Original Article

Effect of soy isoflavones on acne vulgaris

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Abstract

Objective To demonstrate the effect of soy isoflavones on acne vulgaris (AV) lesions in female patients.

Methods In this randomized pretest-posttest control group design, 25 patients were randomized into 5 groups: isoflavones 40 mg, 80 mg, 120 mg, 160 mg and placebo, and treated for 4 weeks.

Results The mean total AV lesions before treatment among the five groups was similar (p=0.259), whereas after treatment significant difference was observed (p=0.001). Intergroup comparison revealed that decrease in the mean total AV lesion count before and after treatment was significant in isoflavone 160 mg group (p<0.05), while in the placebo, 40 mg, 80 mg, 120 mg groups it was insignificant (p>0.05).

Conclusion Soy isoflavones supplementation 160 mg/day can lower total AV lesion.

Key words
Acne vulgaris, soy isoflavones.

Introduction

Acne vulgaris (AV) is a skin disorder that affects nearly 80% of adolescents and young adults.[1-3] Several studies have shown that dihydrotestosterone (DHT), an androgen, is involved in the pathogenesis of acne and DHT levels correlates with the number of AV lesions, especially in women.[4,5]

The active component of soy isoflavones are genistein, daidzein and glycitein.[7-11] Consumption of soy isoflavones in Asian countries is four times more than in the Western countries, with average daily consumption in Asian countries 24-45 mg.[11-13] Soy isoflavones also affect androgen metabolism.[14]

The relationship between the consumption of soy isoflavones and AV is still unknown. The purpose of this study was to demonstrate the effect of oral supplementation of soy isoflavones on AV. This research could usefully contribute to science and technology, and improving the quality of health services. The major hypothesis of research was to test the effect oral supplementation of soy isoflavones on AV, while the minor hypothesis was to find the effect of varied dosing for 4 weeks on the number of AV lesions.

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Methods

The study design was an experimental research with randomized pretest-posttest control group design. This study used a variation of soy isoflavone doses, 40 mg, 80 mg, 120 mg and 160 mg for 4 weeks. A sample of 25 patients was randomized into 5 groups. Study population comprised of female patients of acne vulgaris who were treated in outpatient of hospital Kensaras Ungaran, Central Java, Indonesia. They were selected by consecutive sampling and subjected to the double-blind treatment. Standard drug used was 0.025% tretinoin cream and sunscreen SPF >15, while soy isoflavones used in this study were manufactured and standardized by the

pharmaceutical industry NU Health, California, United States. Inclusion criteria were women with mild to severe AV according to Lehman, not on any systemic medication, who did not suffer from hyperandrogenism, and were willing to sign informed consent. Exclusion criteria were allergy to soy isoflavones., pregnancy or oral contraceptives during past one month.

The independent variable was the soy isoflavones 40 mg/day, 80 mg/day, 120 mg/day, and 160 mg/day, given for four weeks. The dependent variable was the total number of AV lesions, examined by two dermatologist, then calculated interclass correlation coefficient and the coefficient alpha. Controlled confounding variables were age, body mass index, the average consumption of isoflavones from soy foods, stress status measured by Beck Depression Inventory,[15] hyperandogenism clinically assessed as amenorrhea, sound like men and hirsutism (Ferriman-Gallwey score).[16] Uncontrolled confounding variables weres genetic, racial, environmental pollutants and chemicals.

Analysis of the data calculated the difference in the mean lesion count before and after the study, while confounding factors controlled the randomization process. The degree of significance was be determined as $p<0.05$ with 95% confidence intervals. This study was approved by the Ethics Committee of the Faculty of Medicine/Hospital Kariadi Semarang City, Indoneisa.

Results

After screening 40 female patients with AV, 25 patients met the inclusion criteria and 15 patients were excluded from the study, due to refusal to blood sampling in 10 patients and cocurrent acne treatment in 5 patients. 25 patients were randomized into 5 groups, i.e. isoflavones 40 mg, 80 mg, 120 mg, 160 mg, and placebo groups. Mean age of the entire sample was 24.3±5.71 years with a range from 17 years to 34 years. The level of education was junior school in 1 (4.0%), high school in 23 (92.0%) samples, and university level in 1 (4.0%) patient. There were 15 (60.0%) laborers, 6 (24.0%) students, 2 (8.0%) civil servants, and 1 (4.0%) each was self-employed and jobless. The mean body mass index (BMI) was 20.8±1.39 with a range of 17.3 to 23.6 . The mean BMI in the placebo group was 21.2±0.43, isoflavone 40 mg was 20.7±0.79, isoflavone 80 mg was 21.1±2.08, isoflavone 120 mg was 20.6±2.24, isoflavone 160 mg was 20.5±1.39 (**Table 1**).

