Literature Study

Analysis of acupoint-selection patterns in acupuncture-moxibustion treatment of polycystic ovarian syndrome based on data mining

基于数据挖掘分析针灸治疗多囊卵巢综合征的经穴规律

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Abstract

Objective: To analyze the meridian and acupoint-selection patterns in acupuncture-moxibustion treatment of polycystic ovarian syndrome (PCOS) by data mining technique, for exploring acupoints that could be effective for PCOS and providing suggestion and reference in selecting acupoints for the acupuncture-moxibustion treatment of PCOS.

Methods: Literatures related to the acupuncture-moxibustion treatment of PCOS published before April 2018 were collected. By a self-made data mining program developed using Microsoft Excel 2007, a database of acupuncture-moxibustion treatment of PCOS was then established. The correlation analysis was performed for the frequency of use of acupoints and acupoint groups. Cluster analysis was also conducted.

Results: A total of 92 articles were recruited finally. Sanyinjiao (SP 6), Conception Vessel and chest-abdomen region ranked the top on the list of the most frequently used acupoints, meridians and regions, respectively. Correlation analysis showed that the acupoint group with the highest confidence was Sanyinjiao (SP 6) and Zusanli (ST 36), and the group with the highest support was Sanyinjiao (SP 6) and Guanyuan (CV 4). Cluster analysis revealed five effective clusters: Guanyuan (CV 4) and Sanyinjiao (SP 6); Zhongwan (CV 12) and Tianshu (ST 25); Zhongji (CV 3), Zusanli (ST 36) and Qihai (CV 6); Xuehai (SP 10), Shenshu (BL 23), Taichong (LR 3) and Guilai (ST 29); Ganshu (BL 18), Taixi (KI 3), Yinlingquan (SP 9) and Pishu (BL 20).

Conclusion: According to the confidence and support report, Sanyinjiao (SP 6) and Zusanli (ST 36) or Sanyinjiao (SP 6) and Guanyuan (CV 4) are recommended in acupuncture-moxibustion treatment of PCOS, with adjunct points selected for different patterns, e.g. Zhongwan (CV 12) and Tianshu (ST 25) for tonifying spleen and expelling dampness; Zhongji (CV 3) and Qihai (CV 6) for supplementing qi and cultivating blood; Xuehai (SP 10), Shenshu (BL 23), Taichong (LR 3) and Guilai (ST 29) for tonifying kidney and dissolving stasis; Ganshu (BL 18), Taixi (KI 3), Yinlingquan (SP 9) and Pishu (BL 20) for tonifying kidney and spleen and regulating liver.

Keywords: Acupuncture Therapy; Moxibustion Therapy; Acupuncture-moxibustion Therapy; Polycystic Ovarian Syndrome; Infertility; Acupuncture Points; Data Mining; Bibliometrics

【摘要】目的:运用数据挖掘技术分析现代针灸治疗多囊卵巢综合征(PCOS)的经穴规律,挖掘治疗PCOS的潜力穴 位,为针灸治疗PCOS提供选穴思路和参考。方法:收集截至2018年4月针灸治疗PCOS的相关文献,利用Microsoft Excel 2007软件自编数据挖掘程序,建立针灸治疗PCOS的数据库,进行穴位的使用频次及穴位组合的关联分析, 并进行聚类分析。结果:最终纳入92篇文献,使用频次最高的穴位、经络和部位分别为三阴交、任脉和胸腹部, 关联规则结果显示:置信度最高的穴位组合为三阴交和足三里,支持度最高的穴位组合是三阴交和关元。聚类分 析结果显示:存在5个有效聚类群,即关元、三阴交;中脘、天枢;中极、足三里、气海;血海、肾俞、太冲和归 来;以及肝俞、太溪、阴陵泉和脾俞。结论:根据置信度和支持度结果,推荐针灸治疗PCOS时选用三阴交加足三 里,或三阴交加关元,并依据不同证型加用配穴,如加用中脘、天枢以健脾除湿;加用中极、气海以益气养血;加 用血海、肾俞、太冲和归来以补肾化瘀;加用肝俞、太溪、阴陵泉、脾俞以益肾补脾调肝。

