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Research Article

CLINICAL TYPES OF ORAL LICHEN PLANUS AND THEIR CO-RELATION WITH SERUM T3, T4, TSH LEVEL

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A B S T R A C T

Aims and Objectives: To determine the co-relation between the types of oral lichen planus, and serum T3,T4, TSH level. This study also aims at age and sex related serum T3,T4,TSH level and types of Oral lichen planus.

Materials and Method: The whole blood sample(5ml) will be collected from oral lichen planus patient diagnosed by clinical and histopathology examination. The serum of same patients will be analysed for levels of thyroid hormones (free triiodothyronine T3, free thyroxineT4 and thyroid-stimulating hormoneTSH),T3,T4 value is determined by electro-chemiluminescence immunoassay analyzer (ECLIA) however TSH value is determined by ultrasensitive enhanced chemiluminescence(Ultra sensitive 4th generation Chemiflex).

Results: Reticular oral lichen planus(50%) is most common in study population while bullous (6.7%) type of oral lichen planus is least common.Oral lichen planus is most commonly found on right and left buccal mucosa(53.3%) however left buccal mucosa (3.3%) is least common site .The serum T3,T4 and TSH level varies irrespective of clinical subtypes of oral lichen planus(p value<.05).The occurrence of clinical subtypes of oral lichen planus is independent of age and sex (P value<.05%).Theserum T3, T4 and TSH level is statistically not significant in male and females and age groups(P value<.05%).

Conclusion: Serum T3, T4, and TSH level is independent of clinical subtypes of Oral lichen planus i.e. the serum level of T3, T4, and TSH is not specific to particular type of Oral lichen planus. It varies from type to type of oral lichen planus.

INTRODUCTION

Oral lichen planus (OLP) is one of the most common and debilitating oral mucosal lesions in the adult population. Despite large research effort over the last decades, the aetiology of OLP remains an enigma. It is well established that the pathogenesis of OLP is mediated by T cells which presumably are targeted against the oral epithelium and trigger apoptosis of basal keratinocytes, leading to chronic inflammation[1]. However, despite large research effort over the last decades, the mechanisms responsible for T-cell activation in Oral lichen planus remain to be determined. Oral lichen planus has traditionally been considered a specific disorder caused by a single antigen or factor, but the widespread use of this monocausal model has added little insight to the aetiology of this condition. Conversely it is likely that Oral lichen planus represents different forms of idiopathic Oral lichen planus and thus should not be regarded as a specific disease but a common clinical and histopathological reaction pattern elicited by a broad range of environmental and/or self-antigens in genetically susceptible patients.

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Any scientific effort to identify factors that may be related to the aetiology will consequently require the investigation of an extensive number of patients that allows the identification of possible subgroups. The current studies aimed to identify new potential aetiological factors for Oral lichen planus. The morbidity and prevalence of oral lichenoid reactions in a non-referral adult Swedish population of 6448 subjects was determined (Study I). The medication profile of patients with OLP (n=956) was compared with dental patients with no oral mucosal lesions (Study II). Based on the results from studies I and II, the prevalence of levothyroxine supplementation and profile of thyroid disease was established in a cohort of patients with OLP (n=1611) and compared to the general population (n=1615) (Study III). The clinical characteristics of patients with concomitant OLP and thyroid disease (n=108) were also investigated (Study III). Serum levels of antithyroid antibodies and thyroid hormones were analysed in patients with OLP (n=108) and compared with different control groups (Study IV). Finally, the expression of thyroid proteins in OLP lesions (n=5) was determined and compared to healthy oral mucosa (n=5) (Study IV). It was demonstrated that Oral lichenoid reactions still represent one of the most common and debilitating oral mucosal lesions in the adult population (Study I). OLP is strongly associated with the use of levothyroxine

(Study II). The prevalence of thyroid disease in patients with OLP is significantly higher compared to the general population (Study III). The clinical characteristics and the natural course of OLP lesions in patients with thyroid disease are different compared to those in patients with no thyroid disease (Study III). Patients with OLP without a previously diagnosed thyroid disease have high levels of TSH and low levels of FT4, indicative of thyroid disease (Study IV). Elevated levels of antithyroid antibodies could not explain the high prevalence of thyroid disease in patients with OLP (Study IV). Thyroid-stimulating hormone receptor is highly expressed in basal keratinocytes of OLP lesions (Study IV). In conclusion, a subgroup of patients with OLP may have an aetiological background in common with thyroid disease. The reason for this connection remains to be determined, but it is likely that some mechanisms in autoimmune thyroid disease are involved in the pathogenesis of this group of patients suffering from OLP[2,3,4,5].

