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COMPREHENSIVE THERAPY FOR POLYCYSTIC OVARY SYNDROME: KEY POINTS TO IMPROVE QUALITY OF LIFE

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ABSTRACT

Background: *Polycystic Ovary Syndrome (PCOS) is an endocrine disorder that affects the hypothalamus, pituitary, and ovary. PCOS prevalence has increased from 4 -6% to 8 -10%. This syndrome results in both physical illnesses and psychological disorders. Women with PCOS tend to be more prone to psychological disorders compared to healthy women. PCOS increases the risk of anxiety by 7 folds. This study aims to analyze measures to reduce psychological disorders caused by PCOS based on numerous psychological disorder parameters and hormonal biomarkers with psychological therapies.*

Methodology: *This study is based on the PRISMA protocol guidelines. The literature review was performed by accessing ScienceDirect, PubMed, Sage Publications and Google Scholar. The inclusion criteria for the articles are full-text papers written by English from 2009 to 2018. The keywords used to find suitable articles are "anxiety, stress, distress, depression, and quality of life management in polycystic ovary syndrome". Nine articles were subsequently reviewed.*

Results: *Psychological therapies that can be applied for PCOS include holistic yoga, acupuncture, spiritual guidance, mindfulness stress management, relaxation, and guided imagery, progressive muscle relaxation and administration of herbal, probiotic and selenium medication. Those therapies have proven to lower anxiety, stress, depression, and psychological fatigue as they were measured using instruments of Montgomery Åsberg Depression Rating Scale (MADRS-S), Brief Scale for Anxiety (BSA-S), Swedish Short-Form36 (SF-36), PCOS Questionnaire (PCOSQ), Beck Depression Inventory, DASS 21 and STAI. Meanwhile, observed biomarker responses include lower levels of cortisol, adrenalin, testosterone, and malondialdehyde (MDA) and a higher level of endorphin.*

Conclusion: *Psychological therapies for PCOS have proven to lower psychological disorders as measured by numerous parameters and biomarkers. Therefore, psychological therapies have to be further developed to decrease psychological disorders because of Polycystic Ovary Syndrome. Such as symptoms of anxiety and prevent deterioration of social mental health.*

Keywords: *Anxiety, stress, distress, depression, and quality of life management in polycystic ovary*

INTRODUCTION

Polycystic Ovary Syndrome (PCOS) is an endocrine disorder that affects the hypothalamus, pituitary, and ovary. The exact etiology of this syndrome is still being investigated, but it is very likely to be genetic [1-4]. Stein and Leventhal made the first mentioned of Polycystic Ovary Syndrome in modern health literature in 1953. Both scientists wrote that they came across seven reproductive women who were suffering from health problems of amenorrhea, hirsutism and ovary enlargement with symptoms of PCOS [3].

Some journals show that PCOS prevalence has increased from 4 –6% to 8 –10% [1, 5]. PCOS prevalence in Australia even reaches 12 –21 % among reproductive women and has become the main topic discussed by most health researchers due to its relation to increased risk of metabolic and cardiovascular diseases [6]. The increasing trend of PCOS prevalence among reproductive women is in part due to imbalances between calorie intake and exercise that results in insulin retention, which is the pathophysiology of such syndrome [5].

A woman with PCOS suffers from physical illnesses including menstrual dysfunction, acne, obesity, hirsutism, and anovulatory infertility. This syndrome also increases the risk of metabolic diseases such as type-2 diabetes, cardiovascular disorder, and cancer, especially endometrium cancer [3, 7, 8]. Physical illnesses and infertility suffered by reproductive women with PCOS affect their quality of life, mental health and sexual satisfaction. Women with PCOS tend to be more prone to psychological disorders compared to healthy women. Symptoms of psychological disorder include heightened interpersonal sensitivity, psychosomatic symptoms, depression, anxiety, as well as unsatisfactory marriage and sexual activities. Out of 22 women diagnosed with PCOS, 9 also suffer from depression. The likelihood of women with PCOS to suffer from anxiety increases 7 folds, compared to that of healthy women [9–12].

