RESEARCH ARTICLE

Urinary Iodine Concentrations in Cancer Patients

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Abstract

Background: It has been suggested that incidence of some cancers, especially examples in the breast and stomach may be influenced by the iodine intake. However, only few studies are available at present. Therefore, we have conducted the present assessment of iodine status in Iranian patients diagnosed with a malignancy. **Materials and Methods:** This cross-sectional study was conducted in 85 patients diagnosed with different types of cancer at Shahid Sadoughi Hospital, Yazd, Iran. The method used was based on the Sandell–Kolthoff reaction. **Results:** The median urinary iodine concentration (UIC) was 17.4 μg/L, with ≤20 μg/L indicative of severe iodine deficiency. According to the WHO/IC C IDD/UNIC EF classification, 88.1%, 7.1% and 2.4% of patients had a UIC <20 (severe), 20–49 (mild), and 50–99 μg/L (moderate), respectively. There was no statistically significant differences in UIC between men and women. **Conclusion:** The UIC values indicate that Iranian cancer patients were seriously iodine deficient according to WHO/UNIC EF/ IC C IDD, and that this is a suitable index to assess iodine status in Iranians. Daily consumption of salt fortified with iodine or other approaches to increase intake might be effective strategies for prevention or reduction of malignancies.

Keywords: Iodine- Iodine deficiency- urinary iodine concentration- cancer

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Introduction

Iodine deficiency is associated with increased risk of some cancers which have thyroid hormone receptors, such as breast, thyroid and stomach (Verheesen et al, 2008). However, the overall incidence for a relationship between iodine and cancer is poor. It has known that iodine deficiency is associated with fibrocystic breast disease and breast cancer (James et al, 2008). Treatment of the fibrocystic breasts with iodine causes the fibrocystic turn into normal tissues (Ghent et al. 1993; Kessler 2004; Bezpalov et al., 2005). Actually, Iodine induces apoptosis in breast cancer cells at concentrations which are healthy for the body as a whole. These concentrations can be attained by ingesting 50 mg per day of iodine and/or iodide (Ghent et al, 1993). In addition, treatment of the prostate cancer with iodine is associated with shrink of the size of the prostate. Iodine deficiency in adult may cause to enlargement of the testes, due to the enlargement of the thyroid gland without concomitant production of androgenic hormones and virilization (Zhuang et al, 1998).

Over 90% of dietary iodine eventually appears in the urine. Therefore Urinary iodine concentration is recommended by the WHO for assessing iodine nutrition worldwide. Iodine deficiency is defined by the World Health Organization (WHO) as a population median urinary iodine concentration (UIC) that falls below 100 μg/L, while a median UIC of 50–99 μg/L, 20-49 μg/L, and <20 μg/L indicates mild, moderate, and severe iodine deficiency, respectively (WHO 2007).

In 1989, IDD has been accepted as a priority health problem in Iran. Iran first achieved the WHO/UNICEF/ ICCIDD indicators for sustained IDD control back in 1996. In 1989, the median urinary iodine concentration was less than 100 μg/L, but since 1996 it has consistently been over 100 μg/L. Mild iodine deficiency has re-emerged in Iran due to dramatic changes in food consumption patterns. In 2007, the goiter rate was significantly lower than 1996 in all 30 provinces of Iran (Delshad et al, 2012). Therefore, we have conducted this study to provide iodine status in Iranian cancer patients.

Material and Methods

This study was approved by the appropriate human research committee of Shahid Sadoughi University of Medical Sciences. The study population consisted of 85 patients (43 males and 37 females) diagnosed with different types of cancer including lung, stomach, prostate, breast, thyroid, and skin cancer. All patients were diagnosed with a cancer between 2012 and 2015 in the pathology department were between 4 and 76 years of age and lived in Yazd, Iran.

Casual or spot urine samples were collected from the

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patients, refrigerated, and couriered to the laboratory unit, Shahid Sadoughi training hospital the next day. Urine samples were kept frozen at –20°C until assayed at the end of the study.

Urine samples were treated according to the method of Pino et al, being digested with 750 µL HCLO3 (28% by vol) at 110 C for 50 mm (Pino et al, 1996). Iodine content of urine samples was measured by modified Sandell–Kolthoff digestion method, in which iodine acts as a catalyst for the reduction of cerium (IV) to cerium (III) by arsenic (III). The arsenious acid solution contained 5 g As2O3 and 25 g NaCl, dissolved in 1 L 5 mol H_2SO_4/L. The ceric ammonium sulfate solution contained 24 g Ce(NH4)4(SO4)4. 2H2O in 1 L 3.5 mol H2SO4/L.

The median urinary iodine concentration was defined as a concentration of iodine in a spot urine sample and the results were expressed as micrograms per liter (µg/l). In this study it was considered values <25 µg/L as severe deficiency, 25–50 µg/L moderate deficiency and > 50 µg/L normal (Delshad et al, 2012).

Results

The median UIC of the patients was 17.4 µg/L (Table1), which falls within the range ≤20 µg/L that WHO/UNIC EF/IC C IDD categorizes as severe iodine deficiency [5].The concentration was <20 µg/L in 88.1% (severe), 20–49 µg/L in 7.1% (moderate) of the patients and 50-99 µg/L in the remaining 2.4% (mild).