Hypothesis

Is serum level of T3, T4 and TSH is related to occurrence of lichen planus?

Aims and Objectives

1. To determine the co-relation between the types of oral lichen planus and serum T3,T4,TSH level.
2. Co-relation between the types of oral lichen planus , site of occurrence and serum T3,T4,TSH level.
3. Age and sex related T3,T4,TSH level and types of Oral lichen planus

MATERIALS AND METHODS

The study population consists of 30 study subjects. The study subjects were recruited on the basis of inclusion and exclusion criteria. The Inclusion criteria includedPatients with clinically and histopathologically diagnosed lichen planusandpatients with stress history without clinical evidence of oral lichen planus. However the study subjects were excluded from study having Lichenoid reactions, systemic diseases and those not interested to participate in study.The whole blood sample(5ml) will be collected from oral lichen planus patient diagnosed by clinical and histopathology examination. The serum of same patients will be analysed for levels of thyroid hormones (free triiodothyronine T3, free thyroxineT4 and thyroid-stimulating hormone TSH). T3,T4 value is determined by electro-chemiluminescence immunoassay analyzer (ECLIA) method usingthe Cobas6000/8000 system (Roche Diagnostics Scandinavia AB, Stockholm, Sweden) however TSH value is determined by ultrasensitive enhanced chemiluminescence (Ultra sensitive 4th generation Chemiflex).

RESULTS

The study population consists of 30 study subjects with minimum age of 25 years to 56 years. The serum tri-iodothyronine (T3) ranges from .75nmol/l to 4.29 nmol/l. The serum thyroxine (T4) ranges from 73.9 to 136.2 nmol/l. The serum thyrotropin (TSH) ranges from .27 to 126.3 micIU/Ml.(Table.1).Based on the age group, study population has been divided in 3 age groups. The maximum number of study subjects (23) belongs to 25 to 40 years of age followed by 41-50 years of age (3) and 2 in 51-60 yrs age group (Table.2).The study population is dominated by male (63.3%) population followed by female population (36.7 %)(Table.3). The type of oral lichen planus in study population consists of 50% cases of reticular oral lichen planus followed by erosive lichen planus(26.7%),Atrophic type (16.7%) and bullous (6.7%) type of oral lichen planus.(Table.4). In the study population on the basis of site of occurrence,oral lichen planus is most commonly(highest in) found on right and left buccal mucosa(53.3%) followed by right buccal mucosa and gingiva (16.7%), tougue(10%) and left buccal mucosa (3.3%)(Table.5).For serum Triiodothyronine T3, four group of reference have been considered in study population. The group 2 consists of maximum number (17) of study subjects followed by group 3, group 1 and group 4 (Table.6).For serumthyroxine T4, 2 groups of reference have been considered in study population. The group 1 consists of 63.3% while group 2 consists of 36.7% of study population (Table.7).For the serum thyrotropin (TSH), 4 groups of reference have been considered in study population, group 2 and group 4 has 26.7 % population while group 1 and group 3 have 23.3% of study population(Table.8).The 4 groups of serum reference level for T3 (Serum Tri-iodothyronine) have been co-related with subtypes of Oral lichen planus and it was found that the serum T3 level is independent of types of Oral lichen planus i.e. the serum T3 level varies irrespective of clinical subtypes of oral lichen planus.(p value<.05)(Table.9).The 2 groups of serum reference level for T4 (Serum thyroxine) have been co-related with clinical subtypes of Oral lichen planus and it was found that the serum T4 level is independent of clinical subtypes of Oral lichen planus i.e. the serum T4 level varies irrespective of clinical subtypes of oral lichen planus.(p value<.05)(Table.10).For the serum thyrotropin (TSH) level, 4 groups of reference have been co-related with clinical subtypes of oral lichen planus and it was found that the serum thyrotropin (TSH) level varies irrespective of clinical subtypes of oral lichen planus.(p value<.05) (Table.11).

