

USE OF SHENLING BAIZHU IN PREPARING MEDICAMENT FOR TREATING POST-RECOVERY SEQUELAE OF COVID-19 PATIENT

Cross-Reference to Related Application

This application claims the benefit of the priority of the Chinese Patent Application with the application No. 202211652297.0, filed to the China National Intellectual Property Administration on December 21, 2022 and entitled "Use of Shenling Baizhu in Treating Post-recovery Sequelae of COVID-19 patient and Improvement of Quality of Life", the disclosure of which is hereby incorporated by reference in its entirety.

Technical Field

The present disclosure belongs to the field of medicine and traditional Chinese medicine, and specifically relates to use of Shenling Baizhu in treatment of post-recovery sequelae of a COVID-19 patient, especially a patient with pneumonia caused by SARS-CoV-2, and improvement of quality of life.

Background

Coronavirus Disease 2019 (hereinafter referred to as "COVID-19") is one of the most serious public health and safety incidents in this century. According to the latest real-time statistical data of World Health Organization (WHO), as of December 5, 2022, the cumulative number of confirmed cases of COVID-19 worldwide exceeds 644 million, and the cumulative number of death cases is 6.652 million. According to domestic and foreign literature reports, COVID-19 not only damages the respiratory system, but also damages lung, heart, liver, kidney, blood systems, reproductive system and the like, and causes serious damage to multiple systems of patients in the recovery period, and a series of sequelae, including weakness, cough, short of breath, poor appetite, low fever, night sweat, constipation or diarrhea, chest tightness, palpitation, chronic bleeding, sensory disorder, motor dysfunction and the like, appear. In January 2021, "The Lancet", the world's top medical journal, publishes a follow-up study of 1733 COVID-19 patients after discharge conducted by Wuhan Jinyintan Hospital and other multi-centers, and results show that more than 70% (76%) of patients continue to have at least one symptom after 6 months of acute infection. Fatigue or muscle weakness (63%) and sleep disorder (26%) are the most common symptoms (Huang C, et. al.

6-month consequences of COVID-19 in patients discharged from hospital: a cohort study [J]. Lancet.2021; 397(10270):220-232). The above sequelae greatly affect the quality of life of COVID-19 patients after recovery, and may delay the complete recovery of the patients, so that it is difficult for the patients to recover their immunity, thereby increasing the risk of re-infection. According to experts' prediction, COVID-19 undergoes constant variation, although its virulence is declined, the infectivity is increased and the infection is more secretive. COVID-19 may coexist with humans for a long time, and patients with pneumonia caused by COVID-19 infection may continue to appear in the population. Therefore, there is a continuous clinical demand for a medicament to treat the sequelae and improve the quality of life of clinically cured COVID-19 patients.

Shenling Baizhu granules produced by Beijing Handian Pharmaceutical Co., Ltd. are the only Shenling Baizhu granules (SFDA Approval No. Z20040416) approved by the former State Food and Drug Administration (SFDA), with a specification of 3 g per bag and a daily crude drug dose of 27.9 g. This specification of the Shenling Baizhu granules is an exclusive product of Handian, and other Shenling Baizhu granules on the market are medicaments with the same name but different formulations and foreign substances (the specification is 6 g per bag, and the daily crude drug dose is 13.95 g). The process of Beijing Handian Pharmaceutical Co., Ltd. is divided into 4 parts: extracting volatile oil, water extraction, ethanol extraction, and using Chinese yam powder as an active ingredient; the processes of other granule manufacturers are divided into 2 parts: extracting volatile oil and water extraction; and the substance basis of Shenling Baizhu powders/pills, which are both raw powder used as medicine, differs greatly from that of the Shenling Baizhu granules produced by Beijing Handian Pharmaceutical Co., Ltd. The forming process of preparations also varies greatly. Other Shenling Baizhu granules comply with the 1998 departmental standard and are made from 1 part of extract, 2 parts of sucrose, and 2.5 parts of dextrin. The Shenling Baizhu granules produced by Beijing Handian Pharmaceutical Co., Ltd. comply with the 2005 national standard and are made from 1 part of extract and 0.4 parts of lactose, thereby significantly reducing excipient intake and improving patient compliance.

