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## COMMENTARY

# General anaesthesia for patients with a history of a contrast medium-induced anaphylaxis: a useful prophylaxis?

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## ABSTRACT

Contrast-enhanced radiological examinations are important diagnostic tools in modern medicine. Currently, all approved and available iodinated and gadolinium-based contrast agents are safe and well-tolerated by most patients. However, approximately 2% of patients receiving iodinated contrast media exhibit hypersensitivity reactions. Patients with a history of such a reaction are at increased risk upon reexposure. Therefore, they are subjected to a prophylaxis such as injection of antiallergy drugs or general anaesthesia. The latter procedure is expensive, can burden the patients organism, and besides lacks objective verification. Therefore, the purpose of our review paper is to present and discuss the background and the previous practice, as well as to provide a proposal for a safe individual patient management.

## INTRODUCTION

Currently, available contrast media (CM) are well-tolerated and safe. However, adverse events (AEs) in general and hypersensitivity reactions (HSRs), in particular, still occur in a small percentage of patients. Due to the ongoing trend of increasing contrast media usage, one can estimate that more than 100 million procedures using iodinated radio-contrast media (ICM) and 30 million procedures with gadoliniumbased contrast agents (GBCA) are performed worldwide every year.<sup>1–3</sup>

Patients with a history of previous AEs/HSRs are at increased risk. Therefore, this subgroup needs a special prophylactic management in order to avoid a reaction upon CM-reexposure. Most commonly, radiologists perform a drug premedication with antiallergy compounds (e.g. corticosteroids and/or H1-antihistaminics) before they inject the CM. Unfortunately, efficacy to sufficiently suppress severe CM-HSRs has not yet been shown by pertinent studies. The more severe a HSR, the greater the challenge to prevent a subsequent reaction: upon reexposure, in approximately 85% of cases the reactions are generally as severe as in the formerly observed HSR.<sup>4</sup> Therefore, premedication with an antihistamine (e.g. clemastine) and a steroid (e.g.

methylprednisolone) are administered prior to the CM in order to sufficiently suppress a reaction. However, premedication may be ineffective leading to so-called breakthrough reactions. All grades of severity for breakthrough reactions have been observed including anaphylactic reactions.<sup>4–7</sup> In an attempt to solve this prophylactic dilemma, some physicians and radiologists decided to perform contrast-enhanced examinations under general anaesthesia.<sup>8</sup>

Since, in the literature one can find both pros and cons for general anaesthesia as prophylactic task for CM-AEs/HSRs the goal of our paper is to summarize the current knowledge, and to provide a practical recommendation for patients at risk.

## THE PROS

In both diagnostic (non-invasive) and interventional (invasive) radiology sedation and general anaesthesia has a long tradition, and the indication list ranges from suppression of anxiety including claustrophobia, pain, motion artefacts to a probable inhibition of a severe CM-allergy in all age groups.<sup>8–16</sup> Interestingly, although there are only few papers dealing with this subject,<sup>8–14</sup> in clinical practice many physicians/radiologists are familiar with

general anaesthesia as prophylaxis for patients with a history of CM-allergy/CM-anaphylaxis.

The basis for this prophylactic tool could be probably the 1984 published review article on “Systemic reactions to intravascular contrast media” by Goldberg who stated that no reports of adverse reactions to contrast media during general anaesthesia have been published so far.<sup>8</sup> Another paper that has been also published in 1984 presents the results of a questionnaire of radiologists: 82% of more than 1500 radiologists in the USA held true that anxiety could be the cause of mild CM adverse reactions; 37% believed that it could be the main reason for severe reactions such as shock, pulmonary and cardio-vascular complaints as well as death.<sup>17</sup>

Interestingly enough, neither clinical studies nor case reports could be found that confirm this hypothesis.

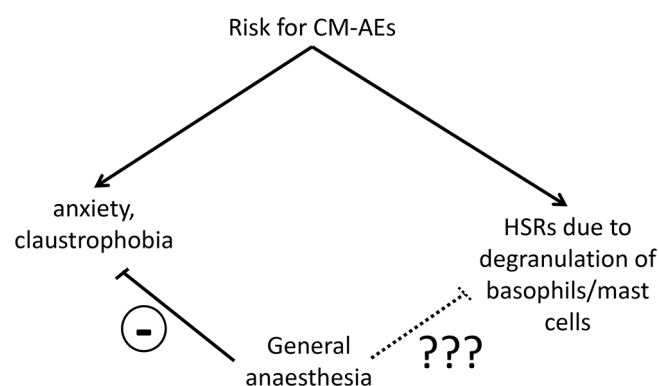
Which cases could benefit from general anaesthesia? Since under general anaesthesia consciousness is switched off, anxious patients in general and patients with claustrophobia in particular could probably benefit from this prophylactic measure. Claustrophobia has been mainly observed in patients undergoing MR-examination, but it is also possible in the context of a CT-scan.<sup>15</sup> Some few severe forms of anxiety have been described who required general anaesthesia to tolerate the MR imaging procedure.<sup>16</sup>

