Seluang (Rasbora agrotyenia) Fish Oil Increases Vitamin D in Autoimmune Patients (Systemic Lupus Erythematosus)

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Seluang (*Rasbora agrotyenia*) Fish Oil Increases Vitamin D in Autoimmune Patients (Systemic Lupus Erythematosus)

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Abstract. Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease which usually affects multiple organ systems. Its patients are prone to 20 povitaminosis D along with its complications such as osteoporosis. The improvement of vitamin D status in SLE patients is associated with better immune modulation, proinflammatory cytokine suppression, calcium absorption improvement, as well as better severity and lower osteoclastogenesis. This double-blind, rand mised clinical trial was conducted in the Allergology-Immunology Polyclinic in the Internal Medicine Department of Mohammad Hoesin General Hospital, Palembang, Indonesia, over the period April 2017 - February 2018. Samples were given either seluang (Rasbora agrotyenia) fish oil or placebo for 12 weeks. On the start and the end of the study, vitamin D levels were examined. 32 patients, all female, were divided evenly into the two groups. On the end of the study, the seluang oil group had significant vitamin D increase compared to placebo (p = 0.000) we concluded that the administration of seluang fish oil was able to increase vitamin D levels in SLE patients.

1. Introduction

Systemic lupus erythematosus (SLE) is an autoin tune disease which causes chronic inflammation as well as damage to most organs and tissues [1]. Genetic and environmental factors contribute to the pathogenesis of this ailment. SLE affects approximately 30 - 50 out of every 10,000 people worldwide, with young women in productive ages being the most common victims. Females are 12x more likely to get SLE compared to men [2,3].

The initiation of autoimmune disorders, including SLE, is thought to arise from several factors, such as vitamin D deficiency [4]. Vitamin D ha 12 crucial role in mineral metabolism, maintaining cardiovascular functions, and immune regulation. The prevalence of Vitamin D deficiency is relatively high, moreover, it could predict mortality from several chronic diseases, among which SLE. Consequently, vitamin D supplementation should the considered the first and foremost nutritional intervention in these patients. It is also recognised that vitamin D deficiency is not only a risk factor for developing autoimmune disorders (such as multiple sclerosis and type 1 DM), but also plays a role in worsening the created conditions, esepecially in SLE patients [5-7].

Generally, SLE patients will attempt to avoid direct sunlight exposure, unless they seek to develop photosensitive rashes. Most of the vitamin D in our body is synthesised on the skin after ultraviolet light exposure, but thanks to their sunlight avoidance, many SLE patients will not synthesise enough vitamin D [8]. Furthermore, dietary vitamin D sources are so rare that it is only found in fatty fishes. Salmon and mackerel, to name a few, are costly and thus inaccessible to the Indonesian public. IOP Conf. Series: Journal of Physics: Conf. Series 1246 (2019) 012036

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However, the seluang fish (*Rasbora agrotyenia*), which is abundant in the South Sumatran rivers, has been known to be beneficial for bone health. A recent study showed that the oil extracted from this particular fish contains an intensely high vitamin D content, with D3 levels of 4,086 IU/mL [9].

This study was aimed to investigate how the administration of seluang fish oil affect serum vitamin D levels, especially in SLE patients.

2. Methods

This deliber blind randomised clinical trial was conducted in the Allergy and Immunology Polyclinic at the Internal Medicine Department of Mohammad Hoesin General Hospi 13 Palembang, Indonesia, during the period April 2017 – February 2018. The samples were SLE patients who 23 Ifilled the American College of Rheumatology (ARA) criteria. The 32 samples were divided into the treatment group and the placebo group, whose randomisation was performed by computerised means. Following that, the samples were given seluang fish oil or placebo for 12 weeks, as a nutritional supplement to the routine therapy. In the beginning and at the end of the study, each subject were assessed for the severity of their lupus and their serum vitamin D levels.

The inclusion criteria were SLE patients who were diagnosed according to the ARA criteria, from a diverse age range of 15 – 50. Samples were excluded if they meet at least one of the following: (1) Severe SLE, (2) SLE with chronic comorbid diseases that would affect bone degeneration i.e. thyroid diseases, diabetes mellitus, bone malignancy, (3) Severely osteoporotic SLE, and (4) A completed or on-going biphosphonate therapy. This study has been approved with an ethical clearance certificate from the Ethical Committee of the Mohammad Hoesin General Hospital-Universitas Sriwijaya Medical School.

The SLE severity was assessed using the MEX-SLEDAI score. A score of < 2 means a mild disease activity, 2-5 means a moderate disease activity, and > 5 means severe activity. In addition, haemoglobin, leukocyte count, platelet count, reticulocyte count, SGOT, SGPT, ureum, creatine, and vitamin D levels were assessed.

The data then were analysed using SPSS version 22.0 $\[Engline{\mathbb{E}}\]$ Windows. We conducted a bivariate analysis using the T-test model with a significance threshold of p < 0.05.

