·新型冠状病毒肺炎专栏·

中医药影响新型冠状病毒肺炎密接者转阳率的研究：一项大样本队列研究

王晓骁，窦莉，邹冲，吴拥军，王威，赵晶晶，于茜，沈照峰，倪平敏，章雯，陆亚文，奚肇庆，方祝元

（南京中医药大学附属医院,江苏 南京　210023）

摘要：目的　观察中医药对新型冠状病毒肺炎（COVID-19）密切接触者的核酸检测转阳率的影响,为中医药预防新型冠状病毒肺炎的应用提供依据。方法　将扬州隔离点中使用和未使用中药（清肺排毒汤、扶正益清方）的 COVID-19 密接者纳入本研究,通过倾向性评分匹配和 logistic 回归分析对核酸扩增试验（NAATs）的阳性率、核酸阳性者的病毒载量、阳性者的病情等级进行分析,以评估中医药预防新型冠状病毒肺炎的作用。结果　共收集了 30 000 余例观察对象,基于数据筛选、核对,以 1 286 例密接者作为研究对象,包括中药组 1 016 例（79.00%）和对照组 270 例（21.00%）,共有转阳患者 55 例。在倾向性评分匹配分析前后,结果均显示在男性和大于 60 岁的老年人群中,中药组的转阳率低于对照组,差异具有统计学意义（$P<0.05$）。多因素 logistic 回归（不纳入 N 值和 O 值）结果显示中药组转阳的风险与对照组相比降低了 0.547 倍。另外,密接者转阳后,中药组的总体和女性的病毒 CT 值高于对照组,差异具有统计学意义（$P<0.05$）。结论　中医药有利于降低 COVID-19 密接者的转阳率和病毒载量。

关键词：新型冠状病毒肺炎；密切接触者；中医药；预防；阳性率

Effectiveness of Traditional Chinese Medicine in Reducing the Positive Rate of COVID-19 Close Contacts: A Large Population Cohort Study

WANG Xiao-xiao, DOU Li, ZOU Chong, WU Yong-jun, WANG Wei, ZHAO Jing-jing, YU Qian, SHEN Zhao-feng, NI Ping-min, ZHANG Wen, LU Ya-wen, XI Zhao-qing, FANG Zhu-yuan

(The Affiliated Hospital of Nanjing University of Chinese Medicine, Nanjing 210023, China)

ABSTRACT: OBJECTIVE　Corona-virus disease 2019 (COVID-19) is an infectious disease caused by SARS-CoV-2 virus. The variant of corona-virus first identified in India, known as Delta, has become the dominant strain in China. Unfortunately, more contagious and unknown variants are coming, leading to a number of close contacts under quarantine. Chinese medicine (TCM) has been recommended to prevention and treatment due to the satisfactory therapeutic effects. However, the effect of TCM to decrease positive rate in close contacts remains unknown. METHODS　We conducted an retrospective cohort study in Yangzhou, China to assess the effect of Chinese medicine on decreasing positive rate in close contacts under quarantine. The primary observation outcome was positive rate of Nucleic Acid Amplification Tests (NAATs). The secondary observation outcome was a composite of viral load of positive NAATs, severity levels of confirmed cases (asymptomatic, mild, moderate, or severe), daily body temperature, and levels of close contact (primary or secondary). RESULTS　A total of 1 286 subjects were collected, of which 1 016 (79.00%) in TCM group and 270 (21.00%) in control group with 55 participants tested positive. The incidence of the primary outcome, positive rate of NAATs was significantly lower in the Chinese medicine group than in the control group, occurring in male and age≥60 years subjects. Multi-variable logistic regression (excluding NO viral load) indicated that the risk of testing positive was reduced by 0.547 times in TCM group

compared to control group. CT value of TCM group was higher than that of control group in all subjects and female subjects, and the result showed statistically significant difference. **CONCLUSIONS**　In our study involving close contacts under quarantine, Chinese medicine resulted in lower positive rate of NAATs and viral load than control.

KEYWORDS: COVID-19; close contacts; traditional Chinese medicine; prevent; positive rate

The severe acute respiratory syndrome corona-virus 2 (SARS-CoV-2) is a rapidly emerging virus causing corona-virus disease 2019 (COVID-19) and the global pandemic since the outbreak in Wuhan, China in late 2019[1-2]. Current strategies to protect oneself include getting vaccines, ensuring personal hygiene, using face masks, and practicing social distancing[1]. With constant mutations of the virus, multiple variants of concern (VOC) continue to emerge. The Delta variant (also referred to as B. 1. 617. 2) appears to spread more easily than other variants. It is characterized by increased transmissible, shorter incubation period, stronger pathogenic, faster progression, and higher risks to cause severe illness[3]. It was once the predominant variant of the virus worldwide, which was already predicted by the WHO in July that the Delta variant was expected to be the main strain in the world in the upcoming months[3]. Due to its high infectivity, a rebound in cases has occurred in multiple countries and territories in the past year.