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Polycystic ovarian syndrome (PCOS) is a reproductive endocrine disorder commonly seen in women of childbearing age, mainly manifested by abnormal follicular development or anovulation, and elevated androgen/ hyperandrogenism, and accompanied by glucose and lipid metabolism disturbance^[1]. Women are bearing increasing stress with the development of the society, along with some improper lifestyles, which result in a rising incidence of PCOS among women at pubertal and child-bearing age. It's reported that the prevalence of PCOS among women of child-bearing age in foreign countries is 5%-10%^[1], the prevalence in the similar age group in China is $5.6\%^{[2]}$, and 30%-60% of the patients with ovulation failure or anovulation have PCOS^[3]. PCOS can be highly diversified in pathogenesis and symptoms, since it involves multiple factors, such as hypothalamus, sexual gland (ovary), adrenal gland and adrenal factor. PCOS not only can affect the reproductive system, but also may induce pregnancy complications, metabolic syndrome, hypertension, diabetes, and endometrial carcinoma^[4-5]. Currently, Western medicine commonly treats this disease symptomatically, which usually requires long-term use of drugs and thus cause a series of adverse reactions. One of its possible symptoms, anovulation, may affect the fertility of patients at child-bearing age and bring great grief to the patients and their families^[6]. There have been numerous clinical studies of acupuncture- moxibustion treatment of PCOS, but the regularities are still vague. It's significant to extract valuable contents from all these data to provide reference for acupuncture-moxibustion treatment of PCOS. By data mining, this study arranged the relevant literatures in China and summarized the acupoint selection rules in acupuncture-moxibustion treatment of PCOS, for providing systematic standardized reliable scientific evidence for this topic. The report is given as follows.

1 Data and Method

1.1 Literature retrieval

By retrieving both subject terms and free words and taking 'PCOS' AND 'acupuncture' OR 'moxibustion' OR 'acupuncture-moxibustion' OR 'electroacupuncture' as a combination, the China National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database (CBM), Wanfang Academic Journal Full-text Database (Wanfang) and Chongqing VIP Database (CQVIP) were searched; time range was from November 1996 till April 2018.

1.2 Literature evaluation criteria

1.2.1 Inclusion criteria

Study: Clinical studies that recruited those diagnosed with PCOS; primary literatures published in Chinese; only the first publication was identified for multiple submissions.

Subject: Diagnosed with PCOS; no limitation regarding age and source.

Intervention: With acupuncture-moxibustion as the intervention, including acupuncture, electro-acupuncture, moxibustion, etc., and these methods could be monotherapy or used in combination.

Literature type: Clinical trials.

1.2.2 Exclusion criteria

Abstracts, reviews, single case study, theoretical discussion, experience summary and animal experiments; those with tuina, massage, acupressure, acupoint blocking, acupoint thread embedding, acupoint application, Chinese medication, sham acupuncture-moxibustion or Western medications as intervention method; duplicate publications.

1.3 Data entry

After screened by the inclusion and exclusion criteria mentioned above, the eligible literatures were recorded by extracting the title, authors, journal, date, control intervention, acupoints used in the treatment group. Only the major acupoints selected in the treatment group were applied for data analysis. The adjunct points, syndrome-based point selections or alterations were not extracted. The recorded acupoint nomenclatures and meridians were standardized based on *Science of Acupuncture and Moxibustion*^[7]. The database was established by Microsoft Excel version 2007. Once an acupoint appeared, it would be put as '1'; otherwise, it would be '0'.

1.4 Study method

1.4.1 Descriptive analysis

The acupoints were analyzed in terms of frequency of use, frequency rate, meridian distribution, body region distribution, and special acupoint distribution.

The frequency of use of an acupoint meant how frequent this acupoint had been used. The frequency rate referred to the relation between the frequency of use and the identified literatures. Meridian distribution told which meridian the acupoints belonged to and how they were distributed. Body region distribution studied how these acupoints distributed in different body regions. Special acupoint distribution referred to how the special acupoints were used and distributed.

