Prevention and Treatment of Polycystic Ovarian Syndrome using Antidiabetic Plants in Cameroon

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Abstract

PCOS is a multifactorial disorder that touches globally between 5% - 10% of women of reproductive age. The syndrome is recognized to be the foremost cause of an ovulatory sterility due to menstrual cycle variations. PCOS sterility is a multifaceted, multivariate syndrome with dysfunction interlaced by multiple parts of the endocrine, metabolic and neurological systems. PCOS often presents with a unique set of symptoms in each individual, requiring treatment against many vectors and careful critical thinking. Neuropathic medicine is an ideal paradigm for approaching the treatment of PCOS because it focuses on individualized treatment and on the treatment of the individual as a whole. The objective of this work was to inform the indigenous population that PCOS is not infectious disorder, but metabolic, neurological systems and hormonal disease which may leads to sterility and to identify credible plants to fight against this pathology in Cameroon. To achieve these goals a survey was carried out during 20 years among 1000 interviewers with only 153 women who presented at least three non-harmful (dominated by anxiety and regular anovulation) symptoms retained our attention. Thirteen anti-PCOS plants are used in Cameroon. Among them seven are for symptomatic treatment and six for direct treatment. *Ficus deltoides*, *Momordica charantia Aloe bulbicaulis* and *Aloe marlothii* are the most important plants. Indigenous drugs have gifted role in the treatment of PCOS and show stable effect with negligible side effects. Yet the investigation in their toxicity is required.

Keywords: Polycystic Ovary Syndrome; Metabolic; Neurological Systems and Hormonal Disease; Anti-PCOS Plants; Cameroon

Abbreviations

PCOS: Polycystic Ovary Syndrome; LH: Luteinizing Hormone Levels; SHBG: Sex Hormone-Binding Globulin; LDL-C: Low Density Lipid Concentration; CC: Clomiphene Citrate

Introduction

Polycystic ovary syndrome (PCOS), the foremost chronic endocrine disorder among women at age of reproduction, is not yet professed as an important health problem worldwide. It global prevalence is estimated to be between 6% and 26% [1]. The exact cause of PCOS isn't

known. There are several possible mechanisms that have been proposed as the causes of PCOS, including insulin resistance, hormonal imbalance, genetic predisposition, inflammation, strong stimulation in adrenals in childhood, and contraceptive pills [2].

Insulin resistance

The pancreas is responsible for the production of the hormone insulin, which is involved in the regulation of blood glucose alongside glycogen. It plays a role in lowering blood glucose levels by encouraging the uptake of glucose into cells for energy. Insulin resistance refers to when the tissues of the body become resistant to the effects of insulin, leading to an increase in the concentration of glucose in the bloodstream. The pancreas begins to produce more insulin to regulate glucose to compensate, but it continues to have a reduced effect. High levels of insulin can then cause the ovaries to produce excess testosterone, which interferes with the normal process of follicle development and ovulation. As a result, anovulation may occur regularly and the woman may develop PCOS and may become sterile. Although being overweight or obese does not cause PCOS, it is believed that excess fat contributes to the worsening of symptoms in women with the syndrome. This is presumably linked to the effect of excess fat on insulin resistance, leading to PCOS [2].

Hormonal imbalance

An imbalance of hormones in the body is another possible cause of PCOS. Many women with the condition have abnormal levels of hormones, which may be responsible for causing PCOS. These hormonal imbalances include;

1. Increased testosterone levels: Testosterone is usually produced in small amounts in women and is present in higher concentration in women with PCOS;

2. Increased luteinizing hormone levels (LH): the left hand is needed to stimulate ovulation but may have a reverse effect on the ovaries at high concentrations;

3. Increased Prolactin Levels: Prolactin stimulates the breast glands to produce milk, but the elevated levels are only evident in some women with PCOS;

4. Decreased sex hormone-binding globulin (SHBG) levels: SHBG is a protein that usually binds to testosterone in the blood to reduce the effect of testosterone. However, it is not clear whether these hormonal changes are involved in the pathogenesis of PCOS to cause the condition or if they are a result of the condition [2].

