

ORIGINAL ARTICLE

Correlation of iodine concentration in urine with muscle mass and reaction speed in young adults

Stjepan Ištvanić^{1,2}, Ivan Dusper¹, Tomislav Ištvanić^{2,3}, Vedran Farkaš^{2,3}, Ines Banjari⁴, Tatjana Bačun^{5,6,7}

¹School of Medicine, Josip Juraj Strossmayer University of Osijek, ²Division of Vascular Surgery, Department of Surgery, University Hospital Centre Osijek, ³Department of Surgery, Urology, Orthopaedics and Physical and Rehabilitation Medicine, School of Medicine Osijek, Josip Juraj Strossmayer University of Osijek, ⁴Faculty of Food Technology, Department of Food and Nutrition Research, Josip Juraj Strossmayer University of Osijek, ⁵Division of Endocrinology, Department of Internal Medicine, University Hospital Centre Osijek, ⁶Department of Internal Medicine and History of Medicine, School of Medicine Osijek, Josip Juraj Strossmayer, University of Osijek, ⁷Department of Clinical Medicine, Faculty of Dental Medicine and Health Osijek, Josip Juraj Strossmayer University of Osijek, Croatia

ABSTRACT

Aim To examine dietary iodine intake and urinary iodine concentration in young adults, as well as the relationship between iodine concentration in urine and muscle mass and speed of muscle reaction.

Methods Seventy euthyroid participants aged between 18 and 24 participated, 35 (50%) males and 35 (50%) females. The participants were young adults who live, study and work in the region of Osijek, Osijek-Baranja County, Croatia. Exclusion criteria were the diagnosed thyroid disease and iodine metabolism disorder. Spot urine samples were analysed, dietary iodine intake was assessed, muscle mass and reaction speed were measured.

Results The median concentration of iodine in urine was $120.77 \mu g/L$, and the estimated iodine intake was $624.66 \mu g$. The median muscle mass was 32.55%, and the median speed of muscle reaction 274.5 ms. A significant, negative and weak correlation between iodine concentration in urine and speed of muscle reaction was observed (Rho = -0.289). Other associations of urine iodine concentration and muscle mass percentage, muscle tissue and reaction speed were not significant.

Conclusion The estimated dietary iodine intake was higher than the reference values of the World Health Organization. The urinary iodine concentration was within the reference values. Urinary iodine concentration was not related to the muscle mass. Urinary iodine concentration in urine was significantly, negatively and weakly related to reaction speed.

Keywords: diet surveys, population health, thyroid hormones

INTRODUCTION

A previously unknown chemical element was discovered in 1811 during algae processing and was later named iodine (1). Iodine is important for thyroid function, especially for its synthetic function (2). Iodine deficiency has been fought by adding iodine to salt, Switzerland and the USA being the first countries to do so (3) termed iodine deficiency disorders, due to inadequate thyroid hormone production. Globally, it is estimated that 2 billion individuals have an insufficient iodine intake, and South Asia and sub-Saharan Africa are particularly affected. However, about 50% of Europe remains mildly iodine deficient, and iodine intakes in other industrialized countries, including the United States and Australia, have fallen in recent years. Iodine deficiency during pregnancy and infancy may impair growth and neurodevelopment of the offspring and increase infant mortality. Deficiency during childhood reduces somatic growth and cognitive and motor function. Assessment methods include urinary iodine concentration, goiter, newborn

TSH, and blood thyroglobulin. But assessment of iodine status in pregnancy is difficult, and it remains unclear whether iodine intakes are sufficient in this group, leading to calls for iodine supplementation during pregnancy in several industrialized countries. In most countries, the best strategy to control iodine deficiency in populations is carefully monitored universal salt iodization, one of the most cost-effective ways to contribute to economic and social development. Achieving optimal iodine intakes from iodized salt (in the range of 150-250 µg/d for adults. Approximately a fifth of absorbed iodine is taken in the thyroid gland. About 90% of iodine is excreted through the kidneys. Therefore, the best method to quantify the iodine status of an individual is a 24-hour urine sample. Since this method is not practical, the most used method for scientific research is a spot urine sample (4-6).

