U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Drug Safety Communications

FDA advises of rare cases of underactive thyroid in infants given iodine-containing contrast agents for medical imaging

Safety Announcement

[11-17-2015] The U.S. Food and Drug Administration (FDA) is advising that rare cases of underactive thyroid have been reported in infants following the use of contrast media containing iodine, also called "contrast dye," for X-rays and other medical imaging procedures. In all of the reported cases, the infants were either premature or had other serious underlying medical conditions. Available evidence leads us to believe that this rare occurrence is usually temporary and resolves without treatment or any lasting effects.

We have approved changes to the labels of all iodinated contrast media (ICM) products to include information about these cases. We do not recommend changes to current prescribing, administration, or monitoring practices. We will continue to evaluate this issue and will update the public when we have additional information. Manufacturers of ICM products have been required to conduct a study to investigate this safety issue further.

Parents and caregivers should contact their baby's health care professional for additional information or if they have questions or concerns about their baby receiving an ICM product. Infants typically do not show any visible signs of underactive thyroid. The thyroid is a gland in the neck that releases hormones. Health care professionals should continue to follow the label recommendations for ICM products. They should continue to use their clinical judgment to determine if testing for underactive thyroid is necessary.

ICM are drugs containing iodine that are given to patients to enhance the ability to see blood vessels and organs on medical images such as X-rays or computed tomography (CT) scans (see Table 1 below for a list of products). These images provide greater detail when necessary to help health care professionals diagnose potential problems.

A search of the FDA Adverse Event Reporting System (FAERS) database identified 10 cases of underactive thyroid reported between 1969 and early 2012 in infants younger than 4 months who received ICM. FAERS includes only reports submitted to FDA, so there may be additional cases about which we are unaware. In addition to ICM, several of these infants also received a topical iodine product that is no longer recommended for young infants, and that may have contributed to their underactive thyroids. All of the infants were diagnosed with underactive thyroid within a month of receiving ICM. Some infants were treated and improved while others improved without treatment.

We will continue to evaluate this safety issue and will update the public when additional information is available. The goals of the study that we are requiring the manufacturers to conduct are to determine how often underactive thyroid occurs with ICM use, how long this temporary condition lasts, and if treatment is needed.

We urge health care professionals and parents/caregivers to report side effects involving ICM to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of the page.

Table 1. FDA Approved Marketed Iodinated Contrast Media Products

Generic name	**Brand name(s)**
diatrizoate meglumine	Cystografin Cystografin Dilute
diatrizoate meglumine and diatrizoate sodium	MD-76R
iodipamide meglumine	Cholografin Meglumine
iodixanol	Visipaque 270, 320
iohexol	Omnipaque 140, 180, 240, 300, 350
iopamidol	Isovue-200, 250, 300, 370 Isovue-M 200, 300 Scanlux-300, 370
iopromide	Ultravist 150, 240, 300, 370
iothalamate meglumine	Conray Conray 30, 43
ioversol	Optiray 240, 300, 320, 350
ioxaglate meglumine and ioxaglate sodium	Hexabrix
ioxilan	Oxilan-300, 350

Facts about Iodinated Contrast Media (ICM)

- Also known as "contrast dye" or "X-ray dye," ICM are drugs that contain iodine and are used to enhance the ability to see blood vessels and organs during medical imaging procedures.
- Procedures that use ICM include X-rays of blood vessels, joints, organs, and the spinal area; and some computed tomography (CT) scans.
- ICM products can be given as injections into the veins, by mouth as a drink, or rectally.
- Common side effects associated with ICM include flushing in the face, nausea or vomiting, mild itchiness, and skin rash.

Additional Information for Parents and Caregivers

- Rare cases of underactive thyroid have been reported in infants following the use of contrast media containing iodine for routine imaging procedures such as X-rays and computed tomography (CT) scans. The thyroid is a gland in the neck that releases hormones.

- Available evidence leads us to believe this rare occurrence of underactive thyroid is usually temporary and may resolve without treatment or any lasting effects. Infants typically do not show any visible signs of underactive thyroid.
- Talk to your baby's health care professional if your baby has received or will receive an iodinated contrast media (ICM) product and/or you have questions or concerns about ICM.
- Report side effects from ICM to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of this page.

Additional Information for Health Care Professionals

- Results of thyroid function tests indicative of hypothyroidism or transient thyroid suppression have been uncommonly reported following administration of iodinated contrast media (ICM) to infants. Some of the infant patients were treated for hypothyroidism.
- Continue to follow the label recommendations for ICM products.
- At this time, we are not recommending any changes to current ICM administration practices, or any additional routine patient testing or follow-up. Health care professionals should continue to use their clinical judgment to determine if testing for hypothyroidism is necessary.
- Report adverse events involving ICM to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of this page.

Data Summary

A search of the FDA Adverse Event Reporting System (FAERS) database between 1969 (database initiation) and February 14, 2012, identified 11 cases of hypothyroidism reported with iodinated contrast media (ICM). Ten of the 11 cases were reported in infants younger than 4 months old, and there was one case in an adult. Seven of the 10 infant cases were also reported in the medical literature.[1,2] Six of the 10 infants were born full-term with major cardiac abnormalities and four were prematurely born. Hypothyroidism in these infants occurred after intravenous ICM administration (n=7), rectal ICM administration (n=1); rectal and intravascular ICM administration (n=1), and through the breast milk of a mother receiving intravenous ICM (n=1). The average time to diagnosis of hypothyroidism following ICM administration was 15 days (range 7 to 30 days). Coadministration of a topical iodine product was also reported in four of the 10 cases. Systemic absorption of iodine in infants may occur from multiple sources, including topical iodine product application, which may also cause hypothyroidism.

Eight of the 10 cases reported clinical improvement, and the remaining two cases did not report an outcome. Four of the 10 infants received treatment for hypothyroidism. In two of these four cases, treatment was continued for 6 and 10 months, respectively. In one case, the duration of treatment was not specified; in the other case, the infant died from other causes while being treated for hypothyroidism.

A 2014 publication reported three infants with congenital heart disease who developed hypothyroidism after exposure to ICM and iodine in surgical dressings: one infant had a spontaneous improvement in thyroid function; another received thyroid hormone replacement from day 14 to approximately day 23 of life; and the third was receiving thyroid hormone replacement at 15 months.[3]

References

1. Ahmet A, Lawson ML, Babyn P, Tricco AC. Hypothyroidism in neonates post-iodinated contrast media: a systematic review. Acta Paediatr 2009;98:1568-74.

2. Hallett A, Evans C, Moat S, Barton J, Warner J, Gregory JW. Hypothyroidism in preterm infants following normal screening. Ann Clin Biochem 2011;48:572-4.

3. Thaker VV, Leung AM, Braverman LE, Brown RS, Levine E. Iodine-induced hypothyroidism in full-term infants with congenital heart disease: more common than currently appreciated? J Clin Endocrinol Metab 2014;99:3521-6.