Genetic patrimony

Women with a family history of PCOS and other hormonal related conditions are more likely to be affected by PCOS, which suggests that there may be a genetic link to the condition. So far, there have not been any specific genes identified to be associated with causing the condition, although this is an area of current research that verifies the possibility of a genetic origin.

Inflammation

Women with PCOS appear to have low grade inflammation, which stimulates the polycystic ovaries to produce androgen hormones. Inflammation is a normal reaction of the body to fight an infection and involves the production of white blood cells by the immune system. However, the role of inflammation in causing PCOS is not completely clear [2].

Major clinical features of PCOS

The major clinical features of PCOS include

1. Varian: Ovarian cysts which can interrupt ovulation and eventually leads to infertility;

2. Irregular menstrual cycles: infrequent, irregular or prolonged menstrual cycles are the most common sign of PCOS;

3. Weight gain: PCOS makes it more difficult for the body to use the hormone insulin, which normally helps convert sugars and starches from foods into energy. This condition called insulin resistance can facilitate insulin and glucose to build up in the bloodstream [3];

4. Fertility problems: the prevalence of barrenness in women with PCOS is about 70 to 80% [4]. PCOS has also been found to increase the risk of miscarriage, anxiety and depression;

5. Elevated levels of male hormones or excess androgen may result in physical signs, such as excess facial and body hair or hirsutism, and occasionally severe acne and male-pattern hairlessness;

6. Excess insulin: Insulin is the hormone produced in the pancreas that allows cells to use sugar, your body's primary energy supply. If your cells become resistant to the action of insulin, then your blood sugar levels can rise and your body might produce more insulin. Excess insulin might increase androgen production, causing anovulation, amenorrhea and oligomenorrhoea;

7. Heredity: Research suggests that certain genes might be linked to PCOS.

8. Early diagnosis and treatment along with weight loss may reduce the risk of long-term complications [4,5]; PCOS leads to anovulation.

Complications of PCOS may embrace (4,5)

1. Sterility;

2. Gestational diabetes;

3. Pregnancy-induced high blood pressure;

4. Miscarriage;

5. Premature birth;

6. Nonalcoholic steatohepatitis is a severe liver inflammation caused by fat amassing in the liver;

7. Metabolic syndrome is a collection of conditions including high blood pressure, high blood sugar, and abnormal cholesterol or triglyceride levels that significantly increase the risk of cardiovascular disease;

8. Type 2 diabetes or prediabetes;

9. Sleep apnea;

10. Unhappiness;

11. Anxiety;

12. Acne;

13. Pain in Pelvic region;

14. Eating disorder;

15. Abnormal uterine bleeding

16. Cancer of the uterine lining (endometrial cancer) (5).

Obesity is associated with PCOS and can worsen complications of the disorder.

Histological features of PCOS [6]

The histological features of PCOS include

1. Complete ovarian hypertrophy

2. Condensed capsule (> 100 μ)

3. Augmented number of sub capsular follicle cysts

4. Scarcity of corporea lutea or albicantia

5. Hyperplasia and fibrosis of the ovarian stroma

6. Untimely luteinization of theca cells.

Forthcoming complications of PCOS [6]

The upcoming of complications PCOS embraces

1. Cardio vascular syndromes;

2. Diabetes mellitus;

3. Obesity;

4. Metabolic syndrome;

5. Endometrial carcinoma.

Many Cameroonian women suffering from PCOS are marginalized because they are considered as witches. Symptoms like excess facial and body hair, sleep apnea, abnormal uterine bleeding, cancer of the uterine, miscarriage or premature birth for example are strange to populations. This disease is treated in its early stages as female infertility complicated. Local therapists confuse this illness with infectious diseases. Since PCOS is a curable disorder, it can be cured by use of natural remedies or allopathic medication. The natural remedies include treatment with phytoestrogenic and non-estrogenic herbs. Due to the connection of diabetes with PCOS, antidiabetic plants can better control this disease in infertile women with diabetes.

