Iodine absorption and thyroidal uptake: a novel ^{129}I tracer method for their assessment in humans

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1 Introduction

Thyroidal iodine uptake and turnover has been measured in adults using radioactive iodine tracers, but these cannot be used safely in women or children. Iodine requirements for these populations groups have never been directly measured.
Our objective was to assess ^{129}I, a semi-stable isotope safe for use in human, as a novel tracer for the measurement of fractional absorption (^{129}IFA) and thyroidal uptake (^{129}ITU).

2 Study design

We administered an oral physiological dose of ^{129}I (^{129}IDose) to euthyroid adults with adequate iodine intake. Three days before until three days after the oral tracer administration, the participants consumed an iodine standardized diet. For the following 4 days, they kept a food diary and were advised to restrain from consuming high-iodine containing foods. At baseline (on the third day) and after tracer consumption, we collected complete urines (over 8 days), complete feces (over 4 days), and frequent spot plasma (over 5 days) (**Fig. 1**). We measured ^{129}I in alkaline-extracted urine (^{129}IU) by multicollector inductively coupled plasma mass spectrometry (ICP-MS) using isotope dilution analysis (IDA) with a known amount of ^{129}I and a Te standard for mass bias correction. We measured ^{129}I in plasma (^{129}IP) and feces (^{129}IF) by accelerator mass spectrometry (AMS) using IDA to samples previously spiked with a known amount of ^{127}I (Woodward iodine). ^{129}IFA is calculated as ^{129}IDose minus ^{129}IF; ^{129}ITU is calculated as ^{129}IFA minus ^{129}IU. The ^{129}IP kinetic patterns allows the evaluation of thyroid uptake patterns.

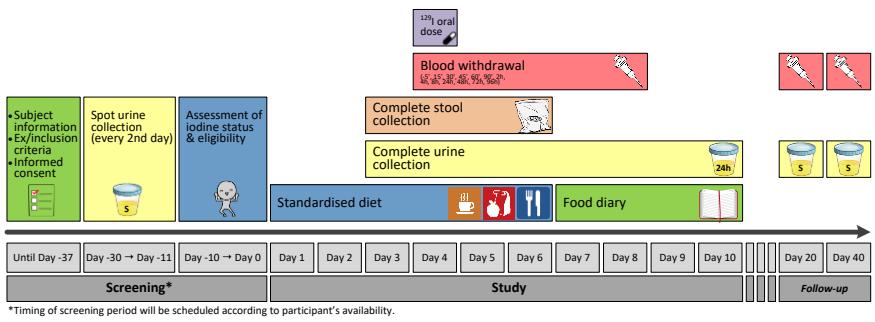

Fig. 1. Study flowchart.

3 Results and discussion

Four male and four female adults (mean±SD age: 26.1±4.0 y) with normal BMI (23.6±1.4 kg/m^2), adequate thyroid function (median (IQR) TSH: 1.3 (1.2-1.4) mU/L; T_4: 106.3 (97.6-122.9) nmol/L) and adequate iodine intake (UIC: 123 (101-140) µg/L), consumed 12.42±0.05 µg ^{129}I as an oral solution together with breakfast. The iodine-standardized diet successfully maintained constant urinary iodine excretion during the study (**Fig. 2**). In urines, ^{129}I was first detected ≈1h after administration and a 96.8, 98.7 and 99.3% of the total ^{129}IU excretion was recovered within 48, 72, and 96h after administration. Cumulatively, 8.3 (7.1-8.6) µg ^{129}I were excreted in urines (^{129}IU), corresponding to 64.3±7.4% of the administered ^{129}IDose (range: 55-75%; inter-subject CV: 11.5%) (**Fig. 3**). Cumulative ^{129}I excretion in feces (^{129}IF) was 0.4 (0.3-0.7) µg (4.7±3.2% of ^{129}IDose; range: 2-11%; inter-subject CV: 67.8%). Cumulative total ^{129}I excretions (^{129}ITE) are shown in **Fig. 4**.

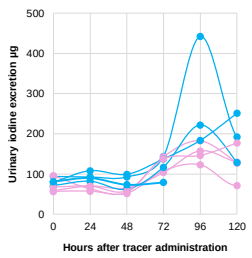

Fig. 2. Daily urinary iodine excretion.

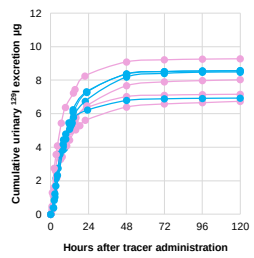

Fig. 3. Cumulative urinary ^{129}I excretion.

