Journal of Medical Sciences

ISSN 1682-4474

science alert

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Research Paper

J. Med. Sci., 3 (5-6): 423-428
September-December, 2003

Continuous Use of Iodized Salt May Cause Thyrotoxicoses in Plain Areas of North West Frontier Province (NWFP) of Pakistan

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The effect of iodized and uniodized salt on the concentration of thyroid hormones (T_3 and T_4) and thyroid stimulating hormone (TSH) was studied in 411 individuals, who were the residents of Peshawar and its vicinity and were referred by physicians to the radio immunoassay (RIA) laboratory of the Institute of Radiotherapy and Nuclear Medicine (IRNUM), Peshawar during 1998 for thyroid hormones tests. Out of these 411 individuals, 148 were using iodized salt and 263 were using uniodized salt. The iodized and uniodized salt users were called experimental and control groups, respectively. Blood samples were taken form both the groups and T_3 and T_4 in the blood serum were determined by radio immunoassay (RIA) while TSH was determined by immunoradiometricassay (IRMA). The mean concentration of T_3 was 2.337 and 2.287 nmol L^{-1} in the experimental and control groups respectively. The mean concentration of T_4 was 109.415 and 105.918 nmol L^{-1} in the experimental and control groups, respectively. The mean concentration of TSH was 3.99 and 4.55 miu L^{-1} in the experimental and control groups respectively. The result indicated that continuous use of iodized salt increased both T_3 and T_4 and decreased TSH in the experimental group which is an indication for thyrotoxicoses. However the increase in T_3 and decrease in TSH were non significant but the increase in T_4 was significant and at $p<0.05$ as compared to the control group. The data suggest that long and un-necessary use of iodized salt may produce sub clinical hyperthyroidism and thyrotoxicosis in the plain areas of NWFP. Close monitoring of T_3, T_4 and TSH of individuals, who are using iodized salt, is recommended.

Key words: Iodized salt, thyroid hormones, thyroid stimulating hormone, hyperthyroidism, thyrotoxicosis

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JMS (ISSN 1682-4474) is an International, peer-reviewed scientific journal that publish original article in experimental & clinical medicine and related disciplines such as molecular biology, biochemistry, genetics, biophysics, bio-and medical technology. JMS is issued six times per year on paper and in electronic format.

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Introduction

The thyroid gland secretes thyroid hormones namely triiodothyronine (T_3) and thyroxine (T_4). Iodine is an integral part of thyroid hormones (Guyton and Hall, 1996). Availability of iodine to the thyroid gland affects the production of thyroid hormones. Iodine is mainly available through food and water and if these sources are deficient in iodine, then iodine supplementation in the diet is required. When food and water are deficient in iodine and the element is not supplemented, hypothyroidism problems like goiter, cretinism and other iodine deficiency disorders can develop. Iodine deficiency disorder (IDD) prevails in the northern hilly region and some plain areas of Pakistan. To eliminate the IDD problem, the Government of Pakistan has made iodization of table salt mandatory and the people are required by law to use iodized salt (IDD News Letter, 1998). However, excessive iodine intake in the form of iodized salt can produce thyrotoxicosis or hyperthyroidism. The amount of iodine mixed in the salt by commercial salt producers is highly variable. Some salt producers add it abundantly without knowing the exact amount needed to be mixed. Generally, salt producers do not have even proper mixing arrangement. Also all plain areas of NWFP are not so iodine deficient, so it is feared that continuous use of iodized salt may not cause thyrotoxicoses in normal individuals.

Human being can tolerate high levels of iodine, however, some individuals are sensitive to high iodine levels and when these individuals are given iodine in greater amount, they may develop untoward reactions. Therefore, iodine supplementation is contra-indicated in individuals who are sensitive to higher intakes of iodine and in those who are suffering from thyrotoxicosis (Welt and Blythe, 1978). Rapid introduction of even ordinary amount of iodine to a severely deficient population has induced hyperthyroidism with nodular goiter in older population (World Health Organization, 1996). The present study reports the effect of constant use of iodized salt on the concentration of thyroid and thyroid stimulating hormones, which are used as predicting factor for the incidence of thyrotoxicoses or hyperthyroidism.

