Safety of Indocyanine Green Angiography During Pregnancy

A Survey of the Retina, Macula, and Vitreous Societies

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Objectives: To establish current practice patterns and assess the general knowledge among vitreoretinal-trained physicians regarding the use of indocyanine green (ICG) angiography during pregnancy, and to review the literature regarding the established safety of ICG angiography in pregnant women.

Methods: A survey was mailed to 1101 members of the Retina, Macula, and Vitreous Societies.

Results: Of the 520 respondents, 434 (83%) had seen at least 1 pregnant woman who required ICG angiography or fluorescein angiography. Of these, 385 (89%) withheld fluorescein angiography and 105 (24%) withheld ICG angiography, largely because of fear of teratogenicity or lawsuit. Diabetic retinopathy and choroidal neovascular membrane were the most common indications for fluorescein angiography, and choroidal neovascular membrane and choroidal tumor were the most common indications for ICG angiography. Only 24% thought it was safe to use ICG angiography in a pregnant patient, and only 5% thought it was safer than fluorescein angiography.

Conclusions: Despite the documented safety of ICG when used for retinal angiography and the extensive experience with the use of intravenous ICG to measure hepatic blood flow in pregnant women, the results of this survey suggest widespread hesitation to use ICG for retinal angiography in pregnant women. Current practice patterns regarding the use of ICG angiography in pregnant patients may be unnecessarily restrictive.


Indocyanine green (ICG) is a water-soluble tricarbocyanine dye introduced in 1957 by Fox et al to measure systemic blood flow. In 1961, Caesar et al first reported the use of ICG in the measurement of hepatic blood flow and hepatic function. Since that time, it has been used intravenously for the evaluation of hepatic function and cardiac output and, more recently, for ophthalmic angiography and in the calculation of venous contrast transit time during cardiac ultrafast computed tomography. The properties that make indocyanine green favorable for these uses are its very high degree of hepatic clearance, predictable volume of distribution, absence of extrahepatic uptake, lack of enterohepatic circulation, unchanged excretion into the bile, and high binding affinity for serum lipoproteins.

Although ICG has been used to evaluate and further the understanding of retinal diseases that are associated with pregnancy or that occurred in pregnant patients, there is little information in the ophthalmic literature regarding the safety of its use during pregnancy. We surveyed vitreoretinal-trained physicians to identify the current practice patterns and general knowledge regarding the use and safety of ICG angiography in pregnant patients.

RESULTS

Of the 1101 physicians surveyed, 520 responded. Of these, 434 had examined at least 1 pregnant patient who had an ocular condition necessitating either IVFA or ICG angiography, and 270 had performed at least 1 IVFA or ICG angiography.

Three hundred eighty-five respondents had withheld IVFA from at least 1 pregnant patient. The reasons were as follows: fear of teratogenicity in 137, ability to treat without test in 96, fear of lawsuit in 118, patient request in 30, and no reason was given in 4. One hundred five respondents had withheld ICG angiography from at least 1 pregnant patient. The reasons were as follows (multiple responses were possible):

- Fear of teratogenicity
- Ability to treat without test
- Fear of lawsuit
- Patient request
- No reason given
Indocyanine green has a documented record of use for nonophthalmic purposes and has been given to pregnant women without adverse effect on mother or fetus. Before its present clinical use in ophthalmic angiography, ICG was used extensively as a chromodiagnostics agent in the evaluation of hemodynamic changes that occur during pregnancy. Indocyanine green clearance has been used to measure apparent liver blood flow and cardiac output in pregnant women. In a study by Robson and associates,7 ICG, 0.5 mg/kg of body weight, was given intravenously to 12 women at 12 to 14, 24 to 26, and 36 to 38 weeks of pregnancy and then at 10 to 12 weeks after delivery. Intravenous ICG, 0.5 mg/kg of body weight, has also been used in the assessment of hepatic excretion in pregnant women afflicted with hyperemesis gravidarum.8

