase in flow followed by a prolonged period of reduced flow in normal kidneys. It is caused by intrenal vasoconstriction and reduced in RBC flexibility induced by CM.26 there is increased production and reduced removal of O2 free radicals. It correlates with reduced GFR. (Morcos). The TGF response is osmolality dependent HOCM > LOCM > IOCM.

The vascular events are due to CM induced impaired production of vasodilators like Nitric Oxide and Prostaglandins (help in maintaining the perfusion and oxygen supply of poorly perfused and hypoxic medulla) and by inducing the synthesis and release of intra-renal vasoconstrictors like Endothelin (ET) and Adenosine, important mediators of CM induced renal haemodynamic effect, from the endothelial cells and increase their levels in plasma and urine in pts with reduced renal function, accentuated following CM administration.26,27,28

**Direct Tubular Toxicity (Effects of CM on Tubular Cells)**

CM are directly toxic to tubular epithelium. The mechanism is Vacular response, wherein there is active engulfing of CM by tubular epithelial cells and lysosomal cells. Its activation plays an important role in nephron injury and renal failure. Cell organelles remain intact. Apoptosis (programmed cell death) is noted in by the presence of
extensive DNA fragmentation. It is detected selectively along thick ascending limbs of loops of Henle as early as 15 minutes post HOCM administration. Vacuolization of the epithelial cells of proximal tubules has been seen in cases of LOCM and IOCM, due to lesser diuresis induced by them and slow transit in renal tubules and hence prolonged exposure of epithelial cells.29

**Prevention of Contrast Medium Induced Nephropathy**21,32,33

There is extensive research focusing on ways of preventing and ameliorating CIN like:

- Various hydration regimens
- N-acetyl cysteine (Tepel et. al.)
- Dopamine receptor agonist Fenoldapam
- Substitution with low or iso-osmolar CM
- Dialysis: Haemodialysis and peritoneal dialysis

**Renal Effects in Our Study**

In our study, the normal baseline S creatinine value was taken as <1.2 mg/dl which indicated normal GFR of 60-120 ml and a patient was considered to have developed CIN, if S creatinine level was >1.5 mg/dl 48 hours post CM administration.

In our study no significant change in renal parameters like S creatinine, Blood urea and GFR were noted post CM administration. There was no proteinuria or oliguria or any other relevant urinary finding suggesting contrast nephropathy

A large study by Schwab et al.13 comparing ionic and nonionic CM in patients with predominantly normal renal function suggested no differences in nephrotoxicity between ionic and nonionic Contrast medium.

Barret et al11 in a study of relative nephrotoxicity of ionic versus nonionic CM suggested that osmolarity plays a significant role but in patients with underlying renal failure and in a healthy patients the overall relative risk of nephrotoxicity was negligible with nonionic as with ionic CM.

Several parameters are identified which are associated with adverse effects of contrast media. With respect to frequency more mild type and moderate type reactions occur with ionic compared to nonionic contrast media which have allergy like manifestation. Nevertheless, we can still expect infrequent adverse reaction with nonionic contrast media.

**REFERENCES**