1.4.2 Correlation analysis

The SPSS Clementine version 12.0 was used and the correlation rules of the major acupoints selected in the identified literatures were analyzed by Apriori method. The support and confidence of the acupoint groups were calculated.

1.4.3 Cluster analysis

The SPSS Clementine version 12.0 was adopted and the cluster analysis was performed by K-means.

2 Results

Initially, 339 articles were identified, but 92 were finally recruited after 247 articles were removed. The screening process is shown in Figure 1.

Since each trial had one set of major acupoints, there were altogether 92 acupoint prescriptions.



Figure 1. Screening process

2.1 Result of descriptive analysis

2.1.1 Frequency of use of acupoints

There were 67 acupoints in the 92 acupoint prescriptions, and the total frequency was 920. The acupoints with a frequency of use >10 and a frequency rate >10.0% are shown in Table 1.

2.1.2 Analysis of meridians

The total frequency of the fourteen meridians in the 92 prescriptions was 836, covering 62 meridian acupoints. The analysis showed that the acupoints used to treat PCOS came from 13 meridians, including 11 ordinary meridians except the Small Intestine Meridian and the Conception and Governor Vessels. The total frequency of the 22 acupoints from the Conception Vessel, Spleen Meridian of Foot Taiyin and Stomach Meridian of Foot Yangming was 555, accounting for 66.39% of the total frequency, and these 22 acupoints occupied 35.48% of all the involved points. The meridian distribution is presented in Table 2.

2.1.3 Body region analysis

The acupoints selected to treat PCOS were mainly located in the chest-abdomen region, knee region and the region below the knees (Table 3).

2.1.4 Special acupoint analysis

The total frequency of the special acupoints used in the treatment of PCOS was 782, involving 48 points. The top 5 special acupoints were Sanyinjiao (SP 6), Guanyuan (CV 4), Zhongji (CV 3), Zusanli (ST 36) and Fenglong (ST 40). The Front-Mu points had the highest frequency, occupying 22.39%, followed by the Five Shu-Transmitting points (19.95%) and crossing points (13.04%). The details were shown in Table 4.

Table 1. Acupoi	ints with a	a frequency	>10	and	a	frequency
rate >10%						

Rank	Acupoint	Frequency	Frequency rate (%)
1	Sanyinjiao (SP 6)	88	95.65
2	Guanyuan (CV 4)	84	91.30
3	Zigong (EX-CA 1)	70	76.09
4	Zhongji (CV 3)	56	60.87
5	Zusanli (ST 36)	53	57.61
6	Qihai (CV 6)	45	48.91
7	Fenglong (ST 40)	44	47.82
8	Xuehai (SP 10)	43	46.74
9	Shenshu (BL 23)	39	42.39
10	Taichong (LR 3)	35	38.04
11	Guilai (ST 29)	35	38.04
12	Ganshu (BL 18)	24	26.09
13	Taixi (KI 3)	23	25.00
14	Yinlingquan (SP 9)	22	23.91
15	Pishu (BL 20)	21	22.83
16	Zhongwan (CV 12)	18	19.57
17	Diji (SP 8)	17	18.48
18	Tianshu (ST 25)	15	16.30
19	Hegu (LI 4)	15	16.30
20	Neiguan (PC 6)	14	15.22
21	Luanchao (Extra)	13	14.13
22	Ciliao (BL 32)	13	14.13
23	Geshu (BL 17)	12	13.04
24	Dahe (KI 12)	12	13.04

