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RESEARCH ARTICLE

The Effect of Inositol On *Malondialdehyde* Serum Levels in Medical Students With PCOS

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Abstract

Introduction: *Polycystic ovary syndrome involves the endocrine system, metabolic system, as well as the reproductive system contributing to anovulatory infertility. Polycystic ovary syndrome affects 5-20% of reproductive age and 6-12% of adolescents. Oxidative stress is known to play an important role in the pathogenesis of PCOS resulting in excessive formation of ROS (malondialdehyde). ROS can be controlled by the antioxidant inositol and has minimal side effects. To determine the effectivity of inositol antioxidant on malondialdehyde serum levels in female students Medical faculty, Andalas University with clinical PCOS.*

Methods: *This study is a clinical trial research with a pure experimental study design (true experimental design). There were 23 samples for the experimental group and 23 samples for the control group selected by probability sampling. Normality test using Shapiro-Wilk test. Data analysis using Independent T test and Mann Whitney Test.*

Results: *There was a significant decrease in malondialdehyde serum levels in PCOS students who consumed inositol therapy for 3 months.*

Conclusion: *There is an effect of inositol antioxidant consumption on malondialdehyde serum levels in female students Medical faculty, Andalas University with clinical polycystic ovary syndrome.*

Keywords: *PCOS, oxidative stress, malondialdehyde, Inositol*

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is a female reproductive disorder characterized by two of the following three symptoms: clinical findings of *hyperandrogenism*, ovulatory dysfunction, or polycystic ovary appearance on ultrasound.[1] Based on World Health Organization, more than 116 million women worldwide experience PCOS.[2] Currently 1 in 10 women worldwide experience PCOS, and 70% of women are not diagnosed with PCOS because they feel they are asymptomatic and do not interfere with their activities.[1,3,4] Polycystic ovary syndrome affects 5-20% of reproductive age and 6-12% of adolescents.[5,6] PCOS can cause fertility disorders, psychological disorders, social behavioral disorders, eating disorders and diabetes mellitus in the future.[7]

PCOS occurs due to disruption of the hypothalamic-pituitary-ovarian signaling pathway (a feedback mechanism), resulting in increased production of *luteinizing hormone* (LH) and decreased production of *follicle stimulating hormone* (FSH). Increased LH production, accompanied by hyperplasia and hypertrophy of theca cells in the ovaries, results in increased production of androgens, which are subsequently converted to testosterone. In theca cells, testosterone is converted to *dihydrotestosterone* (DHT) by *5α-reductase*, while in granulosa cells, testosterone is aromatized into estrogen by *CYP19A1*. Increased LH production results in increased free testosterone, which then circulates in the bloodstream and binds to its receptors in the skin and hair, causing symptoms of hirsutism. Decreased FSH production results in failure of follicle maturation, follicular atresia, and anovulation.[8,9]

Oxidative stress is known to play an important role in the pathogenesis of PCOS. Accumulation of androgens in follicular fluid causes free radicals for oocytes, thereby reducing oocyte quality, resulting in the formation of excessive amounts of *reactive oxygen species* (ROS).[10,11] PCOS results in a more significant increase in *malondialdehyde* production compared to other ROS products. *Malondialdehyde* is more chemically stable and readily found in plasma, serum, body tissues, and urine, making it more frequently used as a marker of oxidative stress than other compounds.[11]

Treatment of PCOS with insulin sensitizing drugs such as metformin, troglitazone, and pioglitazone has been shown to improve ovulatory function and reduce circulating androgens. Of these therapies, metformin is the most commonly used in the treatment of PCOS. However, metformin has gastrointestinal side effects such as nausea, vomiting, diarrhea, and weight gain, which can interfere with patient activity and reduce patient compliance and the appropriateness of metformin use.[12,13] Many studies have shown the success of inositol therapy in reducing *malondialdehyde* levels. Inositol is also thought to increase insulin sensitivity and improve menstrual cycles. Inositol has fewer side effects than other therapies.[12-15]

Based on this information, the author is interested in conducting research on the effect of administering the inositol antioxidant on *malondialdehyde* serum levels by comparing the levels of the biomarker ROS (*malondialdehyde*) before and after administering inositol to female students of the Faculty of Medicine, Andalas University with clinical polycystic ovary syndrome.

