EJMO

DOI: 10.14744/ejmo.2017.02996
EJMO 2017;1(3):145–148

Research Article

Thyroid Hormone and Ultrasonographical Analyses in Patients with Nickel Allergy

Mumtaz Takir,[1] Ozlem Turkoglu,[2] Zafer Turkoglu[3]

[1] Department of Internal Medicine, Clinic of Endocrinology and Metabolism, Istanbul Medeniyet University Goztepe Training and Research Hospital, Istanbul, Turkey
[2]Department of Radiology, Haydarpasa Sultan Abdulhamid Han Training and Research Hospital, Istanbul, Turkey
[3]Department of Dermatology, Haseki Training and Research Hospital, Istanbul, Turkey

Abstract

Objectives: Nickel allergy and thyroid functional disorders have been associated via various mechanisms. We aimed to biochemically and radiologically investigate the relation of thyroid disorder with nickel dermatitis, the frequency of which varies between 4% and 13% in the society.
Methods: Seventy-nine patients diagnosed with nickel dermatitis who visited to our clinic and a healthy control group of 43 individuals were included in the study. Hemogram; peripheral smear; serum Fe, TDBK, ferritin, 25-OH vit D3, total IgE, thyroid hormone, and antibody levels; and thyroid ultrasonography of both groups were evaluated and compared statistically.
Results: MPV and total IgE levels were significantly high in the patient group ($p<0.01$). In addition, monocyte and eosinophil levels were also low in patients with nickel allergy. Anti-TPO and anti-Tg levels in both groups were similar. On ultrasonography evaluation, there was a significant difference in the patients with nickel allergy with respect to thyroid findings ($p<0.01$).
Conclusion: We observed that the incidence of nickel allergy increases in patients who were radiologically diagnosed with thyroiditis.
Keywords: Dermatology, radiology, thyroid autoimmunity, thyroid function

Cite This Article: *Takir M, Turkoglu O, Turkoglu Z. Thyroid Hormone and Ultrasonographical Analyses in Patients with Nickel Allergy. EJMO. 2017; 1(3): 145-148*

Nickel dermatitis has been the subject of etiologic studies in recent years because of its frequent nature in the allergic contact dermatitis (AKD) group. The peripheral connection between inorganic nickel and autoimmune thyroid diseases mentioned in the literature makes us think of a correlation between these two disease groups.[1–8]

We examined hematologic, biochemical, and radiologic thyroid parameters of patients with nickel dermatitis by comparing then with a control group.

Materials and Methods

A total of 79 patients diagnosed with nickel dermatitis who visited to our clinic and a healthy control group of 43 individuals who have no reactions on European Standard, Dental, and Cosmetic serial patch tests were included in this study. Hemogram; peripheral smear; serum Fe, TDBK, ferritin, 25-OH vit D3, total IgE, thyroid hormone, and antibody levels; and thyroid ultrasonographies of both groups were evaluated and compared statistically. The 79

Address for correspondence: Mumtaz Takir, MD. Department of Internal Medicine, Clinic of Endocrinology and Metabolism, Istanbul Medeniyet University Goztepe Training and Research Hospital, Istanbul, Turkey
Phone: +90 216 566 40 00 **E-mail:** mumtaztakir@yahoo.com
Submitted Date: June 08, 2017 **Accepted Date:** August 13, 2017 **Available Online Date:** September 26, 2017
©Copyright 2017 by Eurasian Journal of Medicine and Oncology - Available online at www.ejmo.org