Table 2. Meridian distribution

Meridian	Total	Number of	Point and frequency (time)
	frequency	acupoints	
Conception Vessel	218	7	Guanyuan (CV 4) (84), Zhongji (CV 3) (56), Qihai (CV 6) (45), Zhongwan (CV 12) (18), Xiawan (CV 10) (7), Shuifen (CV 9) (5), Shangwan (CV 13) (3)
Spleen Meridian	180	8	Sanyinjiao (SP 6) (88), Xuehai (SP 10) (43), Yinlingquan (SP 9) (22), Diji (SP 8) (17), Gongsun (SP 4) (5), Daheng (SP 15) (2), Taibai (SP 3) (2), Tianxi (KI 18) (1)
Stomach Meridian	157	7	Zusanli (ST 36) (53), Fenglong (ST 40) (44), Guilai (ST 29) (35), Tianshu (ST 25) (15), Shuidao (ST 28) (7), Huaroumen (ST 24) (2), Wailing (ST 26) (1)
Bladder Meridian	126	13	Shenshu (BL 23) (39), Ganshu (BL 18) (24), Pishu (BL 20) (21), Ciliao (BL 32) (13), Geshu (BL 17) (12), Daimai (GB 26) (6), Shangliao (BL 31) (3), Sanjiaoshu (BL 22) (2), Guanyuanshu (BL 26) (2), Jueyinshu (BL 14) (1), Qihaishu (BL 24) (1), Gaohuangshu (BL 43) (1), Huantiao (GB 30) (1)
Liver Meridian	46	6	Taichong (LR 3) (35), Xingjian (LR 2) (4), Qimen (LR 14) (2), Yinlian (LR 11) (2), Ququan (LR 8) (2), Ligou (LR 5) (1)
Kidney Meridian	45	7	Taixi (KI 3) (23), Dahe (KI 12) (12), Fuliu (KI 7) (4), Henggu (KI 11) (2), Siman (KI 14) (2), Yingu (KI 10) (1), Zhaohai (KI 6) (1)
Governor Vessel	22	4	Baihui (GV 20) (9), Mingmen (GV 4) (9), Dazhui (GV 14) (2), Yaoyangguan (GV 3) (2)
Large Intestine Meridian	16	2	Hegu (LI 4) (15), Quchi (LI 11) (1)
Pericardium Meridian	14	1	Neiguan (PC 6) (14)
Gallbladder Meridian	6	4	Yanglingquan (GB 34) (3), Zulinqi (GB 41) (1), Guangming (GB 37) (1), Wushu (GB 27) (1)
Triple Energizer Meridian	3	1	Zhigou (TE 6) (3)
Heart Meridian	2	1	Shenmen (HT 7) (2)
Lung Meridian	1	1	Lieque (LU 7) (1)

Table 3. Body region distribution

De hereiten	Total	Number of	of Point and frequency (time)	
Body region	frequency	acupoints		
Chest-abdomen	389	22	Guanyuan (CV 4) (84), Zigong (EX-CA1) (70), Zhongji (CV 3) (56), Qihai (CV 6) (45), Guilai (ST 29) (35), Zhongwan (CV 12) (18), Tianshu (ST 25) (15), Luanchao (Extra) (13), Dahe (KI 12) (12), Shuidao (ST 28) (7), Xiawan (CV 10) (7), Daimai (GB 26) (6), Shuifen (CV 9) (5), Shangwan (CV 13) (3), Daheng (SP 15) (2), Qimen (LR 14) (2), Huaroumen (ST 24) (2), Siman (KI 14) (2), Henggu (KI 11) (2), Tianxi (SP 18) (1), Wailing (ST 26) (1), Wushu (GB 27) (1)	42.3
Lower limbs: knees and below	307	18	Sanyinjiao (SP 6) (88), Zusanli (ST 36) (53), Fenglong (ST 40) (44), Taichong (LR 3) (35), Taixi (KI 3) (23), Yinlingquan (SP 9) (22), Diji (SP 8) (17), Gongsun (SP 4) (5), Xingjian (LR 2) (4), Fuliu (KI 7) (4), Yanglingquan (GB 34) (3), Ququan (LR 8) (2), Taibai (SP 3) (2), Yingu (KI 10) (1), Zhaohai (KI 6) (1), Zulinqi (GB 41) (1), Guangming (GB 37) (1), Ligou (LR 5) (1)	33.4
Back	132	14	Shenshu (BL 23) (39), Ganshu (BL 18) (24), Pishu (BL 20) (21), Ciliao (BL 32) (13), Geshu (BL 17) (12), Mingmen (GV 4) (9), Shangliao (BL 31) (3), Dazhui (GV 14) (2), Sanjiaoshu (BL 22) (2), Guanyuanshu (BL 26) (2), Yaoyangguan (GV 3) (2), Jueyinshu (BL 14) (1), Gaohuangshu (BL 43) (1), Qihaishu (BL 24) (1),	14.4
Lower limbs: above knees	46	3	Xuehai (SP 10) (43), Yinlian (LR 11) (2), Huantiao (GB 30) (1)	5.0
Upper limbs: elbows and below	36	6	Hegu (LI 4) (15), Neiguan (PC 6) (14), Zhigou (TE 6) (3), Shenmen (HT 7) (2), Quchi (LI 11) (1), Lieque (LU 7) (1)	4.0
Head and face	9	1	Baihui (GV 20) (9)	0.9