Methodology

A total of 1000 interviewees were contacted during 20 years. Only 153 women who presented at least three non-harmful symptoms were selected to accept and share their information, corresponding to percentage of 15, 30%. These symptoms are: the production of milk by the breast glands in non-pregnant women, the absence of menstruations for long, the family genetic link to PCOS, the women with low-grade inflammation, the regular anovulation, and prolonged menstrual cycles, the increasing risk of miscarriage, the anxiety, depression, the amenorrhea, and the oligomenorrhoea. They were used for distinguish suspected PCOS women.

Criteria of plants inclusion

Plants include in this study must be confirmed antidiabetic, used in the treatment of childless women with diabetes type 2. The antidiabetic plants may treat at least three complications of polycystic ovary syndrome. The antidiabetic plants may treat imbalance hormones. Indeed, many women with PCOS have increased levels of testosterone and luteinizing hormone, which may be responsible for causing this syndrome. Three engines of research were determined from these three criteria as follow:

1. "a given antidiabetic plant treated sterile women with polycystic ovary syndrome";

2. "a single given antidiabetic plant treated three complications of polycystic ovary syndrome"

3. "a given antidiabetic plant may treat women with increased levels of testosterone and/or luteinizing hormone".

Complications of polycystic ovary syndrome described overhead in the introduction were grouped 3 by 3 (Table 1). If a single antidiabetic plant is used to treat three complications of polycystic ovary syndrome, we consider it as anti-polycystic ovary syndrome plant.

Samples of plants identified were harvested and presented to volunteer people and a number of times an antidiabetic plant was used in the treatment of PCOS were recorded.

To compare the set of direct plants and the group of symptomatic plants the kh-2 test was used. The purpose of this test is to determine whether a difference between the observed data and the expected data is due to chance, or if they are due to a relationship between the variables studied. It is expressed by the mathematical formula Khi-2 = $\sum$ (Oi-Ei)^2) / Ei where Khi-2 represents the test, Oi represents the observed value and Ei the expected value. To apply this test to our work, we pre-processed the data, defined hypotheses of Ho and H1 for the two groups such as: Ho = There is no significant difference between the two groups; H1 = There is significant differences between the two groups and subsequently establish contingency and frequency tables between the two groups.

Results

Distribution of non-harmful symptoms for identifying suspected PCOS women.

