

Prescription patterns of herbal medicine for polycystic ovarian syndrome in major Korean medicine hospitals: a multicenter retrospective study

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Background: Few studies investigated the prescription patterns of traditional Korean medicine (TKM) therapies for PCOS in clinical practice. The purpose of this study was to identify the common symptoms, herbal prescription patterns and types of adjunctive treatment for treating polycystic ovary syndrome (PCOS) in major traditional Korean medicine (TKM) hospitals. **Methods:** A retrospective chart review of PCOS patients was used for the study. The study involved the analysis of medical records (ICD-10, polycystic ovary syndrome: E28.2) from four TKM-based university hospitals in South Korea. **Results:** A total of 120 PCOS patients were analyzed. We found that PCOS patients had a wide range of symptoms, including menstrual irregularity, oligomenorrhea, amenorrhea, acne, infertility, and metrorrhagia. The most commonly prescribed prescriptions for PCOS treatment were Chokyung-san (Tiaojing-san), Gamiguibintang (Jiawei Guipi-tang), and Changbudodam-tang (Cangfu Daotan-tang). In addition, patients were most often treated with adjunctive acupuncture and moxibustion. **Conclusion:** Our study presents the major gynecological herbal prescriptions and other adjunctive therapies used for the treatment of PCOS in TKM-based hospitals. However, further pharmacological investigations and effective clinical trials should be developed to ensure the objectivity of efficacy assessments.

Keywords

Herbal medicine; Polycystic ovary syndrome; Clinical practice based; Retrospective study

1. Introduction

Recently, polycystic ovary syndrome (PCOS) has emerged as one of the most common endocrine disorders in women of reproductive age worldwide. It is considered to affect the

menstrual cycle or fertility period of 5–10% of women, account for nearly 19% of female infertility, and increase the potential risk of female reproductive diseases such as endometrial hyperplasia and endometrial cancer [1–4]. Women suffering from PCOS are also at increased risk of menstrual irregularities, chronic anovulation, hyperandrogenism, and metabolic abnormalities due to ovulation disorders [5].

Women diagnosed with PCOS commonly have two of the following abnormalities: hyperandrogenism (clinical, biochemical, or both), ovulatory dysfunction, or polycystic ovarian morphologic features [1–4, 6]. Some of the pharmaceutical treatments proposed for PCOS include pharmacologic and hormone therapies. However, these long-term treatments not only show low efficacy but also have potential side effects, thereby making complementary and alternative treatments a valuable option [7–9]. Traditional Chinese medicine (TCM) and complementary and alternative medicine (CAM) have been regarded as effective remedies for PCOS [10–13]. A current studies demonstrate the beneficial effects of several herbs and herbal formulae for PCOS treatment, it is important to understand the clinical characteristics of and TCM-based therapies for women with PCOS. Additionally, it is essential to analyze symptoms, prescriptions, and therapies in clinical practice to identify commonly used CAM therapies for PCOS.

There have been few analyses of the prescription patterns of TCM or CAM for PCOS symptoms. Two studies in Taiwan have reported frequently prescribed TCM for PCOS in clinical practice through the analysis of a nationwide prescribing database [12, 14]. However, the number of stud-

ies that investigate frequently prescribed traditional Korean medicine (TKM) therapies for PCOS in clinical practice is still relatively low. This study aims to examine the common symptoms of PCOS and the herbal prescription patterns and types of adjunctive treatments used for PCOS.

2. Patients and methods

2.1 Study design

This multicenter retrospective chart review was conducted at four geographically diverse TKM-based university hospitals in South Korea. The four major sites were Kyung Hee University Korean Medicine Hospital at Gangdong, Daegu Korean Medicine Hospital of Daegu Haany University, Korean Medicine Hospital of Daejeon University, and Dongshin University Suncheon Oriental Medicine Hospital.

2.2 Participants

We reviewed the outpatient medical records of PCOS patients who received on-site TKM-based treatment from 1st January 2010, to 31st May 2016.

2.3 Inclusion and exclusion criteria

Patients were considered eligible if PCOS symptoms were their key concerns. Clinicians from each site were also required to use International Classification of Diseases, 10th version (ICD-10, polycystic ovarian syndrome: E28.2) codes to report the outpatient visits. Patients who did not have the corresponding code, use herbal medicines, or show symptoms of PCOS were excluded from this study.