The outbreak in Nanjing, China since July 2021, which spread to Yangzhou, was caused by Delta variant. Since then, a large number of local residents were under quarantine in centralized medical quarantine sites since the standard of care is to observe and quarantine for 14 days as the incubation period[4]. However, there were no specific interventions carried out onto these population. In order to implement national and provincial requirements trying to prevent people from getting sick and treat the disease and to maximize the effect of Chinese medicine based on previous experiences to control the spread in Guangdong, China, Chinese medicine is encouraged to use for its effectiveness in the treatment of COVID-19[5-7].

According to the requirements by provincial leading group for COVID-19 prevention and control, TCM expert teams were established in all parts of Jiangsu Province at the earliest time since the outbreak. Chinese medicine prescriptions for close contacts were formulated taking local experiences into account, including Qingfei Paidu Decoction, Fuzhengyiqing prescription. In the meantime, local TCM prevention teams were built and TCM practitioners took part in daily rounds to observe and record reactions after using Chinese medicine in close contacts. Experts also went to different quarantine sites to train medical personnel and to supervise daily work. Considering the contagious characteristic of the virus, a unified QR code was used as pharmaceutical service platform to guide health professionals and quarantined residents in quarantine sites for drug use and monitoring.

TCM is a treasure of ancient Chinese medicine with a history of more than 2 000 years and rich experience. Evidence from clinical trials showed that TCM can effectively treat several chronic diseases, such as cerebral infarction and chronic kidney disease. TCM is beneficial for immunity, antivirus, anti-inflammatory and relieved side effects. During last two years, the advantages of TCM for the treatment of COVID-19 have been found, including delay the disease progression from mild and moderate to severe. Some mild symptoms like cough or dizziness could be treated with TCM. In addition, WHO expert meeting confirmed Chinese medicine (TCM) in the treatment of COVID-19. In China, TCM could shorten the time of nucleic acid turning negative and reduce the possibility of disease exacerbation. Importantly, fewer adverse events related to TCM were founded. Lianhua Qingwen capsule has been recommended to treat COVID-19 patients with mild symptoms, which could reduce the fever time. Studies shown TCM could improve immune function and hypoxia resistance, protect pulmonary micro-vascular endothelial cells, and inhibit pulmonary fibrosis, which is suitable for the pathological changes of lung tissue injury.

1　METHODS

1.1　Participants

An estimate of at least 5 000 residents who had a recent history of close-contact exposure to a case patient of COVID-19 under centralized quarantine in Jiangsu Province were included based on tripartite database. Participants were excluded if they were confirmed cases of COVID-19, while pregnant or breast-feeding, had complications of severe primary heart, lung, kidney, blood, or other diseases affecting survival, or with psychiatric, cognitive impairment, or legally disabled. Statisticians and main researchers shall determine whether the participants should be eliminated who did not meet inclusion criteria but met exclusion criteria before statistical analysis started.

1.2　Study Design and Oversight

This was an retrospective cohort study, and data of close contacts in centralized medical quarantine sites in Yangzhou, China from August 4 to September 5, 2020 was collected. Study candidates were screened using tripartite database (pharmaceutical database, Yangzhou on-site database, and provincial CDC database) to explore the efficacy of TCM in prevention of COVID-19. Tripartite database first underwent matching, cleaning, and desensitizing (removing identifiable personal information), and was later performed on mining and analysis.

A query list was provided in case of any question. The researchers shall answer the questions in the query list and review each copy of electronic document. The database would be locked once the data verification report was completed. Any documents related to quality control need to be filed, such as data consistency verification, original records of numerical range and logical check, original records of blind audit, and query records of communication between researchers.

1.3　Exposure

The exposure (main strategies) was the use of TCM (including Qingfei Paidu Decoction and Fuzhengyiqing prescription) in the prevention of COVID-19 among close contact in various parts of Jiangsu Province, twice a day for 6 days. Close contacts without using TCM were considered control group.