Table 1. Demographic features of the patient and healthy control groups

	Patients with nickel allergy (n=79)	Healthy control group (n=43)	*P*
Age (year)	40±13	42±14	0.57
Gender (F/M)	65/14	35/8	0.91
WBC (x10^3/mm^3)	7.3±2.1	7.1±1.7	0.70
Hemoglobin (g/dL)	13.1±1.7	12.7±1.7	0.37
MCV (fL)	85.7±7.1	84.3±11.1	0.46
Platelet (x10^3/mm^3)	254±65	251±56	0.81
MPV	9.5±1.6	8.1±1.3	**<0.001**
Neutrophile (x10^3/mm^3)	4.1 (3.2–5.1)	3.9 (3.2–4.9)	0.64
Lymphocyte (x10^3/mm^3)	2.1 (1.7–2.4)	2.0 (1.8–2.5)	0.48
Monocyte (x10^3/mm^3)	0.46±0.14	0.55±0.19	**0.02**
Eosinophi (x10^3/mm^3)	0.10 (0.04–0.20)	0.16 (0.09–0.21)	**0.03**
NLR	1.9 (1.5–2.7)	1.7 (1.4–2.1)	0.21
Total Ig E	60 (18–287)	25 (10–59)	**0.01**
Fe (µg/dL)	75±32	78±38	0.71
Ferritin (ng/mL)	43 (16–160)	24 (8–63)	0.15
25-(OH) vitD	13.6 (10.5–46.9)	16.6 (12.3–26.1)	0.79

WBC: White Blood Cells; MCV: Mean Corpuscular Volume; MPV: Mean Platelet Volume; NLR: Neutrophil to lymphocyte ratio.

patients were only diagnosed with nickel allergy "AKD" on European Standard, Dental, and Cosmetic serial skin patch tests between March 2014 and March 2015 at Medeniyet University Faculty of Medicine, Goztepe Training and Research Hospital, Allergy clinic and the 43 patients showed no allergy in these three-series test. Smokers, alcohol users, and patients with acute and chronic pathologies such as dyslipidemia, obesity, and diabetes were excluded. All participants are informed to avoid chemical substances.

Demographic features, such as age and gender of the patients; skin patch test results; hemogram; peripheral smear; serum Fe, TDBK, ferritin, 25-OH vit D3, total IgE, T4, TSH, anti-TPO, and anti-Tg levels were recorded and thyroid ultrasonography results were evaluated. While patch tests were conducted at our polyclinic with European Standard Series including 28 allergens, Dental Series including 30 different allergens, and Cosmetic Series including 57 different allergens (Chemotechnique Diagnostics Malmo, Sweden), all allergens were attached on the patients' back using IQ Ultra Chambers. Readings were recorded when the patch was removed 48h after its application. The patients back was re-evaluated at 72nd h and at the end of the 7th day. Patch test results were scored between 0 (no reaction) and +3 according to the reaction severity as recommended by the International Contact Dermatitis Research Group. Positive reaction was determined as +1, +2, and +3. Suspicious reactions were excluded from the study. Endocrinology clinic consultations for biochemical readings and thyroid functions of the patient and radiology clinic consultations for thyroid ultrasonography were retrospectively obtained from the hospital system.

This retrospective study design was approved by the ethics committee of Medeniyet University Goztepe Education and Research Hospital.

Statistical evaluation of the findings, Student's t-test, Mann–Whitney U test, Chi-square test, and Wilcoxon's rank test were used. $p<0.05$ was considered to be significant.

Table 2. Thyroid hormone and ultrasonographical profiles

	Patients with nickel allergy (n=79)	Healthy control group (n=43)	*P*
Autoimmunethyroidismn (%)	23 (29)	17 (39)	0.59
Antibodypositivityn (%)			
Isolated Anti-TPO	7 (8.8)	4 (9.3)	0.55
Isolated Anti-TG	1 (1.2)	3 (6.9)	
Both of Anti-TPO/TG	15 (18.9)	10 (23.2)	
Thyroid stimulating hormone	1.84 (1.22–3.34)	1.99 (1.40–3.84)	0.72
Free T3	2.92 (2.78–3.29)	2.67 (2.56–3.10)	0.23
Free T4	0.94 (0.84–1.06)	1.01 (0.90–1.10)	0.08
Anti-TPO	1.51 (0.50–37.93)	0.51 (0.50–36)	0.66
Anti-TG	1.10 (0.90–37.93)	2.16 (1.37–14.29)	0.33
Ultrasonogrpahicfindingsn (%)			
Thyroidcyst	6 (100)	–	0.16
Thyroidnodule	18 (22.7)	3 (6.9)	0.03
Thyroiditis	24 (30.3)	5 (11.6)	0.04

TPO: thyroid peroxidase, TG: thyroglobulin.