The thyroid gland excretes hormones thyroxine (T4), triiodothyronine (T3) (2). T3 and T4 influence the metabolism in many tissues of the body (2,7). After entering the cells of the tissues, the hormones encourage gene transcription in the cell nucleus (2). They increase the metabolic activity of the cell, the activity and number of mitochondria, they increase thermogenesis and oxygen expenditure, they also control lipid and glucose metabolism (2, 8). They encourage the growth and

Division of Endocrinology, Department of Internal Medicine, University Hospital Centre Osijek; Josip Hutler Street 4, HR-31000 Osijek, Croatia Phone: +385 31 511 735; fax: +385 31 512 222; E-mail: tbacun@mefos.hr;

^{*}Corresponding author: Tatjana Bačun

development of the brain, musculoskeletal system and heart function. They increase blood pressure, accelerate peristalsis and respiration, encourage muscle contractions and endocrine functions of other glands. They also have a stimulative effect on the central nervous system (2, 8).

Skeletal muscles make up around 40% of body mass (9). Muscle tissue is specific for its plasticity, which is conditioned by extrinsic and intrinsic factors (10). Thyroid hormones play a key role in normal muscle contractility, metabolic function, regeneration and myogenesis (9, 10). The important factors for myogenesis are muscle load, contraction, tissue regeneration and hormones (testosterone, β -adrenergic agonists and thyroid hormones) (9, 11). Body composition is expressed as total body water (intracellular and extracellular water), fat mass and fat-free mass. Considered as fat free mass are bones, ligaments, tendons and organs (12, 13). Body composition can be assessed with bioelectrical impedance analysis measuring the opposition to the flow of electrical energy through the body, approximating the relationship between total body water, fat mass and fat-free mass (12).

Males and females have different relationships between muscle mass and fat (14). A reaction receives stimulus, it is processing, deciding on an answer and the answer to the stimulus (15). Time elapsed between receiving stimulus to the answer is called reaction speed. Iodine is connected to reaction speed with the stimulative effects of thyroid hormones on the central nervous system and muscle contraction (2, 8). People with hypothyroidism have slow cognitive and muscle function. The reaction speed of such persons accelerates after T4 introduction to their therapy (15, 16).

Inadequate iodine intake is a still a big public health issue in the 21st century, especially for women of reproductive age and pregnant women (4). Daily recommended intake of iodine for grownups is 150 μ g (17, 18). Historically, iodine deficiency and endemic congenital iodine deficiency syndrome have been a problem in Croatia. Measures against them were introduced in 1953 when the first law mandating iodination of kitchen salt was introduced and is now considered solved (19).

In Croatia iodine status studies have been conducted on general population, children and pregnant women, however, studies looking at possible connections of iodine, muscle mass and reaction speed have not been done.

Knowing the importance of iodine, we wanted to research young adults around Osijek, Croatia (Slavonija and Baranja region) to have a better understanding of our iodine status, our dietary habits and analyse possible connections between the iodine status of individuals and their muscle mass and reaction speed.

PARTICIPANTS AND METHODS

Participants and study design

The study was conducted as a cross-sectional study in Osijek (Croatia) in spring of 2024. All measurements and sampling were done once. The participants were euthyroid people between 18 and 24 years of age. A total of 70 participants, 35 males and 35 females, were included in the study. The participants were invited to participate in the study via e-mail and oral invitations. Before signing appropriate consent forms, it was confirmed that the participants fulfilled the inclusion criteria. Inclusion criteria were: euthyroid young adults between 18 and 24 years of age who agreed to participate in the study,

confirming their intentions by signing an informed consent form. The participants were young adults who lived, studied and worked in the region of Osijek, Osijek-Baranja County, Croatia. Exclusion criteria were: thyroid disease and iodine metabolism disorder.

The study analysed the following data: estimated daily iodine intake, the correlation between concentration of iodine in urine and muscle mass, and the correlation between concentration of iodine in urine and reaction speed.

The study was approved by the Ethics Committee of the Osijek School of Medicine.

Methods

Daily iodine intake was approximated using a semiquantitative questionnaire about the frequency of food intake. The questionnaire included 49 food items, including salt, meat, sea fish, seafood and food items that interfere with thyroid hormone production (white bread, semi-white bread, cornbread, integral bread, other types of bread, baked goods, peanuts, soy flakes, tofu, cooked potatoes, baked potatoes, cooked sweet potatoes, spinach, mangold, radish, cabbage, cale, brussels sprouts, beans, lentils, chickpeas, peas, legumes, green zucchinis). The food quantity was defined using standardized quantitative food item models and Croatian meals during the questionnaire development at the Faculty of Food Technology of Osijek or standards available on FoodData Central (20, 21). The quantity of iodine in food items was taken from Frida, a publicly available food composition dataset (22). Iodine concentration in urine was analysed from a spot urine sample at the Faculty of Food Technology of Osijek using the spectrophotometric method based on the Sandell-Kolthoff reaction between iodine and ammonium cerium (IV) sulphate on VIS Spectrophotometer (ONDA Touch V-11 Scan, Giorgio Bormac, Capri, Italy) (23). Muscle mass was measured by Omron BF500 (Tokyo, Japan scale) using bioelectrical impedance. Reaction speed was measured using the online test "Human benchmark test" (24). The test is validated for rough estimation of reaction speed. The reaction speed was measured five times and the result was represented as the average of the five measurements (25).