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METHODS

This study was a clinical trial with a *true experimental design*. The hallmark of experimental research is the randomized trial or intervention of a variable. This study administered inositol to the sample for three months, and observed changes in *malondialdehyde* serum levels. This study used a *pretest-posttest control group* design, with two randomly selected groups given a pretest to determine the baseline conditions of the experimental and control groups.

This research was conducted at the Faculty of Medicine, Andalas University during the period from August 2024 to December 2024. The population in this study was all female students of the Faculty of Medicine Andalas University under 20 years of age, within a maximum age range of 8 years after menarche. The sample size for each research group (experimental and control) was 23 blood serum samples from preclinical female students of the Faculty of Medicine, Andalas University.

The study was conducted after the subjects were provided with information and a statement of consent stating their willingness to participate. This study received ethical clearance from the Health Research Ethics Committee of the Faculty of Medicine, Andalas University, Padang (No : 416/UN.16.2/KEP-FK/2024).

RESULT

Tabel 1. Characteristics Female Students of faculty of medicine Andalas University with PCOS :

Characteristics	**Intervention (n=23)**	**Control (n=23)**
	Mean ± SD	
Age (years)	17,65 ± 0,49	
Menarche age	12,39 ± 1,12	
BMI (kg/m^2)	25,35 ± 3,64	
	f (%)	
BMI		
Obese (>30 kg/m2)	1 (4,35%)	4 (17,39%)
Overweight (25,1 – 29,9 kg/m2)	13 (56,52%)	9 (39,13%)
Normoweight (<25 kg/m2)	9 (39,13%)	10 (43,48%)
Disturbed menstrual cycle	23 (100%)	23 (100%)
Clinical hyperandrogenism	23 (100%)	23 (100%)

Based on table above, the average age of female students with PCOS is 17.65 years. The average age of menarche among female students with PCOS is 12.39 years. The average BMI for female students with PCOS is 25.35 kg/m^2. BMI in the experimental group included 1 person obese (4.35%), 13 people overweight (56.52%), and 9 people normoweight (39.13%). BMI in the control

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group included 4 people obese (17.39%), overweight 9 people (39.13%), and normoweight 10 people (43.48%). All PCOS students who met the inclusion criteria in this study were found to have menstrual cycle disorders (100%) and clinical hyperandrogenism (100%).

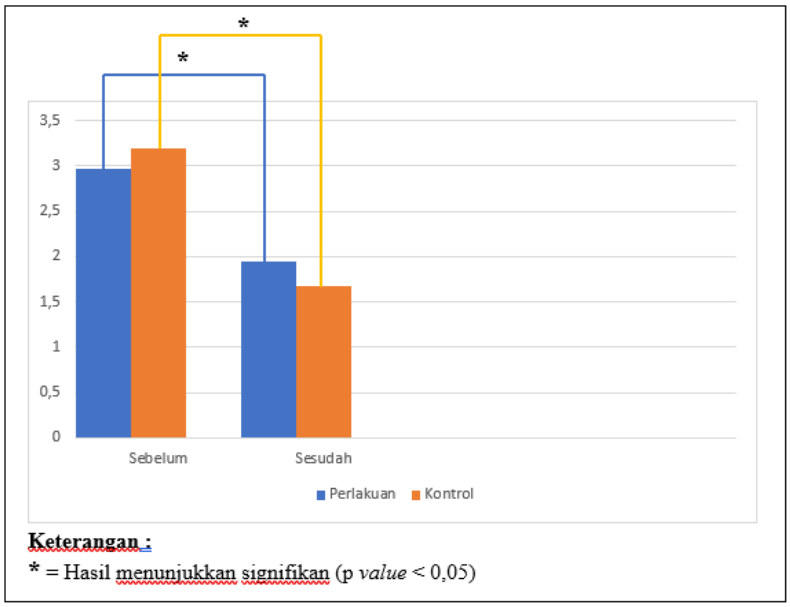


Figure 1. Comparison of Serum Malondialdehyde Levels Before and After Inositol Consumption

Based on Figure above, the mean *malondialdehyde* serum level in the experimental group (the group that will be given inositol for 3 months) is 2.97 nmol/mL. The mean *malondialdehye* serum level in the control group (the group without inositol) was 3.20 nmol/mL.