The production of milk by the breast glands in non-pregnant women (103), the absence of menstruations for long (91), the family genetic history of PCOS (45), the women with low-grade inflammation (44), the regular anovulation (108), the prolonged menstrual cycles (57), the increasing risk of miscarriage (34), the anxiety (127), depression (70), the amenorrhea (67), and the oligomenorrhoea (47), were non-harmful symptoms for selecting suspected PCOS women. The numbers in brackets represent the number of repetitions of a symptom (Figure 1).
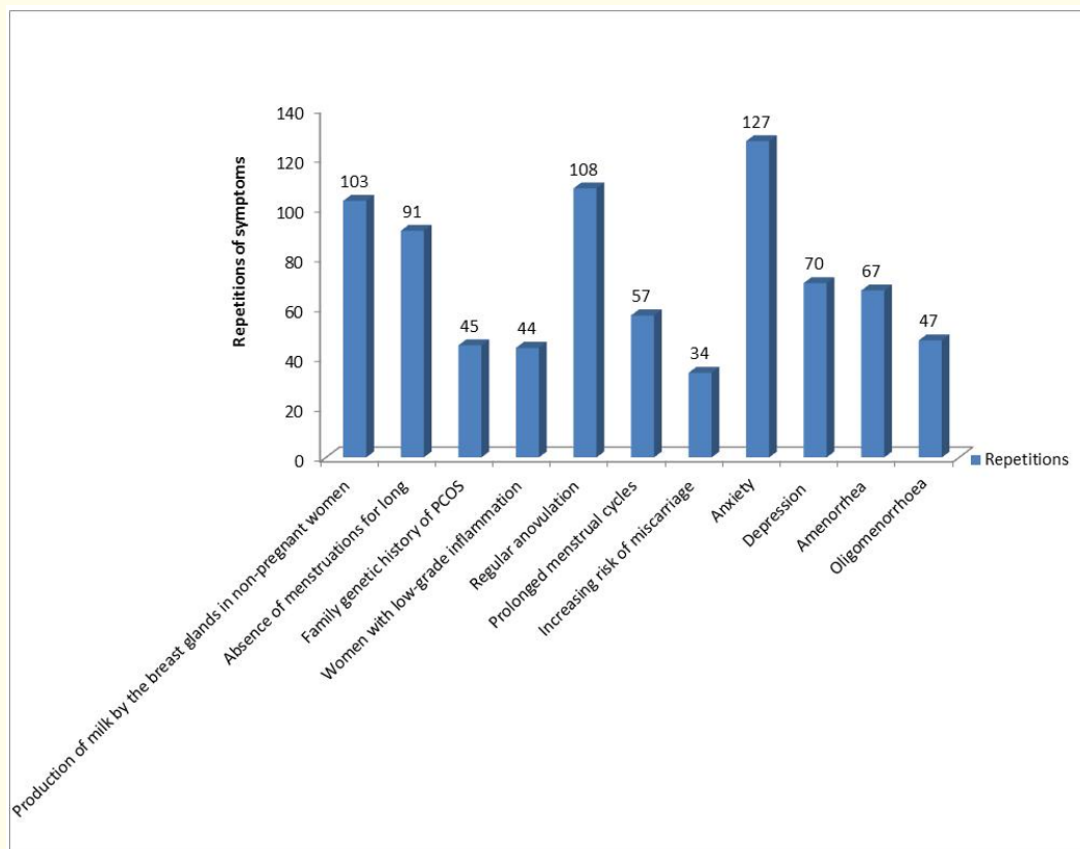

Figure 1: Distribution of non-harmful symptoms used for identification of suspected women with PCOS
The chi-square test shows that there is a very significant difference between the number of repetitions of symptoms permitting the identification of women suspected of having PCOS (chi-square = 33.477, Degree of freedom = 10, P = 0.00022639 < 0.05). We can therefore conclude that the numbers of repetitions differ globally (Figure 1).

For the symptoms of strong repetitions (production of milk by breast glands in non-pregnant women, absence of menstruation for long, regular anovulation, increasing risk of miscarriage and anxiety), there is no significant difference between them (chi-square = 1, 2603, Degree of freedom = 3, P = 0.73858 > 0.05) (Figure 1).

For the second group composed of symptoms at repetitions between 34 and 70, there is not a significant difference between them (chi-square = 6.2158, Degree of freedom = 6, P = 0.39946 > 0.05) (Figure 1).

The clinic symptoms of PCOS in 153 women suspected with PCOS were investigated by the interview of this group of women. These symptoms were used to identify symptomatic treatment (Table 1).

Table 1: *Ethnopharmacological preparation, phytochemicals, pharmacological activities and Repeti-Tions of recorded plants.*

