Development of a novel 129I tracer method to quantify iodine absorption, retention and excretion in humans

Project 484

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Background and objective:
Thyroidal iodine uptake and turnover has been measured in adults using radioactive iodine tracers (^{125}I,^{131}I), but these cannot be used safely in women or children. Iodine requirements for these population groups have never been directly measured and are derived from male adult requirements. Our objectivewas to assess ^{129}I (a semi-stable isotope that is considered safe for use in human trials) as a novel tracerfor the measurement of iodine fractional absorption (^{129}IFA) and iodine thyroidal uptake (^{129}ITU) that can be safely used in all population groups.

Methods:
We administered an oral physiological tracer dose of 12.42±0.05 µg ^{129}I (^{129}IDose) to four male and fourfemale euthyroid adults with adequate iodine intake. Starting at baseline, we collected complete urines over 8 days, complete faeces over 4 days, and spot plasma over 5 days. We measured ^{129}I in alkaline- extracted urines (^{129}IU) previously spiked with a known amount of ^{129}I by multicollector inductively coupled plasma mass spectrometry (ICP-MS) using isotope dilution analysis (IDA). We measured ^{129}I in plasma (^{129}IP) and faeces (^{129}IF) previously spiked with a known amount of ^{127}I by accelerator mass spectrometry (AMS) using IDA. We then calculated ^{129}IFA as ^{129}IDose minus ^{129}IF, ^{129}ITU as ^{129}IFA minus ^{129}IU. We constructed ^{129}IP kinetic curves to evaluate the thyroid uptake patterns and number of body compartments.

Results:
^{129}IU was first detected ~1 hour after tracer administration. A median (IQR) cumulative ^{129}IU of 8.3 (7.1-8.6) µg was excreted, corresponding to 64.3±7.4% of the ^{129}IDose. Cumulative ^{129}IF was 0.4 (0.3- 0.7) µg, corresponding to 4.7±3.2% of the ^{129}IDose. Therefore, ^{129}IFA was 11.9 (11.7-12.1) µg, meaning that 95.3±3.2% of ^{129}IDose was absorbed at the gastro-intestinal level. ^{129}ITU was 3.9 (3.5-4.2)µg, meaning that 31.0±5.2% of ^{129}IDose reached the thyroid as the sole site of utilization. However, the log ^{129}IP kinetic curves typically described a 3-compartment model, thus, other than plasma and thyroid,a third compartment may be involved in iodine metabolism.

Conclusions:
This novel and safe ^{129}I tracer-based method successfully quantified ^{129}I urinary and faecal excretion, allowing the quantification of iodine fractional absorption and an estimation of thyroidal uptake. The pharmacokinetic preliminary analysis showed that iodine metabolism is best described by a multiple- compartment model, suggesting that additional compartments, other than plasma, urine and thyroid, may be involved in iodine metabolism. Due to a high variability, patterns of iodine thyroid uptake couldnot be drawn as conclusive. Further analysis of the collected pharmacokinetic parameters is needed in order to refine estimations of iodine thyroid uptake, that are key for defining iodine requirements.