Majority of the patients i.e. 19 (76.0%) were unmarried. Age of menarche varied from 11 to 14 years. It started by the age of 11 years in 3 (12.0%) patients, 12 years of age in 17 (68.0%), 13 years in 4 (16.0%), and by the age of 14 years in 1 (4.0%). All patients among 5 groups had regular menstrual cycle of 28 days. Length of mentrual cycle was 4 days in 4 (16.0%) patients, 5 days in 17 (68.0%) and 6 days in 4 (16.0 %) patients, (**Table 2**).

Clinical signs and symptoms of hyperandrogenism were not seen in any patient. Majority of the patients 21 (84%) did not experience stress while mild stress was seen in 4 (16%) patients. All five groups were comparable in terms of disease severity The mean total AV lesion count before treatment did not show significant difference (unpaired one-way ANOVA, $p>0.05$). However, after treatment, the mean total lesion count showed significant difference (unpaired Kruskal-Wallis test, $p<0.05$) as shown in **Table 3**.

In individual groups, difference in the mean total lesion count before and after treatment in the group with 160 mg isoflavones demonstrated significant difference (paired t-test, $p<0.05$), whereas the placebo group isoflavones 80 mg, and 120 mg isoflavones results paired t-test did not differ significantly ($p>0.05$) and 40 mg of isoflavones with

Table 1 Characteristic data regarding age, education, and employment variable.

Variable	*Group*					*P*
	Placebo n=5	*Isoflavones 40 mg* n=5	*Isoflavones 80 mg* n=5	*Isoflavones 120 mg* n=5	*Isoflavones 160 mg* n=5	
Age (mean±SD, year)	20.2 ± 2.28	22.2 ± 6.73	25.6 ± 6.73	26.0 ± 5.96	27.4 ± 6.66	0.307[a]
Education level (n, %)						
Junior school	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	0.408[b]
High school	5 (100)	4 (80)	4 (80)	5 (100)	5 (100)	
University	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	
Employment (n, %)						
Did not work	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0.559[b]
Student	2 (40)	2 (40)	0 (0)	1 (20)	1 (20)	
Labour	3 (60)	3 (60)	3 (60)	2 (40)	4 (80)	
Self-employed	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	
Civil servants	0 (0)	0 (0)	1 (20)	1 (20)	0 (0)	
Body mass index	32.1±0.43	20.68±0.79	21.1±2,08	20.59±2.24	25.9±4.33	0.911[b]

[a] Kruskal-Wallis [b]Chi square, [b] One way ANOVA

Table 2 Marital status, pregnancy, family planning, menarche and long menstruation variable.

Variable	*Group*					*p*
	Placebo n= 5	*Isoflavones 40 mg* n=5	*Isoflavones 80 mg* n=5	*Isoflavones 120 mg* n=5	*Isoflavones 160 mg* n=5	
Married						
Yes	0 (0)	0 (10)	2 (40)	2 (40)	2 (40)	0.261*
No	5 (100)	5 (100)	3 (60)	3 (60)	3 (60)	
Pregnancy						
Yes	0 (0)	0(0)	0 (0)	0 (0)	0 (0)	
No	5 (100)	5(100)	5 (100)	5 (100)	5 (100)	
Family planning						
Yes	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
No	5 (100)	5 (100)	5 (100)	5 (100)	5 (100)	
Menarche						
<12 year	1 (20)	1 (20)	1 (20)	0 (0)	0 (0)	0.790*
≥ 12 year	4 (80)	4 (80)	4 (80)	5 (100)	5 (100)	
Long menstrual						0.439*
4 days	2 (40)	0 (0)	1 (20)	0 (0)	1 (20)	
5 days	3 (60)	3 (60)	3 (60)	5 (100)	3 (60)	
6 days	0 (0)	2 (40)	1 (20)	0 (0)	1 (20)	

* Chi square

Table 3. The mean difference of total AV lesions before and after treatment

Total AV lesions	*Placebo*	*Isoflavones 40 mg*	*Isoflavones 80 mg*	*Isoflavones 120 mg*	*Isoflavones 160 mg*	*p*
Before treatment	112.4 ± 64.47	65.4 ± 58,70	94.6 ± 24.07	88.0 ± 19,65	140.0 ± 70,.2	0.259[a]
After treatment	109.8 ± 59.92	64.4 ± 60,24	93.2 ± 26.08	82.4 ± 22,20	44.8 ± 32.24	0.001[b]

[a] One way ANOVA, [b] Kruskal Wallis, $p<0.05$ = significant

Table 4 . The mean difference of total AV lesions in all groups.