The complex nature of health issues due to PCOS requires comprehensive treatment. Comprehensive *treatment covers features of reproduction, metabolism and psychology* [6]. Life style intervention includes diet, exercise, and healthy routines. And these make up the first line treatment for PCOS. The success of this first line treatment is closely related to the treatment of *psychological disorders*. *Treating psychological disorders* is one measure to restore *self-efficacy and* to improve Quality of Life (QoL), which are the key elements for successful healthy life style intervention that is founded on individual positive spirit [6, 13]. *QoL is the difference between the condition in real life and what it should be like* [14]. Psychological therapies must be developed to help women with PCOS, as it is a chronic condition that may manifest throughout life cycle. The protocol for comprehensive treatment of PCOS in Australia compiled using evidence-based practice stresses the importance of evaluating and treating psychological condition along with medical intervention by health professionals [6]. Some of the techniques being developed to treat psychological aspects of PCOS include: holistic yoga, acupuncture, relaxation and guided imagery, progressive muscle relaxation, spiritual healing, mindfulness stress management, and also administration of herbal, probiotic and selenium medication.

Therefore, this paper aims to review the literature that analyze psychological therapies used to complement treatment for PCOS to help health professional in providing comprehensive treatment for ultimate treatment result.

METHODS

Study Design and Study Selection

Literature review was performed by accessing journals from the databases of ScienceDirect, PubMed, Sage Publications and Google Scholar from 3rd January to 19th February 2019. There were 15 publications from PubMed, 4 publications from Science Direct, 1 publication from Sage Publications and 11 publications from Google Scholar. The keywords used for article search were ‘anxiety’, ‘stress’, ‘distress’, ‘depression’, ‘quality of life’ and ‘management’ also ‘polycystic ovary syndrome’.

Inclusion Criteria

Selected articles are written in English and are available in full-text from 2009-2018. There was no limitation in terms of study design.

Exclusion Criteria

Undergraduate thesis, thesis, guidelines, and proceedings are out of scope. Duplicate articles and those with non-matching keywords are not included either.

Data Collection Technique

The standard protocol used to select articles was PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). The 31 articles identified were further screened for title and abstract match. This process resulted in 19 selected articles. The next steps was article fitness screening for relevance and whether those articles were full-text or otherwise. Ten relevant articles were found to have duplicates, and hence, only 9 articles were found to meet all criteria of systematic review in this research.

Data Extraction

Out of 31 articles obtained, only nine articles meet the criteria herein.

