

The influence of oil-soluble iodinated contrast medium (Lipiodol) on child's thyroid function in mice.

Tadashi Hongyo, Masahiro Namise, Yukimitsu Sawai, Yasuyuki Ueda

Osaka University Medical School, Division of Health Science, Radiation Biology

e-mail: hongyo@sahs.med.osaka-u.ac.jp

【Introduction】

Hysterosalpingography(HSG) using oil-soluble iodinated contrast medium (ethiodized oil; Lipiodol) is a common examination for patients with infertility. Lipiodol remains in the body long after the examination, and there are some reports suggesting that Lipiodol induces thyroid dysfunction not only to the mother but also the fetus and the newborn. However, since there are no known mouse models of Lipiodol-induced thyroid dysfunction, we examined the influence of Lipiodol on child's thyroid function in mice by administering Lipiodol to its mother.



Fig.1 Hysterosalpingography

【Materials and Methods】

Twelve-week-old ICR female mice were intraperitoneally administered with Lipiodol once before mating or during pregnancy or after delivery, and the thyroid uptake rate of I-131 (74 kBq / mouse) in their newborn mice was examined 24 hours after oral administration of I-131. The dose of Lipiodol used was either equivalent to that used in humans (10mL/50kgBW=0.2 μL/g BW, iodine amount=96 μg/g BW) or its 1/2 or 1/10 amount.

Lipiodol was diluted with corn oil, and all were set to a total of 10 μL/g BW.

The same volume of corn oil was used as a control.

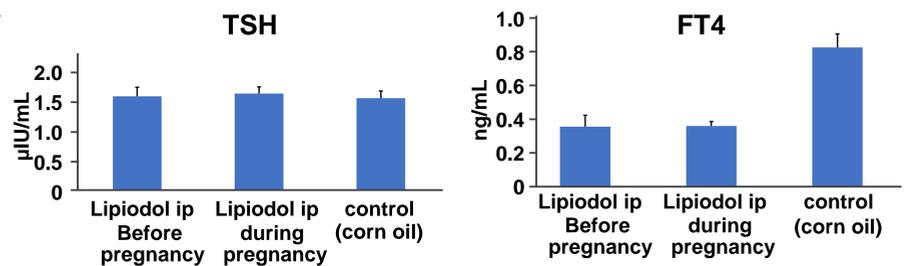
When the offspring mice reached 4 weeks of age, serum TSH and FT4 were measured by ELISA method.

The number of mice in each experiment was 6 or more.

It is noteworthy that thyroid uptake of I-131 was suppressed to almost the same degree even in 1/2 dose administration, suggesting that the effect of Lipiodol on the thyroid gland does not change even if the amount of Lipiodol is reduced from 10 mL to 5 mL for HSG.

When 0.2 mL/g BW of Lipiodol was administered to mice during pregnancy (10th gestation) or immediately after birth, thyroid uptake rate of I-131 in 5-day-old neonatal was decreased to 5.8% and 2.4% compared to control, respectively.

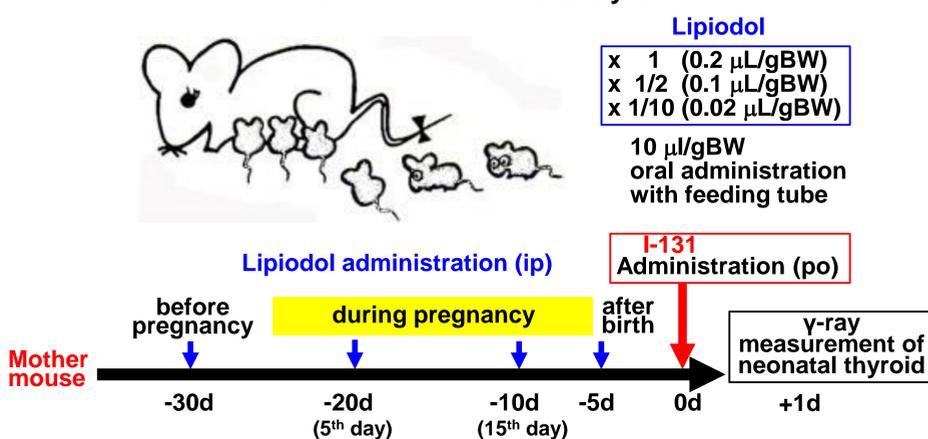
Fig.4 Thyroid hormone level of 28-day-old female mice



There was no change in TSH level in children mice at 4 weeks of age, but a significant decrease in FT4 was observed.