Plants Names	Plant Parts Used	Three Symptoms of PCOS Treated By A Single Plant	Ethonopharmacological Preparation	Repetitions of Recipes	Active Ingredients or Previous Studies
1- *Angelina* sp (Umbelliferae)	Root	Liver disorder Cardio-vascular diseases High blood pressure	Macerate 200g of root in 2 litters of water for a day. Filter and drink 3 glasses daily for a week. Repeat the treatment monthly three times.	15	Coumarin Sesquiterpene in *Angelina glauca* [6]
2- *Aloe elegans* Tod. (Xanthorrhoeaceae) 3- *Aloe marlothii* A. Berger subsp. marlothii (Xanthorrhoeaceae) 4- *Aloe bulbicaulis* Christian (Xanthorrhoeaceae) 5- *Aloe arborescens* × inyangensis [Hell.]. (Xanthorrhoeaceae)	Gel of leaves		Macerate 300g of Aloe gel in 2 litters of water for a day. Filter and drink 3 glasses daily for a week. Repeat the treatment monthly three times.	67 61 104 17	The doses 5 mg, 10 mg and 15 mg of dry weight of *Aloe* gel during 60 days, were significantly used to treat PCOS induced rats as compared to control rats ($p < 0.05$) Particularly Also, *Aloe elegans* gel treated rats demonstrated consistent estrus cyclicity similar to control rats at all doses. Histological slices of PCOS positive rat ovary showed small cysts in follicles as compared to control ovary in which Aloe vera gel treatment changed the ovarian structure. It is interesting to realize that a treatment with a high dose of Aloe dry gel for a longer period of time demonstrate a decrease in atretic follicles and a return to normal of the affected ovary in the rat PCOS. Also the level of plasma insulin was significantly raised in untreated PCOS rats ($p < 0.001$) compared to the control group, while Aloe-treated PCOS rats had significantly reduced insulin levels in all groups of dose ($p < 0.001$). PCOS rats demonstrated insulin resistance whereas Aloe treatment reduced resistance in all groups as similar to the control group [7].

6-*Cinnamomum zeylanicum* Blume (Lauraceae)	Stem bark	Gestational diabetes Infertility Pregnancy induced high blood pressure	Boil 500g of stem bark in.5 litters for 15mn. Filter the decoction after 2 hours. Drink 3 glasses a day, for one week Repeat the treatment one a month three times	23	In 33 women treated group, participated in clinical trial, fasting insulin, LDL-C, and insulin resistance were decreased later 12 weeks in compared with 33 women who ingested placebo in control group. Fasting insulin, LDL-C, and insulin resistance were reduced after 12 weeks in Interventional group compared with control group. 3 capsules contained each one 333 mg of cinnamon, or placebo ingested daily by 15 women with PCOS demonstrated significant decreasing in abstaining glucose and insulin resistance. This supplementation Improved significantly the reduction in abstaining glucose and insulin resistance. Throughout 6 months treatment, menstrual cycles were more frequent in women with PCOS who ingested 1.5 g/day of cinnamon supplements compared with group received placebo. The concentration of progesterone in the luteal phase confirmed the ovulatory period [7].
7-*Camellia sinensis* L (Theaceae)	Leaves		Boil 150g of leaves in 2.5 litters for 10mn. Filter the decoction after 1 hour. Drink 3 glasses a day, for one week Repeat the treatment one a week three times	46	In 96 mature Wistar rats the doses 50, 100 and 200 mg/kg of green tea extract a day for 10 days; significantly change the number of follicles and the layer width and reduce LH serum level, insulin resistance body and ovarian weight between treated-groups related to PCOS [6-8].
8-*Ficus deltoidea* Jack (Moraceae)	Capsules	Human fertility Obesity Diabetes Heart disease Cancer Hypertension	Boil 300 of capsules in 3 litters of water for 15 mn. Drink 250 ml 3 times daily for a week.	24/78 Sympto- matic/Direct treatment	Tannins, alkaloids, saponins, phenols, flavones, isoflavones, and flavonoids [9].

9- *Mentha Piperita* Lin. (Piperaceae)	Leaves		Boil 100g of leaves in 2.5 litters for 10mn. Filter the decoction after a hour. Drink 3 glasses a day, for one week Repeat the treatment one a month three times	77	The treatment with 50 mg/kg spearmint oil or 300 mg/kg spearmint oil of *Mentha piperita* decrease body weight, testosterone concentration, ovarian cysts, and atretic follicles in PCOS rats [8].
10- *Momordica charantia* Lin. (Cucurbitaceae)	Fruit	Anti-diabetic Amenorrhea Infertility	Boil 100g of fruits in 2.5 litters for 10mn. Filter the decoction after 2 hours. Drink 3 glasses a day, for one week Repeat the treatment one a month three times	86	
11- *Sesamum indicum* Lin. (Pedalliaceae)	Seeds	High blood pressure Pregnancy induced high blood pressure Eating disorder	Infuse 200 g of leaves in 200 litters of water for a day. Drink 3 glasses a day for a week	34	Proteins [6]
12- *Smilax anceps* Willd. (Similacaceae)	Rhizome	Premature birth Obesity Gestational diabetes	Infuse 200 g of rhizome in 200 litters of water for 3 hours. Drink 3 glasses a day for a week	13	Resin [6]
13- *Vitex doniana* Sweet (Lamiaceae)	Dried fruit	Infertility Normalized menstrual cycles Miscarriage	Infuse 200 g of dried fruits powder in 200 litters of water for 3 hours. Filter and drink 3 glasses a day for a week	12	Seven women who ingested the infusion affirm that they come pregnant after the treatment.