So it was concluded that serum T3, T4, and TSH level is independent of clinical subtypes of Oral lichen planus i.e. the serum level of T3, T4, and TSH is not specific to particular type of Oral lichen planus. It varies from type to type.The clinical subtypes of oral lichen planus are compared in age groups and it was found that the occurrence of clinical subtypes of oral lichen planus is independent of age (P value<.05%).

The clinical subtypes of oral lichen planus are compared gender wise and it was found that the occurrence of clinical subtypes of oral lichen planus is irrespective of gender (P value<.05%) (Table.13). The serum T3, T4 and TSH level is compared gender-wise and it was found that theserum T3, T4 and TSH level is statistically not significant in male and females(Table.14,15,16). The serum T3, T4 and TSH level is compared in age group and it was found that theserum T3, T4 and TSH level is statistically not significant in age groups.(Table.17,18,19).

Table 1 Showing the range of T3, T4 and TSH

	N	Range	Minimum	Maximum	Mean	Std. Deviation
Age	30	31.00	25.00	56.00	36.0000	9.04395
T3nmol/l	30	3.54	.75	4.29	1.5453	.78849
T4nmol/l	30	62.25	73.95	136.20	98.2767	20.14940
TSH micIU/Ml	30	126.03	.27	126.30	11.8227	28.64040

Table 2 Showing the age wise distribution of study population

Age intervals	N	Percent
25 to 40 years	23	76.7
41 to 50 years	5	16.7
51 to 60 years	2	6.7
Total	30	100.0

Table 3 Gender-wise distribution of study population

Gender	N	Percent
Male	19	63.3
Female	11	36.7
Total	30	100.0

Table 4 Distribution of type of oral lichen planus in study population

Types of lichen Planus	N	Percent
Atrophic	5	16.7
Bullous	2	6.7
Erosive	8	26.7
Reticular	15	50.0
Total	30	100.0

Table 5 Site-wise distribution of oral lichen planus in study population

Site of lichen Planus	N	Percent
Gingiva	5	16.7
Tongue	3	10.0
Leftbuccal mucosa	1	3.3
Rightbuccal mucosa	5	16.7
Right and leftbuccal mucosa	16	53.3
Total	30	100.0

Table 6 Distribution of study population at 4 serum reference level of T3

T3 category (Serum Triiodothyronine)	N	Percent
0.5 to 0.75	1	3.3
0.76 to 1.5	17	56.7
1.6 to 3.0	11	36.7
>3.0	1	3.3
Total	30	100.0

Table 7 Distribution of study population at 2 serum reference level of T4

T4 category (Serum thyroxine)	N	Percent
40-100	19	63.3
101-150	11	36.7
Total	30	100.0

Table 8 Distribution of study population at 4 serum reference level of TSH

TSH category (Serum thyrotropin)	N	Percent
0.25 to 1.5	7	23.3
1.51 to 3.0	8	26.7
3.0 to 4.0	7	23.3
>4.0	8	26.7
Total	30	100.0

Table 9 Showing the correlation between types of oral lichen planus and all 4 levels of T3

		Types of Oral lichen Planus (OLP)				
		Atrophic OLP	Bullous	erosive (OLP)	reticular (OLP)	Total
T3 category	0.5 to 0.75	0	0	0	1	1
		.0%	.0%	.0%	6.7%	3.3%
	0.76 to 1.5	3	1	3	10	17
		60.0%	50.0%	37.5%	66.7%	56.7%
	1.6 to 3.0	2	1	5	3	11
		40.0%	50.0%	62.5%	20.0%	36.7%
	>3.0	0	0	0	1	1
		.0%	.0%	.0%	6.7%	3.3%
Total		5	2	8	15	30
		100.0%	100.0%	100.0%	100.0%	100.0%

p-value=0.787; consider not significant

Table 10 showing the correlation between types of oral lichen planus and all 2 levels of T4