UIC did not differ by sex and age. There was no difference between females and males in terms of UIC. The UIC of females and males were 17.1±1.2 and 16.9± 1.4 µg/L, respectively.When patients who were older than 45 yr old and the ones who were younger than 45 yr old were compared, there was no statistically significant difference in the UIC. The UIC of patients older and younger than 45 yr old were 16.8 ±1.49 and 16.3± 2.1 µg/L, respectively.

Discussion

Most of the investigations of iodine status in humans and animals have been focused on the role of iodine in thyroid function. In recent decades, researchers have been investigating molecular iodine, induced apoptosis by iodine, sodium iodide symporter (NIS), and various other mechanisms that may be involved in cancer development and or treatment (Zhang et al., 2003; Chung et al., 2010; Aceves et al 2013).

It is suggested iodine is an anticancer nutrient that promotes apoptosis when taken in doses far exceeding the RDA, and that chronic deficiencies and the body's inability to properly utilize iodine set the stage for cancers of hormone-sensitive tissues and glands, such as the breasts, ovaries, uterus and prostate (Brownstein 2008). Stadel et al. has postulated that given the geographical distribution of iodine deficiency, there is low incidence of cancers of the prostate, endometrium, ovary and breast in populations consuming diets with high iodine content (Stadel 1976).

Iodine deficiency is associated with a higher rate breast cancer. Similarly, higher dietary Iodine intake is associated with less goiter and breast cancer. In other hand, the incidence of breast cancer has been increased dramatically in recent years in Iran (Forat-Yazdi et al., 2015; Neamatzadeh et al., 2015). It is reported in countries such as Japan and island that has the highest dietary intake of iodine lowest rates for goiter and breast cancers have reported (Zava et al., 2011; Zimmermann et al., 2015). In Japan, where the incidence of breast cancer and infant mortality is very low, people consume about 13.8 milligrams of iodine per day (Konno et al, 1993). It is proven that iodine deficiency can lead to fibrocystic breast disease and/or ovarian cysts. Iodine can similarly reduce uterine fibroids and one of the first conventional medical treatments for severe fibroids was to paint the uterus with iodine (Lungo et al., 2000; Venturi 2001; Jang et al., 2013).

Table 1. Iodine Status in Iranian Patients Diagnosed with Cancer

Iodine status	Reference	Frequency (%)
Normal	≥100	2 (2.4)
IDD		
Mild	50-99	2 (2.4)
Moderate	20-49	6 (7.1)
Severe	≤20	74 (88.1)

Lower urinary iodine concentration in patients with stomach cancer was reported recently (Behrouzian et al, 2004; Gulaboglu et al, 2005). This cancer is the most common cancer in parts of northeastern Turkey where iodine deficiency is common, and iodine levels in gastric cancer tissue were markedly lower than those in surrounding healthy tissue (Gulaboglu et al, 2005). In Iran stomach cancer patients in a non-coastal area were 2.5 times as likely to have severe iodine deficiency as control patients (Behrouzian et al, 2004). Observed association between improved iodine supply and decrease of incidence of stomach cancer could indicate the protective role against stomach cancer of iodine prophylaxis in iodine deficient areas. Stomach lining cells in particular concentrate iodine, capitalizing on its antioxidant effects (Gołkowski et al, 2007).In the stomach, iodine protects against abnormal growth of bacteria, in which Helicobacter pylori is the most clinically significant. Iodine in the stomach can also deactivate all biological and most chemical poisons (Stadel 1976). Failure to trigger the apoptosis in gastric cancer cells resulting from decreased iodine might be harmful (Gulaboglu et al, 2005).Guloglu et al., (2005) have suggested that urinary and blood iodine concentration might be a useful marker for following Gastric Cancer.

Zhang et al have shown that increased intracellular levels of iodine is associated with enhance tumor apoptosis in most of the modified non-small cell lung cancer. They assessed a nonradioactive approach in the non-small cell lung cancer with retroviral vectors containing NIS and thyroperoxidase (TPO) genes. They for first time demonstrated that a therapeutic dose of nonradioactive iodide has potent efficacy and high selectivity against lung cancer (Zhuang et al, 1998).

An increased risk of thyroid cancer has been reported in humans with goiter and those living in some iodine-deficient areas of the world (Ohshima et al, 1984).

Studies suggest that a major role of iodine is to prevent the formation of thyroid tumors in humans (Ward et al., 1986). Iodine deficiency is also associated with increased risk for thyroid carcinoma in animal models. Mutaku JF and et al have shown anti-proliferative effects of excess iodine on thyroid cells (Mutaku et al, 2002).

To the best of our knowledge this was the first study evaluated the iodine status in Iranian patients diagnosed with a malignancy. However, results of the present study showed severe iodine deficiency in the patients. Therefore, check the status of iodine in normal populations and cancer patients may be crucial. In addition, we suggest that daily consumption of salt fortified with iodine or other approaches might be an effective strategy for prevention or reduction of malignancies.

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