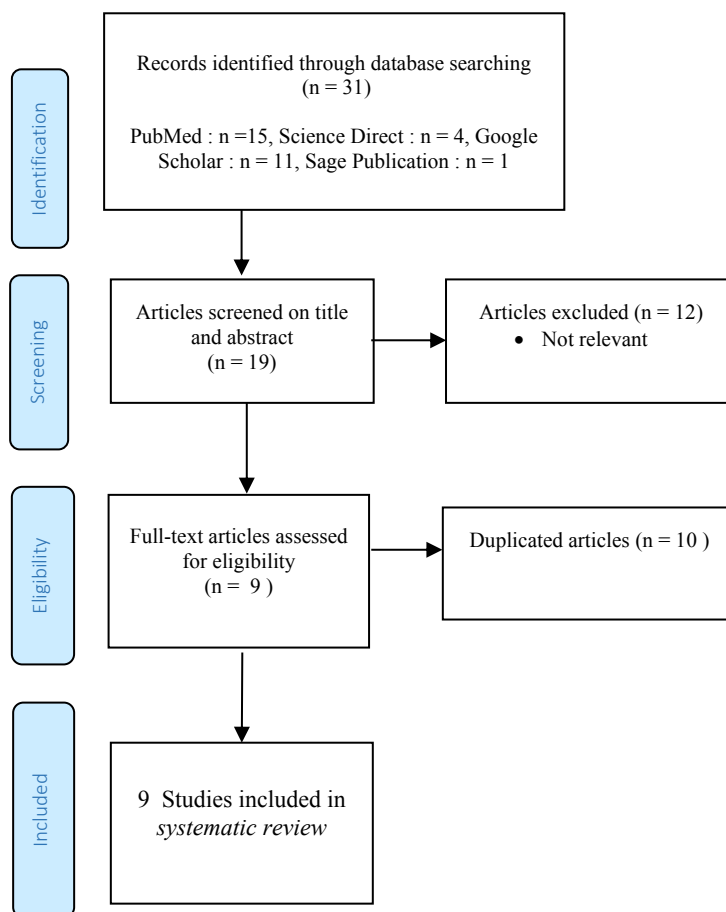


Figure 1: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

RESULTS

Nine articles were obtained for review, one article reviewed holistic yoga therapy, one article reviewed acupuncture therapy, two articles reviewed spiritual therapy, two articles reviewed relaxation therapy, one article reviewed cognitive-behavioral therapy and two articles reviewed administration of herbal, probiotic and selenium medication. Data extraction results are given in the tables below:



Table 1. Article on holistic yoga therapy (1 article)

Author	Title	Methods	Variables	Results
Ram Nidhi, Venkatram Padmalatha, Raghuram Nagarathna, et al (2013) [15]	Effect of holistic yoga program on anxiety symptoms in adolescent girls with polycystic ovarian syndrome: A randomized control trial	<i>Randomized Controlled Trial</i> <i>Treatment group = 30 teenagers</i> <i>Control group = 30 teenagers performing regular exercises</i>	Dependent variable: Holistic yoga program 1 hour/ day for 12 weeks Independent variable: Anxiety level in state - trait anxiety inventory (STAI).	State anxiety is not reduced with p value of 0.243, but anxiety score decreases. Trait anxiety is reduced with p value of 0.002.

Table 2. Article on acupuncture therapy (1 article)

Elisabeth Stener-Victorin, Göran Holm, Per Olof Janson, Deborah Gustafson, et al (2013) [16]	Acupuncture and physical exercise for affective symptoms and health-related quality of life in polycystic ovary syndrome: secondary analysis from a randomized controlled trial	<i>Randomized Controlled Trial</i> Acupuncture treatment group = 24 women Exercise treatment group = 24 women Control group = 24 women.	Dependent variable: Acupuncture (treatment 1) Exercise program (treatment 2) Treatments were performed for 32 weeks with evaluations on weeks 16 and 32. Independent variable: Montgomery Åsberg Depression Rating Scale (MADRS-S), Brief Scale for Anxiety (BSA-S), Swedish Short-Form36 (SF-36), PCOS Questionnaire (PCOSQ)	There is no difference in depression (MADRS-S), anxiety (BSA-S), quality of life (SF-36), and PCOS scores among the three groups after 16 weeks. Depression and anxiety are decrease in the acupuncture treatment group. There is a difference in anxiety score (BSA-S) between the acupuncture treatment group and the other two groups after week 32, with p value of 0.027.
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Table 3. Article on spiritual therapy (2 articles)

Farideh Zangeneh, Reza Salman	Effect of Ramadan Fasting on Stress Neurohormones in	Clinical trial	Dependent variable: Ramadan fasting	There is a decrease in cortisol and adrenaline levels for the Ramadan fasting group, with p value of 0.049 and 0.047.
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Yazdi, Mohammad Mehdi Naghizadeh, et al (2015) [17]	Women with Polycystic Ovary Syndrome	<i>Treatment group (Ramadan fasting)= 20 women</i> <i>Treatment group (no fasting)= 20 women</i>	Evaluation was conducted before fasting and after breaking it. Independent variable: The amount of neurohormone syndrome: cortisol, adrenalin (A), noradrenalin (NA), beta endorphin (β-End) and insulin, and also sexual hormones.	There is no difference in endorphin level, but there is an increase of it after breaking the Ramadan fasting. There is no difference in terms of sexual hormone.
Charikleia Stefanaki, Flora Bacopoulou, Sarantis Livadas, et al (2015)[18]	Impact of a Mindfulness Stress Management Program on Stress, Anxiety, Depression and Quality of Life in Women with Polycystic Ovary Syndrome: a Randomized Controlled Trial	<i>Randomized Controlled Trial</i> <i>Treatment group = 23 women</i> <i>Control group = 15 women</i>	Dependent variable: Mindfulness Stress Management Program Performed 30 minutes a day for 8 weeks, before going to bed. Follow ups were carried out once a week. <i>Independent variable:</i> Depression, anxiety, stress, and quality of life, as well as cortisol level Instrument: DASS 21 (Depression, Anxiety, Stress Scales), PSS-14 (Perceived Stress Scale), PCOSQ (Polycystic Ovary Syndrome Health-related Quality of Life) questionnaires.	There is a decrease in anxiety and stress from DASS 21 and in stress perception from PSS-14, but there is an increase in health satisfaction. There is a decrease in saliva cortisol with p value of 0.0001. There is a decrease after an average intervention of 0.17iu/mL.