		Types of lichen Planus				
		atrophic olp	Bullous olp	erosive olp	reticular olp	Total
T4 category	40-100	2	2	5	10	19
		40.0%	100.0%	62.5%	66.7%	63.3%
	101-150	3	0	3	5	11
		60.0%	.0%	37.5%	33.3%	36.7%
Total		5	2	8	15	30
		100.0%	100.0%	100.0%	100.0%	100.0%

p-value=0.493; consider not significant

Table 11 showing the correlation between types of oral lichen planus and all levels of TSH

		Types of lichen Planus				
		Atrophic (OLP)	Bullous (OLP)	Erosive (OLP)	Reticular (OLP)	Total
TSH category	0.25 to 1.5	1	2	1	3	7
		20.0%	100.0%	12.5%	20.0%	23.3%
	1.51 to 3.0	2	0	3	3	8
		40.0%	.0%	37.5%	20.0%	26.7%
	3.0 to 4.0	2	0	1	4	7
		40.0%	.0%	12.5%	26.7%	23.3%
	>4.0	0	0	3	5	8
		.0%	.0%	37.5%	33.3%	26.7%
Total		5	2	8	15	30
		100.0%	100.0%	100.0%	100.0%	100.0%

p-value=0.275; consider not significant

Table 12 showing the co-relation between age group and types of oral lichen planus

		Types of lichen Planus				
		Atrophic (OLP)	Bullous (OLP)	Erosive (OLP)	Reticular (OLP)	Total
Age intervals	25 to 40 years	4	2	6	11	23
		80.0%	100.0%	75.0%	73.3%	76.7 %
	41 to 50 years	1	0	2	2	5
		20.0%	.0%	25.0%	13.3%	16.7 %
	51 to 60 years	0	0	0	2	2
		.0%	.0%	.0%	13.3%	6.7%
Total		5	2	8	15	30
		100.0%	100.0%	100.0%	100.0%	100.0 %

p-value=0.812; consider not significant

Table 13 Gender-wise co-relation between types of oral lichen planus

		Types of lichen Planus				Total
		Atrophic (OLP)	Bullous (OLP)	Erosive (OLP)	Reticular (OLP)	
Gender	Male	3 60.0%	1 50.0%	5 62.5%	10 66.7%	19 63.3%
	Female	2 40.0%	1 50.0%	3 37.5%	5 33.3%	11 36.7%
Total		5 100.0%	2 100.0%	8 100.0%	15 100.0%	30 100.0%

p-value=0.969; consider not significant

Table 14 Gender-wise distribution of T3

		Gender		Total
		Male	Female	
T3 category	0.5 to 0.75	1 5.3%	0 .0%	1 3.3%
	0.76 to 1.5	9 47.4%	8 72.7%	17 56.7%
	1.6 to 3.0	8 42.1%	3 27.3%	11 36.7%
	>3.0	1 5.3%	0 .0%	1 3.3%
Total		19 100.0%	11 100.0%	30 100.0%

p-value=0.500; consider not significant

Table 15 Gender-wise distribution of T4

		Gender		Total
		Male	Female	
T4 category	40-100	12 63.2%	7 63.6%	19 63.3%
	101-150	7 36.8%	4 36.4%	11 36.7%
Total		19 100.0%	11 100.0%	30 100.0%

p-value=0.979; consider not significant.

Table 16 Gender-wise distribution of TSH

		Gender		Total
		Male	Female	
TSH category	0.25 to 1.5	4 21.1%	3 27.3%	7 23.3%
	1.51 to 3.0	6 31.6%	2 18.2%	8 26.7%
	3.0 to 4.0	4 21.1%	3 27.3%	7 23.3%
	>4.0	5 26.3%	3 27.3%	8 26.7%
Total		19 100.0%	11 100.0%	30 100.0%

p-value=0.873; consider not significant.

Table 17 Co-relation between age group and Serum T3 levels

		Age intervals			Total
		25 to 40 years	41 to 50 years	51 to 60 years	
T3 category	0.5 to 0.75	1 4.3%	0 .0%	0 .0%	1 3.3%
	0.76 to 1.5	10 43.5%	5 100.0%	2 100.0%	17 56.7%
	1.6 to 3.0	11 47.8%	0 .0%	0 .0%	11 36.7%
	>3.0	1 4.3%	0 .0%	0 .0%	1 3.3%
Total		23 100.0%	5 100.0%	2 100.0%	30 100.0%

p-value=0.323; consider not significant.

