Effect of Nonsurgical Periodontal Therapy on Thyroid Stimulating Hormone in Hypothyroid Patients with Periodontal Diseases

Abstract
Background: The endocrine and the immune system demonstrate a mutual relationship under pathophysiologic conditions. Thyroid hormone plays an important role in the regulation of normal growth and development. Although there is proven bidirectional influence of systemic diseases on periodontium, there are fewer studies on the effect of periodontal therapy on the hormone levels. This study aims to assess the effect of nonsurgical periodontal therapy (NSPT) on serum thyroid stimulating hormone (TSH) levels in hypothyroid patients with periodontal diseases. Materials and Methods: A total of 30 randomly chosen subjects of which 15 known hypothyroidism patients (13 females and 2 males) who were under medication for the same and 15 healthy individuals were enrolled into the study. Clinical parameters and serum TSH levels were recorded at baseline in both the groups, whereas TSH levels were recorded again at 3 months after NSPT in hypothyroid patients. Intergroup comparison was carried out by Tukey Kramer multiple comparisons test and the difference in variables was analyzed using one-way analysis of variance. Results: Mean values of TSH in hypothyroid patients $3.48 \pm 1.41 \mu IU/ml$ showed significant reduction to $2.31 \pm 1.24 \mu IU/ml (P \leq 0.05)$ at 3 months follow up of NSPT. Clinical parameters improved significantly in both the groups after NSPT ($P \leq 0.05$). Alveolar bone loss was greater in hypothyroid patients than the control group at baseline. Conclusion: NSPT plays a major role in improving periodontal conditions by reducing inflammatory markers and thereby influencing the thyroid hormone. Thus, immune system serves as an important link between thyroid dysfunction and periodontal diseases.

Keywords: Hypothyroidism, immune system, nonsurgical periodontal debridement, periodontal diseases, serum, thyroid stimulating hormone

Introduction
The communication of the immune system to central nervous system is mainly via hypothalamic–pituitary–adrenal axis. Thyroid hormones play an important role in maintaining homeostasis of the body by regulating normal physiologic growth and development, skeletal maturation and bone turnover. Furthermore, they are involved in the maintenance of immune function in response to environmental stimuli and stress-mediated immunosuppression.

There are two venues through which thyroid stimulating hormone (TSH) modulation takes place by the immune cells. One by the direct effect of TSH on cells of the immune system, the second being an indirect effect mediated by TSH-induced thyroid hormone. The role of cells of immune system in the production of TSH has been demonstrated since a long time. The production of TSH by leukocytes gives a reasonable assumption that it may act like a cytokine-like regulatory molecule within the immune system. There is a positive association of thyroid hormone with markers of inflammation such as interleukin-1 (IL-1), IL-2, IL-6, natural killer T cells, memory helper T-cells, tumor necrosis factor-α (TNF-α), and transforming growth factor-β. As thyroid hormones play a major role in bone turnover, an excessive increase in TSH levels may lead to bone resorption. Bone resorption in hypothyroid patients is seen more as compared to hyperthyroid due to slower bone turnover rate causing retarded bone growth and maturation. Periodontal disease, an immune and inflammatory disorder shows alveolar bone resorption under the influence of IL-1 β, IL-6, osteoprotegerin, and receptor activator of nuclear factor kappa-B ligand (RANKL).
mechanism.[3] Similar bone destruction mechanism is seen with thyrotropin (TSH) levels.[9,10] Nonsurgical periodontal therapy has shown to reduce the oxidative stress within the periodontium and also reduce the inflammation, affecting the levels of pro-inflammatory cytokines.[11]

So to know the effect of periodontal therapy on thyroid hormone levels, we investigated the levels of serum TSH before and after nonsurgical periodontal therapy (NSPT) in hypothyroid patients.

Materials and Methods

Source of data

Totally 30 subjects of both the sexes (26-females and 4 males; age range: 18–50 years) were selected from the out-patient Department of Darshan Dental College and Hospital, Udaipur, Rajasthan. All procedures performed were in accordance with the ethical standards of the institutional committee and with the 1975 Helsinki declaration and its later amendments. All the subjects were asked to sign an informed consent. Of 30 subjects, 15 subjects of good general and oral health with no thyroid dysfunction and no periodontal disease were included in Group I, whereas 15 subjects with known hypothyroidism who were under medication for the same were included in Group II. Thyroid dysfunction was diagnosed by the endocrinologist based on clinical signs and laboratory examinations, such as TSH, T3, and fT4 serum levels.

Inclusion criteria

Subjects in the age range of 18–50 years, the presence of at least 20 permanent teeth in oral cavity, known hypothyroidism patients who are under medication for the same (thyroid supplements) in Group II and no periodontal treatment within the last 6 months.

Exclusion criteria

Subjects over 50 years of age, smokers, subjects with any other endocrine disorder that could influence the thyroid hormone or alter the course of periodontal disease, intake of antibiotics or anti-inflammatory drugs 3 months before the study. Furthermore, patients with history of radiation therapy or evidence of osteoporosis, pregnant or lactating women were excluded from the study.

