Fluorescein and Indocyanine dyes for angiography

**Fluorescein sodium**

Fluorescein sodium is a yellow water-soluble dibasic acid xanthine dye which produces an intense green fluorescent colour in alkaline solution (pH less than 5). It is used as a topical eyedrop to show defects in corneal epithelium but as a diagnostic aid in ophthalmic angiography it is given by direct intravenous injection. Fluorescein angiography allows examination of the fundus and assessment of iris and retinal blood vessels. Oral fluorescein has been used for diagnosis of retinal vascular disease.

Contraindications;
Hypersensitivity to fluorescein. A prior reaction to fluorescein should be entered in the patient’s notes.

Cautions;
Where patient has a history of hypersensitivity, allergies or asthma. Discontinue if signs of sensitivity develop.

Pregnancy;
Category C. Avoid during pregnancy, especially in the first 3 months. There are no reports of fetal complications during pregnancy.

Breastfeeding;
Fluorescein is excreted in breast milk.

Adverse Reactions;
The injection can cause nausea, headache, gastro-intestinal upset & vomiting. Signs or hypersensitivity include hypotension. There have been incidents of cardiac arrest, thrombophlebitis at injection site, severe shock and convulsions. Hives, itching, bronchospasm, anaphylaxis, fever, transient shortness of breath and dizziness may occur. Where a serious adverse event occurs report it using the Yellow Card Scheme (www.mhra.nhs.uk) Extravasation at injection site causes intense pain locally and a dull aching pain in the injected arm.

Patient information;
May give patient a strong taste in use.
Can cause temporary yellowing of the skin which fades in 6 to 12 hours. Urine becomes bright yellow up to 36 hours after injection of the dye.

Off license use;
There is no licensed product available in the United Kingdom for administration of fluorescein for angiography by intravenous or oral route.
Companies making these agents therefore do not have a duty to provide professional information or written information for patients. (Ophthalmic Drug Facts 2000)

Administration and dosage;

Sodium fluorescein 10% or 20% injection is given rapidly into the antecubital vein, taking precautions to avoid extravasation. If the needle has extravasated stop the injection. When injection of the dye is complete luminescence appears in the retina and choroid vessels in 9 to 15 seconds. If allergy is suspected, perform an intradermal skin test prior to i.v. administration. 0.05ml is injected intradermally and the site examined after 30-60 minutes.

I.V. doses; Adult : 500 - 750mg
   Children: 7.5mg/kg

Oral fluorescein has been used to study lesions of the fundus. Dye begins to appear at the fundus at 15 minutes post ingestion with maximum affect at 45-60 minutes. Fasting can enhance dye serum concentration. Oral administration has a lower incidence of side effects.

Oral doses; 1 to 2 grams as powder, capsules or as a solution in fruit juice. (Noble MJ et al 1984)

Extravasation;

Because of its high pH extravasation can result in severe local tissue damage. Complications can include sloughing of the skin, superficial phlebitis and toxic neuritis along the curve of the antecubital area. Administration procedure should involve drawing back blood or using sterile saline to check for correct placement of the cannula before injecting the dye. Solutions should not be used if they contain precipitate and any unused solution should be discarded.

Management of adverse events;

Procedures should be in place for the care of patients experiencing adverse events and drugs such as adrenaline 1 in 1000, antihistamines, steroids and oxygen should be available.

Complications of intravenous fluorescein angiography

Based on the Fluorescein Angiography Complication Survey (FACS) (1984), complications are classified as mild, moderate or severe. FACS evaluated 222,000 cases in 1984 and the findings are tabled below.
<table>
<thead>
<tr>
<th>Mild</th>
<th>Nausea or extravasation resolving rapidly</th>
<th>Reassurance.</th>
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<tbody>
<tr>
<td>Moderate</td>
<td>Urticaria, fainting, taking some time to resolve but no long term problems</td>
<td>Consider systemic antihistamines, e.g. diphenhydramine or chlorpheniramine. Raise legs, consider smelling salts.</td>
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<tr>
<td>Severe (1 in 9,000 - death 1 in 222,000)</td>
<td>Respiratory, cardiac, neurological- prolonged.</td>
<td>Treat intensively as threat to patient safety.</td>
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Butner and Macpherson (1983) reported 241 adverse reactions in 5000 patients. Pacurariu (1982) in a study of 2,600 patients observed men and younger patients to experience side effects more frequently. Cavallerno (1996) has recommended that the procedure should not be performed on pregnant or nursing mothers.

Managing side effects

Side effects such as the warm flush or early nausea within 30 seconds of injection can be explained to the patient in advance. There is no conclusive benefit to giving antihistamines before hand although this may be justified for patients with a history of urticaria. For some patients, anxiety surrounding the whole experience may need controlling with a dose of a benzodiazepine, such as diazepam.

It is good practice to have a local policy in place for the management of patients should extravasation occur.

**Indocyanine Green**

It is a sterile, water soluble, tricarbocyanine dye with a peak spectral absorption and emission at 800 to 810 nm in blood or plasma. Indocyanine green contains about 5% sodium iodide. Transmission of energy by the pigment epithelium is more efficient than in visible light. As the dye is nearly 98% bound to blood proteins there is minimal leakage of dye from the choroidal vessels. It is useful in angiography of the choroid. Outside of ophthalmic use it is used to determine cardiac output, liver function and liver blood flow.

Contra-indications:
Prior allergy to shell fish, iodine or ICG.

Warnings:

Pregnancy; category C- It is not known if ICG can harm the foetus or can affect the normal gestation. Avoid using in the first 3 months of pregnancy. Breastfeeding; It is not know if this dye is excreted in breast milk.
Precautions;
Radioactive iodine uptake studies should not be done within a week of having ICG.
Use with caution in patients with a prior allergy to iodides.

Adverse Reactions;
Anaphylaxis or urticaria has occurred in patients with no prior allergy to iodides. Ensure resuscitation equipment and trained staff are available.

Administration and dosage;
Use 40mg ICG in 2ml of aqueous solvent. It is stable for up to 10 hours once reconstituted and must be protected from light.

Patient information;
Symptoms reported include restlessness, itching, urticaria, tachycardia, hypotension and breathlessness.
Very rarely injections of ICG can cause nausea and anaphylaxis.
There are no known effects with ICG that impair ability to drive.
Alcohol should be avoided before and after ICG angiography.

Toxicity of ICG;
Hope-Ross and colleagues (1994) evaluated 1,923 procedures in 1,226 patients and identified a 0.3% rate of adverse reactions. Regillo’s study of literature identified 18 severe reactions and 3 deaths. An estimated incidence of death for ICG approximates at 1 in 300,000 patients compared to 1 in 200,000 patients with iv fluorescein.