

Masking Iodine Side Effects

Introduction

In order to reduce undesirable side effects, radiologists made the change from ionic to non-ionic iodinated contrast media for intravenous use despite the considerably higher costs. Yet, most physicians do not take the same precautions with oral contrast, and persist in using the older, less safe, ionic contrast medium diatrizoate.

Perception

The perception exists that oral solutions of iodine are not absorbed from the gastrointestinal tract and, therefore, cannot have a systemic effect. Clinical evidence refutes this perception. Oral iodine is absorbed particularly in inflamed bowel caused by IBD, radiotherapy, diverticulitis or other intestinal pathologies.¹ It has even been suggested that renal excretion of oral iodine could be used as a diagnostic test for inflamed bowel.

Once absorbed, iodine has the potential to cause adverse systemic effects. One reported case of oral iodine use resulted in a severe anaphylactoid reaction², but the hospital dismissed the possibility that the reaction could have been caused by diatrizoate because a literature search yielded no previously recorded reactions of this type. Another dose was then administered resulting in a second, more severe reaction. Fortunately, the patient survived with prompt emergency care, but as the author of the report wrote: **"All physicians administering this drug [diatrizoate] must be made aware of its potentially lethal effects."**² Another single case report concluded that, **"...failure to recognize this complication may have resulted in underreporting."**³

A Theory of Masking

The majority of CT studies in which patients are given oral contrast also use an IV iodinated contrast agent. Because the doses of iodine received by the patient are much higher (and by definition systemic), whenever side effects occur, they are always attributed to the IV iodinated contrast agent, even if it is a modern, non-ionic contrast agent. There is a theory that the IV iodinated contrast agent may, in fact, be better tolerated than clinicians realize. The theory is that IV iodinated contrast agents are masking the adverse events actually caused by the ionic iodinated oral agents. A recently published paper⁴ is of interest.

Recent Studies

Researchers from Japan published a prospective study in 7,505 patients in *European Radiology* looking at adverse reactions to IV iohexol (a modern, non-ionic contrast medium) and comparing rates in association with a number of factors. One particularly interesting fact emerged which suggests the possibility of a masking effect with oral iodine:

- The incidence of delayed adverse drug reactions (DADRs) in CT patients (the vast majority of whom received oral contrast) was three times higher (4.4% vs. 1.5%) than in urography patients (who would not have received oral contrast).

The authors did not comment on the statistical significance of these differences.

Dr. Peter Dawson of University College London Hospitals, a world authority on contrast media, wrote the authors to clarify the use of oral contrast in the study group. In their reply they stated that they did not record data on whether patients received oral contrast or not. This omission demonstrates how little oral contrast is considered as a potential source of adverse drug reactions (ADRs).

Additional Evidence

One paper published in 1998 gives anecdotal support to the masking theory.⁵ The paper reported three cases of minor systemic reactions to oral diatrizoate:

1. Patient 1 had a history of allergy to iodine, and so received no IV agent, but was still given oral diatrizoate. He went on to develop a generalized rash and mouth ulcers. There are two interesting points:
 - The radiology team knew that the patient had an allergy to iodine, and yet still gave diatrizoate orally.
 - In subsequent discussion it transpired that the medical team had attributed the rash and ulcers to the use of an IV contrast, even though none had been given.
2. Patient 2 developed an urticarial rash after oral administration of diatrizoate; as a result of this a decision was made not to give IV contrast.
3. Patient 3 had been scanned three times previously, each time receiving both IV and oral iodinated contrasts, and each time developing a rash (despite premedication with oral steroids on the third occasion). On the occasion reported he was scanned without IV contrast, but he developed the same rash within three minutes of taking the initial dose of oral diatrizoate.

One possible explanation is that on each of the three occasions Patient 3 was scanned previously, his rash was caused by the oral diatrizoate, with the IV agent (iopromide, a modern, non-ionic contrast) having no adverse effects. Any suggestion that the rash might have been non-organic in origin is refuted by the fact that the patient has been scanned since the reported case with neither IV nor oral contrast without developing a rash.⁵ It would be interesting to see if the patient developed the same, or any other, rash when receiving IV iopromide but no oral diatrizoate; since such an investigation would not be good medical practice it, therefore, remains a speculative point.

Conclusion

As long as the ADRs caused by iodinated oral contrasts are underreported or attributed to IV agents, this situation will continue. It is hoped that increased realization of the ADR potential of oral iodinated agents will lead to future research and better understanding of less allergenic agents such as those containing pharmacologically inert barium sulfate.[†]

Fact Box

What are Anaphylactoid Reactions?

Anaphylactic reactions are severe, rapid reactions mediated by immunoglobulin E (IgE). They occur when the body has been previously "sensitized" to an allergen by a prior exposure. Rather than the first exposure generating immunity as might be expected from a "normal" antibody/antigen reaction (prophylaxis), a paradoxical reaction occurs on second (and subsequent) exposure, which is far more severe than the original reaction (anaphylaxis).

If a reaction has a clinical manifestation similar to anaphylaxis, but IgE does not mediate the mechanism, then the reaction is said to be "anaphylactoid".

Because the observed clinical effect is always noted but the immunological status is not, such reactions are always referred to as anaphylactoid unless there is suitable evidence to prove them anaphylactic.

In practical terms, the mechanism of the reaction is rarely investigated since the symptoms and treatment of the condition are the same whether IgE is a mediator or not.

*E-Z-EM manufactures and markets a wide range of CT oral contrast products. All products in the range have essentially similar clinical properties, and the decision to choose one over another is based on non-medical criteria such as convenience or taste preference. Not all products manufactured by E-Z-EM are available in all global markets. Brand names used for E-Z-EM CT oral contrast products in various global territories include Smoothie, Read-Cat®, E-Z-Cat®, E-Z-Cat® Dry and BARICAT®.

† Barium sulfate formulations are contraindicated for patients with known gastro or intestinal perforations or hypersensitivity to barium sulfate products. Rarely, severe allergic reactions of an anaphylactoid nature have been reported during the administration of barium sulfate agents.

References:

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