Materials and Methods

Size of Sample and Location of the Study

Four hundred and eleven individuals were referred by physicians to radio immunoassay (RIA) laboratory of the Institute of Radiotherapy and Nuclear Medicine (IRNUM) Peshawar for T_3, T_4 and TSH tests during 1998. These individuals were interviewed about the use of iodized salt and were grouped into iodized and uniodized salt users

Collection of blood sample

Blood samples were collected from the patients through a disposable syringes of suitable volume. The samples were transferred into properly labeled sterilized test tubes and were left for 30-60 minutes at room temperature for coagulation. The Coagulated blood samples were centrifuged at 1500-2000 rpm for approximately five minutes. Serum were separated and transferred into sterile plastic tubes that were appropriately labeled for the required test and the date of sample collection. The samples were analyzed either on the same working day or stored at -20^{o}C until analyzed.

Determination of T_3, T_4 and TSH

T_3 and T_4 were determined by radio immunoassay (RIA) and TSH was determined by immunoradiometric assay (IRMA). Concentrations of T_3, T_4 and TSH in the serum were measured by using AMERSHAM, RIA and IRMA kits for each hormone. All the kits were provided with standards, tracer antibody in case of T_3 and T_4 and antibody coated tubes in case of TSH. The samples were taken out of the freezer, arranged in order and were left for complete thawing. Assay tubes were labeled as standards, non-specific binding (NSB), total count, patient samples and quality control in duplicate. Procedures recommended by the manufacturer for sample dispensing, incubation and decanting were adopted (Ortho-clinical Diagnostics Amersham, UK, 1998). Gamma Counter (Oakfield instrument LTD, UK, 1995) was used for counting the assay tubes. Hormones concentration were measured by using a computer program (RIASTAT software package).

Statistical analysis

The data was statistically analyzed using t test for knowing the difference between the two groups using the available SAS statistics package (SAS, 1990).

Results

The mean concentration of T_3, T_4 and TSH in the blood samples of iodized and uniodized salt users are given in Table 1.

Table 1: Concentration of T_3, T_4 and TSH in iodized and uniodized salt user groups

	Salt group[1]		Standard error	
Hormone determined	Iodized[2]	Uniodized[3]	Iodized	Uniodized
T_3 (nmol L^{-1})	2.337[a]	2.287[a]	0.1176	0.1413
T_4 (nmol L^{-1})	109.415[a]	105.918[b]	3.7933	3.3188
TSH (miu L^{-1})	3.990[a]	4.550[a]	1.2265	0.9476

1. Means followed by different superscript in a row are significantly different at $p<0.05$ as determined by t- test.
2. N = 148 3. N = 263.

The data indicated that intake of iodized salt increased the concentration of both T_3 (2.337 nmol L^{-1} for experimental group versus 2.287 nmol L^{-1} for control group) and T_4 (109.415 nmol L^{-1} for experimental group versus 105.918 nmol L^{-1} for control group). The T_3 concentration in the iodized salt group (experimental) was not statistically higher at $p<0.05$ than the T_3 concentration in the uniodized salt group (control). The concentration of T_4 in the iodized salt user group was significantly higher at $p< 0.05$ than the concentration of T_4 in the uniodized salt group. The use of iodized salt decreased the concentration of TSH, however, the decrease was not statistically significant at $p<0.05$.

Discussion

The intake of iodized salt increased the concentration of both T3 (2.337 versus 2.287 nmol L^{-1}) and T4 (109.415 versus 105.918). However, the increase in T3 was not significant statistically

and the increase in T4 was statistically significant at P<0.05 level. The TSH level was decreased (3.99 versus 4.55) with the intake of iodized salt. However, this decrease was not statistically different at P<0.05 level. The trend in increase in T_3 and T_4 and decrease in TSH is providing a clue that long usage of iodized salt may produce sub clinical hyperthyroidism and thyrotoxicosis or hyperthyroidism in normal individuals. For this reason, the monitoring of iodine amount in the iodized salt is necessary and iodine status of individuals are required to be checked at regular interval.