Table 18 Co-relation between age group and Serum T4 levels

		Age intervals			Total
		25 to 40 years	41 to 50 years	51 to 60 years	
T4 category	40-100	14 60.9%	3 60.0%	2 100.0%	19 63.3%
	101-150	9 39.1%	2 40.0%	0 .0%	11 36.7%
Total		23 100.0%	5 100.0%	2 100.0%	30 100.0%

p-value=0.537; consider not significant.

Table 19 Co-relation between age group and Serum TSH levels

		Age intervals			Total
		25 to 40 years	41 to 50 years	51 to 60 years	
TSH category	0.25 to 1.5	6 26.1%	0 .0%	1 50.0%	7 23.3%
	1.51 to 3.0	4 17.4%	3 60.0%	1 50.0%	8 26.7%
	3.0 to 4.0	7 30.4%	0 .0%	0 .0%	7 23.3%
	>4.0	6 26.1%	2 40.0%	0 .0%	8 26.7%
Total		23 100.0%	5 100.0%	2 100.0%	30 100.0%

p-value=0.232; consider not significant.

DISCUSSION

Oral lichen planus (OLP) is a member of the family of oral lichenoid reactions (OLR).The concept of OLR is used to define a number of diverse immune-mediated conditionslinked together by the presence of common clinical and histopathological features[6]. Except for OLP, the other mucosal lesions that belong to the group of OLR are: oral lichenoid contact reactions, oral lichenoid drug reactions and orallichenoid lesions of graft-versus-host disease. Although the pathological process willalways result in the same reaction pattern, each of the OLR is governed by different immunological mechanisms and apparently triggered by different causative factors. Forinstance, oral lichenoid contact reactions are considered to be a delayed hypersensitivity reaction against dental materials, especially mercury-containing amalgam[7,8,9]. Oral lichenoid drug reactions represent an adverse effect of systemic medications [10,11] while oral lichenoid lesions of graft-versus-host disease are a common complication following allogeneic hematopoietic stem cell transplantation[12,13]. In contrast, the aetiology or aetiologies of OLP areyet unknown.

The term lichen planus is derived from the Greek word *leikhēn*, which means "what eatsaround itself", and the Latin wordplanus, which denotes "flat, level". The word *lichen* was probably coined by Theophrastus in the 4th century BC in order to describe a superficialgrowth on the bark of olive trees, but it was not until early 17th century when the term was reintroduced in the botany field. The current definition of lichenis "a simpleslow-growing plant which typically forms a low crust-like, leaf-like, or branching growthon rocks, walls, and trees"[14].

The first to describe and name lichen planus in a medical context was the dermatologistSir William James Erasmus Wilson[15]. He characterized the disease as "aneruption of pimples remarkable for their colour, their figure, their structure, their habitsof isolated and aggregated

development".Although Wilson recorded the coexistence of oral lesions in some of his patients with lichen planus, it was Thibierge[16] (1885) who published the initial clinical report on OLP. Later, Louis-Frédéric Wickham further characterized the lesions adding "*stries et punctuations grisatres*" (greyish striae and dots) tothe previously described features[17]. This remarkable finding, which later received the name of Wickham's striae, still represents the cornerstone in the clinicaldiagnosis of lichen planus. Finally, Dubreuilh[18]was the first to describe thehistopathology of an OLP lesion.Only a few studies, in which representative random samples drawn from the general population were investigated, reveal minor methodological issues[19,20,21,22,23,24]. The overall prevalence of OLP reported in these studies and presented in the review by McCartan & Healy[25] (2008) as age-standardized rates, ranges from 0.47% to 1.27%, with a markedly women predilection. The estimated overall prevalence of OLP (age-standardized rates) in the Swedish population is 1.27%, 0.96% in men and 1.57% in women[22]. It is important to highlight that the clinical criteria used for the diagnosis of OLP in this study did not allow the exclusion of other forms of OLR, which may have overestimated the reported figures. The incidence of OLP has been reported in a Japanese population to be 59.7 in men and 188.0 in women per 100.000 person-years (0.06% and 0.19%, respectively)[26].

