Iodine (I)

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Iodine (I) is an essential element required for synthesis of the thyroid hormones triiodothyroine (T3) and thyroxine (T4) which participate in regulating multiple metabolic processes. The main symptoms of severe I deficiency (ID), termed I deficiency disorders (IDDs), include endemic goiter, hypothyroidism, cretinism, decreased fertility rate, increased infant mortality, and mental retardation.

Keywords: Iodine (I) ; hormones triiodothyroine (T3) ; thyroxine (T4)

1. Introduction

ID is described as the single greatest global cause of preventable mental impairments [1]. More recent studies have found that even mild ID is associated with lower educational levels of children and cognitive impairment. Thyroid hormones are essential for brain development and this is especially true in early pregnancy prior to the onset of fetal thyroid function [2][3]. Iodine deficiency (ID) is recognized by the World Health Organization (WHO) as the most common cause of damage brain [4].

Pregnant and lactating women need adequate intake of I for maternal T4 production which is of special importance for fetal development in the first trimester and for brain development during the first years of life [1]. Increased renal clearance during pregnancy increases I requirements for pregnant women [5]. According to the World Health Organization (WHO), the recommended nutritional I intakes are 150 µg for adolescents (above 12 years) and adults; 250 µg for pregnant and lactating women, respectively [6][7]. About 90% of I absorbed dose eventually appears in the urine. Therefore, the urinary I content is considered as a good marker for the recent dietary intake of I. Although its excretion varies considerably both between and within days, these variations tend to even out on a population level [8]. The WHO epidemiological criteria for assessing I status based on median urinary I concentrations (UIC) (µg/L of I) for school-age children (>6 years) is as follows; <20 (severe ID); 20–49 (moderate ID); 50–99 (mild ID) and 100–199 (adequate intake). For pregnant women, the criteria are <150 (insufficient) and 150–249 (adequate intake).

ID is a major health challenge worldwide. Although in 1990 the World Health Assembly and the World Summit for Children established a global goal to eliminate severe IDD by 2000 it is obvious that the goal was not reached but some progress in improving global I status has been achieved [9]. In the former Soviet Union severe IDD was reported eliminated by the 1960s and Government programs directed at IDD prevention were discontinued in the 1970s [10]. After the break-up of the USSR in 1991 IDD re-emerged in nearly all former Soviet republics including the Russian Federation where the population is facing insufficient I intake [11]. Russia is the largest country in the world by area and has a multiethnic population. Thus, national data may mask regional variations in both I intake and prevalence of IDD.

Cold environments require an additional amount of thyroid hormones [12], enhancing triiodothyronine (T3) production from thyroxine (T4) to activate the heat production at the local level in brown adipose tissue which is essential in the cold adaptation of Arctic residents [13]. Hypothyroidism increases human susceptibility to cold-induced health effects [14]. Due to extreme climatic conditions in a large part of Russia studies on the prevalence of IDD and adequate I supplementation are important public health issues in Russia. However, the evidence on the prevalence of ID in Russia published in the international peer-reviewed literature is scarce. At the same time, research data published in local biomedical journals is of limited availability to the international audience and may suffer from methodological limitations [15].

2. Iodine Status of Women and Infants in Russia: A Systematic Review

In all studies, with the exception of the Kamchatka territory, the recommended median UIC level for lactating women was not achieved. Children also fail to achieve the optimal level of median UIC, with the exception of the Kamchatka territory and the Khabarovsk territory (Vanino village)

Two of the 19 reviewed papers included data of lactating women taking IS. The range of median UIC values in nursing women who took IS was 41–118 μg/L [16]. However, the median UIC values were below the WHO recommended level for lactating women.

Iodine intake is an important determinant of I status, which is difficult to assess. Therefore, median UIC is one of the most appropriate and commonly used indicators of I status. Reference intervals of the I concentrations recommended by WHO [17] help researchers to characterize the I status of the population in a proper way using median UIC as a marker of I status. The limitation of spot urine sampling as the matrix for I status determination is the inability to evaluate the individual I status due to a significant within-day and day-to-day variability of the individual's I intake [18]. Because of that, all the studies reviewed in the present manuscript used median UIC as an indicator of the population's I status.

It should be noted that most of the reviewed articles do not provide a sufficient description of the analytical method used in the measurement of I in the urine. Most of the measurements were performed by the cerium-arsenate reaction or the colorimetric Sandell–Kolthoff-methods which were introduced decades ago [19]. These methods with some modifications are still used and even recommended by WHO for epidemiological studies where I status is to be assessed [17]. However, more accurate methods based on inductively coupled plasma mass spectrometry (ICP-MS) have been introduced a few decades ago and are today a gold standard for UIC measurements [20]. The Sandell–Kolthoff-method with some modification is still quite often used when the relatively cheap method is needed. A recent study has shown [18] that a microplates Sandell–Kolthoff-method obtained similar results as ICP-MS confirming that the Sandell–Kolthoff-method is a reliable alternative method for UIC measurements.

Quality assurance information in the reviewed articles, however, is unfortunately not available for documentation of detection limits, accuracy, and repeatability. Thus, there is no complete confidence that the reviewed data of the UICs of the Russian population are accurate.

The median UICs measured in pregnant women across Russia clearly indicate that almost all groups studied had not sufficient I intake. An exception is the group of pregnant women from the Pacific coastal area (Petropavlovsk-Kamchatski) presumably due to high consumption of lean white sea fish and other sea products (the yearly fish consumption per capita in the Pacific region is of 31.5 kg in contrast to the national average of 21.7 kg) [21].