Qingfei Paidu Decoction composes of 21 herbs, which are Ma huang (*Ephedra Herba*) 9 g, Zhi gan cao 6 g, Ku xing ren

(*Amygdalus Communis* Vas) 9 g, Sheng shi gao 15−30 g, Gui zhi (*Cinnamomi* Ramulus) 9 g, Ze xie (*Alisma Orientale* Juz.) 9 g, Zhu ling (*Polyporus Umbellatus* Fr.) 9 g, Bai zhu (*Atractylodes Macrocephala* Koidz.) 9 g, Fu ling (*Poria Cocos* Wolf.) 15 g, Bei chai hu 16 g, Huang qin (*Scutellariae Radix*) 6 g, Jiang ban xia 9 g, Ginger (*Zingiber Officinale* Roscoe) 9 g, Zi wan (*Asteris Radix* Et Rhizoma) 9 g, Kuan dong hua (*Farfarae Flos*) 9 g, She gan (*Belamcandae Rhizome*) 9 g, Xi xin (*Asari Radix* Et Rhizoma) 6 g, Shan yao (*Rhizoma Dioscoreae*) 12 g, Zhi shi (*Aurantii Fructus Immaturus*) 6 g, Chen pi (*Citrus Reticulata*) 6 g, Huo xiang (*Pogostemon Cablin* Benth.) 9 g[8]. Raw herbs were boiled with water and made into a 400 mL decoction, which could be taken in 2 days with 100 mL b. i. d. for the entire course of treatment for 6 days. Studies have found over 210 possible targets of Qingfei Paidu Decoction and 50 common targets with COVID−19, which are associated with major immunological pathways including T cell, B cell, tumor necrosis factor (TNF), etc, by inhibiting the invasion and replication of virus directly[8−9].

Fuzhengyiqing Prescription include Ren shen (*Panax Ginseng* C. A. Mey.) 5g, Huang qi (*Hedysarum Multijugum* Maxim.) 5 g, Shan yao (*Rhizoma Dioscoreae*) 10 g, Chen pi (*Citrus Reticulata*) 5 g, Fu ling (*Poria Cocos* Wolf.) 15 g, Jin yin hua (*Lonicerae Japonicae* Flos) 5 g, Mint (*Menthae Herba*) 3 g, Sang ye (*Mori Follum*) 5 g, Lu gen (*Phragmitis Rhizoma*) 15 g, Huo xiang (*Pogostemon Cablin* Benth.) 5 g, Sheng gan cao (*Licorice*) 3 g, Lian zi xin (*Nelumbinis Plumula*) 3 g. Raw herbs were processed into granules and taken with water b. i. d. for the entire course of treatment for 6 days.

1. 4　Covariable and outcome

Age, sex, underlying disease of close contacts, N value and O value of cases which relate to those close contacts, were considered covariables. Age was categorized as dichotomous variable: <60 years old and ≥60 years old. Underlying diseases were categorized according to whether the close contacts had underlying diseases (i. e. hypertension, diabetes, chronic bronchitis). The primary outcome was the result (Positive and Negative) of Nucleic Acid Amplification Tests (NAATs), the positive rate of NAATs was reported. The secondary outcome was the N value and O value of close contacts who turn positive subsequently.

1. 5　Statistical analysis

All data of study were analyzed statistically using R software including actual number of participants, expulsion and exclusion cases, demographic and other baseline characteristics, and efficacy.

Because three data sets form site Yangzhou, EDC system and CDC include different information, the three data sets were merged by ID number to get the final analysis data set before data analysis. The analysis data set included age, sex, underlying diseases, N value, O value, TCM use and the testing result of NAATs.

Qualitative variables were reported as frequency and percentage. Chi−square test or Fisher′s exact test were used for comparison of qualitative variables between TCM group and control group. Quantitative data were reported as means and standard deviation ($\bar{x}\pm s$), or Median and inter−quartile range (IQR). T−test was used for comparison between two groups if under normal distribution (homogeneity of variance between groups was tested with 0. 05 as the test level and Satterthwaite method was used for correction when variance was not uniform) whereas Wilcoxon rank sum test was used for comparison when normal distribution failed to be consistent with logarithmic transformation. Two groups were matched at a ratio of 1∶1 using propensity score matching method before comparison with matching factors of gender and age. Multi−variable logistic regression analysis was performed to explore the association between TCM use and positive status adjusting age, gender, viral load (N value and O value), underlying disease history. Two−sided test was adopted to use as the standard. Given test statistics and their corresponding P values with $P<0. 05$ as statistically significant.

2　RESULTS

2. 1　Statistical results after data handover

A total of 7 793 subjects were collected on site Yangzhou, of which 7 314 in TCM group and 479 in control group. A total of 8 440 subjects were collected using EDC system, of which 4 995(59. 18%) in TCM group and 3 445 (40. 82%) in control group.

After removing duplicate cases and non−close contacts by processing with tripartite matching and cleaning according to tripartite database (on site, EDC system and CDC), a total of 1 286 subjects were collected, of which 1 016 (79. 00%) in TCM group and 270 (21. 00%) in control group with 55 participants tested positive. A total of 54 cases missed age and 9 cases missed gender. The results of comparison of characteristics between TCM group and control group were listed in Table 1. The detail of underlying diseases of close contacts was shown as Table 2.