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Туре	Total frequency	Number of points	Point and frequency (time)
Front-Mu points	175	5	Guanyuan (CV 4) (84), Zhongji (CV 3) (56), Zhongwan (CV 12) (18), Tianshu (ST 25) (15), Qimen (LR 14) (2)
Five Shu-Transmitting points	156	14	Ying-Spring: Xingjian (LR 2) (4) Shu-Stream: Taichong (LR 3) (35), Taixi (KI 3) (23), Shenmen (HT 7) (2), Taibai (SP 3) (2), Zulinqi (GB 41) (1) Jing-River: Fuliu (KI 7) (4), Zhigou (TE 6) (3) He-Sea: Zusanli (ST 36) (53), Yinlingquan (SP 9) (22), Yanglingquan (GB 34) (3), Ququan (LR 8) (2), Quchi (LI 11) (1), Yingu (KI 10) (1)
Crossing points	102	5	Sanyinjiao (SP 6) (88), Baihui (GV 20) (9), Qimen (LR 14) (2), Daheng (SP 15) (2), Huantiao (GB 30) (1)
Back-Shu points	87	5	Shenshu (BL 23) (39), Ganshu (BL 18) (24), Pishu (BL 20) (21), Jueyinshu (BL 14) (1), Sanjiaoshu (BL 22) (1)
Yuan-Primary points	77	5	Taichong (LR 3) (35), Taixi (KI 3) (23), Hegu (LI 4) (15), Shenmen (HT 7) (2), Taibai (SP 3) (2)
Luo-Connecting	65	5	Fenglong (ST 40) (44), Neiguan (SP 6) (14), Gongsun (SP 4) (5), Guangming (GB 37) (1), Ligou (LR 5) (1)
Lower He-Sea points	56	2	Zusanli (ST 36) (53), Yanglingquan (GB 34) (3)
Eight Influential points	30	2	Zhongwan (CV 12) (18), Geshu (BL 17) (12)
Confluent Points of the Eight Extraordinary Meridians	17	4	Neiguan (PC 6) (14), Lieque (LU 7) (1), Zhaohai (KI 6) (1), Zulinqi (GB 41) (1)
Xi-Cleft points	17	1	Diji (SP 8) (17)

Table 4. Special acupoint distribution

2.2 Correlation analysis

The correlation rules of the top 15 acupoints on the list of frequency were analyzed by Clementine 12.0. The first 10 correlation rules with support \geq 10% and confidence \geq 80.0% are shown in Table 5 and Table 6.

The confidence indicated the odds of the latter item given the former item. The support meant the odds of the concurrent existence of the former and latter items. For example: the occurrence rate of Sanyinjiao (SP 6) was 96.4% given the appearance of Guanyuan (CV 4), and the confidence was 96.4%; the possibility of the

concurrent existence of the two points was 91.3%, and the support was 91.3%.

2.3 K-Means cluster analysis

The K-Means cluster analysis was performed for the top 15 acupoints on the frequency list by Clementine version 12.0. K-Means cluster was to randomly selected K centers, and classified the objects according to the distance from them to each K center. As a result, 5 clusters were obtained and cluster 1 ranked the top according to the frequency, while cluster 2 was at the bottom of the list. The details are shown in Table 7.