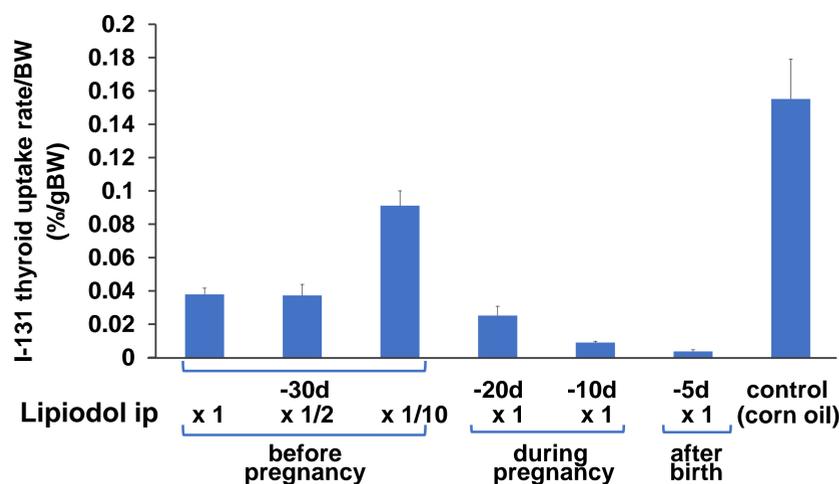
These results suggest that the amount of Lipiodol used in examinations such as hysterosalpingography (HSG) should be kept as little as possible, and that thyroid function in children born after examinations using Lipiodol needs to be carefully observed.

Fig.2 Lipiodol administration to mother and I-131 measurement of neonatal thyroid



【Results and Discussion】

Fig.3 Thyroid uptake rate of I-131 in 5-day-old mice



When 0.2 mL/g BW Lipiodol or its 1/2, 1/10 amount were administered intraperitoneally before pregnancy (5 days before gestation), thyroid uptake rate of I-131 in 5 day old infants was decreased to 24.4%, 24.0% and 58.7% compared to control, respectively.

Tab.1 Frequency of hypothyroidism following HSG (Reports)

object	frequency	remarks	author
neonatal	5/212 (2.4%)	hypothyroidism after maternal HSG	Satoh M ¹⁾
	(0.7%)	congenital hypothyroidism	Tokyo Health Service Association ²⁾
mother	4/180 (2.2%)	euthyroid before HSG	Mekaru K ³⁾
	10/28 (35.7%)	subclinical hypothyroidism before HSG	Mekaru K ³⁾
	3/22 (13.6%)	euthyroid before HSG	Kaneshige T ⁴⁾

As shown in Table 1, occurrence of hypothyroidism in mothers and their children is reported following HSG. This may be a phenomenon often seen in countries with a high iodine uptake as in Japan.

Iodine intake restriction may be needed for pregnant women following HSG who are taking a lot of iodine everyday as well as Japanese during pregnancy and lactation.

【References】

1. Satoh M, Aso K, Katagiri Y. Thyroid dysfunction in neonates born to mothers who have undergone hysterosalpingography involving an oil-soluble iodinated contrast medium. *Horm Res Paediat* 2015;84:370-375.
2. Tokyo Health Service Association: Activity Report Tokyo Health Service Association 2010; 39: 133.
3. Mekaru K, Kamiyama S, Masamoto H, Sakumoto K & Aoki Y. Thyroid function after hysterosalpingography using an oil-soluble iodinated contrast medium. *Gynecol Endocrinol*, 2008; 24: 498-501.
4. Kaneshige T, Arata N, Harada S, Ohashi T, Sato S, Umehara N, Saito T, Saito H, Murashima A, Sago H. Changes in serum iodine concentration, urinary iodine excretion and thyroid function after hysterosalpingography using an oil-soluble iodinated contrast medium (lipiodol). *J Clin Endocrinol Metab* 2015;100:E469-E472.
5. Hongyo T, Namise M, Sawai Y, Nakano T, Yanamoto K. The research about the replacement of the stable iodine tablet which restrains the thyroid bustle of the radioactive iodine. *Euro Associat Nucl Med*. 2017.10 Vienna, Austria.