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THE EFFICACY OF MYO-INOSITOL AND TRANS-RESVERATROL ALONG WITH MELATONIN, LACTOFERRIN, AND OTHER MICRONUTRIENTS IN THE TREATMENT OF PCOS: A PROSPECTIVE COHORT STUDY

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Abstract

Background: Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder affecting women of reproductive age, characterized by a spectrum of symptoms such as menstrual irregularities, hyperandrogenism, and polycystic ovarian morphology. To analyze the efficacy of Myo-inositol and Trans-resveratrol, in conjunction with Melatonin, Lactoferrin, and other micronutrients, in the management of Polycystic Ovary Syndrome (PCOS). **Materials and Methods:** This prospective cohort non-randomized study included 28 women aged 21-30 years diagnosed with PCOS. Participants were treated with a combination of Myo-inositol, Trans-resveratrol, Melatonin, Lactoferrin, and additional micronutrients for 90 days. Baseline and post-treatment evaluations were conducted for Body Mass Index (BMI), Lipid Profile, Ultrasonography (USG) findings, Hemoglobin A1c (HBA1C), Follicle-Stimulating Hormone (FSH), Luteinizing Hormone (LH), and Testosterone levels. **Result:** Among the 28 participants, 20 were aged 20-25 years and 8 were aged 25-30 years. Pre-treatment BMI indicated 18 participants were in the 25.0-29.9 kg/m² range and 10 were above 30.0 kg/m². Post-treatment, 8 were in the 18.5-24.9 kg/m² range and 20 in the 25.0-29.9 kg/m² range. HBA1C levels showed significant improvement, with normal levels (<5.7%) increasing from 10 to 24, pre-diabetes levels (5.7-6.4%) decreasing from 15 to 4, and diabetes levels (>6.4%) dropping from 3 to zero. FSH, LH, and Testosterone levels normalized post-treatment. USG results showed a reduction in bilateral PCOS from 20 to 4, and unilateral PCOS from 8 to 24. **Conclusion:** The combination of Myo-inositol, Trans-resveratrol, Melatonin, Lactoferrin, and other micronutrients significantly improves PCOS symptoms and related metabolic and hormonal profiles.

INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is a common endocrine disorder affecting women of reproductive age, characterized by a spectrum of symptoms such as menstrual irregularities, hyperandrogenism, and polycystic ovarian morphology.[1] The pathophysiology of PCOS is multifactorial, involving insulin resistance, chronic low-grade inflammation, and oxidative stress, which contribute to hormonal imbalances and metabolic disturbances. These factors significantly impact reproductive, metabolic, and psychological health, necessitating multifaceted management strategies.[2-4]

Traditional therapeutic options for PCOS include lifestyle modifications, hormonal therapies, and insulin sensitizers. However, their long-term efficacy and side effects have prompted the exploration of alternative, evidence-based nutraceutical approaches. Recent research highlights the potential of specific

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micronutrients and compounds such as myo-inositol, trans-resveratrol, melatonin, lactoferrin, and other essential micronutrients to improve hormonal balance, reduce oxidative stress, and enhance metabolic function in women with PCOS. Myo-inositol and trans-resveratrol have emerged as promising agents in the management of PCOS due to their unique properties. Myo-inositol, a key mediator in insulin signaling, has shown efficacy in improving insulin sensitivity and restoring ovulatory cycles. It also plays a critical role in ovarian follicular development and hormone regulation.[5,6]

Trans-resveratrol, a polyphenolic compound found in red grapes and berries, possesses anti-inflammatory, antioxidant, and insulin-sensitizing properties. It has demonstrated the potential to reduce androgen levels and improve metabolic parameters in women with PCOS. Melatonin, a hormone primarily known for regulating sleep-wake cycles, is increasingly recognized for its role in ovarian physiology. Its antioxidant properties are crucial in protecting oocytes from oxidative damage, enhancing oocyte quality, and improving fertility outcomes.[7,8]

Lactoferrin, a multifunctional glycoprotein, exerts anti-inflammatory and immunomodulatory effects. Its ability to modulate iron metabolism and support gut health contributes to metabolic homeostasis, making it a valuable adjunct in PCOS management.[9]

The combined use of these nutraceuticals, along with other micronutrients like vitamins and minerals, may offer a synergistic effect in addressing the diverse manifestations of PCOS. However, comprehensive clinical evidence on their efficacy, when used in combination, is limited.

This prospective cohort study aims to evaluate the efficacy of a combined regimen of myo-inositol, trans-resveratrol, melatonin, lactoferrin, and other micronutrients in improving clinical, biochemical, and metabolic outcomes in women with PCOS. By providing robust evidence, this study seeks to bridge the gap between emerging nutraceutical therapies and their practical application in PCOS management.

MATERIALS AND METHODS

This was a prospective cohort, non-randomized study conducted over a period of 90 days. The study aimed to evaluate the efficacy of a combined regimen of nutraceuticals in improving clinical, metabolic, and hormonal parameters in women diagnosed with PCOS.

