

ESMRMB recommendation on

Adverse reactions to gadolinium based contrast agents (Gd-CA)

ADVERSE REACTIONS

1. Acute non-renal adverse reactions
 - a. Urticaria
 - b. Vomiting
 - c. Hypotension
 - d. Vagal reaction
 - e. Anaphylatoid-like reaction
 - f. Larynx edema
 - g. Bronchospastic reaction
2. Acute renal adverse reactions
 - a. Contrast induced nephropathy
3. Site reactions
4. Delayed or late adverse reaction
 - a. Nephrogenic systemic fibrosis

1,2&3 are the same as those seen in relation to iodine-based contrast agents (I-CA). The prevalence of reactions is lower after Gd-CA than I-CA due to the lower molar dose used for MRI than used for X-ray. The preventive measures are the same – see www.esur.org.

NEPHROGENIC SYSTEMIC FIBROSIS

CLINICAL FEATURES OF NSF

Onset: From the day of exposure for up to 2-3 months

Initially

- Pain
- Pruritus
- Swelling
- Erythema
- Usually starts in the legs

Later

- Thickened skin and subcutaneous tissues – ‘woody’ texture and brawny plaques
- Fibrosis of internal organs, eg muscle, diaphragm, heart, liver, lungs

Result

- Contractures
- Cachexia
- Death, in a proportion of patients

AT RISK PATIENTS

Higher risk

- Patients with CKD 4 and 5 (GFR < 30ml/min)
- Patients on dialysis
- Patients with reduced renal function who have had or are awaiting liver transplantation

Lower risk

- Patients with CKD 3 (GFR 30-59ml/min)
- Children under 1 year, because of their immature renal function

CLASSIFICATION OF AGENTS

High risk of NSF

Gadodiamide (Omniscan®)

Ligand: Non-ionic linear chelate (DTPA-BMA)

Incidence of NSF: 3-7% in at-risk subjects

Gadopentetate dimeglumine (Magnevist®)

Ligand: Ionic linear chelate (DTPA)

Incidence of NSF: Estimated to be 0.1 to 1 % in at risk subjects

Gadoversetamide (Optimark®)

Ligand: Non-ionic linear chelate (DTPA-BMEA)

Incidence of NSF: Unknown.

Common

S-creatinine (eGFR) measurement: Mandatory

Hemodialysis: The agents are contraindicated in patients on dialysis.

CONTRAINDICATED in

- patients with CKD 4 and 5 (GFR < 30 ml/min), including those on dialysis
- patients with reduced renal function who have had or are awaiting liver transplantation

USE WITH CAUTION in

- patients with CKD 3 (GFR 30-60 ml/min)
- children less than 1 year old

Intermediate risk of NSF

Gadobenate dimeglumine (Multihance®)

Ligand: Ionic linear chelate (BOPTA)

Incidence of NSF: No unconfounded* cases have been reported.

Special feature: Similar diagnostic results can be achieved with lower doses because of its 2-3% protein binding.

Gadofosveset trisodium (Vasovist®)

Ligand: Ionic linear chelate (DTPA-DPCP)

Incidence of NSF: No unconfounded* cases reported, but experience is limited
Special feature: It is a blood pool agent with affinity to albumin. Diagnostic results can be achieved with 50% lower doses than extracellular Gd-CM. Biological half-life is 12 times longer than for extracellular agents (18 hours compared to 1½ hours, respectively).

Gadoxetate disodium (Primovist®)

Ligand: Ionic linear chelate (EOB-DTPA)

Incidence of NSF: No unconfounded* cases have been reported but experience is limited.

Special feature: Organ specific gadolinium contrast agent with 10% protein binding and 50% excretion by hepatocytes. Diagnostic results can be achieved with lower doses than extracellular Gd-CM.

Common

S-creatinine(eGFR) measurement: Not mandatory

Low risk of NSF

Gadobutrol (Gadovist®)

Ligand: Non-ionic cyclic chelate (BT-DO3A)

Incidence of NSF: No unconfounded* cases have been reported.

Gadoterate meglumine (Dotarem®)

Ligand: Ionic cyclic chelate (DOTA)

Incidence of NSF: No unconfounded* cases have been reported.

Gadoteridol (Prohance®)

Ligand: Non-ionic cyclic chelate (HP-DO3A)

Incidence of NSF: No unconfounded* cases have been reported.

Common

S-creatinine (eGFR) measurement: Not mandatory

**Confounded:* If two different Gd-CA had been injected, it is impossible to determine with certainty which agent triggered the development of NSF and the situation is described as ‘confounded’. However the agent, which is most likely responsible is the one which has triggered NSF in other unconfounded situations.

IMMEDIATE HEMODIALYSIS AFTER ADMINISTRATION OF Gd-CM

- At least 9 hours of hemodialysis (3 sessions) is required to remove a Gd-CM. The efficacy of hemodialysis can be variable and depends on many factors.
- There is no evidence that immediate hemodialysis protects against NSF.

- In patients already being dialysed, it may be helpful to schedule the dialysis session after the gadolinium contrast examination. However, this is optional and should not cause delays in obtaining important diagnostic information.
- Initiating hemodialysis for the sole purpose of removing a Gd-CM is not recommended in patients who have not already been stabilized on hemodialysis as a replacement therapy. The procedure itself can be associated with significant morbidity, which is higher than the risk of inducing NSF with the most stable gadolinium agents.

Pregnant patients.

In the absence of specific information, it seems wise to manage pregnant patients, whatever their renal function, in the same way as children aged under 1 year to protect the fetus.