Based on Figure above, the mean *malondialdehyde* serum level in the experimental group after 3 months of inositol consumption was 1.95 nmol/mL. Meanwhile, in the control group, the median *malondialdehyde* serum level was 1.67 nmol/mL, where the highest *malondialdehyde* serum level was 3.20 nmol/L and the lowest *malondialdehyde* serum level was 1.20 nmol/L.

The results of the *Saphiro-Wilk* normality test form the basis for using the bivariate analysis of the *Mann-Whitney Test* or *Independent T-test* to determine the comparison of *malondaldehyde* serum levels before and after inositol consumption. The *Independent T-test* was used for normally distributed data, while the *Mann-Whitney Test* was used for non normally distributed data.

Bivariate analysis with the *Independent T-Test* gave a p value of 0.000 for the experimental group. This shows that there is a significant comparison of *malondialdehyde* serum levels between before and after consumption of inositol for the experimental group in this study.

Bivariate analysis with the *Mann-Whitney Test* gave a p value of 0.000 for the control group. This shows that there is a significant comparison of *malondialdehyde* serum levels for the control group in this study.

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DISCUSSION

All samples in this study were adolescents and less than 8 years after menarche. PCOS in adolescence ranks second in prevalence after young adulthood.[1,3] Pelvic ultrasound should not be used to diagnose PCOS in adolescents less than 8 years post menarche. This is due to the hormonal and reproductive transitions that occur in adolescence. Ovarian volume is greater in adolescents than in adults, and the incidence of multifocal ovaries is higher in adolescents. Therefore, the diagnostic criteria for PCOS in adolescents are ovulatory dysfunction and hyperandrogenism.[7,16]

In this study, it was found that there were more female students with overweight and obese than with normoweight. A meta analysis showed that obese women have a 2.77 fold increased risk of developing PCOS compared to non-obese women.[17] Increased adipose tissue volume, particularly visceral adipose tissue, is closely associated with insulin resistance, which leads to decreased glucose uptake and significantly inhibits lipid breakdown (lipolysis). Excess fatty acids are stored in skeletal muscle and the liver, leading to increased lipogenesis.[18,19] There is a reciprocal relationship between excess weight and PCOS, with PCOS also contributing to weight gain. Androgen hormones also function to regulate lipid metabolism, adipocyte differentiation, and induce the accumulation of abdominal adipose tissue. Hyperandrogenism in PCOS causes an excessive increase in adipocyte count, visceral fat accumulation, and decreased insulin sensitivity.[18,19]

All female students with PCOS who met the inclusion criteria in this study were found to have menstrual cycle disorders (100%) and hirsutism (100%) as evidenced by a *Ferriman Gallwey* score of more than 3. Menstrual cycle disorders in this study were caused by a decrease in FSH production which resulted in failure of follicle maturation, follicle atresia, and anovulation.[20,21,22] Accumulation of androgens in the oocyte follicular fluid causes free radicals for the oocyte, thereby reducing the quality of the oocyte.[23] Hirsutism is caused by an increase in the amount of free testosterone circulating in the blood circulation, which then binds to its receptors in the skin and hair.[16,20,21]

In the experimental group there was a significant decrease in *malondialdehyde* serum levels. Inositol is a second messenger for insulin and is thought to increase insulin sensitivity. Inositol reduces hyperinsulinemia, thereby reducing androgen production, which in turn reduces *malondialdehyde* production.[24,25] In addition to this mechanism, inositol is a non-enzymatic antioxidant (vitamin B8) which will send its electrons and then bind to oxidants (free radicals) thereby reducing the oxidative stress process and reducing the formation of *malondialdehyde*.[10,11,12]

CONCLUSION

Characteristics of female students medical faculty Andalas University using PCOS showed that the average age of menarche and female students were classified as teenagers. There are more overweight and obese female students than normoweight. There is a significant decrease comparison of *malondialdehyde* serum levels in medical faculty Andalas University students with polycystic ovary syndrome between before and after consumption of inositol 3 months.

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