Table 4. Article on relaxation therapy (2 articles)

John A. Barry, Noelia Leite, Nagaruban Sivarajah, et al (2017)[19]	Relaxation And Guided Imagery Significantly Reduces Androgen Levels And Distress In Polycystic Ovary	<i>Repeated measures design</i> <i>13 women aged 19 – 33 years.</i>	Dependent variable: Diaphragm respiration, relaxation, and visualization Performed for 15 in each hospital visit. Independent variable:	There is a decrease in anxiety and depression score on both the first and sixth week with p values of 0.037 and 0.034, respectively.
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Syndrome: A Pilot Study		Psychological response (anxiety, depression, quality of life) and levels of (DHEAS/ dehydroepiandrosterone), androstenedione, cortisol, and testosterone Measured before and after <i>treatment</i> on the first, sixth, and follow-up weeks.	There is a decrease in cortisol and adrenalin levels for the sixth week, with ρ value of 0.010 and 0.003. There is a decrease in DHEAS level on both the first and sixth week with ρ value of 0.044 and 0.001, respectively. There is no difference in either free or total testosterone levels, or quality of life.	
Jyoti Parle, Aishwarya D. Savant (2018)[20]	The effect of progressive muscle relaxation on depression in polycystic ovarian syndrome	<i>Experiment</i> 30 women as samples from 40 women with PCOS from both inclusion and exclusion criteria.	Dependent variable: Progressive muscle relaxation Performed 3 times a week for 4 weeks (12 sessions) Independent variable: Depression score from Becks Depression Inventory	There is a decrease in depression after progressive muscle relaxation with ρ value of 0.0001.

Table 5. Article on cognitive-behavioral therapy (1 article)

Leila Abdollahi, Mojgan Mirghafourv and, Jalil Kheyradin Babapour, et al (2018)[21]	Effectiveness of cognitive-behavioral therapy (CBT) in improving the quality of life and psychological fatigue in women with polycystic ovarian syndrome: a randomized controlled clinical trial	<i>Randomized Controlled Trial</i> 74 women aged 18 – 35. Treatment group = 37 women Control group = 37 women.	Dependent variable: Cognitive and behavioral therapy <i>Treatment</i> was performed for 8 weeks at duration of 45 –60 minutes per session a week. Independent variable: Polycystic Ovary Syndrome Health-Related Quality of Life Questionnaire (PCOSQ) and the Fatigue Impact Scale (FIS)	Score of quality of life (PCOSQ) is better for the treatment group compared to the control group (60.2 to 24.4) with ρ value of 0.001. Score of psychological fatigue (FIS) is worse for the treatment group compared to the control group (28.2 to 78.2) with ρ value of 0.001.
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Table 6. Article on administration of herbal, probiotic and selenium medication (2 articles)