Evidence that ICG does not cross the placenta comes from 2 studies where simultaneous measurements were made in the maternal and fetal blood after intravenous administration in the mother. Rudolf and associates9 used intravenous ICG to characterize hepatic excretion function during the course of a normal pregnancy. Intravenous boluses of ICG, 0.5 mg/kg, were given to 168 pregnant women during all 3 trimesters of pregnancy and post partum. No placental transfer of the dye could be detected by simultaneous measurement of ICG in the maternal and fetal cord blood. Probst and associates10 studied the clearance and placental transfer of ICG during labor. Eight of their 9 patients were given intravenous ICG, 5 mg/kg of body weight. Although this dose represents many times the currently recommended dose for ICG angiography, no ICG could be detected in fetal blood samples that were obtained simultaneously with maternal blood or in umbilical vein blood collected immediately after birth.

Recent improvements in digital video technology have led to increased use of ICG for retinal angiography.11 12 The safety of ICG is well established, with severe adverse effects occurring in 0.05% or less.12,13 Despite the documented safety of ICG when used for retinal angiography and the experience of using intravenous ICG in pregnant women to measure hepatic blood flow, there is still hesitation to use ICG for retinal angiography in pregnant women. Valluri and associates14 reported the ICG angiographic finding in 4 women with preeclampsia. However, the ICG angiography was withheld until the postpartum period.

Both ICG and fluorescein are classified by the Food and Drug Administration as pregnancy category C, indicating that studies have not been conducted and therefore it is unknown whether fetal harm will result when administered to a pregnant woman. This is important, because the results of this survey indicate that 434 (83%) of the 520 responding vitreoretinal specialists have, during the course of their careers, examined at least 1 pregnant patient who required either IVFA or ICG angiography. Although the majority reported withholding IVFA, nearly one quarter of the respondents also withheld ICG angiography.

The results support the impression that fear of teratogenicity in the fetus is the major reason for not performing angiography in pregnant patients.4 However, fear of being sued was almost as common a reason to withhold ICG angiography and IVFA. The ability of many respondents to treat the patient without obtaining the test (25% for IVFA and 10% for ICG angiography) raises the question of whether the test was actually necessary.

Not surprisingly, the indications to perform ICG angiography in pregnancy were quite different from the indications to perform IVFA. Diabetic retinopathy and choroidal neovascular membrane were the most common indications for IVFA, and choroidal neovascular membrane and choroidal tumor were the most common indications for ICG angiography.

The overall safety of ICG angiography in pregnancy was unable to be assessed by most respondents. When asked whether ICG angiography was a safe procedure to perform in a pregnant woman, 60% of the respondents indicated that they did not know. Only 24% indicated it was safe and only 16% believed that it was

**MATERIALS AND METHODS**

We surveyed 1101 members of the Retina, Macula, and Vitreous Societies to assess their experience with ICG angiography in pregnant patients. The questionnaires requested information on the following: general use of ICG angiography and intravenous fluorescein angiography (IVFA); experience with pregnant patients requiring angiography; indications for ICG angiography and IVFA; the number of studies performed; whether ICG angiography or IVFA was withheld from a pregnant woman and, if so, the reason for this; opinions as to which trimester was safest to perform an ICG angiogram; whether ICG was a safe procedure to perform in a pregnant woman; and whether ICG was safer than IVFA in pregnancy.
not safe. Fifty percent of the respondents believed that IVFA was safer than ICG angiography in the setting of pregnancy, and only 5% believed that ICG was the safer of the two. A longer “track record” was noted by many of the respondents as the reason to choose IVFA as the safer test.

The results of this survey suggest widespread hesitation to use ICG for retinal angiography in pregnant women. A lack of awareness of the evidence supporting the safety of ICG use in pregnancy for nonophthalmic indications is the most likely explanation for these responses. Current practice patterns regarding the use of ICG angiography in pregnant patients may be unnecessarily restrictive.

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