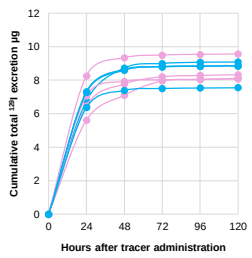

Fig. 4. Cumulative total ^{129}I excretions.

It resulted a calculated ^{129}IFA of 11.9 (11.7-12.1) µg, meaning that 95.3±3.2% of ^{129}IDose (range: 89-98%; inter-subject CV: 3.3%) was absorbed at the gastro-intestinal level, and a calculated ^{129}ITU of 3.9 (3.5-4.2) µg, meaning that 31.0±5.2% of ^{129}IDose (range: 23-39%; inter-subject CV: 16.9%) reached the thyroid, as the sole site of utilization (**Tab. 1**).

Tab. 1. Administered ^{129}I tracer oral dose (^{129}IDose), measured ^{129}I urinary excretion (^{129}IU) , measured ^{129}I fecal excretion (^{129}IF), measured ^{129}I total excretion (^{129}ITE), calculated ^{129}I fractional absorption (^{129}IFA), and calculated ^{129}I thyroidal uptake (^{129}ITU).

	All (n=8)	Males (n=4)	Females (n=4)
^{129}IDose (µg)	12.41 (12.40-12.42)	12.41 (12.41-12.45)	12.4 (12.37-12.42)
^{129}IU (µg)	8.3 (7.1-8.6)	8.5 (8.1-8.6)	7.6 (7.1-8.4)
^{129}IU (%)	64.3 ± 7.4	65.5 ± 6.4	63.2 ± 9.1
^{129}IF (µg)	0.4 (0.3-0.7)	0.4 (0.3-0.6)	0.6 (0.3-1.0)
^{129}IF (%)	4.7 ± 3.2	3.6 ± 1.5	5.8 ± 4.3
^{129}ITE (µg)	8.6 (8.1-8.9)	8.9 (8.5-8.9)	8.3 (8.1-8.7)
^{129}ITE (%)	69.0 ± 5.2	69.1 ± 5.5	69.0 ± 5.8
^{129}IFA (µg)	11.9 (11.7-12.1)	12.0 (11.8-12.2)	11.8 (11.4-12.1)
^{129}IFA (%)	95.3 ± 3.2	96.4 ± 1.5	94.2 ± 4.3
^{129}ITU (µg)	3.9 (3.5-4.2)	3.6 (3.5-4.0)	4.1 (3.7-4.2)
^{129}ITU (%)	31.0 ± 5.2	30.9 ± 5.5	31.0 ± 5.8

Data are mean ± SD for percent of ^{129}IDose or median (IQR) for actual measured or calculated values.

However, visual inspection of the log ^{129}IP concentration curves shows patterns that typically describe a 3-compartment model, suggesting that a third compartment, other than plasma and thyroid, may be involved in iodine metabolism (**Fig. 5**). Further investigations for determining the pharmacokinetic parameters is needed in order to draw thyroid uptake.

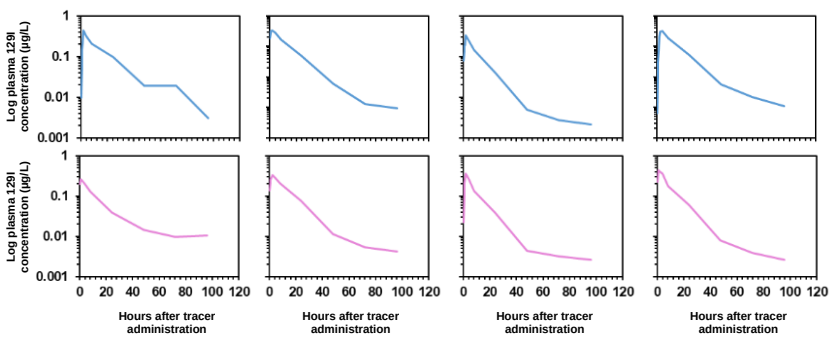

Fig. 5. Kinetic patterns of log 129IP concentration over time for 8 adults.

4 Conclusions

This novel and safe ^{129}I tracer based method successfully quantified ^{129}I urinary and fecal excretion, allowing the quantification of iodine fractional absorption and thyroidal uptake. The pharmacokinetic preliminary analysis shows that iodine metabolism is best described by a 3-compartment model. We will apply this promising methodology to assess iodine requirements in vulnerable population groups and to assess iodine bioavailability from foods.

Partners