Table 1 presents thirteen plants belonging to 10 families and 10 genera that were recorded to treat PCOS. The genus Aloe is represented by four species. Among the thirteen plants six are used directly to treat PCOS and seven used to treat PCOS via its symptoms. Indeed there are two types of PCOS treatment: symptomatic and direct treatment. *Ficus deltoidea* is a plant both of direct treatment and symptomatic treatment (Table 1). Table 1 shows also the distribution of the recorded plants in function of their repetitions.

Global comparison of recorded plants

The chi-square test shows that there is a very significant difference between the number of repetitions of plants used in both symptomatic and direct treatments of PCOS (chi-square = 85,951, Degree of freedom = 13, P = 8, 2668E-13 < 0.001). We can therefore conclude that the numbers of repetitions of plants differ globally from one plant to another (Figure 2). The recorded plants are used independently of each other.
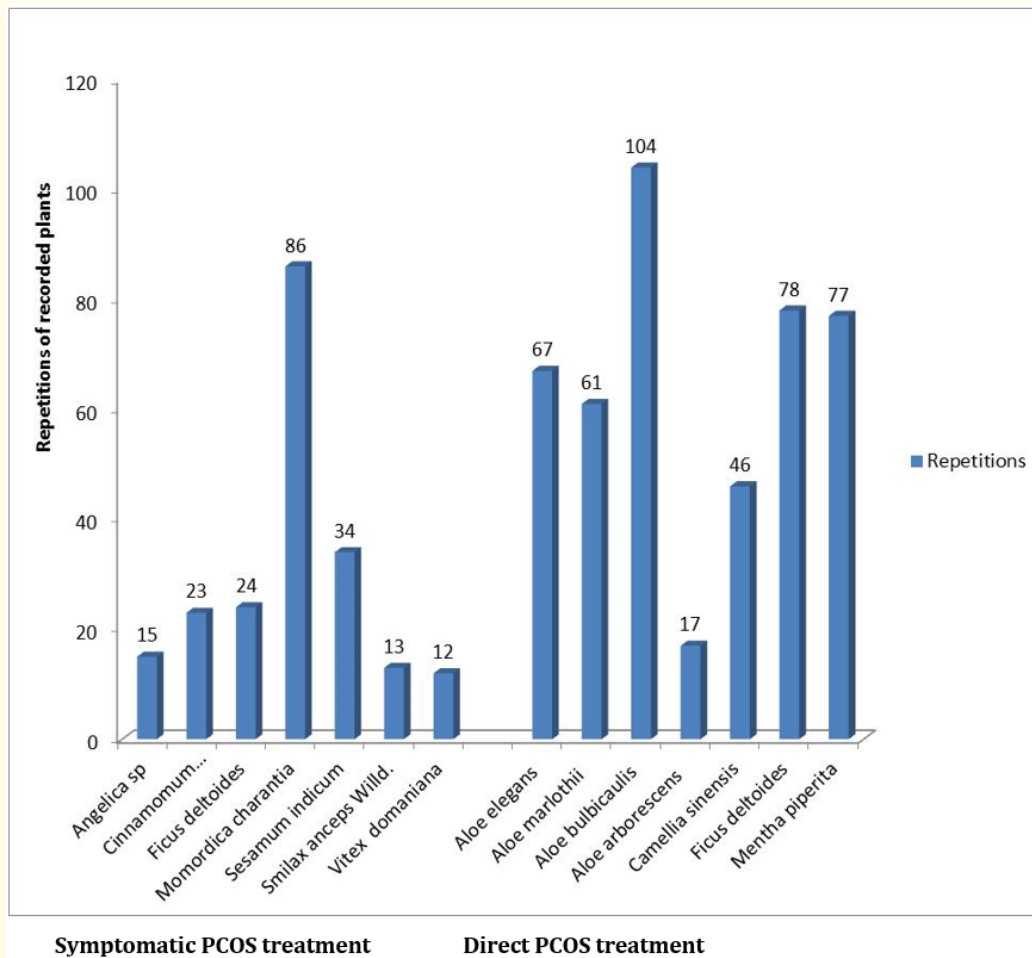
Figure 2: Distribution of the two groups of plants used in the treatment of PCOS.