The unique process of Shenling Baizhu granules produced by Beijing Handian Pharmaceutical Co., Ltd. based on pharmacodynamic substances also acquires a national invention patent, and the patent No. is ZL200510086669.8. In order to alleviate the sequelae of the patients with pneumonia caused by COVID-19, help the patients fully recover as soon as possible and return to normal production and life, the inventor tries the Shenling Baizhu

granules produced by Beijing Handian Pharmaceutical Co., Ltd. to treat the sequelae of the patients with pneumonia caused by COVID-19, and achieves remarkable efficacy.

Summary

In view of deficiencies of existing technologies, the present disclosure provides a new medical use of Shenling Baizhu, especially Shenling Baizhu granules (SFDA Approval No. Z20040416) produced by Beijing Handian Pharmaceutical Co., Ltd., in treating post-recovery sequelae of a patient with COVID-19 and improving quality of life of the patient after recovery.

In order to achieve the above technical effects, the present disclosure adopts the following technical schemes.

Provided is use of Shenling Baizhu in preparing a medicament for treating post-recovery sequelae of a COVID-19 patient and improving quality of life; the sequela is selected from at least one of short of breath, fatigue and weakness, inappetence, and diarrhea; and raw materials of the Shenling Baizhu are composed of the following traditional Chinese medicinal materials in parts by weight.

400 parts of ginseng, 400 parts of poria cocos, 400 parts of rhizoma atractylodis macrocephalae stir-fried with bran, 400 parts of Chinese yam, 300 parts of fried white hyacinth beans, 200 parts of lotus seeds, 200 parts of coix seeds stir-fried with bran, 200 parts of fructus amomi, 200 parts of platycodon grandiflorum, and 400 parts of liquorice.

Optionally, the sequela also includes at least one selected from nausea, epigastric fullness, and asthenic defecation.

Optionally, improving the quality of life of COVID-19 patient after recovery means that after the Shenling Baizhu is administered to COVID-19 patient, the SF12 scale score of the patient is decreased significantly compared with the score before treatment, and the P value is at least less than 0.05.

Optionally, the medicament in the present disclosure is a clinically acceptable preparation.

Optionally, the medicament is selected from decoctions, pills, powders, granules, tablets, or capsules.

As an optional implementation scheme, the medicament is a granule prepared by the following steps.

I. Each traditional Chinese medicinal material is taken in parts by weight.

II. The Chinese yam is crushed into fine powder, and it is passed through a 100-mesh sieve for later use.

III. Volatile oil is extracted from the fructus amomi by using a steam distillation method until it is completely removed, and aqueous solution after distillation is collected in a separate container; a fructus amomi medicinal residue, ginseng, the rhizoma atractylodis macrocephalae stir-fried with bran are soaked in 4-5 times their weight of 95% ethanol for 24 h, it is heated and refluxed for 3 h, and filtered, the ethanol is recovered from a filtrate, and it is concentrated into an extract with a relative density of 1.00-1.15 at 65°C, and an alcohol extract A is obtained; the medicinal residue is then refluxed and extracted with 4-5 times its weight of 50% ethanol for 3 h, it is filtered, the ethanol is recovered from a filtrate, and it is concentrated into an extract with a relative density of 1.12-1.13 at 80°C, an alcohol extract B is obtained, and the medicinal residue after ethanol extraction is used for later use.

IV. The poria cocos, the fried white hyacinth beans, the lotus seeds, the coix seeds stir-fried with bran, the platycodon grandiflorum, and the liquorice are added with 8-10 times their weight of water and boiled for 2 h, it is filtered, a medicinal residue is combined with the medicinal residue for later use after the ethanol extraction in Step III, and then 8 times their weight of water is added to boil together for 1.5 h, it is filtered, the two filtrates and the aqueous solution obtained after the distillation in Step III are combined, it is stillly placed, and filtered, when a filtrate is concentrated to a relative density of 1.20 at 80°C, the alcohol extracts A and B are added, and it is continuously concentrated into an extract with a relative density of 1.30-1.34 at 80°C.

V. The Chinese yam fine powder obtained in Step II is mixed into the extract obtained in Step IV, it is dried at a low temperature of 60°C into a dry extract, and it is crushed, to obtain medicinal powder.

VI. 1 part by weight of the medicinal powder obtained in Step V and 0.4 parts by weight of sugar powder are taken, mixed evenly, and pelletized with 70%-75% ethanol, it is granulated after being dried, and the fructus amomi volatile oil obtained in Step III is sprayed, it is mixed evenly, and 1000 g of the granules are prepared.

