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The Relationship between Triiodothyronine and Thyroid Stimulating Hormone Serum Level into Melasma Severity

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ABSTRACT

Background: Melasma is a chronic acquired hypermelanosis of the skin and relatively common skin disorder that primarily affects sunlight-exposed areas in women. While etiology of melasma is not yet well understood, a possible factor is thyroid hormones. Few studies have been conducted in order to find the relationship between melasma and thyroid disorders with varying results. This study is conducted to investigate the association between thyroid parameters (triiodothyronine and thyroid stimulating hormone) and melasma severity.

Aim: To determine the relationship between triiodothyronine (T3) and thyroid stimulating hormone (TSH) serum level into severeity of melasma.

Subject and method: Thirty six women with melasma aged >18 years old are included in the study group indoor at Dr. M. Djamil Hospital Padang. Exclusion criteria: pregnancy/lactation, using oral contraception, using hormonal therapy, taking photosensitizer systemic antifungi and anticonvulsant and taking topical/systemic of melasma treatment. History of sun protection usages and MASI score are recorded. Triiodothyronine and TSH level are measured by electrochemiluminescence-immunoasay (ECLIA) method.

Result: Mean age of melasma patients in this study: 47.52±8.11 years old. Malar type is more common than centrofacial (61,1%) and we did not find mandibular type. The most common severity of melasma: mild (19 out of 36 people). MASI score: 21.46±10.40. Mean serum level of T3 and TSH: 1.578±0.282 nmol/L and 1.773±1.457 µIU/L (p>0,05).

Conclusion: Mean serum levels of T3 and TSH hormones are not related to the severeity of melasma. Nevertheless, increasing levels of hormones are in accordance with the increase of melasma's severeity degree, although it is not statistically significant. Further study could be done by adding hypothyroidism to patients who have melasma and comparing them with control group by using cross-sectional comparative sampling. An equal sample number of each severity degree of melasma would be ideal and then evaluate psychological/stress factors to the subjects.

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Keyword: Triiodothyronine Hormone, Thyroid Stimulating Hormone, Melasma Severity.

Introduction

Melasma is an acquired hipermelanosis with irregular lesion, colored from light to dark brown, on sun-exposed areas. The lesion could appear either on the upper lip, nose, cheeks, chin, forehead, sometimes on the neck, chest and the dorsal arm. Melasma is usually shaped irregularly, often demarcated, with bright to brown-black pigmentation.

Melasma is epidemiologically found in all races. Based on available data, it is found more often on women rather than men. As much as 90% of the cases are found in people with an age range of 30 to 50 years old, but the exact number is unknown. Melasma is often found in tropical countries, including Indonesia, with a varying incidence rate in different spectrums of population. Melasma prevalence in Southeast Asia reaches 40% in female and 20% in male. Incidence rate of melasma in women during 2012-2014 at the Dermato-Venereology Outpatient Clinic of Dr. M. Djamil Hospital Padang is 129 (0.095%) out of 1,355 patient visits to the Division of Cosmetic Dermatology (non-publication). The etiology of melasma is not yet known for certain, but there are several factors that play a role in melasma pathogenesis such as exposure to ultraviolet radiation, genetic predisposition, pregnancy, oral contraceptives, hormone replacement therapy, cosmetics, phototoxic medications, anticonvulsant drugs and endocrine factors associated with thyroid disorders. Thyroid disorder is known to involve the entire organ system of the body and the skin is no exception. Both hyperthyroidism and hypothyroidism cause changes to structure and function of the skin.

Assessment levels of T3 and TSH serum is a useful indicator to determine the status of clinical hypothyroidism as TSH serum concentration is a sensitive indicator of thyroid dysfunction. If the thyroid function is abnormal, TSH serum level will change even under subclinical conditions. Thyroid stimulating hormone serum levels that exceed 2.5 µIU/mL is referred as subclinical hypothyroidism. Hypothyroidism is clinically defined as endocrine status with a value of TSH> 4.0 µIU/L; T3<1.2 nmol/L. The

relationship between thyroid hormone and the incidence rate of melasma has long been studied, but the relationship between them is very complex and there is only limited research.