Results

Patients with nickel allergy complaints (n=79, 65 male and 14 female) and age-and sex-matched controls (n=43, 35 male and 8 female) were included in our study. Basic demographic features and biochemical results of the patient and control groups are shown in (Table 1). MPV and total IgE levels were significantly high in the patient group ($p<0.01$). In addition, monocyte and eosinophil levels were low in the patient group. There was no significant difference between the two groups in terms of Fe, ferritin, and 25-(OH) vit D3 levels. There was no significant difference between the groups on evaluation of thyroid functions in terms of autoimmune thyroid dysfunction. Anti-TPO and anti-Tg levels in both groups were similar. Meanwhile, according to the ultrasonographic findings, thyroid cyst was similar between groups and the frequency of thyroid nodules and thyroiditis was also significantly higher in patients with nickel allergy ($p=0.03$ and $p=0.04$, respectively) (Table 2).

Discussion

In patients with nickel allergy, we saw a significant difference in terms of thyroiditis by the radiologic evaluation of thyroid that was indicating autoimmunity. Because of high affinity of gold, mercury, nickel, and silver to thiol groups, disulfide bonds are formed with sulfhydryl (-SH) groups. Nickel, arsenic, cadmium, and mercury are strong sulfhydryl-binding metals[9]. Thiols of self-proteins may change the structure of auto-antigens or create hidden epitopes. These sulfide groups stimulate immunity by bonding with cell surface structures on renal or thyroid tissues[10]. The difference in thyroid ultrasonography findings of patients with nickel dermatitis indicates this.

It was reported that keratinocytes produce IL-23 in response to nickel, and this was the potential trigger point of TH 17-related skin inflammation cascade. There are allergen-specific T-helper cells in the peripheral blood of the individuals with nickel allergy[11]. Cytokines, such as IFN-gamma, IL-12, and tumor necrosis factor-alpha, are in front of Th 2 type mechanisms. They are similarly governed by IL-4 and IL-10 in the destruction of thyrocytes in thyroid cells in rat model, suggesting an important role of IFN-gamma in the nickel and thyroid bond[11-13].

In their animal test, Al-Mogairen et al. histopathologically presented that nickel causes autoimmunity and cutaneous sclerosis[6]. In addition, the metal-driven inflammation may affect the hypothalamic-pituitary-thyroid axis (HPT) by a novel, unknown way. New studies indicated mast cell as a sensor point in the homeostatic response control of the HPT axis via toll-like receptor MyD8814. A limitation of our study was that it was not conducted on the cellular level. Because of lack of technical equipment in the present study, patients were evaluated only clinically and radiologically.

The stimulant feature of nickel was presented on the zinc-finger gene (ZFAT) which has been discovered recently and creates a high-risk for autoimmune thyroid diseases. In addition, nickel targets heterochromatins in the cell and distresses eosinophil, monocyte, and megakaryocytes hematologically. In compliance with the literature, we also observed MPV and IgE levels as an indicator of eozinopenia, monocytopenia, and thrombocyte structural disorder in the peripheral smear of our patients. There was no significant increase in the laboratorial thyroid autoimmunity of our patients. However, significant differences determined in the thyroid ultrasonography findings suggest that laboratorial differences may be determined in the future[10-18].

We think that our study, for the first time, has investigated the relation between nickel allergy and thyroid hormone using ultrasonography and hematologic biochemical readings, which were theoretically referred to and presented with animal tests, in a patient population. Present results will contribute in further studies on the relationship between nickel allergy and autoimmunity.