## THE CONS

Interestingly, as early as the mid-1970s and early-1980s, some authors described CM-reactions under general anaesthesia.<sup>9,10,14</sup> Yet, these observations have gone mostly unnoticed by the majority of physicians and by the Goldberg review as well.<sup>8</sup> Both ionic and non-ionic iodinated CM can induce adverse reactions (e.g. including severe ones with cardiac arrest) in anaesthetized patients.<sup>10,13,14,18</sup> If anaesthesia would have a suppressive effect on allergic reactions then one would expect that no CM-allergy should occur in patients under general anaesthesia. But sedation/general anaesthesia does not affect the manifestation of allergy reactions, and only influences subjective reactions (e.g. anxiety claustrophobia and other psychological reactions).<sup>9–14,16</sup> Moreover, even in anaesthetized animals adverse reactions following injection of an iodinated CM have been observed.<sup>19–22</sup>

Anxiety could be a risk factor for both the initialization and aggravation of HSRs,<sup>22,23</sup> but there are neither studies available that provide evidence for the notation that anxiety could trigger the degranulation of basophils nor that show beneficial effects from general anaesthesia in such patients (Figure 1). On the other hand, release of histamine and other biogenic amines of mast cells and basophils—the central cellular events of anaphylaxis—is a process independent of a patients’ alertness. This may be the reason why general anaesthesia does not completely prevent all severe CM-reactions including anaphylactic reactions.<sup>9–12</sup> Moreover, since general anaesthesia bears its own risks for adverse reactions including induction of anaphylactic reactions, this measure cannot be recommended

Figure 1. The diagram displays both anxiety and HSRs as risks for CM-AEs. General anaesthesia is able to suppress anxiety. But there are currently no hints that anaesthesia could block HSRs. CM-AEs, contrast media adverse events; HSRs, hypersensitivity reactions.



to prevent CM-AEs/CM-anaphylaxis. An investigation by Rigsby et al showed that there were 115 adverse reactions experienced by 367 anaesthetized patients (31.3%), and 22 adverse reactions were experienced by 344 (6.4%) non-anaesthetized patients.<sup>24</sup> This means that anaesthetized patients were 5.7 times more likely to experience an AE than non-anaesthetized patients. The authors observed most reactions in anaesthetized patients after the administration of anaesthesia alone.<sup>24</sup> Renaudin et al found that 18.9% of severe drug-induced anaphylaxis occurred during anaesthesia, and only 4.2% after the injection of either iodinated or magnetic resonance imaging contrast media.<sup>25</sup>

## DISCUSSION

Although the manuals on contrast media of the American College of Radiology (ACR) and the European Society of Urogenital Radiology (ESUR) contain a great spectrum of recommendations for different risk groups and circumstances, they both lack some advices concerning the role of general anaesthesia as prophylaxis.<sup>26,27</sup> Without hint to the practice of general anaesthesia in patients at high risk, the ACR-manual on contrast media stated that there is anecdotal evidence that severe adverse effects to contrast media or to procedures can be mitigated at least in part by reducing anxiety.<sup>26</sup> The still ongoing clinical use of general anaesthesia to suppress severe CM-allergy reactions in patients who need contrast-enhanced radiology scans, prompted us review the literature, and present the obtained results.

We presume that the scarce number of papers dealing with this subject do not properly reflect the use of general anaesthesia in clinical practice. To the best of our knowledge, the available literature on that topic reveals only one paper that approves and advises the use of general anaesthesia as a prophylactic tool for patients with a history of severe CM allergy.<sup>8</sup> All other papers reported on patients who acquired adverse CM-reactions under general anaesthesia.<sup>9–14</sup> Even in anaesthetized animals CM-allergy reactions could be observed.<sup>19–22</sup> Since neither evidence-based studies nor clinical observations exist, the clinical use of general anaesthesia in cases with a history of a

CM-induced anaphylaxis is irrational. Therefore, it is tempting to speculate that clinicians favouring this prophylaxis seem to interpret CM-anaphylaxis as mainly emotional-triggered reaction. We recommend the following management program for patients with history of a severe CM-allergy reaction: 1. allergy testing and determining a non-reactive CM; 2. use of a non-culprit CM.

If necessary, anxious patients should receive conscious sedation. In patients at high risk for severe CM-hypersensitivity/CM-anaphylaxis anaesthesia-stand-by is useful for emergency cases. For all other circumstances with elective contrast-enhanced radiological procedures an allergy-work-out should be done with the aim to identify individual tolerable and non-tolerable contrast media materials.<sup>7</sup>

## CONCLUSION

Taken together, general anaesthesia suppresses conscious-dependent reactions such as anxiety and claustrophobia for example, but does not suppress the iodinated CM-/gadolinium-based contrast agents induced release of basophils and mast cells, and subsequent arising immediate reactions. Therefore, the use of general anaesthesia cannot be recommended to avoid CM-related anaphylaxis. Rather, in elective radiological examinations an allergy diagnosis will provide insight into tolerable and non-tolerable (culprit) CM. In patients at high risk for a severe reaction and in emergency cases, anaesthesiology could assist the contrast-enhanced procedure when standing by with the option to intervene as quickly as possible, if the patient demonstrates signs of a HSR. Last but not least, another way to possibly avoid a CM reaction is a modality change.

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