2.4 Variables

- Age distribution.
- Main symptoms of PCOS (menstrual irregularity, oligomenorrhea, etc.).
- Commonly prescribed herbal medicines.
- Major adjunctive treatments used with herbal medicines (acupuncture, moxibustion, etc.).

2.5 Data sources/measurement

The key sources of data included the case report forms (CRF) and the electronic medical records (EMR) of patients in the included hospital sites. Study investigators collected the deidentified patients' data (without names or personal identification numbers) from each research site to assure patient confidentiality.

2.6 Statistical analysis

We used IBM SPSS Statistics Version 20.0 Windows (IBM, Armonk, NY, USA) for the frequency analysis of the collected data. Additionally, we used descriptive statistics to analyze participants' age and the frequency of herbal medicine prescriptions.

2.7 Ethical approval

This study received approval from the Institutional Review Boards (IRBs) of the four participating university hospitals (Daegu Hanny University: DHUMC-D-16010-PRO-10; Daejeon University: DJDSKH-16-E-5; Dong-guk Uni-

versity: 2016-08; Dongshin University: 2016-02; Kyung Hee University: 2016-09-010).

3. Results

In this study, we analyzed the medical records of 129 PCOS patients who visited TKM-based university hospitals in four different regions. The number of patients varied in each region, with the Seoul and Gyeongbuk (Daegu) regions accounting for 80% of the patients and the Chungjeong (Daejeon) and Jeolla (Suncheon) regions contributing to the remaining 20% (**Supplementary 1A**). Regarding age distribution, 11 (8.5%) patients were under the age of 20 years, 75 (58.1%) patients were between the ages of 20 and 29 years, 42 (32.6%) patients were between the ages of 30 and 39 years, and only 1 (0.8%) patient was between the ages of 40 and 49 years (**Supplementary 1B**). This indicates that approximately 90% of the patients with PCOS were between 20 and 39 years old.

Among ovarian dysfunction symptoms, there were 45 (34.9%) cases of menstrual irregularities, 42 (32.6%) cases of oligomenorrhea, 22 (17.1%) cases of amenorrhea, 4 (3.1%) cases of polymenorrhea, 6 (4.7%) cases of metrorrhagia, and 6 (4.7%) cases of infertility, which accounted for over 93% of all symptoms. Additionally, acne, hirsutism, skin discoloration due to an excess of androgens, and weight gain among the major symptoms of PCOS (Table 1).

Table 1. Frequency of polycystic ovarian syndrome symptoms (n = 129).

Symptoms	Frequency		
	(n)	(%)	
Ovarian dysfunction	Menstrual irregularity	45	34.9
	Oligomenorrhea	42	32.6
	Amenorrhea	22	17.1
	Polymenorrhea	4	3.1
	Metrorrhagia	6	4.7
	Infertility	6	4.7
	Hyperandrogenism		
	Acne	6	4.7
	Hirsutism	2	1.6
	Skin discoloration	1	0.8
Metabolic syndrome	Weight gain	5	3.9

Duplicated responses were allowed.

All patients received herbal prescription for treating PCOS. Of the 41 herbal medicine decoctions used to treat them, the most common prescriptions were Chokyung-san (15.5%), Gamiguibi-tang (10.9%), Changbudodam-tang (10.9%), and Onkyung-tang (7.0%), as shown in Table 2.

Table 3 summarizes the frequently prescribed herbal medicines for each PCOS symptom (please see **Supplementary 3** for complete data). Several types of herbal medicines were used for each symptom.

The top 5 TKM treatments used for PCOS patients included the combination of acupuncture and moxibustion

Table 2. Herbal medicines used to treat polycystic ovarian syndrome.

Herbal prescription		Frequency	
Korean	Chinese	(n)	(%)
Chokyung-san	Tiaojing-san	20	15.5
Gamiguibi-tang	Jiawei Guipi-tang	14	10.9
Changbudodam-tang	Cangfu Daotan-tang	14	10.9
Onkyung-tang	Wenjing-tang	9	7.0
Gyejibokryeong-hwan	Guizhi Fuling-wan	7	5.4
Dodam-tang	Daotan-tang	7	5.4
Onpoeum	Wenbao-yin	7	5.4
Shingihwanhapchangbudodam-tang	Shenqi-wan with Cangfu Daotan-tang	6	4.7
Chokyungjongok-tang	Tiaojing Zhongyu-tang	6	4.7
Onpojongok-tang	Wenbao Zhongyu-tang	5	3.9
Youndamsagan-tang	Longdan Xiegan-tang	5	3.9
Pyeongjingeonbi-tang	Pingchen Jianpi-tang	5	3.9

Duplicate responses were allowed. Detailed information on the medicines, including their Korean and Chinese names, is listed in **Supplementary 2**.