Comparison of strong repetitions recorded plants

There is not significant difference between strong repetitions (between 61 et 104) plants (*Momordica charantia, Mentha piperita, Ficus deltoides, Aloe bulbicaulis* and *Aloe elegans* (Chi-square = 3, 9531, Degree of freedom = 5, P = 0, 55619 > 0.05) (Figure 2). In overall, the use of one plant does not predominate over another.

Comparison of low repetitions recorded plants

There is not significant difference between low repetitions (between 15 and 46) plants (*Camellia sinensis, Sesamum indicum, Ficus deltoides, Cinnamomum zeylanicum, Angelina* sp, *Smilax krausiana* and *Vitex doniana*) (chi-square = 11,515, Degree of freedom = 7, P = 0, 11769 > 0.05) (Figure 2). In this group, the use of one plant does not predominate over another.

Comparison of repetitions of plants of symptomatic treatment group

The chi-square test demonstrates that there is a very significant difference between the number of repetitions of plants used in symptomatic treatment of PCOS (chi-square = 28,247, Degree of freedom = 6, P = 8, 4404E-05 < 0.001). We can therefore conclude that the numbers of repetitions of plants for symptomatic treatment differ globally from one plant to another. The plants of symptomatic treatment are not similarly used by the population (Figure 2).

Comparison of repetitions of plants of direct treatment group

The chi-square test reveals that there is not significant difference between the number of repetitions of plants used in direct treatment of PCOS (chi-square = 10,083, Degree of freedom = 6, P = 0, 12122 > 0.05). We can therefore conclude that plants for direct treatment are globally popular (Figure 2).

Discussion

Symptomatic treatment

Ficus deltoidea (leaves) has been formulated, packaged and circulated as a tonic tea or capsules crossways Malaysia country. Previous studies revealed the following treatments of PCOS with *F. deltoidea*:

1. The methanolic extract of *F. deltoidea* leaf has been reported rich in constituents such as tannins, alkaloids, saponins, phenols, flavones, isoflavones, and flavonoids which are advantageous for treating PCOS through its different complications like dyslipidemia, diabetes, heart disease, cancer, and infertility in women [10,11].

2. It has been reported the improved depressive behavior, antihypertensive, chemopreventive and chemotherapeutic activities of *F. deltoidea* in rats [12,13].

3. *F. deltoidea* also promoted fertility and hormonal balance respectively in male and in PCOS female diabatic rats [14].

4. *F. deltoidea* increased cognitive performance and attenuated tissue morphology changes by increasing antioxidant activities in diabetic rats [14].

The treatment symptomatic although less known by the population are very important. Indeed plants like *Ficus deltoides*, *Camellia sinensis*, *Momordica charantia* and *Sesamum indicum* used in this treatment revealed the interesting anti-PCOS activities and possessed active ingredients.

Importance of mixture

Ainehchi N., *et al.* 2019 investigated the effect of herbal mixture supplements including menthe, zingiber, and Cinnamomum with and without Clomiphene citrate (CC) in PCOS women. They revealed that these supplements shows important properties on the antioxidants proportions, glycemic control, menstrual regulation, and pregnancy level [15].