Table 5. The top 1	10 correlation ru	les regarding t	he confidence
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Former item	Latter item	Support (%)	Confidence (%)
Zusanli (ST 36)	Sanyinjiao (SP 6)	57.6	100.0
Xuehai (SP 19)	Sanyinjiao (SP 6)	46.2	100.0
Xuehai (SP 10) and Guanyuan (CV 4)	Sanyinjiao (SP 6)	45.7	100.0
Shenshu (BL 23)	Sanyinjiao (SP 6)	42.4	100.0
Shenshu (BL 23) and Guanyuan (CV 4)	Sanyinjiao (SP 6)	40.2	100.0
Taichong (LR 3)	Sanyinjiao (SP 6)	38.0	100.0
Zhongji (CV 3) and Zusanli (ST 36)	Sanyinjiao (SP 6)	35.9	100.0
Taichong (LR 3) and Ganyuan (CV 4)	Sanyinjiao (SP 6)	33.7	100.0
Xuehai (SP 10) and Zusanli (ST 36)	Sanyinjiao (SP 6)	32.6	100.0
Qihai (CV 6) and Zusanli (ST 36)	Sanyinjiao (SP 6)	31.5	100.0

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Former item	Latter item	Support (%)	Confidence (%)
Guanyuan (CV 4)	Sanyinjiao (SP 6)	91.3	96.4
Zhongji (CV 3)	Sanyinjiao (SP 6)	60.9	94.6
Zusanli (ST 36)	Sanyinjiao (SP 6)	57.6	100.0
Zhongji (CV 3) and Guanyuan (CV 4)	Sanyinjiao (SP 6)	54.3	96.0
Zusanli (ST 36) and Guanyuan (CV 4)	Sanyinjiao (SP 6)	53.2	100.0
Qihai (CV 6)	Sanyinjiao (SP 6)	48.9	97.8
Xuehai (SP 10)	Sanyinjiao (SP 6)	46.7	100.0
Xuehai (SP 10) and Guanyuan (CV 4)	Sanyinjiao (SP 6)	45.7	100.0
Shenshu (BL 23)	Sanyinjiao (SP 6)	42.4	100.0
Taichong (LR 3)	Sanyinjiao (SP 6)	38.1	100.0

Table 6. The top 10 correlations rules regarding the support

Table 7. Cluster analysis

Cluster	Acupoint
Cluster 1	Guanyuan (CV 4), Sanyinjiao (SP 6)
Cluster 3	Zhongji (CV 3), Zusanli (ST 36), Qihai (CV 6)
Cluster 4	Xuehai (SP 10), Shenshu (BL 23), Taichong (LR 3), Guilai (ST 29)
Cluster 5	Ganshu (BL 18), Taixi (KI 3), Yinlingquan (SP 9), Pishu (BL 20)
Cluster 2	Zhongwan (CV 12), Tianshu (ST 25)

3 Discussion

PCOS was first described in 1935^[8], and its main manifestations are hyperandrogenism and decreased ovulation or even anovulation^[9]. There is no such term in traditional Chinese medicine, but it can be classified into delayed menstruation, amenorrhea or female infertility according to its signs and symptoms, or under the scope of Zheng Jia (mass accumulation) because of the polycystic ovarian enlargement^[10-11]. This condition is mainly associated with dysfunctions of Zang-fu organs, predominantly the liver, spleen and kidney, and the major pathological productions are phlegm, dampness and blood stasis^[12]. In the recent years, there had been numerous clinical studies focusing on acupuncturemoxibustion treatment of PCOS. As a result, there occurred some data dining research in this field. However, some problems cannot be ignored, such as insufficient cutting-edge support^[13], and not using data mining software for analysis^[14-15]. The current study collected clinical studies of acupuncture-moxibustion treatment of PCOS published during 1996 and 2018 and conducted correlation and cluster analyses for the frequency and meridian distribution of acupoints by adopting data mining software and K-means method $^{\rm [16]},$ for seeking and summarizing the acupoint selection regularities in acupuncture- moxibustion treatment of PCOS.