As an optional implementation scheme, the above granules should be administered to a subject in need three times a day, 3 g each time, and it is equivalent to a daily crude drug dose

of 27.9 g/day.

Through clinical observation, the Shenling Baizhu granules may effectively treat the post-recovery sequelae of COVID-19 patient, thus the quality of life of the patient is improved.

Brief Description of the Drawings

The present disclosure is further described below in combination with drawings.

Fig. 1 shows a sample table of a quality of life rating scale (SF-12).

Detailed Description of the Embodiments

2019 novel coronaviruses (2019-nCoV) not only cause serious damage to respiratory systems of patients during the infection period, but also have a huge impact on the patients' whole body biological systems, it brings continuous and long-term sequelae to the patients, and greatly affects the patients' physical health and quality of life. The inventor carries out a clinical observation test on the effect of the Shenling Baizhu preparation on the quality of life of the COVID-19 patients after recovery in four hospitals: Tongshan County People's Hospital, Sinopharm Dongfeng General Hospital, Xian'ning Central Hospital, and Yangxin County People's Hospital in Hubei Province. After nearly a month of intervention treatment, the patients' symptoms such as short of breath, fatigue and weakness, inappetence, and diarrhea are significantly improved, and the quality of life is significantly improved.

The present disclosure is described below with reference to specific embodiments. Those skilled in the art may understand that these embodiments are only used to describe the present disclosure, and it does not limit the scope of the present disclosure in any way.

Experimental methods in the following embodiments, unless otherwise specified, are all conventional methods. Medicinal raw materials, reagent materials and the like used in the following embodiments are all commercially available products unless otherwise specified.

In the field of traditional Chinese medicine, there are proprietary terminologies for describing clinical symptoms, such as "fatigue and weakness" is referred to as "tireness and weakness", "inappetence" is referred to as "poor appetite", and "diarrhea" is referred to as "loose stool", In the following embodiments, the relevant clinical symptoms are generally expressed by using the traditional Chinese medicine terminologies.

Embodiment 1: Preparation of Shenling Baizhu granules

Prescription: 400 g of ginseng, 400 g of poria cocos, 400 g of rhizoma atractylodis macrocephalae stir-fried with bran, 400 g of Chinese yam, 300 g of fried white hyacinth beans, 200 g of lotus seeds, 200 g of coix seeds stir-fried with bran, 200 g of fructus amomi, 200 g of platycodon grandiflorum, and 400 g of liquorice.

Production process:

I. Each traditional Chinese medicinal material was taken according to the prescription.

II. The Chinese yam was crushed into fine powder, and it is passed through a 100-mesh sieve for later use.

III. Volatile oil was extracted from the fructus amomi by using a steam distillation method until it was completely removed, and aqueous solution after distillation was collected in a separate container; a fructus amomi medicinal residue was soaked with the ginseng, the rhizoma atractylodis macrocephalae stir-fried with bran, and 4-5 times their weight of 95% ethanol for 24 h, it was heated and refluxed for 3 h, and filtered, the ethanol was recovered from a filtrate, and it was concentrated into an extract with a relative density of 1.00-1.15 at 65°C, and an alcohol extract A was obtained; the medicinal residue was then refluxed and extracted with 4-5 times its weight of 50% ethanol for 3 h, it was filtered, the ethanol was recovered from a filtrate, and it was concentrated into an extract with a relative density of 1.12-1.13 at 80°C, an alcohol extract B was obtained, and the medicinal residue after ethanol extraction was used for later use.

IV. The poria cocos, the fried white hyacinth beans, the lotus seeds, the coix seeds stir-fried with bran, the platycodon grandiflorum, and the liquorice were added with 8-10 times their weight of water and boiled for 2 h, it was filtered, a medicinal residue was combined with the medicinal residue for later use after the ethanol extraction in Step III, and then 8 times its weight of water was added to boil together for 1.5 h, it was filtered, the two filtrates and the aqueous solution obtained after the distillation in Step III were combined, it was stillly placed, and filtered, when a filtrate was concentrated to a relative density of 1.20 at 80°C, the alcohol extracts A and B were added, and it was continuously concentrated into an extract with a relative density of 1.30-1.34 at 80°C.