Statistical analysis

Categorical data were presented as absolute and relative frequencies. Normality of the distribution of numerical variables was tested by the Shapiro-Walk test. Continuous variables that follow a normal distribution were presented by the arithmetic mean and standard deviation (SD), and in other cases by the median and the limits of the interquartile range. The assessment of the association was given by the Spearman correlation coefficient (Rho). The significance level was set at alpha $\alpha\!\!=\!\!0.05.$

RESULTS

This study was done on 70 participants, 35 (50 %) males and 35 (50 %) females. The mean (M) age was 22 (SD \pm 2) years, with the age range 19-24 years.

The median (Mdn) concentration of iodine in urine was 120.77 μ g/L (range 30.71 μ g/L - 762.67 μ g/L. The estimated dietary iodine intake was Mdn=624.66 μ g (range 94.07 μ g - 2672.28 μ g). The median muscle mass of 32.55 % (range 24.70 % -

45.70 %), and the median reaction speed of 274.5 ms, (range 205 ms - 457 ms) was found (Table 1).

Table 1. Results of variable values measured in 70 participants

Variable	Median (interquartile range)
Urine iodine concentration (μg/L)	120.77 (92.3-160.49)
Estimated iodine intake (µg)	624.66 (419.49-842.72)
Muscle tissue (%)	32.55 (28.9-37.3)
Muscle reaction speed (ms)	274.50 (259.75-297.25)

Spearman's rank correlation coefficient was used to assess the correlation between the concentration of iodine in urine with muscle mass and reaction speed. A significant, negative and weak correlation between the concentration of iodine in urine and reaction speed was observed (Rho = - 0.289). Other tested correlations of urine iodine concentration and muscle mass percentage, muscle tissue and reaction speed were not significant (Table 2).

Table 2. Statistical analysis of the correlation between the studied variables

	Spearman's correlation coefficient Rho (p)		
Variable	Urine iodine concentration	Muscle tissue	Muscle reaction speed
Urine iodine concentration	-		
Muscle tissue	-0.053 (0.67)	-	
Muscle reaction speed	-0.289 (0.02)	0.066 (0.59)	-

DISCUSSION

The WHO recommends an intake of 150 μg of iodine daily for adults (23). In this study, we found that the median of estimated dietary iodine intake was 624.66 μg using a standardized semiquantitative questionnaire. A Norwegian study estimated the dietary intake of iodine of healthy Norwegian adults aged between 40 – 69 years at 281 μg (26). Other research showed an increased estimated dietary iodine intake as higher than recommended by the WHO as well (23, 26, 27). Since the median estimated dietary intake of iodine was well over the recommended quantities, the population included in this study was not at risk of deficient iodine intake.

Collecting data on iodine in urine is important to follow the success of the salt iodination program (4). The method used in this study is simple and easily applied to population studies (3-6). The median iodine concentration of urine between 100-199 μg/L is considered a sign of appropriate dietary iodine intake (4); we found the median iodine concentration of urine of 120.77 µg/L. In Korean population iodine concentrations in urine at 292 µg/L were found, which is higher than the WHO's recommendation (28); in Belgian population it was equal to 93.6 μg/L, which represents a slight deficiency (29). There are some studies on the Croatian population showing the level in adults in Croatia at 178 µg/L (30), in children at 248 µg/L, which is higher than the recommended values, and in pregnant women lower than recommended (159 µg/L) (31). This study showed that the studied population was within the recommended range for iodine saturation, according to the WHO guidelines (23).

Normal function of muscles relates to iodine through thyroid hormones (9, 10). T3 has an important role in muscle tissue plasticity. In patients with hypothyroidism delayed contraction and relaxation of the muscles was noticed (10). In this study muscle mass percentage was 32.55 %. A statistical correlation with iodine in urine with muscle mass percentage was not found. The correlation most likely does not exist because many other factors, such as exercise and other hormones (Insulin-like growth factor 1, androgens and $\beta 2$ agonists), influence muscle mass (11,32).

