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CASE REPORT

Fatal anaphylactoid reaction following ioversol administration

Frank GA Jansman · Hans Kieft · Johannes W Harting

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Abstract We report a fatal intravenous ioversol administration in a 60-year old male patient. Although the introduction of new low-osmolar non-ionogenic contrast media with a more favourable efficacy-toxicity balance has diminished the side-effects significantly, everyone involved in radiodiagnostic procedures should be aware of the potential life-threatening effects. Especially patients with risk factors for side-effects should be monitored carefully.

Keywords Contrast media · Anaphylactoid reaction · Adverse effects · Risk factors

Introduction

For several decades, organic iodinated contrast media have been used for diagnostic radiologic imaging purposes. Because of the absorption difference of X-rays by the iodine-molecule and surrounding tissues, radiographic visualisation of structures is possible. Although new compounds with a more favourable efficacy-toxicity balance have been introduced, severe and life-threatening side-effects are still reported.

F. G. Jansman · J. W. Harting
Department of Clinical Pharmacy, Isala klinieken, Zwolle, The Netherlands

F. G. Jansman (✉)
Department of Pharmacotherapy and Pharmaceutical Care, Groningen University Institute for Drug Exploration (GUIDE), Antonius Deusinglaan 1, 9713 AV Groningen, The Netherlands
e-mail: f.g.a.jansman@isala.nl

H. Kieft
Department of Intensive Care, Isala klinieken, Zwolle, The Netherlands

We present a male patient with a fatal cardiac arrest after intravenous ioversol administration.

Case description

A 60-year-old man, with a history of regulated diabetes mellitus type II and hypertension, was referred for an abdominal contrast-enhanced CT-scan, because of presurgical staging of a rectal carcinoma His medication consisted of metformin and a thiazide diuretic. There was no history of allergic reactions.

After ioversol 350, 100 ml had been administered intravenously, the patient complained of headache and nausea. Subsequently, he lost consciousness with discoloration of his skin to red-purple. Immediate basic life support was started. On arrival of the medical emergency team, patient was found in pulseless electrical activity. During endotracheal intubation no signs of glottis edema were noticed. Ventricular fibrillation developed for which (unsuccessful) external electrical defibrillation was performed. After 40 min of cardiopulmonary resuscitation with repeated doses of epinephrine, clemastine, atropine, and amiodarone, with concomitant dexamethasone, calcium, theophylline, transcutaneous pacing and intracardial epinephrine, the transthoracic echocardiogram yielded cardiac standstill without ventricular dilatation. It was then decided to cease resuscitation.

An autopsy found, besides the rectal carcinoma without lymph node metastasis, benign adrenal and prostatic hyperplasia concentric left ventricular hypertrophy.

Discussion

Ioversol, used in the present case, is a low-osmolar nonionic monomeric contrast medium, with a relatively

low risk of (severe) side-effects. According to the information from the manufacturer, anaphylactoid reactions occur in 0.1–1% of cases, life-threatening in less than 0.01% [1]. The Netherlands Pharmacovigilance Centre (LAREB) received no report of pseudo-allergic reactions to ioversol administration since its registration in 2001, although one report of severe dyspnoe was found [2].

Intravenous administration of low-osmolar contrast media is associated with side-effects in 2.1% of patients, being mild in 1.2%, moderate in 0.9%, and severe in 0.01% [3]. For the 52% of patients in this study that had risk factors for adverse effects, not being defined in detail, the side effect rate was 2.7%.

The toxicity of contrast media is determined by the intrinsic toxicity and the osmolarity of the medium.

The intrinsic toxicity is attributed to the ability to bind to biological macro-molecules, such as proteins [4]. Since non-ionic and dimeric contrast molecules bind to proteins to a lesser extent than ionic and monomeric contrast molecules, contrast media with non-ionic dimeric molecules (like ioversol) are less toxic.

Life-threatening hypersensitivity reactions have been reported on intravenous administration of iodinated contrast media [5]. Most frequent symptoms are fever, purpura, skin reactions, cardiovascular collapse (like in the present case), convulsions, dyspnoe, renal impairment, pseudo-allergic and/or anaphylactoid reactions [1]. In contrast to initial exposure, clinically manifest IgE-reactions arise at renewed exposure to the allergenic agent. Therefore, anaphylactic reactions to iodinated contrast media are specified as non-allergic anaphylactic or anaphylactoïd reactions. The clinical symptoms, however, of allergic and non-allergic anaphylactic reactions are similar [6].

Several risk factors are identified for the occurrence of side-effects of iodinated contrast media [1] (Table 1); in the present case, the patient had the following risk factors: diabetes, cardiovascular disease and co-medication (metformine). Recommendations for the prevention of renal side-effects are well known and include the preferred use of low-osmolar over high-osmolar contrast media, avoidance of the administration of high doses, sufficient hydration, and prophylactic administration of antioxidants in order to disable the action of cytotoxic oxygen free radicals causing ischemic renal injury. Moreover, calcium-channel blockers can be considered for their positive effects on renal haemodynamics and their cytoprotective effects on renal cells. Furthermore, pre-heating of the contrast fluid before administration decreases its viscosity, reducing side-effects as well [7].

Table 1 Risk factors for side-effects of contrast media

Previous reactions on iodinated contrast media
Positive allergic anamnesis
High osmolar contrast medium
High dose contrast medium (>100 ml)
Intra-arterial injection
Dehydration
Cardiovascular disease, e.g. congestive heart failure, hypertension
Pre-existing renal impairment
Diabetes mellitus
Hyperuricaemia
Proteinuria
Nephrotoxic co-medication (e.g. metformine, vasopressor drugs, nonsteroidal anti-inflammatory drugs, diuretics, aminoglycosides)
Co-medication (neuroleptic drugs, antidepressants, analeptic drugs, MAO-inhibitors)
Hyperthyroidism
Severe hepatic impairment/liver cirrhosis and necrosis
Pheochromocytoma
Cerebro-vascular disease
Homocystinuriae
Sickel cell anaemia
Uraemia
Morbus Kahler
Epilepsy
Alcoholism/liver cirrhosis and necrosis
Asthma
Drug addiction
Age >70 years

Conclusion

In the present case, ioversol administration evidently caused the death of this patient. Despite adequate intervention of the medical emergency team, cardiopulmonary resuscitation was not successful. Although the introduction of low-osmolar noniogenic contrast media has diminished the side-effects significantly, every radiologist and others involved in radiodiagnostic procedures should be aware of the potential life-threatening effects. Especially patients with risk factors for side-effects, including cardiovascular disease, diabetes, renal impairment, and particular co-medication, should be monitored carefully with an adequately organized and operating medical emergency team on duty. Appropriate guidelines for the treatment of acute adverse reactions and equipment available in the room where the contrast medium is given, are provided by the Contrast Media Safety Committee of the European Society of Urogenital Radiology and the American College of Radiology [8, 9].

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