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An Update From The Contrast Media Safety Committee of the European Society of Urogenital Radiology



Dr. Fulvio Stacul, Professor of Radiology

*****@***aots.sanita.fvg.it

D - University Of Trieste

The Contrast Media Safety Committee (CMSC) of the European Society of Urogenital Radiology (ESUR) first produced guidelines on contrast medium-induced nephropathy (CIN) and on the use of metformin in patients receiving contrast medium in 1999. The committee decided to critically review the new literature and update its guidelines for reducing the risk of CIN and for the management of diabetic patients on metformin who receive contrast agents.

Definition of CIN

In 1999, the CMSC gave the following definition of CIN: "Contrastmedium nephrotoxicity is a condition in which an impairment in renal function (an increase in serum creatinine by more than 25 percent or 44 $\mu\text{mol/l}$) occurs within three days following the intravascular administration of a contrast medium in the absence of an alternative etiology". This definition is still widely used but the subject of extensive debate: Is it still appropriate to consider absolute and relative increases in serum creatinine (SCr) together? Can the same thresholds still be used? Should the same time interval be considered? Can alternative explanations for the serum creatinine changes be confidently excluded? The topic is complex and our understanding of it continues to evolve. Following its review, the CMSC considers it still appropriate to maintain the definition agreed in 1999.

Risk Factors for CIN

In the previous guidelines, a number of risk factors were listed, for example:

- Raised S-creatinine levels, particularly secondary to diabetic nephropathy;
- Dehydration;
- Congestive heart failure;
- Age over 70 years; and
- Concurrent administration of nephrotoxic drugs, e.g. non-steroid anti-inflammatory drugs.

The significance of these risk factors has been confirmed. Recent data on other risk factors indicate the significance of:

- Haemodynamic instability (for example when an intra-aortic balloon pump is used);
- Reduction of the renal blood supply during vascular procedures (hypotension); or
- Reduction of the renal oxygen supply (anaemia). These factors have been added to the list of risk factors in the guidelines.

Other Recent Data

Recent data support a higher risk of CIN after intra-arterial contrast administration above the level of the renal arteries than after intravenous administration. Intravenous contrast medium for enhanced CT is usually given in lower doses than for arteriography and lower concentrations of contrast medium reach the kidneys. Also, with enhanced CT, there are usually fewer haemodynamically unstable patients and dislodged atheroemboli, which may occur during intra-arterial procedures resulting in cholesterol embolisation that can mimic CIN, and are not a risk.

The CMSC agreed that the risk of CIN is significantly lower following intravenous contrast medium administration and concluded that patients referred for enhanced CT are genuinely at risk of CIN if they have an $\text{eGFR} < 45 \text{ ml/min/1.73m}^2$. Patients referred for arteriography are considered at risk if they have an $\text{eGFR} < 60 \text{ ml/min/1.73m}^2$.

The previous CMSC guideline suggested the use of contrast media (CM) with low or iso-osmolality in patients with risk factors for CIN. Having considered the many studies published in recent years, the Committee considers that this previous guideline should not be changed.

The CMSC agrees that the incidence of CIN is related to the dose of CM and therefore only the minimum amount necessary to answer the clinical diagnostic question should be used.

Multiple studies applying CM within a short period of time in at-risk patients should be avoided and the interval between procedures should be 2 weeks, if acceptable clinically.

Prophylactic Strategies

The literature published since the original CMSC guidelines has favoured volume expansion with intravenous fluid over oral hydration. However, there has not been adequate research on this topic. Preventive strategies for CIN include hydration (volume expansion), pharmacological support, extracorporeal therapy (haemodialysis and haemofiltration) and withdrawal of nephrotoxic drugs.

It appears that volume expansion with sodium bicarbonate provides equal or superior protection to isotonic saline. Therefore, the CMSC considers that there is enough evidence to recommend that either volume expansion regimen may be used. When normal saline is used, the CMSC recommends an intravenous regime of 1.0-1.5 ml/kg/h for at least six hours before and after contrast medium administration. For sodium bicarbonate, the most widely used regimen (3 ml/kg/h for 1 h before contrast medium followed by 1 ml/kg/h for 6 h after) seems appropriate.

Additionally, the current opinion of the CMSC is that the efficacy of N-acetylcysteine (NAC) and other drugs in reducing the incidence of CIN remains unproven and their use cannot be recommended.

The CMSC does not recommend prophylactic haemodialysis and has concerns in recommending haemofiltration because it requires management in the intensive care unit (ICU), is costly and affects creatinine levels *per se*.

Lack of evidence makes it difficult to produce a definitive statement about nephrotoxic drugs. The CMSC therefore recommends that the possible withdrawal of nephrotoxic drugs before contrast medium in patients at risk of CIN should be discussed with the referring physician and that the judgement should balance the relative benefits and harms.

Guidelines for Patients on Metformin

Finally, the CMSC updated the 2009 guideline on the use of metformin in patients receiving iodinated contrast media in the light of its new CIN recommendations and of the recent NICE guidelines. The new ESUR guideline has been relaxed and states that patients with an eGFR of 45 ml/min/1.73 m² or greater can continue to take metformin normally if they receive intravenous iodinated contrast medium. Patients receiving intra-arterial iodinated contrast medium with an eGFR of 30-59 ml/min/1.73 m² and patients receiving intravenous contrast medium with an eGFR 30-44 ml/min/1.73 m² should stop taking metformin 48 hours before contrast medium administration. Renal function should be re-assessed 48 hours after contrast medium and metformin should only be restarted if it has not deteriorated further.

Prof. Fulvio Stacul Department of Radiology, Maggiore Hospital, Trieste, Italy
fulvio.stacul@aots.sanita.fvg.it

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