Conclusion

At the end of this study we discover that herbal medicines may have beneficial effects on PCOS. The compounds in herbal medicine from symptomatic plants and direct plants in the treatment of PCOS can produce manifold affects including lipid profiles, insulin resistance, blood glucose, the serum levels of hormones (consistent estrus cyclicity), and the ovarian tissue (decrease in atretic follicles and a return to normal of the affected ovary in the rat PCOS). Herbal medicines may improve immunity of the body and also normalize menstrual cycle without unstable hormonal level. Consequently, plants can be considered as a new approach for treating and/or controlling PCOS. Nonetheless, due to the insufficiency of studies, the toxicity of herbal medicines (prolonged use toxicity, acute toxicity), further research are required in this regard in the future.

Acknowledgements

Conflicts of Interest

Bibliography

1. Rao Manisha., *et al*. "Cross-sectional Study on the Knowledge and Prevalence of PCOS at a Multiethnic University". *Progress in Preventive Medicine* (2020): e0028.

2. https://www.news-medical.net/health/Polycystic-Ovary-Syndrome-Causes-(French).aspx

3. https://www.mayoclinic.org/diseases-conditions/pcos/symptoms-causes/syc-20353439

4. Melo AS., *et al*. "Treatment of infertility in women with polycystic ovary syndrome: approach to clinical practice". *Clinics* 70.11 (2015): 765-769.

5. Saei Ghare Naz M., *et al*. "Polycystic ovary syndrome and pelvic floor dysfunction: A narrative review". *Research and Reports in Urology* 12 (2020): 179-185.

6. Priyanka Kantivan Goswami., *et al*. "Natural Remedies for Polycystic Ovarian Syndrome (PCOS): A Review". *International Journal of Pharmaceutical and Phytopharmacological Research* 1.6 (2012): 396-402.

7. Ashkar Fatemeh., *et al*. "The Role of medicinal herbs in treatment of insulin resistance in patients with Polycystic Ovary Syndrome: A literature review". *Biomolecular Concepts* 11.1 (2019): 57-75.

8. Radha M., *et al*. "Evaluation of Aloe Barbadensis Mill. Gel on Letrozole Induced Polycystic Ovarian Syndrome (PCOS) Rat Model- A Dose Dependent Study". I*nternational Journal of Pharmaceutical Sciences and Research* 5.12 (2014): 5293.

9. Bunawan H., *et al*. "Ficus deltoidea Jack: A review on its phytochemical and pharmacological importance". *Evidence-Based Complementary and Alternative Medicine* (2014).

10. Musapha Z and Harun H. "Phytochemical constituents in leaves and callus of Ficus deltoidea Jack var. kunstleri (King) Corner. Walailak". *Journal of Science and Technology (WJST)* 12.5 (2014): 431-439.

11. Melo AS., *et al*. "Treatment of infertility in women with polycystic ovary syndrome: approach to clinical practice". *Clinics* 70.11 (2015): 765-769.

12. Kamal MSA., *et al*. "Standardized ethanol-water extract of Ficus deltoidea angustifolia reduces blood pressure in spontaneously hypertensive rats". *Clinical and Experimental Hypertension* 41.5 (2019): 444-451.

13. May Al-koshab., *et al*. "Antitumor activity of Ficus deltoidea extract on oral cancer: An in vivo study". *Journal of Oncology* (2020).

14. Wang H., *et al*. "Inhibitory Activity of Ficus deltoidea var. trengganuensis aqueous extract on lipopolysaccharide-induced TNF-α production from microglia". *Evidence-Based Complementary and Alternative Medicine* (2017).

15. Ainehchi N., *et al*. "The Effectiveness of Herbal Mixture Supplements with and without Clomiphene Citrate in Comparison to Clomiphene Citrate on Serum Antioxidants and Glycemic Biomarkers in Women with Polycystic Ovary Syndrome Willing to be Pregnant: A Randomized Clinical Trial". *Biomolecules* 9.6 (2019): 215.