Development and Validation of Liver Depression Type Infertility Quality of Life Scale Based on Traditional Chinese Medicine

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Research

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Abstract

Background Traditional Chinese medicine (TCM) liver depression infertility quality of life scale is developed to provide a scientific and reliable tool for TCM treatment and intervention in the treatment of liver depression patients with infertility, as well as basis and assistance for clinical decision-making.

Methods Literature research method: Through the retrieval of Chinese knowledge network (CNKI), Wanfang (WANFANG), Vip (VIP), Springer, PubMed database of existing Chinese life quality scale and infertility dedicated quality of life scale, an entry pool is built with symptoms, emotional state, social function state and satisfaction as dimensions. Using the Delphi method to screen the entries. Screening entries according to the results of expert review, and evaluating the positive degree coefficient, authority degree and coordination coefficient by the experts. Using the clinical questionnaire method to screen the entries further. To form the Chinese medicine liver depression infertility life of quality scale. Scale evaluation: the reliability and validity of the scale were evaluated based on the results of the clinical questionnaire.

Results After two rounds of Delphi method, there are 33 entries remained. The clinical questionnaire rescreened entries, formed the traditional Chinese medicine liver depression infertility quality of life scale containing 4 dimensions of symptoms, emotional states, social function states and satisfaction, with total of 29 entries and VAS score scale. Evaluation results: the Kronbach alpha coefficients performed well in total and each aspect. The validity of the scale: the structural efficiency evaluation results are in good agreement with the scale structure envisioned at the time of design. The relationship between the quality of life scale and the standard scale (FertiQoL International2008) showed a high absolute value.

Conclusion In this study, the quality of life scale of Chinese medicine liver depression type infertility was developed by literature research, Delphi method and clinical questionnaire, with good reliability and validity of the scale evaluated. It could be used as a tool for efficacy judgment tool or quality of life evaluation in Chinese medicine treatment or intervention for patients with liver depression infertility.

1. Background

As the incidence of infertility increases year by year worldwide, infertile couples are 10% to 15% of childbearing couples, especially in developing countries. Infertility is mainly caused by female infertility which is mostly primary infertility. There are many factors that influence the incidence of infertility, varying in different countries and areas. Infertility causes physical and psychological pain, and economic burden.

Traditional Chinese medicine for infertility awareness began more than 2,000 years ago, when the ancient medical scientists differentiated infertility syndrome to form kidney deficiency, liver depression, blood stasis, phlegm as the main causes. Theoretical framework after a long period of clinical practice and experience accumulation[1], developed a large number of treatment of infertility recipe. Clinical practice proves that traditional Chinese medicine treatment of infertility could relieve the symptoms of patients,

and it is an indispensable method for clinical diagnosis and treatment. In recent years, due to the change of environment, society and life style, the incidence of infertility soared. According to the etiology and pathogenesis of infertility from traditional Chinese medicine aspect, infertility is mainly liver depression type.

From traditional Chinese medicine perspective, liver works as main drain, smooth the chi mechanism and emotional catharsis. If liver works well, the pulse would reconciled, the liver's blood is responsible for the repetitive cycles of human life. A woman's menstrual cycle depends on the liver's blood and disharmonious liver blood can make an irregular or painful menstruation and other diseases as well. It could be good for impregnation. Liver depression type infertility always performed as ovulatory dysfunction, endocrine imbalance, fallopian tube obstruction, endometriosis and other connective diseases.

There are 98 scales for infertility quality of life determination so far in China and abroad, including 14 special infertility quality of life scales [2]. However, due to the different cultures, living habits and values, the use of foreign infertility quality of life scales in China has limitations. Therefore, this study is aimed to develop a traditional Chinese medicine liver depression infertility quality of life scale based on the theory of syndrome differentiation and treatment of Chinese medicine, combined with Chinese culture, life and other backgrounds.

2. Methods

The Minimum Standards of Reporting Checklist contains details of the experimental design, and statistics, and resources used in this study.

2.1 Development of scale

2.1.1 Retrieve relative data and scales

Through the retrieval of Chinese knowledge network (CNKI), Wanfang (WANFANG), Vip (VIP), Springer, PubMed database of existing Chinese life quality scale and infertility dedicated quality of life scale by keywords "infertility", "quality of life", "QOL" (in both English and Chinese) scales were subject to statistic and analysis, with consultation to relative experts to build up the entry pool of liver depression type infertility quality of life scale.

2.1.2 Using Delphi method to screen entries

Using Delphi method to screen entries. Delphi questionnaire was distributed to 10~15 experts including doctors, nurses and scholars on the basic theory of Chinese medicine, Chinese medicine gynecology, quality of life, reproductive division and infertility. The initial liver depression type infertility quality of life scale was established according to the consequence of Delphi, with evaluation of the positive degree coefficient, authority degree and coordination coefficient of the experts.

2.1.3 Using the clinical questionnaire method to screen the entries further

We designed clinical questionnaire according to the Delphi experts' advice results and chose patients with liver depression infertility as the standard. Data were recorded using Excel 2010. To form the Chinese medicine liver depression infertility life of quality scale, the scale entries were screened according to the results of clinical questionnaire via methods of frequency distribution, correlation coefficient, discrete trend, Kronbach coefficient and factor analysis. And finally formed the liver depression type infertility quality of life scale.