Mehri Jamilian, Shirin Mansury, Fereshteh Bahmani, et al (2018)[22]	The effects of probiotic and selenium co supplementation on parameters of mental health, hormonal profiles, and biomarkers of inflammation and oxidative stress in women with polycystic ovary syndrome	<i>Randomized Controlled Trial</i> 60 women aged 18 - 40. Treatment group= 30 women Control group = 30 women.	Dependent variable: Administration of 8×10^9 CFU/ day of probiotic and 200 µg/ day of selenium supplement for 12 weeks Independent variable: The hormone profile includes levels of androgen, sex hormone-binding globulin (SHBG), total testosterone, malondialdehyde (MDA), glutathione total (GSH), total antioxidant capacity (TAC), and high-sensitivity C-reactive protein (hs-CRP). The mental health parameter includes Beck depression inventory, DASS 21 (depression, anxiety, and stress) and a questionnaire on general health perception.	Administration of probiotic and selenium supplements results in reduced depression (Beck depression inventory), DASS 21 and increased health perception with p value of 0.003, 0.007 and 0.009, respectively. There is a decrease in total testosterone, high-sensitivity C-reactive protein (hs-CRP), and malondialdehyde (MDA) levels, and there is an increase in total glutathione (GSH) level with p value of 0.03, 0.004, 0.03, 0.001, and 0.02, respectively.
Susan Arentz, Caroline A. Smith, Jason Abbott, et al (2017)[23]	Combined Lifestyle and Herbal Medicine in Overweight Women with Polycystic Ovary Syndrome (PCOS): A Randomized Controlled Trial	<i>Randomized Controlled Trial</i> <i>Treatment group (life style management and herbal medication) = 61 women</i> <i>Control group (life style management) = 61 women.</i>	Dependent variable: A combination of life style management (tablet 1 contains Cinnamomum verum, Glycyrrhiza glabra, Hypericum perforatum and Paeonia lactiflora, while tablet 2 contains Tribulus terrestris). Treatment was performed for 3 months. Independent variable:	The intervention group experienced oligomenorrhea of 32.9% and improve menstrual cycle with p value of 0.01. There is a decrease in body mass index, insulin, LH, and blood pressure with p values of 0.01, 0.02, 0.04 and 0.001. There is an increase in quality of life and a decrease in DASS 21 (depression,



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Oligomenorea, reproductive hormone level, anxiety, stress) with ρ value of 0.01 and anthropometry, quality of life, DASS 21 0.01, respectively.
(depression, anxiety, stress).

DISCUSSION

Results of literature review reveal that there are alternative therapies to treat psychological disorder experienced by women *with PCOS*. *Psychological therapies are developed to improve successful intervention rate of healthy life style against Polycystic Ovary Syndrome.*

Holistic Yoga Therapy

Yoga is a form of mind-body fitness that involves a combination of muscular activity and an internally directed mindful focus on awareness of the self, the breath, and energy to lead a balanced state of mind[24–26]. Ram Nidhi, et al [15], mentions that holistic yoga reduces anxiety due to *PCOS better, compared to routine exercises*. This is because holistic yoga encourages people to be relaxed and hence, improves the balance in the sympathetic nerve system. In turn, this response eases respiration, lowers heart beat rate, blood pressure, and cortisol level, and increases blood supply to vital body organs. The enhanced vagal activity caused by the stimulation of pressure receptors due to yoga would lead to decreased stress hormones such as cortisol[26]. Yoga practice may create a change in attitudes towards stress and life in a more optimistic way in PCOS.

Acupuncture Therapy

Acupuncture helps to reduce anxiety and depression caused by *PCOS*. The acupuncture points used to treat PCOS are the abdomen, feet, and palm. These points are connected to the reproductive, endocrine, and ovary systems, as well as the central nervous system. Stimulation of the central nervous system lowers symptoms of anxiety, as it is connected to neurohumoral mechanism that affects the hypothalamus-hipofisis adrenal [16]. This axis is directly linked to the functions of vegetative systems (sympathetic and parasympathetic). Effects of acupuncture modulation on the autonomous system explain the decrease of symptoms of anxiety [27].

Spiritual Therapy

Spiritual therapy is another measure to reduce psychological disorder in *PCOS* [17, 18]. This therapy for Muslims include reciting Al-Qur'an, chanting dzikir (remembrance of Allah), and fasting [28–30]. Ramadan fasting helps reduce psychological disorder, as evidenced by hormonal biomarkers in *PCOS* [17]. Fasting is an incredible religious practice compared to any worshiping activities as it is solely dedicated to The Almighty. Believe in the sacredness of fasting makes people calm and patient, hence, lower cortisol secretion. Increased endorphin serum is also found among respondents observing Ramadan fasting [30].