3. Results

Table 1 shows the general characteristics of the subjects, which include: age, duration of disease, body mass indices, education, and occupation. Statistically, there were no significant differences between the two subject groups.

It is also evident that there were initially no differences in the serum levels of vitamin D in both groups before treatments were administered (p = 0.474). After being given seluang fish oil for 12 weeks, however, there was a significant difference between the two.

A Wilcoxon analysis of the vitamin D levels before vs. after the administration of seluang fish oil showed a significant change in the treatment (SF(1) group (p = 0.000). On the other hand, using a paired T-test, there were no before-after differences in the placebo group (p = 0.890).

4. Discussion

Vitamin D has both preventive and curative properties on SLE. The former is regulated genetically and repairs the immune system by decreasing the production and regulation of NF-kB, thus inhibiting IFN- γ and thereby reducing IL-2; as well as inhibiting the proliferation of cell B and inflammatory cytokines. While the latter is possible through the modulation of the immune system, thereby stopping the inflammation. The at 7 tion of vitamin D, primarily by diet, is expected to fix the defects of Treg cells, and also controls the activation of T and B cells. These will lead to a significant drop in proinf 16 natory cytokines, namely: IFN, TNF- α , IL-1, and IL-17 [10, 11].

IL-17 and IL-6 have be 21 implicated in the pathogenesis in SLE, thus making them decent biomarkers. High levels of IL-17 is associated with 15 nal damage (lupus nephritis), which may manifest as proteinuria. It has been demonstrated that 12 cells that produce IL-17 are more present in the circulation in SLE patients [12]. In another study, IL-6 is correlated with signs of active nephritis. Therefore, it should be used as the primary biomarker in active inflammation in SLE [13]. An elevated serum IL-6 in SLE patient can also be linked with anaemia of chronic disease [14].

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Table 1. General characteristics of subjects.

Characteristic	Group		– P value	
10 Characteristic	SFO	Placebo	- r value	
Age (years)				
 Mean ± SD 	30.31 ± 9.32	26.75 ± 8.96	0.227^{a}	
 Median (Min-Max) 	28 (16-49)	23.5 (17-46)		
Duration of disease (months)				
 Mean ± SD 	18.63±13.54	21.09±4.80	0.677^{a}	
19 • Median (Min-Max)	18 (3-36)	16 (3-84)		
Body mass index (kg/m ²)				
 Rerata ± SD 	22.44±2.99	22.59±4.35	0.917 ^b	
 Median (Min-Max) 	22.44	21.83		
	(17.31-28.76)	(16.83-29.9)		
BMI cate 6 y (kg/m²)	2 (12 50/)	2 (10 00/)	0.746	
Underweight: <18,5	2 (12.5%)	3 (18.8%)	0.746°	
 Normal: 18,5-22,9 	10 (62.5%) 1 (6.2%)	7 (43.8%) 1 (6.2%)		
 Overweight: 23-24,9 	3 (18.8%)	5 (31.2%)		
Obesity: >25	3 (18.8%)	3 (31.276)		
Education, n(%)				
 Primary school 	3 (18.8)	0 (0.0)		
 Junior secondary school 	0(0.0)	1 (6.2)	0.377c	
 Senior secondary school 	8 (50.0)	10 (62.5)		
 Diploma 	1 (6.2)	1 (6.2)		
Bachelor	4 (25.0)	4 (2.5)		
Occupation	1 (20.0)	1 (2.5)		
Housewife	8 (50.0)	7 (43.8)		
Civil servant	1 (6.2)	0 (0.0)		
Honorary worker	3 (18.8)	2 (12.5)	0.248c	
Private company worker	0 (0.0)	4 (25.0)		
Student (school/university)	4 (25.0)	3 (18.8)		
Serum Vitamin D (mmol/L)	4 (23.0)	3 (18.8)		
Mean + SD	44.91 ± 7.00	46.01 ± 0.16		
• Mean ± SD	44.81 <u>+</u> 7.09	46.91 ± 9.16	0.474 ^b	

^a Mann-Whitney test, p = 0,05; ^b Independent T Test, p = 0,05; ^c Chi Square, Pearson correlation, p = 0,05

Table 2. Vitamin D levels before and after seluang fish oil administration.

Group	Before	After	p-value
 SFO 	$44,81 \pm 7,09$	$60,46 \pm 8,25$	0,000
 Placeho 	46.91 ± 9.16	47.01 ± 9.17	0,890

This finding is consistent with the fact that SLE patients are prone to vitamin D deficiency. This condition could be caused by a variety of factors, one of them being the limited exposure to sunlight due to photosensitivity and the use of sun-block lotions. However, it should be noted that they are also experiencing chronic renal insufficiency, chronic inflammation, and most of them are regular users of steroid [15].

5. Conclusion

The administration of seluang fish oil was able to increase serum Vitamin D levels in SLE patients.

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