V. The Chinese yam fine powder obtained in Step II was mixed into the extract obtained in Step IV, it was dried at a low temperature of 60°C into a dry extract, and it was crushed, to obtain medicinal powder.

VI. 1 part by weight of the medicinal powder obtained in Step V and 0.4 parts by weight of sugar powder were taken, mixed evenly, and pelletized with 70%-75% ethanol, it was granulated after being dried, and the fructus amomi volatile oil obtained in Step III was sprayed, it was mixed evenly, 1000 g of the granules were prepared, and sub-packaged in 3 g per bag.

Dosage and administration: three times a day, and 1 bag each time.

Embodiment 2: Intervention effect of Shenling Baizhu granules on quality of life of COVID-19 patients after recovery

This embodiment was performed from September 2021 to July 2022 in Tongshan County People's Hospital, Sinopharm Dongfeng General Hospital, Xianning Central Hospital, and Yangxin County People's Hospital in Hubei Province.

1. Distribution of cases

A total of 313 subjects were enrolled in the study, and all 313 completed the study, accounting for 100% of the enrolled cases. After excluding 8 cases that were beyond the age range of 18-80 years, 305 cases were included in the analysis set.

2. General information of cases

There were 166 males (54.43%) and 139 females (45.57%), with 303 Han people (99.34%). The average age was 46.34 ± 14.09 years (ranging from 2 to 84 years). The average weight was 63.41 ± 7.51 (kg).

3. Vital signs

At enrollment, body temperature, respiration, blood pressure, and heart rate were all generally normal, and no significant abnormalities in these vital signs were observed during the study period.

4. Administration scheme

The average medication duration during the study period was 28.09 ± 0.88 days, the shortest medication duration was 25 days, the longest medication duration was 32 days, and the median medication duration was 28 days. The day before the subjects started taking medication was counted as day 0, the day that they started taking medication was counted as day 1, and so on until day 28.

The specific administration scheme was that: the Shenling Baizhu granules were

administered 3 times a day, 1 bag each time (3 g/bag), for 28 consecutive days. Herein, the Shenling Baizhu granules were manufactured by Beijing Handian Pharmaceutical Co., Ltd., the production process was the same as Embodiment 1, and the batch numbers were 211032, 211134, and 211232.

5. Efficacy evaluation indicators

The main efficacy indicator was the disappearance rate of symptoms such as short of breath, fatigue and weakness, poor appetite, and loose stool, while the secondary indicator was assessed using SF-12 (quality of life rating scale, see Fig. 1).

6. Data collection

All enrolled subjects were treated on day 0, day 14, and day 28 respectively, to collect the symptoms and scoring records, herein the data on day 0 was recorded as "Visit 1", the data on day 14 was recorded as "Visit 2", and the data on day 28 was recorded as "Visit 3". The three groups of the data were statistically analyzed.

7. Statistics and analysis

The statistical analysis was conducted by using SAS 9.4 (or higher version) statistical analysis software.

All statistical tests were conducted by using a two-sided test, the test statistic and its corresponding P value were provided, and $P < 0.05$ might be considered statistically significant.

Quantitative data, the number of cases, mean, standard deviation, minimum, median, maximum, upper quartile (Q1), lower quartile (Q3), and 95% confidence interval (95% CI) were described. The comparison between each treatment group was conducted by using a t-test. If the influence of covariates was considered, covariance analysis was used. Time sequence data, the median survival time was described and its Kaplan-Meier curve was drawn, and a Log-rank test was used to compare the inter-group difference of the median survival time between two groups. If the influence of central or other factors was considered, Cox regression analysis was used.

Qualitative data, the number and percentage of cases for each type were described. The count data between different treatment groups were compared by using a chi-square test and a Fisher exact probability method; and the ranked data between different treatment groups were compared by using a Wilcoxon rank-sum test. If the influence of central or other factors

was considered, a CMH chi-square test or a Logistic regression was used.

8. Intervention efficacy

8.1. Improvement of main symptoms

Results were shown in Tables 1, 2, and 3.