This study identified a total of 67 acupoints from 92 eligible clinical trials, among which, 39 were special points. According to the data mining analysis, the top three acupoints on the frequency list were Sanyinjiao (SP 6) (88), Guanyuan (CV 4) (84) and Zhongji (CV 3) (56); the identified acupoints were mainly from the Conception Vessel (218), Spleen Meridian of Foot Taiyin (180) and Stomach Meridian of Foot Yangming (157); the top three distributed body regions were chestabdomen (389), lower limbs: knees and below (307) and back (132). We know that acupoints are where gi and blood of Zang-fu organs pour into the body surface, and that's why acupuncture-moxibustion can regulate Zang-fu function via stimulating the corresponding acupoints. Guanyuan (CV 4) and Zhongji (CV 3) are located on the lower belly, so the frequent use of these two acupoints reflects that the acupoints can be used to treat the diseases of where they are located. Sanyinjiao (SP 6) is a crucial point for gynecological diseases. It is the crossing point of the three foot yin meridians which run from the feet to the belly. Hence, the frequent use of Sanyinjiao (SP 6) is an example of using an acupoint to treat diseases related to the path of their meridians. On the other hand, the treatment of gynecological diseases is also guided by meridian-based syndrome differentiation. By data mining, Shen LY, et al^[17] discovered that the hairy regions of PCOS patients showed certain yin-yang and meridian distribution specificities. He found that the yin side was hairier than the yang side, especially along the Conception Vessel, Yangming meridians, and Liver Meridian, and the acupoints often selected to treat PCOS were also mainly from these meridians. The distribution of acupoints in acupuncture-moxibustion treatment of PCOS not only reflects the feature of clinical treatment, but also bears potential value for clinical diagnosis. Liu B^[18] holds that acupoint diagnosis should not be ignored and the theory expects restructuring and renovation. Given the current research condition in acupuncture-moxibustion treatment of PCOS, we also strongly believe that it is

necessary to conduct an integrated study about the acupoint diagnosis and treatment of PCOS.

Confidence and support are key factors in judging the validity of a correlation rule. The support indicates the prevalence and application rate of a correlation rule, i.e. the possibility of the concurrent existence of two items. Confidence reveals the accuracy and reliability of a correlation rule, i.e. the possibility of an event that contains item A also covers item B, reflecting the odds of the occurrence of item B given the appearance of item A. An ideal correlation should have a high support and confidence at the same time^[19]. According to the support and confidence report, the most frequently used acupoint groups were Sanyinjiao (SP 6) plus Zusanli (ST 36) and Sanyinjiao (SP 6) plus Guanyuan (CV 4). Sanyinjiao (SP 6) is the crossing point of the three foot yin meridians, with the function to tonify spleen and kidney and regulate liver; Zusanli (ST 36) is the lower He-Sea point of the Stomach Meridian of Foot Yangming, and it can reinforce qi and harmonize stomach, release dampness and dissolve phlegm/stasis; Guanyuan (CV 4) is the crossing point of the three foot yin meridians and the Conception Vessel and it can consolidate the primordial qi, and modulate the Conception and Thoroughfare Vessels. Huang XS^[20] took Sanyinjiao (SP 6) as the major point to treat obesity-type PCOS and found that the levels of insulin resistance parameters, fasting insulin, low density lipoprotein, total cholesterol and triglyceride all declined after treatment, suggesting that acupuncture at Sanyinjiao (SP 6) can regulate glucose and lipid metabolism disturbance in PCOS and increase insulin sensitivity and pregnancy rate. Anatomic studies have demonstrated that the location of Sanyinjiao (SP 6) is governed by T₅-L₄ spinal nerves and their branches, partially overlapping the afferent nerves of ovary^[21-22]; another study also showed that acupuncture at Sanyinjiao (SP 6) affected hypothalamus and pituitary in the regulation of gonadotropin and gonadotropin-releasing hormone^[23]. Chen PD, *et al*^[24] found that acupuncture at acupoints including Guanyuan (CV 4) and Zusanli (ST 36) improved endometrial dysplasia induced by clomiphene citrate (CC) and cervical mucus score, and ameliorated endometrium thickness and blastocyst implantation environment. Sun J, et al^[25] discovered that by enhancing the levels of P450arom and its mRNA, and inhibiting the levels of P450c17 α and its mRNA in ovary of PCOS rats, electroacupuncture at acupoints including Guanyuan (CV 4) could promote androgen to transform into estrogen, so as to improve the condition of follicular development, ovulation failure and hyperandrogenism in PCOS. In an experimental study, Wang SJ, et al^[26] found that acupuncture at Guanyuan (CV 4), Zusanli (ST 36) and other points could promote the electrical activities in hypothalamus and excitatory nerves related to sexual

