

Original Research Article

Effectiveness of Zinc Supplementation in Regulating Serum Hormonal and Inflammatory Status in Hypothyroidism Patients

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Abstract

This study was designed to investigate the serum level of thyroid-stimulating hormone, thyroxine, triiodothyronine, interleukin-6 and tumour necrosis factor- α in hypothyroidism patients, and to reveal their relationship with serum zinc level in 27 patients with hypothyroidism, and 27 control group. The results disclosed that serum zinc, interleukin-6 and tumour necrosis factor- α levels in hypothyroidism patients are significantly lower ($p < 0.05$) than the control group. While serum thyroid stimulating hormone level, was significantly higher in hypothyroidism patients than the control ($p < 0.05$). After zinc administration, the patients group showed a significant increase in interleukin-6 and tumour necrosis factor- α level ($p < 0.05$) in comparison with control group.

Key words: Zinc, TSH, T3, T4, Hypothyroidism, TNF- α , IL-6

الخلاصة

صممت هذه الدراسة لقياس مستوى هرمون الدرقية (TSH) ، الثايروكسين (T4) وهرمون ثلاثي يود الثايرونين (T3) وبعض المؤشرات الالتهابية (TNF- α و IL-6) في مصلى المرضى المصابين بهبوط الغدة الدرقية . ولأظهار العلاقة مع مستوى عنصر الزنك (Zn) في مصلى 27 مريضا مقارنة مع 27 مشاركا كمجموعة سيطرة . أظهرت نتائج هذه الدراسة انخفاض ملحوظ في مستوى عنصر الزنك (Zn) والمؤشرات الالتهابية (TNF- α و IL-6) في مرضى البحث مقارنة بمجموعة السيطرة ($p < 0.05$). بينما أظهرت النتائج زيادة ملحوظة في مستوى هرمون الدرقية مقارنة بمجموعة السيطرة ($p < 0.05$). وتبين بعد اعطاء جرعات من عنصر الزنك (Zn) لهؤلاء المرضى ارتفاع ملحوظ في مستوى الزنك والمؤشرات الالتهابية التي تم قياسهم في هذا البحث بالمقارنة مع مجموعة السيطرة ($p < 0.05$).

Introduction

Zinc (Zn) is an important element in maintaining normal physiological functions. Deficiency of Zn has been revealed to have clinical manifestations including impaired immune function, increased inflammatory cytokines, and thyroid hormone disorder [1]. In addition,

Zn assists numerous essential enzymatic and hormonal activities; it plays a critical role in homeostasis of thyroid hormone [2]. Basically, Zn required for the proper function of the enzyme 1,5'-deiodinase, the enzyme catalyses the conversion of biologically thyroxine (T4) to its active form triiodothyronine (T3) and

decreases the metabolic rate. In hypothyroidism, the tubular excretion of Zn leads to low levels of plasma zinc [3]. The study by Wada and King (1986)[4], was the first to report the relationship between Zn status and thyroid hormone levels, which showed the impact of Zn treatment on thyroid hormone level. "They revealed a significant decrease in free T3 and free T4 levels during Zn deficiency in hypothyroidism patients. Other studies were in agreement with Wada and King result"[3,5-7]."

"Cytokines are multifunctional protein produced by immune cells and likely play an essential function in autoimmune thyroid disease "[6,8]. Kiziltunc et al (1999) [9], showed that serum thyroid-stimulating hormone (TSH), "tumor necrosis factor- α (TNF- α) and interleukin-6 (IL-6) cytokines" were increased in hyperthyroidism patients but decreased in hypothyroidism patients. In a population based study Prasad et al (2007) demonstrated that Zn supplementation resulting in decreased production of inflammatory cytokines in older adults [10]."

The current study was undertaken to determine a possible relationship of serum zinc levels with thyroid hormones and inflammatory cytokines in hypothyroidism patients following zinc supplementation.

Materials and Methods

Subjects

"The study was conducted on 27 hypothyroid patients and 27 controls in Al-Nahrain and Al-Yarmook Medical College & Hospital. The ages (mean \pm SD) of the hypothyroid patients and control were 59 \pm 4, and 58 \pm 3 years respectively. The patients were diagnosed on the basis of the clinical case and thyroid function test, including determination of serum T3 level, T4 level, and TSH level. The study excluded subjects received medical or surgical treatment for the thyroid at any time of their life or subjects with a history of radio-iodine

treatment". All of patient and control groups were not taking any treatment known to impact thyroid metabolism. In all patients, measurements of thyroid hormones were performed at first diagnosis time and 6 months after daily Zn supplementation (Elemental zinc, 20 mg/day, OD) while in controls they were carried out only at study entry. Before starting the study, all the participants were demonstrated by administration through a consent form about the goal of the study and all agreed to participate and signed the application."