Table 1: Observed Values of Main Symptom Scores

	Visit 1	Visit 2	Visit 3	Statistical quantity	P value	Test method
Short of breath						Mixed effect model
N(Nmiss)	305(0)	305(0)	305(0)	285.79	<.0001	
Mean±SD	2.56±1.78	1.12±1.37	0.16±0.55	Visit 1VS2	<.0001	
Median(Q1,Q3)	2(2,4)	0(0,2)	0(0,0)	Visit 1VS3	<.0001	
Min, Max	0,6	0,6	0,2	Visit 2VS3	<.0001	
Tireness and weakness						Mixed effect model
N(Nmiss)	305(0)	305(0)	305(0)	757.19	<.0001	
Mean±SD	3.38±1.33	1.47±1.27	0.22±0.67	Visit 1VS2	<.0001	
Median(Q1,Q3)	4(2,4)	2(0,2)	0(0,0)	Visit 1VS3	<.0001	
Min,Max	0,6	0,4	0,4	Visit 2VS3	<.0001	
Poor appetite						Mixed effect model
N(Nmiss)	305(0)	305(0)	305(0)	861.72	<.0001	
Mean±SD	3.07±1.27	1.13±1.18	0.05±0.3	Visit 1VS2	<.0001	
Median(Q1,Q3)	4(2,4)	2(0,2)	0(0,0)	Visit 1VS3	<.0001	
Min,Max	0,6	0,4	0,2	Visit 2VS3	<.0001	
Loose stool						Mixed

N(Nmiss)	305(0)	305(0)	305(0)	140.28	<.0001	effect model
Mean±SD	1.67±1.69	0.62±1.02	0.1±0.45	Visit 1VS2	<.0001	
Median(Q1,Q3)	2(0,2)	0(0,2)	0(0,0)	Visit 1VS3	<.0001	
Min,Max	0,6	0,4	0,2	Visit 2VS3	<.0001	

Table 2: Main symptom score difference

	Visit 2-Visit 1 score difference	Visit 3-Visit 1 score difference
Short of breath		
N(Nmiss)	305(0)	305(0)
Mean±SD	-1.44±1.32	-2.4±1.8
Median(Q1,Q3)	-2(-2,0)	-2(-4,-2)
Min, Max	-6,4	-6,2
Statistical quantity	-9291.5	-13225.5
P value	<0.0001	<0.0001
Test method	Wilcoxon signed-rank test	Wilcoxon signed-rank test
Tireness and weakness		
N(Nmiss)	305(0)	305(0)
Mean±SD	-1.91±1.24	-3.16±1.45
Median(Q1,Q3)	-2(-2,-2)	-4(-4,-2)
Min,Max	-6,2	-6,2
Statistical quantity	-15114	-20893
P value	<0.0001	<0.0001
Test method	Wilcoxon signed-rank test	Wilcoxon signed-rank test
Poor appetite		

N(Nmiss)	305(0)	305(0)
Mean±SD	-1.94±1.22	-3.02±1.29
Median(Q1,Q3)	-2(-2,-2)	-4(-4,-2)
Min,Max	-6,2	-6,2
Statistical quantity	-15609	-21323.5
P value	<0.0001	<0.0001
Test method	Wilcoxon signed-rank test	Wilcoxon signed-rank test
Loose stool		
N(Nmiss)	305(0)	305(0)
Mean±SD	-1.05±1.54	-1.57±1.65
Median(Q1,Q3)	0(-2,0)	-2(-2,0)
Min, Max	-6,2	-6,2
Statistical quantity	-4699.5	-7299
P value	<0.0001	<0.0001
Test method	Wilcoxon signed-rank test	Wilcoxon signed-rank test

Table 3: Disappearance rate of main symptoms

	Number of cases of symptom disappearance in Visit 3 (N)	Proportion (%)	Number of causes of baseline symptoms present (N)
Short of breath	216	90	240
Tireness and weakness	270	89.7	301
Poor appetite	285	97.94	291
Loose stool	161	91.48	176

8.1.1. Symptoms of short of breath: Through intervention treatment, the average score of Visit 2 was decreased by 1.44 ± 1.32 scores compared to the baseline score during the study period, and the average score of Visit 3 was decreased by 2.4 ± 1.8 scores compared to the baseline score. Through mixed effect model and Wilcoxon signed-rank test analysis, it was found that the differences were statistically significant ($p < 0.05$), it was indicated that the symptom score of short of breath was significantly decreased by the treatment. At the end of the study, the disappearance rate of the symptoms of short of breath was 90%.