A short reaction speed is important in some professions and is considered a good sign of health (25). People with hypothyroidism have a significantly longer reaction speed in comparison to euthyroid people however, this prolongation can be remedied with hormone replacement therapy (15, 33). Relevant literature describes a decrease of reaction speed in persons with hypothyroidism because of the lack of stimulative effect of the hormones on the central nervous system (15, 33). In this study, the "Human benchmark test" was used to measure reaction speed, as it is validated for rough estimation of reaction speed (24,25). Median reaction speed was 274.5 ms. A significant, negative and weak correlation between iodine concentration in urine and reaction speed was noticed. The more iodine in urine, the faster muscle reaction. The results of this study are in accordance with the results from the relevant literature and the results on the online test "Human benchmark test" (24,25). Our study was one of the few studies that researched the iodine status of individuals in the region, since the question of hypothyroidism in our region is considered solved. However, researching the nutritional intake of salt, closely connected to intake of iodine, gives us important data, since the modern diet contains more salt, hidden in the so-called ultra-processed food. To explain the faster reaction speed in persons with higher iodine concentration in urine, a study with a larger sample size and more parameters is needed.

In conclusion, our study has opened the door to the possibility of further iodine status and reaction speed research. The study itself, showing the iodine status of young adults, is an invaluable epidemiological resource for the region of Slavonija and Baranja in Croatia.

AUTHOR CONTRIBUTION STATEMENT:

[Conceptualization], [T.B.], [I.B.]; [Methodology], [T.B], [I.B.]; [Investigation], [S.I.], [I.D.]; [Resources], [T.B.], [I.B.]; [Writing (Original Draft)], [S.I.]; [Writing (Review & Editing)], [T.B.], [I.B.], [T.I.]; [Supervision], [V. F.]

ACKNOWLEDGEMENTS:

This paper is a version of the Master's Thesis by Stjepan Ištvanić, mentored by prof. Tatjana Bačun, MD, MA, PhD, presented publicly on 25 June 2024 at School of Medicine, Osijek, Croatia.

FUNDING

No specific funding was received for this study.

TRANSPARENCY DECLARATION

Conflict of interest: None to declare.

REFERENCES

- 1. De Laeter JR, Böhlke JK, De Bièvre P, Hidaka H, Peiser HS, Rosman KJR, et al. Atomic weights of the elements: Review 2000 (IUPAC Technical Report). Pure and Applied Chemistry 2003; 75(6):683–800.
- 2. Sinha RA, Yen PM, Metabolic Messengers: Thyroid Hormones. Nat Metab 2024; 6(4):639-50.
- 3. Zimmerman MB. Iodine deficiency. Endocr Rev 2009; 30(4):376–408.
- 4. Hatch-McChensey A, Liberman HR. Iodine and Iodine Deficiency: A Comprehensive Review of a Re-Emerging Issue. Nutrients 2022; 14(17):3474.
- Vejvjerg P, Knudsen N, Perrild H, Laurberg P, Andersen S, Rasmussen LB, et al. Estimation of Iodine Intake from Various Urinary Iodine Measurements in Population Studies. Thyroid 2009; 19(11):1281–6.
- 6. Eriksson J, Barregard L, Sallsten G, Berlinger B, Weinbruch S, Manousou S, et al. Urinary iodine excretion and optimal time point for sampling when estimating 24-h urinary iodine. Br J Nutr 2023; 130(8):1289–97.
- 7. Brent GA. Mechanisms of thyroid hormone action. J Clin Invest 2012; 122(9):3035–43.
- 8. Zupo R, Castellana F, Sardone R, Lampignano L, Paradiso S, Giagulli VA, et al. Higher Muscle Mass Implies Increased Free-Thyroxine to Free-Triiodothyronine Ratio in Subjects With Overweight and Obesity. Front Endocrinol 2020; 11:565065.
- 9. Bloise FF, Cordeiro A, Ortiga-Carvalho TM. Role of thyroid hormone in skeletal muscle physiology. J Endocrinol 2018; 236(1):R57–68.
- Salvatore D, Simonides WS, Dentice M, Zavacki AM, Larsen PR. Thyroid hormones and skeletal muscle–new insights and potential implications. Nat Rev Endocrinol 2014; 10(4):206–14.
- 11. Schiaffino S, Dyar KA, Ciciliot S, Blaauw B, Sandri M. Mechanisms regulating skeletal muscle growth and atrophy. FEBS J 2013; 280(17):4294–314.
- 12. Holmes CJ, Racette SB. The Utility of Body Composition Assessment in Nutrition and Clinical Practice: An Overview of Current Methodology. Nutrients 2021; 13(8):2493.
- 13. De Ritter R, Sep SJS, Van Greevenbroek MMJ, Kusters YHAM, Vos RC, Bots ML, et al. Sex differences in body composition in people with prediabetes and type 2 diabetes as compared with people with normal glucose metabolism: the Maastricht Study. Diabetologia 2023; 66(5):861–72.
- 14. Janssen I, Heymsfield SB, Baumgartner RN, Ross R. Estimation of skeletal muscle mass by bioelectrical impedance analysis. J Appl Physiol 2000; 89(2):465–71.
- 15. Kale JS, Katole NT, Rode SB, Gade SA. Effect on Reaction Time in Primary Hypothyroid Patients Before and After Thyroxin Treatment. Cureus 2022; 14(6):e26074.
- 16. Rakugi H. Cognitive Dysfunction in Hypothyroidism. Sci Insights 2023; 42(2):813–8.
- 17. Niwattisaiwong S, Burman KD, Li-Ng M. Iodine deficiency: Clinical implications. Cleve Clin J Med 2017; 84(3):236–44.