Group	*Mean total lesions before treatment*	*Mean total lesions after treatment*	*p*
Placebo	112.4 ± 64,47	109.8 ± 59,92	0.480[1]
Isoflavones 40 mg	65.4 ± 58,70	64.4 ± 60,24	0.715[2]
Isoflavones 80 mg	94.6 ± 24,07	93.2 ± 26,08	0.624[1]
Isoflavones 120 mg	88.0 ± 19,65	82.4 ± 22,20	0.098[1]
Isoflavones 160 mg	140.0 ± 70,92	44.8 ± 32,24	0.007[1]*

[1] Paired t test, [2] Wilcoxon signed ranks test * $p<0.05$

Table 5 Kruskal-Wallis test of differences in delta AV lesions between the placebo group, isoflavones 40 mg, 80 mg, 120 mg, and 160 mg.

Groups	*Mean±SD, delta AV lesions*	*p*
Placebo	-2.6 ± 7.470	
Isoflavones 40 mg	-1.0 ± 6.325	
Isoflavones 80 mg	-1.4 ± 5.899	0.013*
Isoflavones 120 mg	-5.6 ± 5.814	
Isoflavones 160 mg	-95.2 ± 42.287	

**Kruskal Wallis, p*<0,05 or significantly different.*

Table 6 Mann Whitney test of difference between the delta lesions AV placebo group, isoflavones 40 mg, 80 mg, 120 mg, and 160 mg.

Variable	*Isoflavones 40 mg*	*Isoflavones 80 mg*	*Isoflavones 120 mg*	*Isoflavones 160 mg*
Placebo	0.753	0.917	0.402	0.009*
Isoflavones 40 mg	-	0.465	0.295	0.009*
Isoflavones 80 mg		-	0.251	0.009*
Isoflavones 120 mg			-	0.009*

* Value of different test unpaired Mann-Whitney to delta AV lesion 160 mg isoflavone group (p=0.009) or significant (p< 0.05)

Wilcoxon signed ranks test, did not differ significantly (p>0.05), (**Table 4**).

Results of Kruskal-Wallis test between the delta AV lesion values obtained in 5 groups were statistically significant (p<0.05), (**Table 5**) and differences between groups as measured by Mann-Whitney test showed that mean delta value of 160 isoflavone group was significantly superior (p<0.05) to that of placebo, 40 mg of isoflavones, isoflavone 80 mg, and 120 mg isoflavones, whereas among other groups it was not significant (p>0.05), (**Table 6**).

Discussion

This study used varying doses of soy isoflavones, with the aim to see a dose response and determine the most effective dose of soy isoflavones that affects the amount of total AV lesions. The doses used in the study were 0 mg/day, 40 mg/day, 80 mg/day, 120 mg/day and 160 mg/day for 4 weeks. The duration of treatment was selected as four weeks as this corresponds to regeneration time of epidermis.[17] Decrease in the mean total lesion before and after treatment in the placebo group, 40 mg of isoflavones, 80 mg, 120 mg did not differ significantly (p>0.05), while the 160 mg isoflavone group found significant differences (p<0.05). Differences delta AV lesions after 4 weeks of the study was significantly different between groups (p<0.05), and effect of a dose of 160 mg of soy isoflavones in reducing the total AV lesions was significant (p<0.05), as compared to placebo, 40 mg of isoflavones, 80 mg and 120 mg, thus proving the hypothesis to be minor.

The effect of soy isoflavones on AV lesions has not been studied previously, but it seems to be multidimensional. Some studies have shown that soy isoflavones have antiandrogen effect,[10] especially in women, there is a correlation between the number of lesions and DHT.[4,6] The antiandrogenetic effect of soy isoflavones is mediated through inhibition of 3ß-hydroxysteroid dehydrogenase enzyme (3ß-HSD), 17ß-hydroxysteroid dehydrogenase (17ß-HSD) and 5α-reductase.[14] Decreased levels of DHT improve the milieu of the pilosebaseus duct, decrease the secretion of sebaceous glands, thus fix keratinization of infundulum region, cohesion and prevent the formation of corneocytes microcomedo, resulting in a decreased closed and open comedones, and lead to a decrease in AV lesion counts.[4,6]

Isoflavones also have antiinflammatory properties. It has been shown that isoflavones

in dose of 160mg/day for 12 weeks in postmenopausal women decrease the expression of inflammatory mediators.[18] The antiinflammatory effect of soy isoflavones in AV results in reduction in papules, pustules, and nodules; it also reduces the total number of lesions.

Conclusion

Soy isoflavone supplementation 160 mg/day for 4 weeks in women with AV would lead to a significant reduction in the number of lesions AV.

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