Experiment protocol

The participants of both the groups were asked to report on the study day after an overnight (>12 h) fast at 09.30 h. Clinical parameters to evaluate periodontal condition such as oral hygiene index-simplified (OHI-S) by Greene and Vermillion (1964), papillary bleeding index (PBI) by Muhlemann (1977), periodontal screening and recording index (PSR), and clinical attachment level (CAL) were recorded in both the groups at baseline. Radiographic assessment of bone loss was carried out by orthopantamogram.

Blood collection and sampling

A volume of 2 ml of venous blood from subjects of both the groups was obtained from median cubital vein by venipuncture using an adequate closed system sample and stored in plain vacutainer tubes at 4°C/30 min. Tubes were then centrifuged at 3000 rpm/10 min, serum was separated and stored at −20°C until analyzed. Serum TSH levels were measured by electrochemiluminescence immunoassay, a three-step sandwich immunoassay by COBAS INTEGRA E 411 autoanalyzer (Roche Diagnostics).

Nonsurgical periodontal therapy

After recording clinical parameters and blood sample collection, NSPT which included supragingival scaling, subgingival scaling, and root planning was carried out on the same appointment in both the groups. Detailed oral hygiene instructions were given to the subjects and asked to report for maintenance phase every 1 month for 3 months. At 3 months follow-up after NSPT, periodontal evaluation and serum TSH measurement were performed again.

Statistical analysis

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS; Chicago, IL, USA) version 16.0 and the data obtained was expressed as mean and standard deviation. Mean and standard deviation of different variables such as OHI-S score, PBI score, PSR score, clinical attachment loss (CAL), and serum TSH levels in both the groups at baseline and 3 months follow-up was calculated by Multi Variant Analysis Of Variance. Intergroup comparison was performed by Tukey–Kramer multiple comparisons test. The level of significance was set at $P \leq 0.05$ and $P < 0.01$ with confidence interval at 95% and 99%, respectively.

Results

Clinical parameters

The mean and standard deviation were calculated for various clinical and blood parameters such as OHI-S, CAL, PBI, PSR and TSH at baseline and 3 months after NSPT as shown in Table 1. Intergroup comparison of the indices (OHI-S, PBI and PSR) between control and hypothyroid group at baseline and at 3 months after NSPT is shown in Figure 1.

Comparison between Group I and Group II as performed using Tukey Kramer multiple comparisons test at baseline is shown in Table 2. Intergroup comparison for OHI-S between the control (0.55 ± 0.25) and hypothyroid patients (4.09 ± 0.53) showed statistically significant difference at baseline ($P < 0.001$). After NSPT in both the groups, there was significant reduction in the mean OHI-S score in hypothyroid patients at 3 months follow-up (1.85 ± 0.41) ($P < 0.001$).
Similarly, there was a significant reduction in the PBI score in hypothyroid patients at 3 months follow-up after NSPT (2.08 ± 0.44) as compared to baseline (3.65 ± 0.60) (P < 0.0001). Furthermore, a significant difference was seen when hypothyroid group was compared with control group at baseline (1.23 ± 0.18) (P < 0.001).

PSR system showed significant reduction in mean score when comparison was done between control group (1.05 ± 0.19) and hypothyroid patients at baseline (3.85 ± 0.65). In hypothyroid patients at 3 months follow-up (2.18 ± 0.88) after NSPT, PSR score showed significant reduction as compared to baseline (P < 0.001).

An important periodontal parameter CAL was recorded in both the groups which showed statistically significant difference in the mean values when control group (0.33 ± 0.51) was compared to hypothyroid group at baseline (5.21 ± 0.60). In hypothyroid patients at 3 months follow-up (2.18 ± 0.88) after NSPT, mean CAL showed significant reduction as compared to baseline (P < 0.001) as shown in Figure 2.

Blood parameter (serum Thyroid Stimulating Hormone levels)

The reference range for TSH levels was 0.27–4.20 µIU/ml. Comparison between the control (2.60 ± 1.11 µIU/ml) and the hypothyroid group (3.48 ± 1.41 µIU/ml) at baseline showed no statistically significant difference in the levels of TSH (P > 0.05). At 3 months follow-up after NSPT, there was a significant difference in the TSH levels in hypothyroid patients (2.31 ± 1.24 µIU/ml) as compared to baseline (P < 0.05). Intergroup comparison of TSH levels between control and hypothyroid group is shown in the Figure 3. Intra-group comparison within group II at baseline and at 3 months is shown in Table 3.

Discussion

To the best of our knowledge, this is the preliminary study to assess the levels of thyrotropin or TSH after NSPT in patients with thyroid dysfunction and periodontal diseases.

This study showed that hypothyroidism patients in group II had compromised periodontal condition in older adults after evaluation of their clinical parameters. The clinical condition in these patients at baseline showed higher amount of local factors, positive gingival bleeding on probing, deeper probing depth, and loss of attachment. Alveolar bone resorption was also greater in these patients.
Bhankhar, et al.: Changes in the serum TSH levels after nonsurgical periodontal therapy in hypothyroid patients

Figure 2: Intergroup comparison of clinical attachment level at baseline and at 3 months after nonsurgical periodontal therapy

Figure 3: Intergroup comparison of serum thyroid stimulating hormone levels at baseline and at 3 months after nonsurgical periodontal therapy

as compared to control group. The presence of high amount of inflammation was suggested to be due to excessive amount of inflammatory cytokines which also has a role in periodontal tissue destruction.