Clinical Characteristics

Lichen planus The most common is the reticular form which is characterized by white keratotic dots and lines (the so-called Wickham's striae) that coalesce to create an annular or lacypattern. The striae are often surrounded by an erythematous area, which reflects asubepithelial inflammation. The papular form is considered to be an early phase ofOLP[27] and is seen as small white dots that frequently appear in combination with a reticular pattern. The plaque-like form shows a homogeneous and relatively well-demarcated white plaque that resembles a homogeneous oralleukoplakia. However, the presence of striae and erythema in the periphery of the lesionis not a finding compatible with oral leukoplakia. The reticular, papular and plaque-like forms constitute the white OLP lesions. These types of OLP may be detected in all regions ofthe oral mucosa either unilaterally or bilaterally and also on the lips, although the buccal mucosa is usually the most affected area with a bilateral distribution.The erythematous form appears as homogeneous red patches accompanied by whitestriae or papules in the periphery. When this form exclusively affects the attachedgingiva, the white dots and striae are frequently absent and the lesion resembles mucous membrane pemphigoid or any other lesion associated with erythema. The ulcerative form is the most disabling type of OLP. It displays a fibrin-coated ulcer in the centreof the lesion surrounded by an erythematous area and white striae in the periphery.

Diagnostic Criteria for OLP and Other Oral Mucosal Lesions

In study I, the diagnostic labels and criteria for oral mucosal lesions were in accordance with the WHO, the Application of the International Classification of Diseases to Dentistry and Stomatology and with the modifications and complementary additions suggested by Axéll[21,22]and Axéll *et al*[28]. In studies II, III and IV, specialists in oral medicine established the diagnosis of OLP following the clinical and histopathological criteria according to the WHO[29]. However, biopsies were only taken when the disease was divergent from thetypical clinical manifestations, as has been previously suggested[30].All lesions had to present with reticular or papular features with or without plaque,erythema or ulcerations. OLP lesions were clinically classified as papular, plaque-like,reticular, erythematous or ulcerative, based on the most predominant form of the lesion.Gingival OLP with erythema but without striae or papules, which is sometimes referred to as an OLL[31]was also included. Patients who presented with other types of oral mucosal lesions, including oral lichenoid contact reactions, were excluded from these studies.

Triiodothyronine (T3)

Thyroid hormones (T3 and T4) are normally synthetized and secreted by the thyroidgland. T3 constitutes approximately 20% of the total hormone production in the thyroid;the rest is produced by the conversion (deiodination) of T4 to T3 in peripheral tissues. T3and T4 regulate a number of developmental, metabolic and neural activities throughoutthe body. Circulating levels of T3 are much lower than levels of T4, but T3 is morebiologically active (3-4 times more potent than T4). Thyroid hormones circulate primarilybound to carrier proteins; only a small fraction (less than 1%) circulates unbound (free).Only the free forms are biologically active. Free T3 (FT3) is therefore a measurement ofthe fraction of circulatory T3 that exists in free state in the blood and is important inevaluating the effectiveness of thyroid replacement therapy, in ruling out T3thyrotoxicosis, and in detecting protein-binding abnormalities. Elevated FT3 values areindicative of T3 toxicosis (if T4 values are normal) or hyperthyroidism, whereas decreasedFT3 values are found in primary and secondary hypothyroidism. However, FT3 is not a reliable marker for hypothyroidism.

Thyroxine (T4)

T4 is the major hormone derived from the thyroid gland. It is metabolized to T3 peripherally by deiodination, and is therefore considered a reservoir or prohormone for T3. Approximately 0.05% of circulating T4 is in the free or unbound portion. Free T4 (FT4) may more accurately measure the physiologic amount of T4 and is usually measured together with thyroid-stimulating hormone when thyroid disease is suspected. FT4 testing is also used to monitor the appropriateness of thyroid replacement therapy. Elevated FT4 values suggest hyperthyroidism or over-replacement in patients treated with levothyroxine sodium, whereas decreased levels are compatible with hypothyroidism orunder-replacement.