Thyrotoxicosis is not a common condition in Pakistan. However, cases of thyrotoxicosis have been reported in patients with thyroid related problems. For better health care planning, the knowledge of prevalence of the disease and its relation with iodized salt intake and the thyroid hormone levels is important. Prevalence of thyrotoxicoses and hyperthyroidism in North West Frontier province (NWFP) of Pakistan and other countries have been reported (Khan ***et al.***, 2000 and 2001; Mengistu, 1993 and IDD Newsletter, 1998).

Iodine excess is toxic and may lead to thyrotoxicosis. Families with the history of thyrotoxicosis should avoid unnecessary iodine supplementation in their diets. Many workers have suggested that a normal healthy individual must not take iodized salt until and unless prescribed by a doctor (ICCIDD, 1997).

Connolly (1971; 1973) and Vidor ***et al.*** (1973) have reported iodine-induced thyrotoxicosis in Tasmania and Australia. Iodine supplementation of bread in Tasmania was initiated in 1966 to correct moderate iodine deficiency. After iodine supplementation they observed an increase in the prevalence of thyrotoxicosis in the area. They further noted that the increase in the prevalence of thyrotoxicosis involved primarily middle-aged to older individuals who lived in iodine deficient sections of Tasmania and had histories of long standing nodular goiters. They suggested that iodine was a regulator of thyroxine production in the autonomous tissues and that increased dietary intake resulted in increased hormonal production. They concluded that because the development of autonomous tissue was correlated with aging, a population with a significant number of individuals of 40 to 50 years old or above could be at risk of epidemic thyrotoxicosis if iodine intake was increased.

Braverman ***et al.*** (1971) reported that iodide goiter could be developed in normal individuals whose diets contain excessive amounts of iodine. Excess iodine in medication caused iodine induced thyrotoxicosis in ten patients who were euthyroid with no thyroid abnormalities before taking iodine-containing drugs. However, after cessation of iodine medication they returned to euthyroid status (Savoie ***et al.***, 1975).

Autoimmune thyroiditis (Hashimoto's disease) occurred in areas of iodine deficiency after iodine supplementation in susceptible individuals. Foley (1992) observed that the disease was less common in susceptible individuals who lived in the regions with dietary iodine deficiency. The autoimmune disease particularly thyroiditis increased after the therapeutic administration of iodized salt, bread and oil. Lymphocytic infiltration of the thyroid occurred after dietary iodine supplementation. Thyroid antibodies were not detected in serum from patients with endemic goiter, but 43% subjects became positive after therapy with iodized oil and hyperthyroidism

developed. Also these medication and diet containing iodine increased the frequency and severity of autoimmune thyroid diseases.

Galofre ***et al.*** (1994) reported thyrotoxicosis before and after mandatory introduction of iodized salt in Vigo, Span. The prevalence of thyrotoxicosis was increased in the area after iodine supplementation and it was more prevalent in women than man. Wolff (1969) studied the prevalence of dietary iodine induced goiter in Hokkaido, an island of Japan, where the residents were consuming large amounts of iodine-rich seaweed. He reported that the prevalence of iodine induced goiter was 6 to 12% among the coast dwellers of the island.

In conclusion, the increase in concentration of T_3, T_4 and TSH in the group of iodized salt users is providing a clue that long term usage of iodized salt may produce sub clinical hyperthyroidism and thyrotoxicosis in normal individuals and close monitoring of T_3, T_4 and TSH of individuals, who are using iodized salt, is recommended. Continuous use of iodized salt in the plain areas of North West frontier Province of Pakistan may not be necessary. Well designed studies on the effect of iodized salt on the concentration of thyroid hormones in normal individuals are needed to decide whether the intake of iodized salt should be continued or not in the plain areas of the province.

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