Although many studies have shown the correlation between thyroid disorders and periodontal diseases, there is no adequate literature regarding the mechanism. In this study, higher amount of inflammation and periodontal destruction was seen in hypothyroid patients, which is consistent with the findings of McGee et al. who showed inflammatory cytokines spread into periodontal tissues by entering the systemic circulation where they induce production of matrix metalloproteinases (MMP’s) responsible for connective tissue and further alveolar bone destruction by activation of the resident cells of periodontium.[12] Bartalena et al. reported IL-6 and TNF-α as major proinflammatory cytokines produced locally in pathological conditions such as thyroid dysfunction. [13] The findings of our study could be due to the presence of excess proinflammatory cytokines such as IL-1, IL-6, PGE2, and TNF-α in the periodontium of hypothyroid patients.

Our assumption was also supported by Monea et al. who suggested that cytokines IL-6 and TNF-α produced in thyroid disorders play a major role in initiation and amplification of the inflammatory cascade in the periodontal tissues. The endotoxins produced by the bacteria in dental plaque combines with these cytokines further aggravating the inflammatory cascade by production of more cytokines responsible for MMP’s activation and periodontal breakdown.[14]

Babior suggested that polymorphonuclear leukocytes (PMN’s) play a major role in bacterial phagocytosis by respiratory burst mechanism through the nicotinamide adenine dinucleotide phosphate-oxidase complex and leads to production of ROS which generates oxidative stress within periodontal tissues. These ROS lead to bone resorption by acting at the ruffled border of osteoclasts.[15] Similarly, Mezosi et al. and Palmblad et al. have shown that thyroid hormones stimulate free radical production and impaired phagocytosis by PMNs mainly in hypothyroid patients.[16,17]

In this study, NSPT was performed in both the groups at baseline after evaluating clinical parameters and serum TSH levels. After maintenance phase at every 1 month till 3 months after NSPT, clinical parameters, and serum TSH levels were measured again in Group II. A 3 months, follow-up was taken as it is considered ideal time for periodontal evaluation after any NSPT.[18]

Clinical parameters such as OHI-S, PSR score, PBI, and CAL improved at 3 months follow-up after NSPT as compared to baseline in both the groups. A study conducted by Aziz et al. supported the finding of our study who concluded that SRP improves periodontal condition by reducing gingival inflammation and lowering oxidative stress markers such as C-reactive protein (CRP), malondialdehyde, and superoxide dismutase.[11]

Although, there was no significant difference in TSH levels in both the groups at baseline, the levels reduced significantly in hypothyroid patients when measured at 3 months after NSPT. The nonsignificance in the levels of TSH could be due to constant dose of thyroid medication taken by hypothyroid patients. The reduction in the levels of thyroid hormone following NSPT seen in this study could be due to reduction in the proinflammatory cytokines such as IL-6, TNF-α, and certain lipopolysaccharides playing a role in regulation of thyroid hormone in hypothyroid condition. George and Janam evaluated effect of NSPT on the levels of IL-6 and CRP in chronic periodontitis patients and concluded a significant reduction in their levels following periodontal therapy.[19] Furthermore, supporting our study Zhou et al. reported a decrease in levels of serum TNF-α, IL-6 and CRP in chronic periodontitis patients with stable CHD.[20]

In the present study, greater alveolar bone loss was seen in hypothyroid patients as compared to control group. Feitosa et al. studied the effect of thyroid hormone on alveolar bone loss using a rat model of ligature-induced
periodontitis and the results showed significantly greater alveolar bone loss in hypothyroid subjects as compared to control. They also speculated progression of periodontal disease in hypothyroidism to be relative to immune system negatively.[21] Kanatani et al. also showed a negative effect of thyroid dysfunction on IL-6 and TNF-α, which are responsible for osteoclast differentiation and function independent of RANKL mechanism.[22]

As known our study is the first known interventional study among the hypothyroidism patients with periodontal diseases. The focus here was more on the clinical importance of NSPT in reducing the levels of TSH in blood. This study had some limitations. Exact cause for the changes in the levels could not be determined as the individual inflammatory markers were not estimated. In addition, diet affecting thyroid hormones was not considered in the study. Therefore, we acknowledge an unrecognized confounding factor in the thyroid hormone level changes due to therapy.

Conclusion

Our results suggest a reciprocal relationship between endocrine system, especially thyroid dysfunction and periodontal disease which is mediated through immune system. Furthermore, the decrease in serum TSH levels within the normal range among hypothyroid patients following NSPT is due to reduction in inflammatory markers responsible for periodontal as well as thyroid dysfunction condition. Further studies must be carried out with inclusion of larger sample size, comprehensive assessment of immune status with exact identification of more inflammatory markers responsible in both the diseases and further surgical periodontal treatment modalities to clearly confirm the changes in TSH levels.

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Conflicts of interest

There are no conflicts of interest.

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