In countries neighboring Russia (Norway, Denmark, Mongolia, China, Belarus, Ukraine) iodized salt is a source of I [22][23][24][25][26][27][28]. In Norway and Denmark, products such as milk, dairy products, fish, and fish products make up almost 80% of the dietary I intake [22][23]. In Ukraine, along with iodized salt, one of the most accessible sources of I is algae [25]. In Belarus, the mandatory use of high-quality iodized salt in the food industry has led to the elimination of I deficiency among the population [27].

The experiences of neighboring countries and the USSR show that salt iodization is an effective strategy to prevent ID [29]. In the United States, the median UIC for women of reproductive age is also below the WHO recommended level [30]. China generally had adequate I intake with significantly higher average UIC among pregnant women in Shandong (244 μg/L) than in Tianjin (159 μg/L). No difference was found in median UIC during pregnancy in Shandong. The I status of pregnant women in Tianjin and Shandong was sufficient, but various changes in median UIC and thyroid function during pregnancy were reported. The authors of the study call for attention to I nutrition of pregnant women, even in areas with sufficient I content [31].

In Norway, a study of pregnant women and newborns showed that low I intake (lower than ~150 μg/day) was associated with fetal growth retardation in three exposure indicators: I from food, median UIC, and use of I supplements. In addition, low dietary I intake (lower than ~100 μg/day) and lack of I supplementation have been associated with an increased risk of preeclampsia. The use of I supplements can satisfy the increased need for I during pregnancy. The risk of hypothyroidism is reduced in women with severe I deficiency, while studies in women with mild to moderate deficiency are not consistent [32]. This inconsistency in findings is related to a range of measurement, design, and location factors [2][4]. However, an increasing amount of evidence suggests that even mild ID is associated with mild cognitive difficulties particularly in expressive language and working memory tasks [2][3][4][33]. Starting I supplementation in the first trimester can lead to temporary "thyroid stunning", which can adversely affect the developing fetus. Therefore, it is necessary to pay special attention to the intake of I by women before pregnancy, as well as during pregnancy [32].

The three studies raise concerns regarding excessive and uncontrolled excess intake of I, which can lead to deleterious health effects for women and children.

When interpreting the quantitative data on I status assessment in epidemiological studies of the prevalence, distribution, and severity of ID it is important to pay special attention to a number of environmental confounders and effect modifiers such as cold climate, vitamin D deficiency, and some chemical food contaminants that may influence the I-related health effects.

For example, vitamin D deficiency might be a contributing risk factor to non-autoimmune hypothyroidism which is also associated with ID [34]. This is specifically important for the Russian population residing in northern areas due to lack of solar UV-radiation and low consumption of seafood which is one of the main nutritional sources of I and vitamin D. Thus, vitamin D deficiency in Arctic areas may enhance the impact of ID on the vulnerable groups of the population such as pregnant women, infants, and children.

Other lifestyle challenges in Russia today are nutritional habits resulting in increased obesity [35], food may also be an important source of environmental contaminants such as persistent organic pollutants (POPs), lead, and mercury. These environmental contaminants have similar adverse effects as ID on the neurocognitive development of children among other impacts, such as the perturbation of thyroid hormones [36]. Thus, any risk assessment of exposure to these environmental neuro-toxicants should take into consideration the potential confounding of the I status.

Iron (Fe) and zinc deficiencies continue to be global health problems and especially iron deficiency anemia (IDA) during pregnancy and infancy. IDA is a strong factor for cognitive, motor, and socioemotional impaired development of children [37]. Recent studies have shown that among individuals with IDA the thyroid hormone metabolism is impaired most likely because of the reduced activity of the Fe-dependent enzyme—thyroid peroxidase. This argues for improving the Fe-status in areas of overlapping deficiencies, not only to combat IDA but also ID with dual-supplementation with both Fe and I [38][39].

In a recent study, there were found multidirectional associations of serum concentrations of POPs and I-containing thyroid hormones [40]. Researchers found that perfluorooctanesulfonic acid (PFOS) was positively associated with TSH (thyroxine-binding globulin); polychlorinated biphenyls (PCBs), hexachlorobenzene (HCB), and nonachlors were inversely associated with T3, T4; and new emerging compounds viz perfluorodecanoic acid (PFDA) and perfluoroundecanoic acid (PFUnDA) were also inversely associated with T3.

Effects of persistent contaminants were found on vitamin metabolism, immune functioning, and hormones in the arctic wildlife as well [41].

The Russian guidelines recommend a daily I intake of at least 150 µg for women of reproductive age, whereas a daily dose of 250 µg is recommended for residents of endemic ID areas. Despite these recommendations, only 9% of Russian women take dietary vitamin and mineral supplementation [42]. It has been reported that three-quarters of pregnant women are affected by micronutrient deficiency [42]. All women and children need I deficiency prevention. Special attention should be paid to women of reproductive age before they become pregnant, because of the time lag to fully synthesize I into thyroid hormones.

The main reason for the lack of significant progress in Russia to prevent ID is the absence of a national-wide regulatory act on the prevention of IDD and a centralized system for monitoring the implementation of preventive measures [11]. Only in 2020, the use of iodized salt has become mandatory in Russia when catering to children in schools and institutions of secondary education . At present, a draft Federal Law “On Prevention of Iodine Deficiency Disorders” dated 27 March 2019 has been developed, which will be important for establishing a further legal foundation of state policy .

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