Table 3. Frequently prescribed herbal medicines for the treatment of polycystic ovarian syndrome symptoms.

Symptoms	Frequently prescribed herbal medicine
Menstrual irregularity	Chokyung-san, Gamiguibi-tang
Oligomenorrhea	Changbudodam-tang, Chokyung-san, Onkyung-tang
Amenorrhea	Shingihwanhapchangbudodam-tang, Chokyungjongok-tang
Polymenorrhea	Dodam-tang
Metrorrhagia	Gagam-Sukhongjeon
Infertility	Youndamsagan-tang
Acne	Chokyung-san
Hirsutism	Youndamsagan-tang
Skin discoloration	Chokyung-san
Weight gain	Gamiguibi-tang

We selected top frequent one and the detailed information was listed in **Supplementary 3**.

(37.2%); herbal medicine only (16.3%); the combination of acupuncture, moxibustion, and cupping (9.3%); the combination of acupuncture, moxibustion, and pharmacopuncture (9.3%); and the combination of acupuncture, moxibustion, cupping, and pharmacopuncture (7.0%) (**Supplementary 4**).

4. Discussion

4.1 Summary of the main results

This study presented the common symptoms of PCOS, prescription patterns of herbal medicines for PCOS and related adjunctive treatments based on the records of PCOS patients at four TKM-based hospitals. Symptoms such as menstrual irregularities, oligomenorrhea, and amenorrhea occurred very frequently in PCOS patients. Additionally, Chokyung-san (Tiaojin-san), Gamiguibi-tang (Jiawei Guipi-tang), Changbudodam-tang (Cangfu Daotan-tang), Onkyung-tang (Wenjing-tang), and Guizhi Fuling-wan were the most frequently prescribed herbal medicines for PCOS. We also found that TKM physicians frequently prescribed acupuncture and moxibustion adjunctively with herbal medicines to treat other symptoms associated with PCOS.

4.2 Agreements and disagreements with other studies

Few previous studies have evaluated herbal medicine prescription patterns for PCOS. In one study, a nationwide prescription database in Taiwan was analyzed to investigate the use of herbal medicines for PCOS. According to those findings, Gamisoyo-san (Jiawei Xiaoyao-san) and Hyangbuja (Xiang-fu, Cyperi Rhizoma) were the most commonly used formulas and single herbs for treating PCOS [14]. Another study also investigated the pattern of herbal medicines used to treat gynecological problems and infertility related to PCOS. The results showed that the three most frequently recommended herbal formulas were Bosinhwadambang (Bushen Huatan), Onkyung-tang (Wenjing-tang), and Cheongyegyong (Tian Gui capsules) [15].

The findings of the current study are partially consistent with the results of the aforementioned studies in terms of patient characteristics. Regarding the methods of prescribing herbal medicines for the treatment of PCOS symptoms, there was no significant difference between perceived and actual use in clinics and large major hospitals in three countries: Korea, China, and Taiwan.

4.3 Potential mechanism and implication for research

Recent studies have demonstrated various approaches for the use of traditional or herbal medicine to treat PCOS and have thoroughly assessed their mechanisms and efficacy [10, 16–19]. Many studies have analyzed the direct effects of herbal medicine decoctions on various PCOS symptoms, such as reproductive issues, irregular menstruation, hyperandrogenism, and metabolic disorders. Their findings showed the potential use of a range of herbal medicines to improve the symptoms of ovarian failure.