- 18. Lisco G, De Tullio A, Triggiani D, Zupo R, Giagulli VA, De Pergola G, et al. Iodine Deficiency and Iodine Prophylaxis: An Overview and Update. Nutrients 2023; 15(4):1004.
- 19. Jukić T, Dabelić N, Rogan SA, Nõthing-Hus D, Lukinac L, Ljubičić M, et al. The Story of The Croatian Village of Rude after Fifty Years of Compulsory Salt Iodination in Croatia. Coll Antropol 2008; 32(4):1251–54.
- 20. Senta A, Pucarin-Cvertković J, Doko Jelinić J. Kvantitativni modeli namirnica i obroka (Quantitative models of foodstufs and meals) [In Croatian]. Zagreb: Medicinska naklada, 2004.
- 21. U.S. Department of Agriculture. FoodData Central. https://fdc.nal.usda.gov/ (accessed May 29, 2024).
- 22. National Food Institute, Technical University Denmark. Frida. https://frida.fooddata.dk/?lang=en (accessed May 28, 2024).
- World Health Organization. Assessment of iodine deficiency disorders and monitoring their elimination: a guide for programme managers. Geneva: World Health Organization, 2007.
- 24. Human Benchmark. Reaction Time Test. https://human-benchmark.com/tests/reactiontime (ccessed May 25, 2024).
- 25. Abbasi–Kesbi R, Memarzadeh–Tehran H, Deen MJ. Technique to estimate human reaction time based on visual perception. Health Technol Lett 2017; 4(2):73–7.
- 26. Madar AA, Heen E, Hopstock LA, Carlsen MH, Meyer HE. Iodine Intake in Norwegian Women and Men: The Population-Based Tromsø Study 2015–2016. Nutrients 2020; 12(11):3246.
- 27. Gostas DE, Larson-Meyer DE, Yoder HA, Huffman AE, Johnson EC. Dietary Relationship with 24 h Urinary Iodine Concentrations of Young Adults in the Mountain West Region of the United States. Nutrients 2020; 12(1):121.
- 28. Ahn J, Lee JH, Lee J, Baek JY, Song E, Oh HS, et al. Association between urinary sodium levels and iodine status in Korea. Korean J Intern Med 2020; 35(2):392–9.
- 29. Vandevijvere S, Ruttens A, Wilmet A, Marien C, Hautekiet P, Van Loco J, et al. Urinary sodium and iodine concentrations among Belgian adults: results from the first national Health Examination Survey. Eur J Clin Nutr 2021; 75(4):689–96.
- 30. Itterman T, Albrecht D, Arohonka P, Bilek R, de Castro JJ, Dahl L, et al. Standardized Map of Iodine Status in Europe. Thyroid 2020; 30(9):1346–54.
- 31. Kusić Z, Jukić T, Rogan SA, Jureša V, Staničić J, Borić M, et al. Current Status of Iodine Intake in Croatia The Results of 2009 Survey. Coll Antropol 2012; 36(1):123–8.
- 32. Lim C, Nunes EA, Currier BS, McLeod JC, Thomas ACQ, Phillips SM. An Evidence-Based Narrative Review of Mechanisms of Resistance Exercise—Induced Human Skeletal Muscle Hypertrophy. Med Sci Sports Exerc 2022; 54(9):1546–59.
- 33. Vedavathi K, Shekharappa KR. Reaction Time Study as a Tool to Identify Central Nervous System Affect due to Hypothyroidism. Int J Health Sci 2013; 3(5):29–32.