Biochemical Analyses

Blood was sampled in the morning after overnight fasting. Plasma was immediately isolated from blood cells by centrifugation at 1000 x g for 15 min at 4°C (Sorvall @ 4K15 centrifuge) ; the resulting plasma samples were stored at -70°C until usage. Serum concentrations of T3 and T4 were determined by radioimmunoassay; and TSH concentrations by immunoradiometric assay (Gamma counter, Oakfield, England, SD-12, 2000). Serum Zn levels were determined using Shimadzu model AA-670 Flame Atomic Absorption Spectrophotometer (FAAS)(Shimadzu, Japan). IL-6 and TNF- α were determined via linking to enzymatic immunosorbent test "(Quantikine™, Human TNF- α immunoassay, CN DTA 50; Quantikine™, Human IL-6 immunoassay, CN D 6050)"."

Statistical Analysis

Descriptive analysis was used to show the mean and standard deviation of variables. Pearson's correlation analysis was used to test the linear relationship between parameters. ANOVA was used to determine differences between group variables. P-value less than 0.05 were considered to have significant difference

Results

The statistical analysis of the data in this study showed that Zn supplementation has

an effect on thyroid hormone level and cytokine level.

Figure 1 shows serum levels of Zn (Fig. 1A), TSH (Fig.1B), T4 (Fig 1C), and T3 (Fig 1D) in hypothyroidism patients before and after Zn treated compared to control.

Serum Zn level of hypothyroidism patients before Zn supplementation is significantly lower ($p < 0.05$) than the level in control, whereas increased after Zn supplements. A

significant elevation in serum "TSH level was revealed in patients before treatment in comparison with that of the control subjects, while after supplements the TSH level in the patients was decreased. T₃ and T₄ results showed decrease in hypothyroid patients when compared with controls. However, after six months of Zn supplementation, T₃ and T₄" levels were increased."