A study evaluating the effectiveness of an herbal-based obesity management program on an obese PCOS patient concluded that Changbudodam-tang (Cangfu Daotan-tang) is effective in treating oligomenorrhea associated with obesity in PCOS [20]. Additionally, herbal prescriptions such as Chokyung-san (Tiaojing-san), Changbudodam-tang (Cangfu Daotan-tang), Onkyung-tang (Wenjing-tang), Gyejibokryeong-hwan (Guizhi Fuling-wan), and Chokyungjongok-tang (Tiaojing Zhongyu-tang) were found to alleviate ovulatory dysfunction and apoptosis of granulosa cells, normalize the endometrium, and improve acne vulgaris, oligomenorrhea and excess androgen-related conditions associated with female ovarian dysfunction [21–23]. Several studies using animal PCOS models also tested the effectiveness of major herbal medicine prescriptions, such as Chokyung-san (Tiaojing-san), Gamiguibi-tang (Jiawei Guipi-tang), and Changbudodam-tang (Cangfu Daotan-tang) [23–27], and presented favorable results. This corresponds with our study results, which showed that herbal prescriptions such as Chokyung-san (Tiaojing-san), Changbudodam-tang (Cangfu Daotan-tang), Onkyung-tang (Wenjing-tang), Gyejibokryeong-hwan (Guizhi Fuling-wan), and Chokyungjongok-tang (Tiaojing Zhongyu-tang) have a high frequency of use in treating PCOS. More rigorous clinical studies of those prescriptions should be conducted to validate their clinical efficacy in treating PCOS. Such findings would broaden the scope of future clinical research to evaluate the efficacy of these therapies.

4.4 Limitations

In this study, we conducted an analysis of the clinical information of 129 PCOS patients using data from 4 TKM-based hospitals in South Korea. However, this study was limited to a retrospective chart review. Consequently, large-scale, multicenter research may be required to validate the effectiveness of TCM and the long-term response of symptoms associated with PCOS, such as menstrual irregularity and metabolic disease. Second, although we aimed to generate larger sample sizes by using a wide range of medical records from major TKM-based hospitals in South Korea, this effort was limited by the lack of patients. Additionally, there was a lack of objective posttreatment information that would indicate changes and improvement in major complaints and supplement future research. Therefore, we were unable to design a study that focused the correspondence between an individual single herbal formula/combined formula

and a particular PCOS symptom that could allow us to analyze the treatment routine and its specific effects. Furthermore, the academic background and working experience of on-site TKM physicians may affect the prescription pattern of herbal medicine for PCOS, but this information was not available. We also limited our focus to herbal prescriptions only and did not evaluate each single herb. This restricted our ability to provide information on the potential use of eligible herbs for the treatment of PCOS. Last, as this study was based on case files/records, it was not feasible to monitor the outcome of symptom improvement.

5. Conclusions

In conclusion, we found that three major gynecological herbal prescriptions, Chokyung-san (Tiaojing-san), Gamiguibi-tang (Jiawei Guipi-tang), and Changbudodam-tang (Cangfu Daotan-tang), were used to treat PCOS in TKM-based hospitals. Based on the study results and limitations, additional well-designed clinical trials are essential to provide an objective efficacy evaluation and to build an herbal prescription database.

Abbreviations

CAM, complementary and alternative medicine; CRF, Case Report Form; EMR, Electronic Medical Record; PCOS, polycystic ovary syndrome; TCM, traditional Chinese medicine TKM, traditional Korean medicine.

Author contributions

Conceptualization, HWL and MSL; methodology, HWL and MSL; software, LA and MSL; validation, TYC, KSP, JML, CHL, DCK, JEY, SJY; formal analysis, HWL and MSL; investigation, HWL and MSL; resources, KSP, JML, CHL, DCK, JEY, SJY, data curation, HWL, TYC, and MSL; writing—original draft preparation, MSL and MSL; writing—review and editing, LA, KSP, CHL, DCK, JEY, SJY, TYC; visualization, HWL and MSL; supervision, MSL; project administration, MSL; funding acquisition, MSL.

Ethics approval and consent to participate

This study received approval from the Institutional Review Board (IRB) of the four participating university hospitals (Daegu Hanny University: DHUMC-D-16010-PRO-10; Daejeon University: DJDSKH-16-E-5; Dong-guk University: 2016-08; Dongshin University: 2016-02; Kyung Hee University: 2016-09-010).

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Conflict of interest

The authors declare no conflict of interest.

Supplementary material

Supplementary material associated with this article can be found, in the online version, at <https://ceog.imrpess.com/EN/10.31083/j.ceog.2021.03.2471>.

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