8.1.2. Symptoms of tiredness and weakness:

Through intervention treatment, the average score of Visit 2 was decreased by 1.91 ± 1.24 scores compared to the baseline score during the study period, and the average score of Visit 3 was decreased by 3.16 ± 1.45 scores compared to the baseline score. Through mixed effect model and Wilcoxon signed-rank test analysis, it was found that the differences were statistically significant ($p < 0.05$), it was indicated that the symptom score of tiredness and weakness was significantly decreased by the treatment. At the end of the study, the disappearance rate of the symptoms of tiredness and weakness was 89.7%.

8.1.3. Symptoms of poor appetite:

Through intervention treatment, the average score of Visit 2 was decreased by 1.94 ± 1.22 scores compared to the baseline score during the study period, and the average score of Visit 3 was decreased by 3.02 ± 1.29 scores compared to the baseline score. Through mixed effect model and Wilcoxon signed-rank test analysis, it was found that the differences were statistically significant ($p < 0.05$), it was indicated that the symptom score of poor appetite was significantly decreased by the treatment. At the end of the study, the disappearance rate of the symptoms of poor appetite was 97.94%.

8.1.4. Symptoms of loose stool:

Through intervention treatment, the average score of Visit 2 was decreased by 1.05 ± 1.54 scores compared to the baseline score during the study period, and the average score of Visit 3 was decreased by 1.57 ± 1.65 scores compared to the baseline score. Through mixed effect model and Wilcoxon signed-rank test analysis, it was found that the differences were statistically significant ($p < 0.05$), it was indicated that the symptom score of loose stool was significantly decreased by the treatment. At the end of the study, the disappearance rate of the symptoms of loose stool was 91.48%.

8.2. Secondary symptom efficacy results

The results were shown in Tables 4, 5, and 6.

Table 4: Observed Values of secondary symptom

	Visit 1	Visit 2	Visit 3	Statistical quantity	P value	Test method
Nausea						Mixed effect model
N(Nmiss)	305(0)	305(0)	305(0)	283.94	<.0001	
Mean±SD	1.05±0.75	0.29±0.48	0.01±0.11	Visit 1VS2	<.0001	
Median(Q1,Q3)	1(1,2)	0(0,1)	0(0,0)	Visit 1VS3	<.0001	
Min,Max	0,3	0,2	0,1	Visit 2VS3	<.0001	
Epigastric fullness						Mixed effect model
N(Nmiss)	305(0)	305(0)	305(0)	217.34	<.0001	
Mean±SD	0.92±0.73	0.23±0.48	0.03±0.18	Visit 1VS2	<.0001	
Median(Q1,Q3)	1(0,1)	0(0,0)	0(0,0)	Visit 1VS3	<.0001	
Min,Max	0,3	0,2	0,1	Visit 2VS3	<.0001	
Asthenic defecation						Mixed effect model
N(Nmiss)	305(0)	305(0)	305(0)	139.49	<.0001	
Mean±SD	0.78±0.76	0.3±0.51	0.08±0.26	Visit 1VS2	<.0001	
Median(Q1,Q3)	1(0,1)	0(0,1)	0(0,0)	Visit 1VS3	<.0001	
Min,Max	0,3	0,2	0,1	Visit 2VS3	<.0001	

Table 5: Secondary symptom score difference

	Visit 2-Visit 1 scores difference	Visit 3-Visit 1 scores difference
Nausea		
N(Nmiss)	305(0)	313(0)
Mean±SD	-0.76±0.68	-1.04±0.76
Median(Q1,Q3)	-1(-1,0)	-1(-2,-1)
Min,Max	-3,1	-3,0
Statistical quantity	-11046	-13398
P value	<0.0001	<0.0001
Test method	Wilcoxon signed-rank test	Wilcoxon signed-rank test
Epigastric fullness		
N(Nmiss)	305(0)	305(0)
Mean±SD	-0.7±0.66	-0.89±0.76
Median(Q1,Q3)	-1(-1,0)	-1(-1,0)
Min,Max	-2,1	-3,1
Statistical quantity	-9146	-11196.5
P value	<0.0001	<0.0001
Test method	Wilcoxon signed-rank test	Wilcoxon signed-rank test
Asthenic defecation		
N(Nmiss)	305(0)	313(0)
Mean±SD	-0.47±0.67	-0.7±0.73
Median(Q1, Q3)	0(-1, 0)	-1(-1, 0)
Min,Max	-3,1	-3,1
Statistical quantity	-4456.5	-7203.5