Subjects and Methods

This study is an observational analytic study with a cross-sectional design. It is conducted at the Division of Cosmetic Dermatology of Outpatient Clinic of Dr. M. Djamil Hospital Padang and the Regional Health Laboratory Padang. Subjects of research are patients with a diagnosis of melasma who come to the Division of Cosmetic Dermatology of Outpatient Clinic and worked at Dr. M. Djamil Hospital Padang. The study is approved by the the Faculty of Medicine Ethics Committee, Andalas University Padang.

The number of samples are determined by a sampling quota method based on a specified number. The specified number of samples in this study are 36 people who has been verified through the inclusion and exclusion criteria. The study is conducted from January to May 2016.

Inclusion and exclusion criteria

Inclusion criteria: women with melasma aged >18 years old, working indoor between 9am to 3pm local time and willing to participate in the study by signing an informed consent after being given an explanation of the study. Exclusion criteria: pregnant and nursing women, taking oral contraceptives, received hormonal therapy, taking systemic antifungal (griseofulvin) or photosensitiser medication (amiodarone, tetracycline, minocycline, chloroquine, cytostatics such as cyclophosphamide, 5-flourouracil, doxorubicin, daunorubicin and bleomycin, heavy metals, inorganic arsenic), treated by anticonvulsants (hydantoin, dilantin, phenytoin, phenothiazines, chlorpromazine, levodopa and barbiturates) and in treatment of melasma (topical and/or systemic).

Informed consent

All patients are required to provide a written informed consent for participation in the study.

Study Assessments

All patients are assessed for demographics including age, clinical distribution of melasma, melasma severeity degree and MASI score. Patients are examined to identify their distribution of melasma which is divided into three regions: centrofacial (cheeks, forehead, upper lip, nose and chin), malar (cheeks and nose) and mandibular (ramus of the mandible). All the patients are examined by a certified dermatologist.

Data collection

The data of all patients are collected in study protocol report forms and are saved to computer using Microsoft Excel for review.

Statistical Analysis

The mean age of all patients is calculated using observational analytic statistics. One-way analysis of variance (ANOVA) is performed to determine statistical difference in T3 and TSH mean value. The mean value of T3 and TSH to melasma severeity (for each degree of melasma) is obtained and evaluated for statistical significance using one-way ANOVA. A $p<0.05$ is considered as statistically significant.

A total of 36 female patients (ranged from 27 to 56 years old) with mean age of 47.52±8.11 years old suffering from melasma are included in the study. Observation at pattern of clinical features mostly found malar type in 22 (61.1%) while no mandibular type found on research subjects. Based on the severity of melasma, mild degree is mostly found in 19 people (52.8%). The mean value MASI scores in this study is 21.46±10.40 (table 1).

Table 1

Characteristic	f (n = 36)	p (%)
Age		
15 – 19 year-old	0	0
20 – 24 year-old	0	0
25 – 29 year-old	1	2,7
30 – 34 year-old	4	11,1
35 – 39 year-old	1	2,7
40 – 44 year-old	3	8,3
45 – 49 year-old	9	25
> 50 year-old	18	50
Mean ± standard deviation	47,52 ± 8,11 year-old	
Pattern of clinical features		
Malar	22	61,1
Centrofacial	14	38,9
Mandibular	0	0
Severity		
Mild	19	52,8
Moderate	12	33,3
Severe	5	13,9
MASI Score	Mean Value	
Mild	13,15	
Moderate	27,54	
Severe	38,42	
Mean ± standard deviation	21,46 ± 10,40	

The mean value levels of T3 and TSH in severe degree of melasma is higher (1.605±0.309 and 2,4±1,158) compared to mild and moderate degree. As seen in each degree, there is an increasing mean value of T3 and TSH (table 2).

Table 2

Melasma Severity	Mean value of T3 serum level (nmol/l)	Mean value of TSH serum level (µIU/L)
Mild	1,572 ± 0,340	1,607 ± 1,723
Moderate	1,574 ± 0,169	1,776 ± 1,089
Severe	1,605 ± 0,309	2,4 ± 1,158

Relationship between T3 and TSH serum level to the severeity of melasma as analysed using ANOVA statistical test does not find a significant association between mean value of T3 and TSH serum levels to the severeity of melasma (1.578±0.282 nmol/L and 1.773±1.457 µIU/L; $p>0.05$) (table 3).