Table 1　Comparison of characteristics between TCM group and control group

Characteristics	Control Group	TCM Group	$W/\chi^2/t$	P value
Age, Median (IQR)	35. 0 (25. 0, 50. 0)	41. 0 (30. 0, 53. 0)	−5. 278	<0. 001
Gender, n (%)				
Male	135 (50. 00)	471 (46. 77)	0. 889	0. 346
Female	135 (50. 00)	536 (53. 22)		
Underlying diseases, n (%)				
No	230 (85. 19)	917 (90. 26)	5. 689	0. 017
Yes	40 (14. 81)	99 (9. 74)		
N value, $\bar{x}\pm s$	24. 91±7. 47	23. 00±7. 67	3. 295	0. 001
O value, $\bar{x}\pm s$	27. 31±6. 79	25. 73±7. 07	3. 001	0. 003

Table 2　The detail of underlying diseases of close contacts

Underlying disease	Frequency/n	Percentage/%
Hypertension	45	32. 37
Diabetes	14	10. 07
Chronic bronchitis	9	6. 47
Chronic nephrosis	7	5. 04
Other	85	61. 15

Note: Some close contacts have multiple underlying disease.

2. 2　Inferential Statistical Results

Positive rate was analyzed between TCM and control groups in different subgroups based on gender and age (whether less than 60 years old), and the result was shown in Table 3. It was shown that the positive rate of TCM group was lower than that of control group for all subjects with statistically significant difference ($P = 0. 019$). Of male close contacts, the positive rate of TCM group was lower than that of control group with statistically significant difference ($P = 0. 048$). And of people $\geqslant 60$ years old, the positive rate of TCM group was lower than that of control group with statistically significant difference ($P < 0. 001$).

Table 3　Comparison of positive rate between TCM and control group before matching

Subgroups		NAATs Result, n (%)		χ^2	P value
		Negative	Positive		
All	Control Group	251 (92. 96)	19 (7. 04)	5. 535	0. 019
	TCM Group	980 (96. 46)	36 (3. 54)		
Male	Control Group	126 (93. 33)	9 (6. 67)	3. 922	0. 048
	TCM Group	457 (97. 03)	14 (2. 97)		
Female	Control Group	125 (92. 59)	10 (7. 41)	2. 590	0. 108
	TCM Group	514 (95. 90)	21 (4. 10)		
Age <60	Control Group	234 (97. 50)	6 (2. 50)	0. 376	0. 540
	TCM Group	796 (96. 72)	27 (3. 28)		
Age $\geqslant$60	Control Group	13 (52. 00)	12 (48. 00)	30. 392	<0. 001
	TCM Group	135 (93. 75)	9 (6. 25)		

Subjects with missing information need to be removed beforehand. The total number of subjects was 1 227 including 962 (78. 40%) in TCM group and 265 (21. 60%) in control group. Taking age and gender as matching variables and setting caliper value as 0. 05, propensity score matching was conducted at a ratio of 1∶1 to match 259 participants in each group. There was no statistically significant difference in age ($t = -0. 402$, $P = 0. 688$) and gender ($\chi^2 = 0. 378$, $P = 0. 538$) between TCM and control groups after matching. The result pattern of propensity score matching was shown as Figure 1.
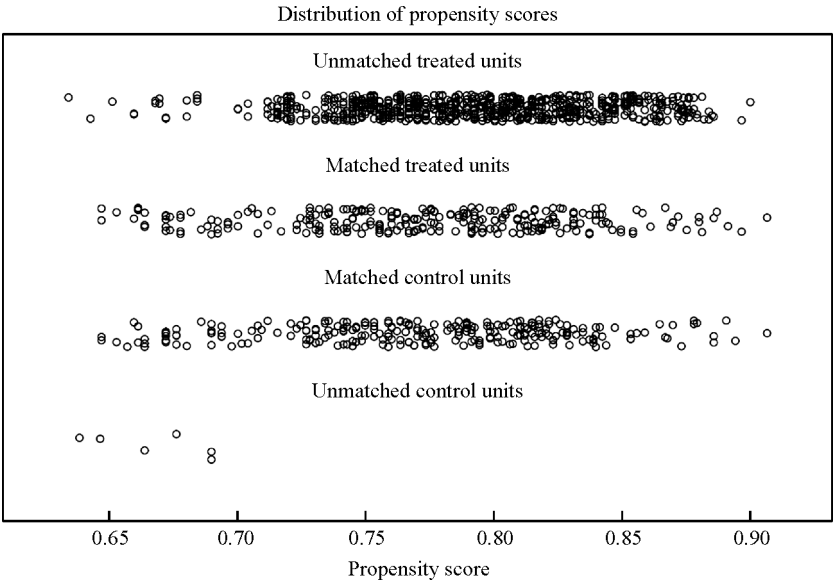
Fig. 1　Result pattern of propensity score matching