arousal imitation. They also discovered that the location of Guanyuan (CV 4) is governed by T_{11} - L_3 spinal nerves and the location of Zusanli (ST 36) is in the charge of L_3 - L_4 spinal nerves, which substantially overlap the nervous distributions of reproductive organs. Dr. Shi Yin emphasizes the significance of selecting Sanyinjiao (SP 6), Guanyuan (CV 4) and Zusanli (ST 36) in the treatment of PCOS based on different stages, syndromes and types^[27]. The above studies all contributed certain evidence to prove the effectiveness of Sanyinjiao (SP 6), Guanyuan (CV 4) and Zusanli (ST 36) for PCOS.

Clustering or cluster analysis is a method to group a set of objections with similar features. K-means clustering analysis randomly selected k cluster centers and classified objects according to their distance to the nearest center^[16]. This type of clustering analysis matched up more with the classification of common syndromes^[28], and thus can be applied to analyze the core acupoints for each syndrome. Guanyuan (CV 4) and Sanvinjiao (SP 6) can supplement the primordial gi, so they are used as the major points for kidney deficiency pattern; Zhongwan (CV 12) and Tianshu (ST 25), which can tonify spleen and dispel dampness, are used to treat spleen deficiency and phlegmdampness syndrome; Zhongji (CV 3), Zusanli (ST 36) and Qihai (CV 6) can supplement qi and nourish blood, so that they can be used for gi-blood deficiency syndrome. The other two syndromes are more complicated. Xuehai (SP 10), Shenshu (BL 23), Taichong (LR 3) and Guilai (ST 29) all function to dissolve stasis and tonify kidney, and they can be used for kidney deficiency and blood stagnation syndrome; Ganshu (BL 18), Taixi (KI 3), Yinlingquan (SP 9) and Pishu (BL 20) can tonify kidneyspleen and regulate liver, so that they are used as the major acupoints for the pattern of kidney-spleen deficiency and liver depression and phlegm-dampness blocking syndrome. So far, although the patterns of PCOS in traditional Chinese medicine have not been unified yet, kidney deficiency, spleen deficiency, blood stagnation, phlegm-dampness and liver depression are predominant ones^[28]. Jiang YT, *et al*^[29] hold that sterility in PCOS should be closely related to age, body constitution and disease syndrome, while kidney deficiency is more associated with sterility and usually results in a poor pregnancy outcome. We can see that the five clusters of acupoints concluded in this research conform to the clinical rules. In turn, in clinical practice, the acupuncture-moxibustion treatment should also pay attention to the difference between patterns and enhance the clinical effectiveness via carefully selecting acupoints, tonifying the deficiency and reducing the excess.

In summary, the data mining analysis showed that acupuncture-moxibustion treatment of PCOS should

select acupoints from the chest-abdomen region and the Conception Vessel as the major acupoint, in combination with the points from the knees and below as well as the Spleen and Stomach Meridians. By following the support and confidence report, Sanyinjiao (SP 6) plus Zusanli (ST 36) or Sanyinjiao (SP 6) plus Guanyuan (CV 4) can be used. Besides, the treatment should be modified according to different syndromes to improve the therapeutic efficacy: Zhongwan (CV 12) and Tianshu (ST 25) can be added to tonify spleen and dispel dampness; Zhongji (CV 3) and Qihai (CV 6) for supplementing gi and nourishing blood; Xuehai (SP 10), Shenshu (BL 23), Taichong (LR 3) and Guilai (ST 29) for tonifying kidney and dissolve stasis; Ganshu (BL 18), Taixi (KI 3), Yinlingquan (SP 9) and Pishu (BL 20) for tonifying kidney-spleen and regulating liver^[30-33].

Conflict of Interest

The authors declared that there was no potential conflict of interest in this article.

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