Thyroid-Stimulating Hormone (TSH)

TSH also known as thyrotropin is synthetized and secreted by the anterior pituitarygland in response to a negative feedback mechanism involving FT3 and FT4. Additionally the thyrotropin-releasing hormone (TRH) which is secreted by the hypothalamusdirectly stimulates TSH production. TSH interacts with specific cell receptors on thethyroid cell surface and gives rise to 2 main actions. First, it stimulates cell reproduction and hypertrophy. Second, it stimulates the thyroid gland to synthesize and secrete T3 and T4.TSH testing is useful for detecting thyroid dysfunction (both primary hypothyroidismand hyperthyroidism) and monitoring thyroid replacement therapy. Elevated TSH levelsindicate primary

hypothyroidism whereas decreased levels suggest hyperthyroidism. TSHis also important in the differential diagnosis of primary (thyroid) from secondary (pituitary) and tertiary (hypothalamus) hypothyroidism in which TSH levels are low or normal. Elevated TSH in the presence of normal FT3 and FT4 levels is often referred to as subclinical hypothyroidism.

It could be questioned if dental patients with no oral mucosal lesions are the most appropriate controls when investigating the medication profile of patients with OLP andif they are representative of the general population. In order to tackle this issue, we aimed to compare in study III, the prevalence of levothyroxine supplementation and thyroid disease in the general population with an even larger cohort of patients with OLP. The results from this study confirmed the marked difference presented in study II on the prevalence of levothyroxine supplementation in patients with OLP compared to controls. Although the retrospective design of study III could not establish a temporal relationship between the onset of OLP lesions and the use of levothyroxine, nearly 80%of the patients reported that the start of levothyroxine supplementation preceded the diagnosis of OLP. This indicated that either levothyroxine supplementation or an underlying thyroid disease might play a role in the development of OLP lesions in a subgroup of patients. Furthermore, it was shown that nearly 80% of the patients with OLP using levothyroxine had a diagnosis of primary hypothyroidism for reasons other than surgery or irradiation. OLP has previously been associated with hypothyroidism[32,33,34]. In the study by Siponen *et al*[32], it was established that all patients with OLP who were using levothyroxine (n=15) had an initial diagnosis of hypothyroidism. Hirota *et al*[33] found that 10.9% of patients with OLP (n=110)had hypothyroidism, compared to 5.3% of the controls (n=76). Lo Muzio *et al*[34]reported from a series of 105 OLP patients without a previous diagnosis of thyroiddisease, that 14.3% had Hashimoto's thyroiditis. A high prevalence of hypothyroidismhas also been shown in patients with lichen ruber planus[35]. It was found that 10.0% of these patients (n=1477) had hypothyroidism compared to 5.7% of the control subjects (n=2856). Based on these studies and ours, it is evident that a subgroup of patients with lichen planus may have hypothyroidism, or eventually levothyroxine supplementation, as a common aetiological denominator.

The results from study III also showed that the course of OLP lesions was different between patients with and without thyroid disease. The severity of the lesions was lower and the symptoms were milder in patients with thyroid disease when comparing the oral status between the primary examination and re-examination. In patients without thyroid disease, OLP lesions and subjective symptoms remained more constant over time. OLP is a chronic condition in which periods of remission and exacerbation are frequently observed. A complete resolution of the papular and reticular form may also occur[36] (Andreasen, 1968a). It has been shown that in the natural course of OLP the lesions tend to adopt a reticular pattern and that the initial erythematous/erosive forms are likely to decrease[27,37]. However in those studies, the course of OLP lesions in patients with and without thyroid disease was not examined. In studyIII, reticular forms of OLP were more prevalent and erythematous/erosive less prevalent in patients with thyroid disease than in patients without thyroid disease at the re-examination. Hence, patients with concomitant OLP and thyroid disease may represent aspecific subgroup of OLP patients with a different clinical presentation of the lesions over time.

The analysis of thyroid hormones in study IV showed that more OLP patients without a previously diagnosed thyroid disease have high levels of TSH and low levels of FT4compared to the general population. This finding is indicative of a higher prevalence of hypothyroidism in patients with OLP and corroborates the results from study III.

CONCLUSION

To conclude that a subgroup of patients with OLP may have an etiological background in common with thyroid disease. The reason for the high prevalence of thyroid disease in patients with OLP remains to be determined but it is likely that some mechanisms in sautoimmune disease are involved in the pathogenesis of this group of patients suffering from OLP. One such promising factor which will be evaluated in further research, is the high expression of TSHR in basal keratinocytes of OLP lesions.

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