

Fluorescein and anaphylactic reactions

Introduction

Fluorescein, an indicator dye in the form of fluorescein disodium, was approved for the Dutch market in 1992. As intravenous dosage form it is indicated for *the use in ocular angiography* [1].

The fluorescein disodium SPC mentions the following reactions that could be related to an allergic mechanism as possible ADRs: urticaria, hypersalivation, rhinorrhoea and fever.

Reports

On the 31st of August 2007 the database of the Netherlands Pharmacovigilance Centre Lareb contained 4 reports, concerning 2 events, of anaphylactic reactions in relation to the use of fluorescein.

Patient A is a 49 year old male who was administered i.v. fluorescein for a fluorescein angiography (FAG). After administration the patient experienced an anaphylactic reaction with symptoms such as pruritus, urticaria and hypotension. Patient was treated with clemastine i.v. and recovered. This report was submitted by an ophthalmologist together with a hospital pharmacist.

Patient B was a 56 year old female with a medical history of hypertension. The patient was using betahistidine, furosemide, felodipin and metoprolol. Patient was administered fluorescein for a retinal angiography. One and a half minute after administration the patient had an anaphylactic shock, which started with laryngospasms, vomiting and dissociation. Patient was treated with i.v adrenaline clemastine, dexamethason and sodium carbonate. Cardio-pulmonary resuscitation was stopped after one hour, after which she died. This report was submitted by an ophthalmologist together with a hospital pharmacist.

Other sources of information

Literature

In a prospective study of 2,789 angiographic procedures in 2,025 patients, adverse reactions occurred in 4.8% of the patients undergoing angiographic procedures. These reactions included nausea (2.9%), vomiting (1.2%), flushing/itching/hives (0.5%), and other reactions (dyspnoea, syncope, excessive sneezing) (0.2%). No cases of anaphylaxis, myocardial infarction, pulmonary oedema, or seizures occurred. The percentage of reactions was 1.8% for patients who had had previous angiography without ever having had an adverse reaction. In contrast, the percentage of reactions was 48.6% for patients who had had an adverse reaction to angiography previously [2].

Anaphylactic reactions in relation to the use of fluorescein have been described in a number of case reports starting back in the fifties [3-6].

Trindade-Porto *et al.* describe two cases of patients suffering from an anaphylactic reaction after administration of fluorescein.

A 23-year old woman, with no previous history of adverse reactions to drugs presented with hypotension, respiratory distress and hand oedema with itching and a sensation of warmth after i.v administration of fluorescein. Patient received treatment with i.v anti-histamines and corticosteroids. Hours later the patient presented with facial angio-oedema. A skin prick test was positive for fluorescein sodium.

The second case concerns a 75- year old man who immediately after the administration of fluorescein, presented with intense respiratory distress and loss of consciousness which required medical treatment with epinephrine, serum therapy and corticosteroids. A skin prick test was positive for fluorescein sodium [7].

Databases

On August 31, 2007 the database of the WHO contained 74 reports of fluorescein and anaphylactic shock (ROR 13.8 95%CI 10.9-17.5) and 40 reports of anaphylactoid reaction (ROR 7.4 95% CI 5.4-10.2).

Conclusion

The Netherlands Pharmacovigilance Centre Lareb has received two cases of anaphylactic reactions after administration of intravenous fluorescein. In one of the cases the patient died. Case reports in the literature support this association. The SPC of Fluoresceinedinatrium[®] mentions urticaria, hypersalivation, rhinorrhoea and fever as possible adverse drug reactions. Anaphylactic reactions are not mentioned [1]

The SPC of Fluorescite[®], a sodium fluorescein containing product recently approved for marketing, was accessed on September 4, 2007. In this SPC it is adequately warned for the possibility that fluorescein can cause anaphylactic reactions [8].

References

1. Dutch SPC of Fluoresceinedinatrium[®]. (version date 11-9-1992) <http://www.cbg-meb.nl/IB-teksten/h51727.pdf>.
2. Kwiterovich KA, Maguire MG, Murphy RP, Schachat AP, Bressler NM, Bressler SB, Fine SL. Frequency of adverse systemic reactions after fluorescein angiography. Results of a prospective study. *Ophthalmology* 1991;98(7):1139-42.
3. Ingelsted S, Ivstam B. Hypersensitivity to fluorescein; a case of anaphylactic reaction to the injection of fluorescein sodium. *Int Arch Allergy Appl Immunol.* 1950;1(2):157-9.
4. Hitosugi M, Omura K, Yokoyama T, Kawato H, Motozawa Y, Nagai T, Tokudome S. An autopsy case of fatal anaphylactic shock following fluorescein angiography: a case report. *Med Sci Law* 2004;44(3):264-5.
5. Fineschi V, Monasterolo G, Rosi R, Turillazzi E. Fatal anaphylactic shock during a fluorescein angiography. *Forensic Sci Int* 1999;100(1-2):137-42.
6. Tondriaux A, Andrejak M, Vallet D, Daelman F, Galy C, Turut P, Ossart M. Lethal shock after fluorescein angiography; a case. *Ann Med Interne (Paris).* 1990;141(7):630-1.
7. Trindade-Porto C, onso-Llamazares A, Robledo T, Chamorro M, Dominguez J, Plaza A, Martinez-Cocera C. Fluorescein-induced adverse reaction. *Allergy* 1999;54(11):1230
8. Dutch SPC Fluorescite[®]. (version date 23-1-2007) <http://www.cbg-meb.nl/IB-teksten/h34461.pdf>.