Data after matching was compared on positive rate in all subjects and different subgroups. The result was shown in Table

4, which indicated that the positive rate of TCM group was lower than that of control group for all subjects with statistically significant difference ($P=0.009$). Of male close contacts, the positive rate of TCM group was lower than that of control group with sta- tistically significant difference ($P=0.032$). And of people ≥60 years old, the positive rate of TCM group was lower than that of control group with statistically significant difference ($P<0.001$).

Table 4   Comparison of positive rate between TCM and control groups after matching

Subgroups		NAATs Result, n (%)		χ^2	P value
		Negative	Positive		
All	Control Group	242 (93.44)	17 (6.56)	6.836	0.009
	TCM Group	254 (98.07)	5 (1.93)		
Male	Control Group	121 (94.53)	7 (5.47)	—	0.032*
	TCM Group	134 (99.26)	1 (0.74)		
Female	Control Group	121 (92.37)	10 (7.63)	2.385	0.123
	TCM Group	120 (96.77)	4 (3.23)		
Age <60	Control Group	229 (97.86)	5 (2.14)	<0.001	>0.999
	TCM Group	231 (97.88)	5 (2.12)		
Age ≥60	Control Group	13 (52.00)	12 (48.00)	—	<0.001*
	TCM Group	23 (100.00)	0 (0)		

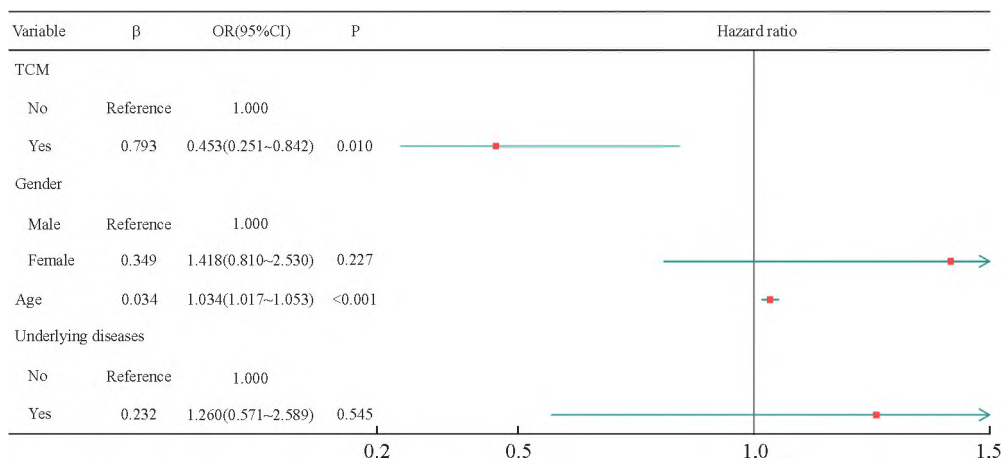Note:　* Fisher´s exact test.

Multi−variable regression analysis was performed before matching data to examine the preventative effect of Chinese medicine on COVID−19 after adjusting gender and age. Compare to control group, the risk of testing positive was reduced by 0.547 times ($OR=0.453$, 95%CI: 0.251−0.842) in TCM group after adjusting age and gender, as shown in Table 5 and Figure 2. After further adjusting N value and O value, no statistically significant difference ($OR=0.933$, 95% CI: 0.131−2.251, $P=0.868$) was observed between taking Chinese medicine and the risk of testing positive, as shown in Table 6.

Table 5   Multivariable logistic regression of TCM reducing positive rate

Variable	β	Std. Error	P	OR	95%CI
TCM vs Control	−0.793	0.307	0.010	0.453	0.251−0.842
Females vs Males	0.349	0.289	0.227	1.418	0.810−2.530
Age	0.034	0.009	<0.001	1.034	1.017−1.053
Underlying diseases	0.232	0.383	0.545	1.260	0.571−2.589

Variable	β	OR(95%CI)	P	Hazard ratio
TCM				
No	Reference	1.000		
Yes	0.793	0.453(0.251~0.842)	0.010	
Gender				
Male	Reference	1.000		
Female	0.349	1.418(0.810~2.530)	0.227	
Age	0.034	1.034(1.017~1.053)	<0.001	
Underlying diseases				
No	Reference	1.000		
Yes	0.232	1.260(0.571~2.589)	0.545	