Mindfulness Stress Management is one type of meditation therapy that is founded on the Buddhist mindfulness meditation in 1979 [31]. The therapy focuses on cultivating mindfulness through formal practices (sitting meditation, body scan and mindful yoga) and on integrating this capacity into everyday life as a coping resource for dealing with intensive physical symptoms and difficult emotional situations[32]. Mindfulness stress management has proven to help reduce depression, anxiety, stress, and also enhance spirituality values and saliva cortisol level [18, 31, 32]. Spiritual therapy is a cognitive knowledge that affects a person's ability to control his/her negative emotion using religious understanding.

Relaxation Therapy

Anxiety and depression responses, as well as cortisol serum secretion are also lower with the use of relaxation therapies in PCOS. Treatment with relaxation and guided imagery results in positive response among respondents. Two of the respondents interviewed state that they feel better, calmer, and more relaxed [19]. Guided imagery has proven to lower anxiety by visualizing symbols/images a person like[33]. Visualization is one of relaxation techniques that improve cognitive experience of subjects in order to turn stressors into positive things. Progressive muscle relaxation that is also based on relaxation technique has proven to lower anxiety caused by *PCOS*. The progressive muscle relaxation therapy

teaches patients to strictly differentiate contraction and relaxation [20]. Relaxation has positive effect on emotional state and prevents deterioration of social mental health.

Cognitive-Behavioral Therapy (CBT)

CBT is psychotherapy aimed at altering dysfunctional thoughts that lead to negative mood states and maladaptive behaviors in order to help people make positive changes in their lives[34–36]. *Three principles of cognitive behavioral therapy are problem-solving skills, perception, ability to control her/his disease effectively* [34]. Leila Abdollahi [21], concludes that cognitive intervention help reduce psychological fatigue and increase quality of life among people with PCOS. *Transfer of knowledge using effective communication in counseling sessions helps to improve an individual's self-esteem.*

Administration of Herbal, Probiotic and Selenium Medication

Administration of herbal, probiotic, and selenium medication has also proven to ease psychological disorder caused by PCOS. Probiotic is a substance that is capable of improving the balance of microorganism in the gut and digestive tract and absorbing nutrition and increasing insulin sensitivity, whereas selenium is a high dose antioxidant. A combination of both substances has proven to lower MDA and testosterone level and to increase antioxidant capacity that allows the body to reduce anxiety [22, 23]. Other than those, consumption of natural substances such as mint tea is also being developed to lower the androgen level in women with PCOS [37].

CONCLUSION

Polycystic Ovary Syndrome (PCOS) is an endocrine disorder that affects the hypothalamus, pituitary, and ovary. Risk of psychological disorder among women with PCOS increases significantly, compared to that among healthy women. Symptoms of psychological disorder related to PCOS include heightened interpersonal sensitivity, psychosomatic symptoms, depression, anxiety, as well as unsatisfactory marriage and sexual activities. Out of 22 women diagnosed with PCOS, 9 also suffer from depression. Psychological therapies must be developed to help women with PCOS, as it is a chronic condition that may manifest throughout their life cycle.

Psychological therapies have proven to be effective in reducing psychological disorder. Indicators showing improved psychological condition among women with PCOS include lower scores of depression, anxiety, stress, fatigue, and psychological fatigue, and higher scores of quality of life and physical biomarkers. Indicators of physical biomarkers include lower cortisol and testosterone levels, and higher endorphin level. Psychological therapies for PCOS include holistic yoga, *mindfulness stress management, acupuncture, spiritual guidance, relaxation and guided imagery, progressive muscle relaxation and administration of herbal, probiotic and selenium medication.* Therefore, psychological therapies have to be further developed to improve the successful intervention rate of healthy lifestyle against Polycystic Ovary Syndrome.

CONFLICT OF INTERESTS

This literature review does not inflict any conflict of interest.

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