P value	<0.0001	<0.0001
Test method	Wilcoxon signed-rank test	Wilcoxon signed-rank test

Table 6: Disappearance rate of secondary symptoms

	Number of cases of symptom disappearance in Visit 3 (N)	Proportion (%)	Number of causes of baseline symptoms present (N)
Nausea	231	98.3	235
Epigastric fullness	207	97.18	213
Asthenic defecation	159	87.85	181

8.2.1. Symptoms of nausea:

Through intervention treatment, the average score of Visit 2 was decreased by 0.76 ± 0.68 scores compared to the baseline score during the study period, and the average score of Visit 3 was decreased by 1.04 ± 0.76 scores compared to the baseline score. Through mixed effect model and Wilcoxon signed-rank test analysis, it was found that the differences were statistically significant ($p < 0.05$), it was indicated that the symptom score of nausea was significantly decreased by the treatment. At the end of the study, the disappearance rate of the symptoms of nausea was 98.3%.

8.2.2. Symptoms of epigastric fullness:

Through intervention treatment, the average score of Visit 2 was decreased by 0.7 ± 0.66 scores compared to the baseline score during the study period, and the average score of Visit 3 was decreased by 0.89 ± 0.76 scores compared to the baseline score. Through mixed effect model and Wilcoxon signed-rank test analysis, it was found that the differences were statistically significant ($p < 0.05$), it was indicated that the symptom score of epigastric fullness was significantly decreased by the treatment. At the end of the study, the disappearance rate of the symptoms of epigastric fullness was 97.18%.

8.2.3. Symptoms of asthenic defecation:

Through intervention treatment, the average score of Visit 2 was decreased by 0.47 ± 0.67 scores compared to the baseline score during the study period, and the average score of Visit 3 was decreased by 0.7 ± 0.73 scores compared to the baseline score. Through mixed effect model and Wilcoxon signed-rank test analysis, it was found that the differences were statistically significant ($p < 0.05$), it was indicated that the symptom score of asthenic defecation was significantly decreased by the treatment. At the end of the study, the disappearance rate of the symptoms of asthenic defecation was 87.85%.

8.3. SF12 scale (quality of life assessment score) score results

The results were shown in Tables 7 and 8.

Table 7: SF12 scale score observed values

	Visit 1	Visit 2	Visit 3	Statistical quantity	P value	Test method
Total score of SF12 scale						Mixed effect model
N(Nmiss)	305(0)	305(0)	305(0)	290.25	<.0001	
Mean $\pm$ SD	- 13.63 $\pm$ 8.08	- 4.48 $\pm$ 11.44	3.42 $\pm$ 9.77	Visit 1VS2	<.0001	
Median(Q1,Q3)	-14(-17,-9)	-5(-12,3)	4(-1,10)	Visit 1VS3	<.0001	
Min,Max	-42,8	-35,18	-32,20	Visit 2VS3	<.0001	

Table 8: SF12 Scale score difference values

	Visit 2-Visit 1 scores difference	Visit 3-Visit 1 scores difference
N(Nmiss)	305(0)	305(0)
Mean $\pm$ SD	9.16 $\pm$ 11.59	17.06 $\pm$ 12.42
Median(Q1,Q3)	8(2,15)	17(10,26)
Min,Max	-19,43	-18,47
Statistical quantity	17027	21744

P value	<0.0001	<0.0001
Test method	Wilcoxon signed-rank test	Wilcoxon signed-rank test

Through intervention treatment, the average score of Visit 2 was increased by 9.16 ± 11.59 scores compared to the baseline score during the study period, and the average score of Visit 3 was decreased by 17.06 ± 12.42 scores compared to the baseline score. Through mixed effect model and Wilcoxon signed-rank test analysis, it was found that the differences were statistically significant ($p < 0.05$), it was indicated that the SF12 scale score was significantly improved by the treatment compared to the baseline.

9. Conclusion

The Shenling Baizhu can significantly treat various sequelae of the COVID-19 patients after recovery, and significantly improve the quality of life scores of the patients.

The above are only optional implementation modes of the present disclosure and are not intended to limit the present disclosure. For those skilled in the art, the present disclosure may have various changes and variations. Any modifications, equivalent replacements, improvements and the like made within the spirit and principles of the present disclosure shall be contained within the scope of protection of the present disclosure.