Fig. 2   Forest plot of multivariable logistic regression

Table 6　Multi－variable logistic regression of TCM reducing positive rate after adjusting N and O value

Variables	β	Std. Error	P	OR	$95\%CI$
TCM vs Control	−0.069	0.416	0.868	0.933	0.131−2.251
Females vs Males	0.109	0.336	0.745	1.116	0.578−2.184
Age	0.007	0.010	0.508	1.007	0.986−1.028
Underlying diseases	0.486	0.489	0.320	1.626	0.571−4.003
N value	0.000 1	0.036	0.998	1.000 1	0.945−1.092
O value	−0.019	0.038	0.616	0.981	0.896−1.045

For the analysis of viral load and classification in 55 close contacts who tested positive, the comparison result of N/O value of TCM and control groups showed that the N value of TCM group (27.00±6.05) was higher than that of control group (22.05± 7.12), which indicated a statistically significant difference ($P=$ 0.017); and the O value of TCM group (28.42±6.01) was higher than that of control group (24.99±5.55), which indicated a statistically significant difference ($P=0.045$). Details were shown on Table 7 and Figure 3−4.

Among 55 close contacts who tested positive, 38 (69.09%) of them had moderate symptoms and 13 (23.64%) had mild symptoms (4 cases missing illness categories). There was no statistically significant difference ($P=0.464$) in composition ratio of categories between TCM and control groups, as shown in Table 8. Multi－variable regression analysis indicating the association between TCM use and illness categories was not significant ($OR=1.761$, $95\%CI$: 0.357−8.696, $P=0.487$), as shown in Table 9.

Table 7　Comparison of N/O values between TCM and control groups

Subgroup	Control Group	TCM Group	t value	P
N value, $\bar{x}±s$				
All	22.05±7.12	27.00±6.05	−2.252	0.017
Males	24.46±6.76	27.36±7.04	−0.974	0.343
Females	19.89±7.06	26.74±5.42	−2.663	0.018
Age<60	25.97±9.97	26.92±5.52	−0.223	0.831
Age ≥60	19.92±4.91	27.24±7.80	−2.365	0.038
O value, $\bar{x}±s$				
All	24.99±5.55	28.42±6.01	−2.068	0.045
Males	27.03±5.20	27.77±6.78	−0.289	0.776
Females	23.16±5.44	28.86±5.57	−2.663	0.015
Age<60	27.48±7.34	28.54±5.97	−0.327	0.753
Age ≥60	23.83±4.56	28.04±6.50	−1.587	0.139

Note: * $P<0.05$.
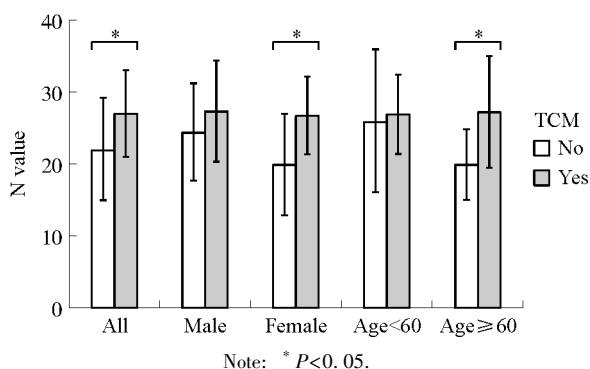
Fig. 3　Comparison of N value between TCM and control groups

Note: * $P<0.05$.
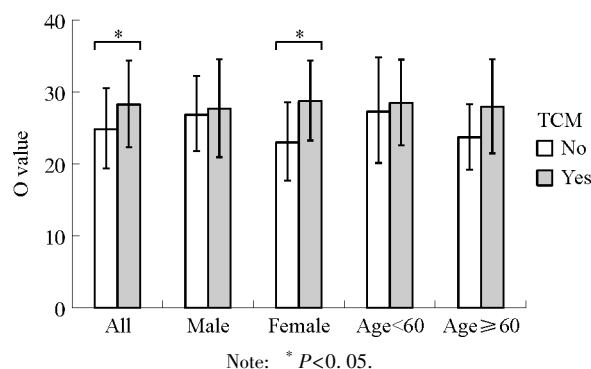
Fig. 4　Comparison of O value between TCM and control groups

Table 8　Illness categories of positive cases between TCM and control groups

Taking Chinese medicine	Moderate illness	Mild illness	χ^2	P
No	15 (83.33)	3 (16.67)	0.535	0.464
Yes	23 (69.70)	10 (30.30)		