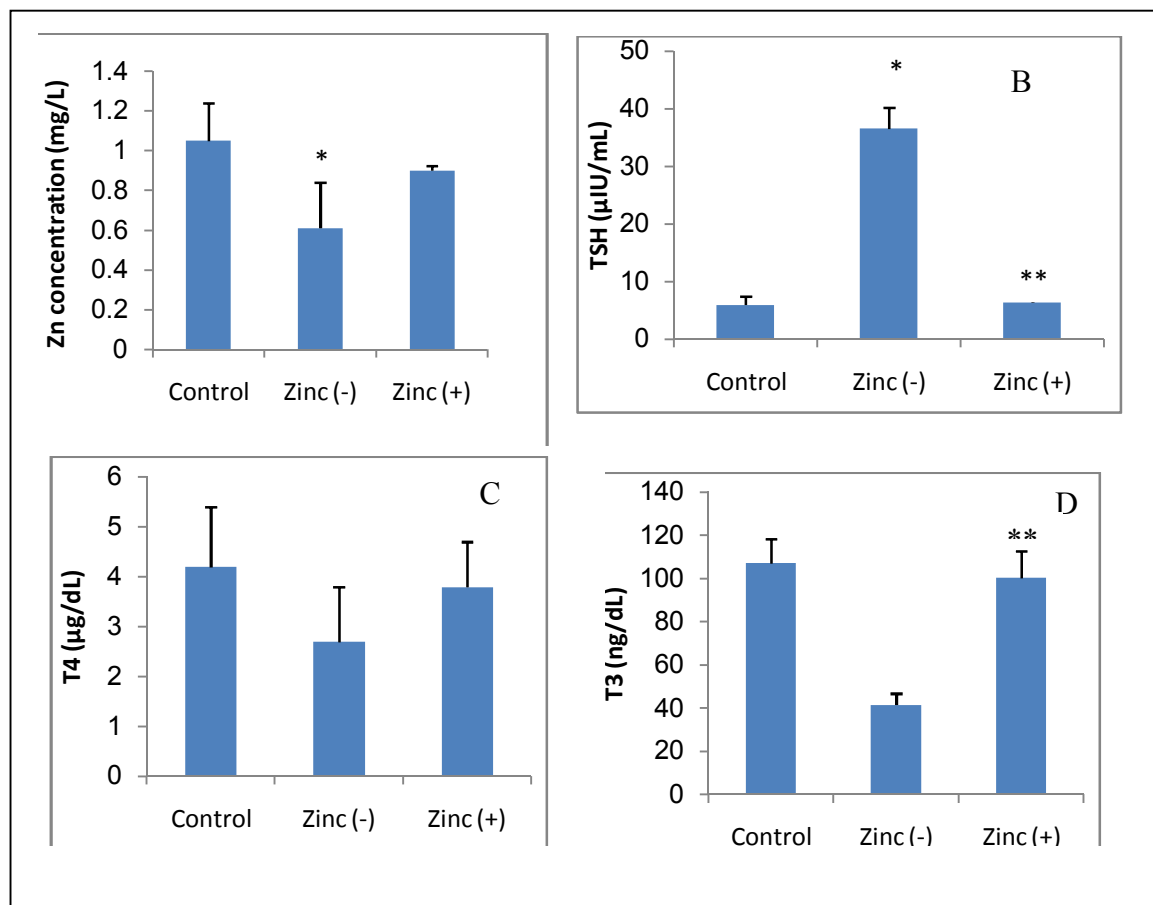


Figure 1: Effect of Zn supplementation on serum levels of Zn (A), TSH (B), T4 (C) and T3 (D) in hypothyroidism patients. Zn = zinc; TSH = Thyroid-stimulating hormone; T4 = thyroxine; T3 = triiodothyronine. (-) zinc = before Zn supplementation; (+) zinc = after Zn supplements (Elemental zinc, 20 mg/daily, OD). Data displayed is a representative experiment. Significant effects compared to the control and after Zn supplementation are indicated as * $P < 0.05$ and ** $P < 0.05$, respectively.

The serum levels of IL-6 and TNF- α of hypothyroidism patients before and after Zn supplementation compared to control group are represented in Table (1). "The

patients had significant low levels of serum IL-6 and TNF- α before Zn administration compared to control, where as their levels

increased significantly after Zn supplementation ($P < 0.05$).

Pearson's correlation analysis showed a positive relationship between serum IL-6,

and TNF- α after Zn supplementation ($r = 0.562$, $p = 0.009$), ($r = 0.518$, $p = 0.01$), Figure 2 and 3, respectively.

Table 1: IL-6, and TNF- α levels in control, hypothyroidism patients' serum before and after treatment expressed as mean \pm SD.

	Control	Hypothyroid	
		Before	After
IL-6 (pg/mL)	10.4 \pm 1.5	8.1 \pm 1.6*	9.7 \pm 0.1**
TNF- α (pg/mL)	13.6 \pm 0.9	11.7 \pm 1.7*	13.1 \pm 0.4**

IL-6 = interleukin-6; TNF- α = Tumor necrosis factor- α

* $p < 0.05$ vs the control group. ** $p < 0.05$ vs before Zn supplementation.

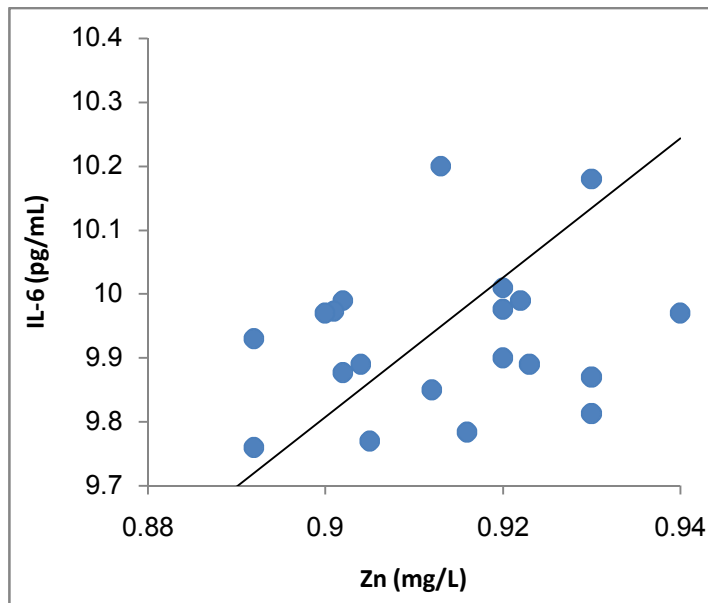


Figure 2: Correlation between Zn levels and serum IL-6 after Zn supplements. $r = 0.562$, $p = 0.009$