The study included 28 women aged between 21 and 30 years, diagnosed with PCOS based on the Rotterdam criteria. The Rotterdam criteria require the presence of at least two of the following three features.[4]

- Oligo- or anovulation.
- Clinical and/or biochemical signs of hyperandrogenism.
- Polycystic ovaries on ultrasound (≥12 follicles measuring 2–9 mm in diameter and/or increased ovarian volume >10 mL).

Inclusion Criteria

- Women aged 21–30 years.
- Diagnosed with PCOS based on the Rotterdam criteria.
- Not receiving any other medications for PCOS during the study period.

Exclusion Criteria

- Women with other endocrine disorders such as thyroid dysfunction or hyperprolactinemia.
- Pregnant or lactating women.
- Individuals with a history of chronic illness such as diabetes mellitus, cardiovascular disease, or renal dysfunction.
- Participants unwilling to comply with the study protocol.

Methodology

Participants were provided with a daily oral regimen containing the following components:

Myo-inositol: Known to improve insulin sensitivity and regulate ovarian function.

Trans-resveratrol: A polyphenol with antioxidant and anti-inflammatory properties.

Melatonin: To support ovarian function and protect against oxidative damage.

Lactoferrin: To modulate inflammation and support metabolic health.

Additional Micronutrients: Including essential vitamins and minerals to address potential deficiencies and support overall health.

Participants were assessed at baseline and after 90 days of treatment. A thorough clinical evaluation and biochemical tests were performed to measure the following parameters:

Body Mass Index (BMI): Calculated as weight in kilograms divided by the square of height in meters (kg/m^2).

Lipid Profile: Total cholesterol, HDL, LDL, and triglycerides to evaluate metabolic health.

Ultrasound (USG) Findings: To assess ovarian morphology and changes in follicular count.

Glycemic Control: HbA1c levels were measured to assess long-term glucose regulation.

Hormonal Profile: Including Follicle-Stimulating Hormone (FSH), Luteinizing Hormone (LH), and testosterone levels.

Ethical Considerations: The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment. Confidentiality of participant data was maintained throughout the study.

Statistical Analysis

Data were collected and recorded systematically for each participant at the two time points (baseline and 90 days). Changes in BMI, hormonal profile, glycemic control, lipid profile, and USG findings were analyzed to evaluate the treatment efficacy. Statistical analyses were performed using paired t-tests or Wilcoxon signed-rank tests as appropriate for comparing baseline and post-treatment values. A p-value < 0.05 was considered statistically significant.

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RESULTS

A total of 28 women aged 21–30 years were included in the study. All participants completed the 90-day study period. Age Distribution: 20-25 years: 20 participants, 25-30 years: 8 participants.

The mean BMI of participants decreased from 27.8 ± 3.1 kg/m² at baseline to 26.4 ± 2.9 kg/m² after 90 days of treatment. This change was statistically significant, with a p-value < 0.001. The reduction in BMI indicates the efficacy of the nutraceutical regimen in promoting weight loss, a critical factor in managing PCOS. [Table 1]

Total cholesterol levels significantly decreased from 210 ± 15 mg/dL at baseline to 190 ± 12 mg/dL post-treatment. A p-value < 0.001 confirms the statistical significance of this reduction. LDL levels dropped from 130 ± 10 mg/dL to 115 ± 9 mg/dL post-treatment. This significant reduction (p-value < 0.001) suggests an improved cardiovascular risk profile. HDL levels improved from 42 ± 5 mg/dL to 48 ± 4 mg/dL, a statistically significant increase (p-value < 0.001). Higher HDL levels are associated with better cardiovascular health and reduced inflammation. Triglyceride levels significantly decreased from 160 ± 20 mg/dL to 140 ± 18 mg/dL post-treatment (p-value < 0.001). [Table 2]

The mean FSH levels showed a slight decrease from 6.8 ± 1.2 mIU/mL at baseline to 6.5 ± 1.1 mIU/mL post-treatment. This change was not statistically significant (p = 0.210), indicating that FSH levels remained relatively stable over the study period. Stability in FSH levels suggests that the treatment regimen did not negatively impact ovarian stimulation processes. LH levels decreased significantly from 11.5 ± 1.8 mIU/mL to 9.6 ± 1.5 mIU/mL post-treatment (p-value < 0.001). A reduction in LH levels indicates improved hormonal balance and reduced hyperandrogenism, as elevated LH is often associated with PCOS. The decreased LH/FSH ratio further suggests improved ovulatory function. Testosterone levels dropped significantly from 65 ± 10 ng/dL to 48 ± 8 ng/dL post-treatment (p-value < 0.001). The reduction in testosterone levels demonstrates a significant improvement in hyperandrogenic symptoms, which are a hallmark of PCOS. This can translate into clinical benefits such as reduced acne, hirsutism, and improved menstrual regularity. [Table 3]

HbA1c levels improved significantly, reflecting better glycemic control. Ultrasound findings revealed a reduction in the number of ovarian follicles, indicating improved ovarian morphology. [Table 4]

Table 1: Baseline and Post-Treatment Changes in BMI.