Table 3

Melasma Severity	Mean value of T3 serum level (nmol/l)	p value	Mean value of TSH serum level (µIU/L)	p value
Mild	1,572	1,000	1,607	1,000
Moderate	1,574	1,000	1,776	1,000
Severe	1,605	0,085	2,400	0,879
Mean ± standard deviation	1,578 ± 0,282	0,975	1,773 ± 1,457	0,571

Discussion

Mean age of patients suffering from melasma the study is 47.52±8.11 years old. Epidemiologically, mean age of patients suffering from melasma in women is aged between 30 and 50 years old. Mean age of patients in this study therefore corresponds to the epidemiology of melasma.

Based on age, T3 hormone levels is reduced at an older age due to secretion of thyroid hormone T3. Although TSH level is relatively stable between 40 and 50 years old, it can be decreased or increased through iodine intake. In case of decreasing level of TSH, it is caused by the increasing sensitivity of pituitary gland to decrease circulating thyroid hormones and TSH secretion. As the secretion of hormones T3 and TSH are influenced by age, in normal circumstances despite T3 hormone declines with increasing age, TSH can either decrease or increase. In this study, mean age of patients suffering from melasma is in the range of epidemiological age (between 30 and 50 years old). Therefore, it can be concluded that in this study, age does not affect the level of hormones T3 and TSH.

The pattern of clinical feature malar type is found in 22 patients (61.1%). There is no mandibular type in this study because of mandibular type is rarely found (16%). Melasma is more commonly found on sun-exposed areas such as forehead, nose, cheeks, chin and upper lip, whereas the mandible area is rarely exposed to sun.

Indonesia is a tropical country, where it is exposed to the sun with strong enough intensity almost all year long. In countries with 4 seasons, people with melasma are more prevalent in the summer and appear to be less in winter. This shows the magnitude of relationship between the severeity of melasma and sun exposure. Based on theories and research results that are previously discussed where T3 and TSH hormone levels are lower in the summe and Indonesia is a tropical country with strong intensity of exposure to the sun, it can be concluded that the patttern of clinical feature of melasma is greatly influenced by the ultraviolet where the malar and centrofacial type are found in this study. However, since the whole subject of research is worked indoor and not exposed to sunlight at peak time (between 10am and 2pm), it can be concluded that exposure to sunlight does not affect thyroid hormone level on the subjects of this study.

Results of melasma severeity mostly found to be mild in 19 (52.8%) out of 36 people. According to the reviews mentioned by Handel AC, et al. (2014) patients who have melasma are often more motivated to go to a dermatologist. Cestari T, et al. (2006) examine 300 patients suffering from melasma with a result of 65% patients report feeling discomfort because of patches on their face, 55% feeling frustrated and 57% feeling ashamed of the disease. This is because melasma appears mainly on the face, although mild, do often cause cosmetic and psychological problems. Women, especially, in turn will quicky go to a dermatologist.

The mean value of MASI score is 21.46±10.40. Validity testing shows that the MASI score is able to provide precise estimation of on melasma severeity. Total MASI score on mild degree is <24, moderate is if the total score is between 25 and 36, whilst severe is if the total score is between 37 and 48. Triiodothyronine hormone level affects the degradation of melanosomes at the time of melanin transfer to keratinocytes and their resillience in kreatinocytes, whereas TSH affects the amount of melanin in melanogenesis. The mean proportion of the number of samples in each degree of melasma is not equal where mild degree has the most subjects (19 people/52.8%).

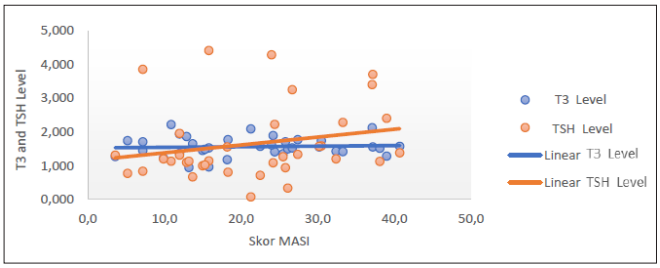
The distribution of mean value of T3 and TSH serum level is in the normal range (1.605±0.309 and 2.4±1.158). The mean value result of the two hormones are relatively normal. It might be caused by the compensation of endocrine hormones' negative feedback loop in the thyroid gland pituitary. Table 2 shows an increase in T3 and TSH serum levels due to the severeity of melasma.