Table 9　Multi-variable logistic regression of the effect of TCM on illness severity

Variables	β	Std. Error	P	OR	95%CI
TCM vs Control	0.566	0.815	0.487	1.761	0.357-8.696
Females vs Males	0.370	0.712	0.603	1.448	0.359-5.846
Age	-0.023	0.018	0.199	0.977	0.943-1.012
Underlying diseases	0.306	1.038	0.768	1.358	0.177-10.394

In conclusion, the data before and after matching revealed that the positive rate of TCM group was lower than that of control group in all subjects, male subjects, and subjects whose age is ≥60 in the analysis of positive rate between TCM and control groups, and the difference in composition ratio showed statistically difference. Multi-variable logistic regression (excluding NO viral load) indicated that the risk of testing positive was reduced by 0.547 times in TCM group compared to control group. Moreover, CT value of TCM group was higher than that of control group in all subjects and female subjects, and the result showed statistically significant difference.

3　DISCUSSIONS

The study used the data collected on site, by EDC system, and provincial CDC. Statistical subjects were filtered out after tripartite matching and cleaning, and a total number of 1 286 were collected as participants, of which 1 016 were in TCM group while 270 in control group. Taking age and gender as matching variables and setting caliper value as 0.05, propensity score matching was conducted at a ratio of 1 : 1 to match 259 subjects in each group. The result showed that data before and after matching both indicated that the positive rate of TCM group was lower than that of control group in all subjects, male subjects, and subjects whose age is ≥60, which elucidated that the use of Chinese medicine in centralized quarantine sites was effective on preventing testing positive of close contacts to COVID-19 exposure, especially in specific population groups showing more remarkable preventative effect, such as males and people whose age is ≥60. This trial did not yet involve the pharmacological mechanism of Chinese medicine, which was believed to have the following effects: ① Most Chinese herbs used in these formulas had function of tonifying Qi, such as Huang qi, Bai zhu, and Shan yao, which could improve immunity of the body.[10-11] Therefore, it can be deduced that Chinese medicine may be effective by regulation the immune function of the close contacts, which is also consistent with the TCM theory of "healthy Qi is stored in the body and the pathogenic factors cannot be interfered"[12]. ② It was believed that bad emotion is a significant pathogenic factor in TCM. Chinese herbal ingredients have the effect of soothing the liver and relieving depression. Use of Chinese medicine could relieve panic and anxiety by reducing psychological stress, so as to improve the immune function of close contacts in centralized quarantine sites. ③ The preventative effect of Chinese medicine is more noteworthy in close contacts whose age is ≥60 since elderly could have more underlying diseases. Chinese medicine may be effective by intervening on those basic problems and improve quality of life. In addition, COVID-19 vaccine rate may be lower in the elderly, which highlights the effect of Chinese medicine in unvaccinated population. ④ The preventative effect is more remarkable in male close contacts in the analysis of subgroups, which may be contributed to the underlying diseases and higher smoking rates in males. Thus, male close contacts are more likely to get sick. More research is required for further illustration of gender specific effect of TCM.

The viral load of close contacts to COVID-19 exposure who tested positive were calculated, and the results showed that the CT value of the virus in TCM group was higher than that in control group for all subjects and females. Our results clarified that Chinese medicine could not only prevent testing positive in close contacts, but also reduce the viral load of confirmed cases, relieving symptoms and shortening infectious period. Based on the result of subgroup analysis, females may benefit more from the use of Chinese medicine, which may be contributed to their low body weight. As the same dosage can get the higher serum concentration, it indicates that taking weight as a reference on dosage may strengthen the effect of Chinese medicine.

The development of Chinese medicine prescriptions for specific diseases is recommended, as well as its preparation, quality control, and adverse reaction monitoring. During COVID-19 outbreak in Yangzhou, the early administrative involvement plays an indispensable role in the early intervention and high coverage rate of Chinese medicine use in centralized quarantine sites, which as well laid the foundation for the implementation of distributing Chinese medicine prescriptions. However, the lack of standard medication plan in the early stage and the use of local empirical prescriptions in different regions increased the difficulty for the preparation of Chinese medicine and pharmaceutical services in later stage. TCM treatment varies on individuals, places, and time, and focuses on the symptom-oriented adjustment and personalized diagnosis. It is considered that "one prescription to one person" is the inevitable result from TCM theory of syndrome