Parameter	Baseline (Mean ± SD)	Post-Treatment (Mean ± SD)	p-value
BMI (kg/m²)	27.8 ± 3.1	26.4 ± 2.9	< 0.001

Table 2: Lipid Profile

Lipid Parameter	Baseline (Mean ± SD)	Post-Treatment (Mean ± SD)	p-value
Total Cholesterol (mg/dL)	210 ± 15	190 ± 12	< 0.001
LDL (mg/dL)	130 ± 10	115 ± 9	< 0.001
HDL (mg/dL)	42 ± 5	48 ± 4	< 0.001
Triglycerides (mg/dL)	160 ± 20	140 ± 18	< 0.001

Table 3: Hormonal Profile

Hormonal Parameter	Baseline (Mean ± SD)	Post-Treatment (Mean ± SD)	p-value
FSH (mIU/mL)	6.8 ± 1.2	6.5 ± 1.1	0.210
LH (mIU/mL)	11.5 ± 1.8	9.6 ± 1.5	< 0.001
Testosterone (ng/dL)	65 ± 10	48 ± 8	< 0.001

Table 4: HbA1c and USG Findings

Parameter	Baseline (Mean ± SD)	Post-Treatment (Mean ± SD)	p-value
HbA1c (%)	5.9 ± 0.4	5.6 ± 0.3	< 0.001
Number of Follicles	16 ± 3	12 ± 2	< 0.001

DISCUSSION

The study demonstrated significant improvements in PCOS symptoms and related metabolic and hormonal profiles with the combined treatment regimen. The decrease in BMI, improvement in HBA1C levels, and normalization of FSH, LH, and Testosterone levels highlight the efficacy of the intervention.

A comparison with previous studies indicates similar positive outcomes. For instance, a study by Genazzani et al. (2014) reported improvements in insulin resistance and hormonal balance with Myo-inositol supplementation in PCOS women. Additionally, studies on Resveratrol have shown its effectiveness in reducing inflammation and androgen levels, further supporting our findings.[1]

The observed reduction in BMI (p < 0.001) is consistent with findings from Gerli et al. (2007), who demonstrated that myo-inositol effectively reduces body weight in women with PCOS by enhancing insulin sensitivity.[5] Improved BMI is a crucial outcome, as obesity exacerbates insulin resistance and hyperandrogenism in PCOS patients. Significant reductions in total cholesterol, LDL, and triglycerides, alongside an increase in HDL levels, were observed in this study (p < 0.001). These

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findings align with Minozzi et al. (2008), who reported similar lipid-modulating effects of myo-inositol in PCOS patients.[6] Trans-resveratrol, known for its anti-inflammatory and cardioprotective properties, likely contributed to these favorable outcomes by modulating lipid metabolism (Banaszewska et al., 2016).[7]

The study showed a significant reduction in LH ($p < 0.001$) and testosterone levels ($p < 0.001$), with FSH remaining stable ($p = 0.210$). Elevated LH levels and the LH/FSH ratio are hallmark features of PCOS, contributing to anovulation. Studies by Ciampelli et al. (2005) demonstrated that myo-inositol supplementation reduces LH and testosterone levels, improving ovulatory function and reducing hyperandrogenism.[8] Additionally, trans-resveratrol has been shown to reduce androgen production by modulating ovarian theca cell activity (Banaszewska et al., 2016).[7]

A significant reduction in HbA1c levels and the number of ovarian follicles post-treatment suggests improved insulin sensitivity and ovarian health. Findings by Genazzani et al. (2008) highlighted that myo-inositol improves insulin sensitivity, resulting in decreased ovarian follicular cysts and enhanced ovulatory function.[9]

The combined effects of the nutraceuticals can be attributed to their complementary mechanisms, Myo-inositol enhances insulin signaling and reduces hyperinsulinemia.Trans-resveratrol exerts anti-inflammatory and anti-androgenic effects. Melatonin regulates reproductive hormone cycles and reduces oxidative stress. Lactoferrin improves gut health and systemic inflammation, further modulating metabolic dysfunction.

Similar improvements in metabolic and hormonal parameters have been documented in studies by Unfer et al,[10] (2011) Sibiraj,[11] Azizz,[12] reinforcing the potential of nutraceutical regimens in managing PCOS. However, this study stands out by evaluating the combined effects of multiple nutraceuticals, offering a comprehensive therapeutic approach.

Clinical Implications

The combined use of these nutraceuticals offers a multifaceted approach to managing PCOS, addressing both metabolic and hormonal disturbances. The study supports the hypothesis that an integrative treatment strategy can provide substantial benefits to PCOS patients.

Limitations and Future Research

While the study presents promising results, the non-randomized design and small sample size limit the generalizability. Future research should involve larger, randomized controlled trials to validate these findings and explore the long-term effects of such treatments.

CONCLUSION

The study provides evidence that a combination of Myo-inositol, Trans-resveratrol, Melatonin, Lactoferrin, and other micronutrients can significantly improve PCOS symptoms and associated metabolic and hormonal profiles. This integrative approach could be a valuable addition to the therapeutic options for PCOS.

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