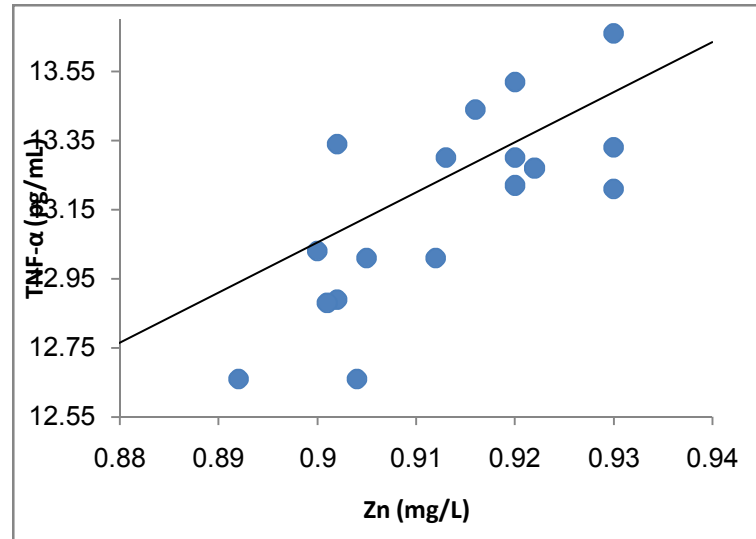


Figure 3: Correlation between Zn levels and serum TNF- α after Zn supplements. $r = 0.518$, $p = 0.01$

Discussion

Zn is identified to have a significant function in regulating clinical, biochemical, and immunological human function [11-12]. Studies showed that Zn has significant function in thyroid metabolism and a basic role in the synthesis of protein. It involves in T3 binding to its nuclear receptor [5].

This study was conducted to find out the importance of Zn in hypothyroid patients. The significant decrease in the value of Zn in hypothyroidism patients compared to controls is reported in other studies [13-14]. This may be explained that gastrointestinal absorption of Zn is severely damaged in hypothyroidism patients. Other explanation may be that TSH has significant influence in the variation of zinc concentration in normal and changed human thyroid tissues. In the current study, the decrease in serum zinc levels in hypothyroidism patients is in agreement with other studies revealing the correlation between Zn deficiency and iodothyronine levels [3,5]. Gupta et al [15] and Hartoma et al [16] who have reported

that Zn deficiency could affect thyroid hormone synthesis and function.

It was shown in this study that Zn administration enhances the levels of T3 and T4 of hypothyroidism serum patients, while decrease the TSH levels, these results are similar to other study [17]. The most probable explanation is the link between endocrine functions with Zn deficiency which are altered in thyroid hormone metabolism and energy consumption [3].

Studies showed that the role of cytokines in pathophysiology have reported that a given inflammatory stimulus results a sophisticated cascade for releasing cytokine [9]. Therefore, in the present study the demonstration of circulating TNF following thyroid deficit has led us to study other cytokines production, in particular IL-6.

IL-6 was examined in the current study because TNF- α has been recorded to be an essential enhancement for IL-6 release" [18]. This investigation showed a significant decrease in serum IL-6 and TNF- α " in hypothyroidism patients as compared to the control group. The current study, provide

support for the idea of a cascade enforcement of these cytokines by reporting a positive relationship between IL-6 and Zn, and also TNF- α with Zn. A significant increase in serum IL-6 and TNF- α level were observed in hypothyroidism participants after supplemented of Zn. This may reflect the functions of Zn as an intracellular signalling molecules, and alters in Zn concentrations can cause both direct and indirect immune modulation [19].

Conclusion

The data of the present study showed that the hypothyroidism case brings about alters in the levels of Zn, TSH, T3, T4, IL-6 and TNF- α . These changes may be associated with decreased zinc levels in hypothyroidism and normalized by Zn supplementation. Further studies are required to determine the clinical significance of this abnormality and the role of zinc supplementation in male and female patients of hypothyroidism.

Conflict of Interest

The authors have declared that there is no conflict of interest

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