Disclosures

Ethics Committee Approval: The study was approved by the Local Ethics Committee.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

References

1. Sterzl I, Procházková J, Hrdá P, Bártová J, Matucha P, Stejskal VD. Mercury and nickel allergy: risk factors in fatigue and autoimmunity. Neuro Endocrinol Lett 1999;20:221–8.
3. Hybenova M, Hrda P, Procházková J, Stejskal V, Sterzl, I. The role of environmental factors in autoimmune thyroiditis. NeuroEndocrinol Lett 2010; 31: 283-289.
4. Al-Mogairen SM. Induction of an Autoimmune Thyroid Disease with Nickel Chloride in Brown Norway Rats. Turk Jem 2009;13:71–4.
5. Al-Mogairen SM, Meo SA, Al-Arfaj AS, Hamdani M, Husain S, Al-Mohimed B, et al. Nickel-induced allergy and contact dermatitis: does it induce autoimmunity and cutaneous sclerosis? An experimental study in Brown Norway rats. Rheumatol Int 2010;30:1159–64. [CrossRef]
6. Al-Mogairen SM. Induction of autoimmunity in brown Norway rats by oral and parenteral administration of nickel chloride. Lupus 2010;19:262–7. [CrossRef]
7. Niedziela M, Bluvshteyn-Walker S. Autoimmune thyroid disease and allergic contact dermatitis: two immune-related

pathologies in the same patient. J Pediatr Endocrinol Metab 2012;25:31–2. [CrossRef]
8. Grandjean P. Human exposure to nickel. In: Sunderman FW Jr, editor. Nickel in the Human Environment (IARC Scientific Publications No. 53). Lyon: IARC; 1984. p. 469–85.
9. Mohammadi-Bardbori A, Rannug A. Arsenic, cadmium, mercury and nickel stimulate cell growth via NADPH oxidase activation. Chem Biol Interact 2014;224:183–8. [CrossRef]
10. Bigazzi PE. Metals and kidney autoimmunity. Environ Health Perspect 1999;107 Suppl 5:753–65. [CrossRef]
11. Larsen JM, Bonefeld CM, Poulsen SS, Geisler C, Skov L. IL-23 and T(H)17-mediated inflammation in human allergic contact dermatitis. J Allergy Clin Immunol 2009;123:486–92. [CrossRef]
12. Chistiakov DA. Immunogenetics of Hashimoto's thyroiditis. J Autoimmune Dis 2005;2:1. [CrossRef]
13. Kono DH, Balomenos D, Pearson DL, Park MS, Hildebrandt B, Hultman P, et al. The prototypic Th2 autoimmunity induced by mercury is dependent on IFN-gamma and not Th1/Th2 imbalance. J Immunol 1998;161:234–40.
14. Rocchi R, Kimura H, Tzou SC, Suzuki K, Rose NR, Pinchera A, et al. Toll-like receptor-MyD88 and Fc receptor pathways of mast cells mediate the thyroid dysfunctions observed during nonthyroidal illness. Proc Natl Acad Sci USA 2007;104:6019–24. [CrossRef]
15. Harris WR. Estimation of the ferrous-transferrin binding constants based on thermodynamic studies of nickel(II)-transferrin. J Inorg Biochem 1986;27:41–52. [CrossRef]
16. Hartwig A, Mullenders LH, Schlepegrell R, Kasten U, Beyersmann D. Nickel(II) interferes with the incision step in nucleotide excision repair in mammalian cells. Cancer Res 1994;54:4045–51.
17. Hartwig A, Asmuss M, Ehleben I, Herzer U, Kostelac D, Pelzer A, et al. Interference by toxic metal ions with DNA repair processes and cell cycle control: molecular mechanisms. Environ Health Perspect 2002;110 Suppl 5:797–9. [CrossRef]
18. Rustemeyer T, von Blomberg BM, van Hoogstraten IM, Bruynzeel DP, Scheper RJ. Analysis of effector and regulatory immune reactivity to nickel. Clin Exp Allergy 2004;34:1458–66.