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Nephrogenic systemic fibrosis in stage 4 kidney disease, what is the alternative?

Dear Sir,

In a past issue, Wetzels[1] advises to avoid gadolinium-based contrast agents in patients with stage 4 and 5 kidney disease, i.e. a GFR <30 ml/min. His advice is in line with the opinion of many more authors and guidelines, such as the one proposed by the Netherlands Federation of Nephrology. All because of the risk of developing nephrogenic systemic fibrosis (NSF), which is indeed a disease to avoid.

In his argumentation, and in the argumentation of others, I miss two aspects. The first is the lack of hard evidence to support their and others' advice on gadolinium or at least some qualification of the emphasis put on the advice to avoid of gadolinium at all costs. The reported 200 to 300 cases of NSF worldwide do not outweigh the probably millions of MRI scans carried out without any problem in patients with a GFR <30 ml/min. Furthermore, as some authors claim, NSF has not been described in patients with an estimated GFR of more than 20 ml/min.[2] Why then advise patients with a GFR <30 ml/min to avoid gadolinium? Moreover, the reported incidence of NSF after exposure to gadolinium in stage 5 kidney disease is 1.5[3] to 2.4%.[4] Given the scarce reports of NSF in patients with stage 4 kidney disease, the risk of acquiring NSF in these patients would be extremely low, as the incidence of stage 4 kidney disease is far higher than the incidence of stage 5 kidney disease. Although the half-life of gadolinium is markedly prolonged in renal insufficiency, which probably contributes to the occurrence of NSF, and although it is logical to assume that patients with stage 4 kidney disease are therefore also at increased risk, this is not yet proven!

The second aspect I miss in the discussion about NSF, is the lack of weighing the avoidance of gadolinium against the toxicity of alternative diagnostic methods. How can I produce vascular images without the risk of contrast nephropathy, contrast allergy or cholesterol emboli (which has a mortality of 50%!)? Why avoid gadolinium at all costs when the alternative is at least as dangerous?

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RESPONSE

The safety of gadolinium compounds

The editorial comment was intended to bring to attention nephrogenic systemic fibrosis (NSF) as a severe side effect of gadolinium-containing contrast media in patients with chronic kidney disease.[1] The comment did not allow me to discuss all aspects extensively. I merely alluded to the guidelines formulated by Kuo *et al.*[2] Even these authors do not forbid any use of gadolinium in patients with chronic kidney disease. My conclusion was that the knowledge of NSF as potential side effect of gadolinium 'must be taken into account when considering the best diagnostic strategy in the individual patient'. This conclusion still holds, meaning that the risk of gadolinium-based imaging procedures must be weighed against the well-known risks of other procedures as put forward by Dr. Stassen.

I am concerned by one of Dr Stassen's conclusions. I do not agree with the statement that 'the reported 200 to 300 cases of NSF worldwide do not outweigh the probably millions of MRI scans carried out without any problem in patients with a GFR <30 ml/min'. NSF was only recently recognised as a problem, there must be many unreported cases. In fact, in recent months the number of case reports is rising at a staggering pace, and in a small country as Denmark a total of 24 patients have been reported until 2006. It seems that we have only seen the tip of the iceberg. Since NSF is a severe, disabling and untreatable disease, with associated mortality, we must take action.

Admittedly, risks are low in patients with a GFR >30 ml/min. The recent FDA warning has cautioned against the use of gadolinium compounds in patients with a GFR <30 ml/min. We do not know the risk in these patients. However, NSF has been described in patients with a GFR of 25 ml/min. In patients with a GFR <15 ml/min the risk of developing NSF after gadolinium exposure is estimated at 3%. Although the risk of NSF in patients with a GFR of 15 to 30 ml/min will be lower than 1%, the total number of patients at risk is large.

I suggest the following: be restrictive when ordering a diagnostic procedure in patients with a GFR <30 ml/min. Do not use linear gadolinium-contrast agents. Although cyclic compounds are relatively safe, use the lowest possible dose, and try to avoid repeated procedures. Lastly, weigh the risks and benefits of the various diagnostic procedures and select the procedure with the lowest risk. Awareness of NSF should reduce the risk of its development.

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