Industrial Applicability

The present disclosure provides uses of Shenling Baizhu in preparing a medicament for treating post-recovery sequelae of a COVID-19 patient and improving quality of life; and the sequela is selected from at least one of short of breath, fatigue and weakness, inappetence, and diarrhea. The Shenling Baizhu provided by the present disclosure may significantly treat various sequelae of the COVID-19 patients after recovery, significantly improve the quality of life scores of the patients, and has the excellent industrial practicability.

Claims

1. Use of Shenling Baizhu in preparing a medicament for treating post-recovery sequelae of a COVID-19 patient and improving quality of life; the sequela is selected from at least one of short of breath, fatigue and weakness, inappetence, and diarrhea; and raw materials of the Shenling Baizhu are composed of the following traditional Chinese medicinal materials in parts by weight:

400 parts of ginseng, 400 parts of poria cocos, 400 parts of rhizoma atractylodis macrocephalae stir-fried with bran, 400 parts of Chinese yam, 300 parts of fried white hyacinth beans, 200 parts of lotus seeds, 200 parts of coix seeds stir-fried with bran, 200 parts of fructus amomi, 200 parts of platycodon grandiflorum, and 400 parts of liquorice.

2. The use according to claim 1, wherein the sequela also comprises at least one selected from nausea, epigastric fullness, and asthenic defecation.

3. The use according to claim 1, wherein the improving the quality of life of COVID-19 patient after recovery means that after the Shenling Baizhu is administered to COVID-19 patient, the SF12 scale score of the patient is decreased significantly compared with the score before treatment, and the P value is at least less than 0.05.

4. The use according to any one of claims 1 to 3, wherein the medicament is a clinically acceptable preparation.

5. The use according to claim 4, wherein the medicament is selected from decoctions, pills, powders, granules, tablets, or capsules.

6. The use according to claim 5, wherein the medicament is a granule prepared by the following steps:

I. taking each traditional Chinese medicinal material in parts by weight;

II. crushing the Chinese yam into fine powder, and sieving by a 100-mesh sieve for later use;

III. extracting volatile oil from the fructus amomi by using a steam distillation method until completely removed, and collecting aqueous solution after distillation in a separate container; soaking a fructus amomi medicinal residue with the ginseng, the rhizoma atractylodis macrocephalae stir-fried with bran, and 4-5 times their weight of 95% ethanol

for 24 h, heating and refluxing for 3 h, and filtering, recovering the ethanol from a filtrate, and concentrating into an extract with a relative density of 1.00-1.15 at 65°C, to obtain an alcohol extract A; then refluxing and extracting the medicinal residue with 4-5times its weight of 50% ethanol for 3 h, filtering, recovering the ethanol from a filtrate, and concentrating into an extract with a relative density of 1.12-1.13 at 80°C, to obtain an alcohol extract B, and using the medicinal residue after ethanol extraction for later use;

IV. adding the poria cocos, the fried white hyacinth beans, the lotus seeds, the coix seeds stir-fried with bran, the platycodon grandiflorum, and the liquorice with 8-10 times their weight of water and boiling for 2 h, filtering, combining a medicinal residue with the medicinal residue for later use after the ethanol extraction in Step III, and then adding 8times its weight of water to boil together for 1.5 h, filtering, combining the two filtrates and the aqueous solution obtained after the distillation in Step III, stillly placing, and filtering, when concentrating a filtrate to a relative density of 1.20 at 80°C, adding the alcohol extracts A and B, and continuously concentrating into an extract with a relative density of 1.30-1.34 at 80°C;

V. mixing the Chinese yam fine powder obtained in Step II into the extract obtained in Step IV, drying at a low temperature of 60°C into a dry extract, and crushing, to obtain medicinal powder; and

VI. taking 1 part by weight of the medicinal powder obtained in Step V and 0.4 parts by weight of sugar powder, mixing evenly, and pelletizing with 70%-75% ethanol, granulating after being dried, and spraying the fructus amomi volatile oil obtained in Step III, mixing evenly, and preparing 1000 g of the granules.

7. The use according to claim 6, wherein the granules are administered to a subject in need three times a day, 3 g each time, and it is equivalent to a daily crude drug dose of 27.9 g/day.