TSH serum level that exceed 2.5 µIU/L is referred as subclinical hypothyroidism. Hypothyroidism is clinically defined as endocrine status with a value of TSH > 4.0 µIU/L and T3 < 1.2 nmol/L. Normal TSH value is ranged from 0.5 to 4.0 µIU/L and T3 from 1.2 to 1.8 nmol/L. T3 and TSH serum levels are useful indicators for determining the status of hypothyroidism. Clinical concentration of TSH serum is a sensitive indicator of dysfunction tiroid.

Melasma is the result of hyperactivity of local dermal-epidermal melanin unit resulting in hypermalanisation. Epidermal hypermalamisation is influenced by thyroid hormones. Hypothyroidism occurs in the case where melanogenesis and intact of melanosomes epidermis increase. In case of hypothyroidism, the levels of T3 and T4 are decreasing and a negative feedback loop on the hypothalamus and the pituitary gland of the brain activate and stimulate the formation of TRH. TSH level then increases and produces pro-hormones T4 and the active from T3.

Research on the relationship between melasma and thyroid hormone has been carried out for years. Perez M, et al. (1983) found a link between hormone in the incidence of melasma, but the data obtains many conflicting views possibly due to various genetic backgrounds on study populations. On the other hand, the relation between thyroid hormone abnormalities and the incidence of melasma has not yet been reported much. Handel AC, et al. (2014) states there is no strong evidence to support a connection between thyroid abnormalities to melasma and melasma or thyroid disease even though it is very common in women.

Statistic analysis result using ANOVA test in this study found no significant relationship between the mean value of T3 and TSH hromone levels to the severeity of melasma. Even so, mean value of both hormones in each of the severeity degree of melasma is associated with an increase to the severeity of melasma (graphic 1).



Graphic

Aetiopathogenesis melasma that has not been evaluated by the researcher is the emotional stress factors. There have been case reports of melasma that is obtained onset after an episode of emotional stress and affective disorders (e.g. depression). Level of stress on a person can be desribed as interference or may cause physiological and psychological malfunctioning to someone. Stressor can come from outside the human body (external stressor) and internal stressor (associated with genetic factors, development and growth). External stressors can be measured using a scale, the one that is used is the Holmes scale. The scale that is used to measure the level of an external stressor which the questions are given is a general perception that could potentially cause stress on the subjects.

Several studies that prove stress affects the skin through nerupeptidergic peripheral nerve fibers and exacerbates beurogenic aspect because melanocytes is derived from the neural crest. This explains why the melanocytes in human skin has been linked with neural fibers. Some hormones that activate the melanocortin receptor that induces melanogenesis which are propiomelanocortin, adrenocorticotropin hormone (ACTH) and melanocyte stimulating hormone (MSH), of which are related to stress. Besides affecting melanogenesis, hormone level changes in response to stress, one of the hormones that are affected by stress conditions is thyroid hormone. Thyroid function usually is down-regulated during stressful conditions. Triiodothyronine and tyroxine levels is decreased in a state of stress. Stress inhibits the secretion of TSH as the action of glucocorticoids on the central nerveous system. Verma K, et al. (2016) in their study shows 40.9% of the total 66 study subjects had a history of stress and emotional factors before contracts melasma.

We did not assess the emotional stress factors on the subject of research. The status of hypothyroidism in this study subjects to melasma studied is not homogeneous. It is expected for further research to get the subject of research number equally to each degree of melasma severeity, homogeneous status of hypothyroidism in melasma patients and assess the emotional stress factors to get significant relationship between T3 and TSH serum level to melasma severeity.

Conclusion

The result of this study shows that mean levels of both T3 and TSH serum in melasma patients are relatively normal, nevertheless increasing level of both hormones are in accordance with an increase in the severeity of melasma. Further study can be done to larger subjects by adding the inclusion criteria of melasma patients with hypothyroidism and comparing them to control patients without hypothyroidism using cross-sectional comparative sampling and assess the stress factors using a scale to get more significant results [1-127].

Conflict of interest

I declare that there are no conflict of interrests regarding the publication of this paper.

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