differentiation. However, the statement ignores the ideology of TCM outlines and empirical effects of specific prescriptions and medications. Modern Chinese medicine should combine syndrome differentiation with disease differentiation especially when being involved in the public health emergencies. Not only should syndrome be targeted, but also the disease. Since the outbreak of COVID-19, the disease and the pathogenesis did not alter even though the place, timing, and strains varied over time. Therefore, the treatment experiences in Wuhan and Guangzhou in the early stage are advisable. Chinese medicine granules or oral liquids are required as their convenience and can be accurately used relying on body weight. Half dose of Qingfei Paidu Decoction is recommended to prevent from getting sick, which is proved to be effective in reducing positive rates in certain population. Ma huang, Ku xing ren, Sheng shi gao and Zhi gan cao has been used for the treatment of common cold, fever, and influenza virus infections, which means remove cold by dispersing Lung-Qi. She gan, Kuan dong hua and Xi xin are benefit to symptoms like cough, asthma, tonsillitis and sore throat. Bei chai Hu, Huang qin, Jiang ban xia, Ginger and Gui zhi have effect on exogenous febrile disorder containing cold and heat. Ze xie, Zhu ling, Fu ling, Bai zhu, Shan yao, Zhi shi and Chen pi can regulate Qi and eliminate turbidity, a prescription for nephritic syndrome, can improve kidney excretion function and inhibit inflammatory response.

Another proscription, Fuzhengyiqing is a Chinese medicine comprising 12 herbs. One the one hand, it is mainly administered in the treatment of "warm disease" characterized by clinical symptoms including cough, fever and headache. Jin yin hua, Lian qiao, Sang ye, Lu gen, Mint and Lian zi xin are good to clear heat and detoxigy. On the other hand, it is typically used strengthen the immune system, improve cells metabolism and promote blood circulation. Ren shen, Huang qi, Shan yao, Fu ling, Chen pi, Huo xiang and Sheng gan cao played significant roles in pathogenesis of multiple organ injury. All of them have been found to supporting health and suppling Qi.

In conclusion, widely use of Chinese medicine to prevent from COVID-19 in centralized quarantine sites is recommended, especially in population whose age is ≥60 to achieve higher benefits.

ACKNOWLEDGMENTS

Reference：

[1] MITJA O, CORBACHO-MONNE M, UBALS M, et al. A cluster-randomized trial of hydroxychloroquine for prevention of COVID-19 [J]. N Engl J Med, 2021, 384(5): 417-427.

[2] SIMONOVICH VA, BURGOS PRATX LD, SCIBONA P, et al. A randomized trial of convalescent plasma in COVID-19 severe pneumonia[J]. N Engl J Med, 2021, 384(7): 619-629.

[3] BIAN LL, GAO QS, GAO F, et al. Impact of the Delta variant on vaccine efficacy and response strategies[J]. Expert Rev Vaccines, 2021, 20(10): 1201-1209.

[4] BOULWARE DR, PULLEN MF, BANGDIWALA AS, et al. A randomized trial of hydroxychloroquine as postexposure prophylaxis for covid-19[J]. N Engl J Med, 2020, 383(6): 517-525.

[5] ZHAO ZH, ZHOU Y, LI WH, et al. Analysis of traditional Chinese medicine diagnosis and treatment strategies for COVID-19 based on *The diagnosis and treatment program for coronavirus disease*-2019 from Chinese authority[J]. Am J Chin Med, 2020, 48(5): 1035-1049.

[6] WANG ZL, YANG LY. Chinese herbal medicine: Fighting SARS-CoV-2 infection on all fronts[J]. J Ethnopharmacol, 2021, 270: 113869.

[7] AN XD, DUAN LY, ZHANG YH, et al. The three syndromes and six Chinese patent medicine study during the recovery phase of COVID-19[J]. Chin Med, 2021, 16(1): 44.

[8] ZHONG LLD, LAM WC, YANG W, et al. Potential targets for treatment of coronavirus disease 2019 (COVID-19): A review of Qing-Fei-Pai-du-Tang and its major herbs[J]. Am J Chin Med, 2020, 48(5): 1051-1071.

[9] HUANG YF, BAI C, HE F, et al. Review on the potential action mechanisms of Chinese medicines in treating Coronavirus Disease 2019 (COVID-19)[J]. Pharmacol Res, 2020, 158: 104939.

[10] CHEN KX, YIN LW, LI ZP. Study on the prescription pattern of traditional Chinese medicine treatment for Corona Virus Disease 2019 in different provinces based on data mining [J]. J Liaoning Univ Tradit Chin Med, 2021, 23(5):100-107.

[11] PAN Y, ZHANG ML. Analysis on medication rule of COVID-19 pneumonia treated by TCM based on Data Mining [J]. TCM Res, 2021, 34(3):48-53.

[12] SHAO CC, WANG HJ, MENG PF, et al. TCM understanding and treatment status of COVID-19[J]. Acta Chin Med, 2020, 35(4): 704-708.

（编辑：董宇）