2.1.4 Liver depression type infertility quality of life scale scientificity evaluation

The reliability and validity of the scale were evaluated based on the results of the clinical questionnaires.

2.2 Scale evaluation

2.2.1 Study group

According to the western medicine diagnosis standard and TCM syndrome differentiation standard, patients who were diagnosed as liver depression type infertility were included in this clinical investigation research.
1) Meeting WHO diagnostic criteria: childbearing couples who has regular sex lives, with no contraceptive measures, and live together for one year without being pregnant.

2) Diagnostic criteria of TCM syndrome differentiation: referring to *Guiding Principles for the Clinical Study of Chinese Medicines*

3) Patients who are diagnosed as liver depression type infertility according to the clinical diagnosis and treatment of TCM terms national standards: liver pathogenesis, qi activity stasis, with emotional depression, unhappy sigh, threats or thoracic abdominal distension stuffy pain, less women breast pain, menoxenia, pulse string, and other common disease syndromes.

4) Excluding patients who have congenital biological defects and malformations of the reproductive system, merger of tumor, mental diseases, and serious chronic diseases.

5) Rejection standard: patients who 1enter the study more than once; 2lack of information; 3are not qualified after enter the study.

This clinical investigation was conducted in a convenient sampling, with the preliminary agreement with the hospital, and finally determined the Dongzhimen affiliated hospital of Beijing university of Chinese medicine. Through the contact with the gynecologist we obtained the consent, patients who met this study inclusion and exclusion criteria were investigated.

Quality of life scale includes many dimensions and entries. Based on the estimation of sample content of general multivariate analysis, according to the demand of the scale, the sample size should satisfy

following requests: 1The ratio of entries to survey objects should better be 1:5; 2The total number of survey objects should be more than 100. This clinical questionnaire contains 33 entries, so the total number of objects should be 33*5=165.

2.2.2 Scoring method

The scoring method of the scale: we used 5 levels Likert scale to do the quantitative measurement distinguished by frequency adverbs including “sometimes”, “medium”, and “general satisfied”. Options were expressed in the scale as “never- seldom- sometimes- often- always”, “very dissatisfied- dissatisfied- general satisfied- satisfied- very satisfied”. As forward entries scored 1-5, and inverse entries scored 5-1, finally we obtained the total score to evaluate patients’ quality of life.

2.2.3 Evaluation content

The reliability and validity of the scale were evaluated according to the results of the clinical questionnaire. Reliability evaluation includes Kronbach coefficient method, split-half reliability, and test-retest reliability[3], while validity evaluation includes content validity, construct validity, standard degree of association, and reactivity evaluation.

2.3 Statistical methods

The study used statistical description correlate on analysis, etc., to conduct statistical processing, with the software SPSS applied.

3. Results

3.1 The literature research method determines the scale dimension and the result of the entry pool

3.1.1 Scale dimension build results

We retrieved TCM quality of life scale from Chinese knowledge network (CNKI), Wanfang (WANFANG), Vip (VIP), Springer, PubMed database of existing Chinese life quality scale and infertility dedicated quality of life scale by keywords "quality of life", "QOL", "traditional Chinese medicine", from building time to March 16, 2016.

So far, China has already developed TCM life quality scales of acute myocardial infarction, chronic liver disease, chronic urticaria, alopecia and acne, etc. By combing through the dimensions and entries of 41 TCM life quality scales, the Chinese medicine life quality scale covers 3 to 7 dimensions and 19 to 69 entries. After removing one scale that used different sorting technique, the 40 TCM life quality scales mainly include physiological dimension, psychological dimension, social function state dimension and symptom dimension which distribution is shown in Table 1. The Pareto chart of 40 TCM life quality scales is shown in Figure 1. Based on the retrieved 41 Chinese medicine quality of life scales and the existing 14 specificity infertility scales to comb and statistics, and combined with liver depression type of

infertility patients clinical syndrome, we finally determined symptoms, emotion state, social function state, satisfaction as dimensions for liver depression type infertility quality of life scale.

Figure 1 Pareto chart of 40 TCM life quality scale

3.1.2 Results for constructing scale entry pool

The results are based on scales used to measure the anxiety level of infertile patients, such as SDS, SAS, SCL-90, and women's infertility scale developed by Qinnan (China)[4], which are according to the characteristics of TCM syndrome differentiation of infertility, and liver depression patients' symptom, and combined with consultation with the clinical experts of TCM infertility to construct item pool of this scale. They were initially settled, excluded entries that were improper, similar and repetitive, and formed the entry pool of liver depression type infertility quality of life scale. Dimensions of Symptom, emotion state, social function state and satisfaction include 19, 12, 6, and 4 entries, respectively, with totally 41 entries, as shown in table 2.

3.2 Filter results after Delphi method

The first round of Delphi expert consultation questionnaire was started on March 10, 2016, while the second was on May 4, 2016. All the questionnaires were filled by experts independently, and returned within 7 days. Double entry and statistics were performed for the returned questionnaire data via Excel 2010.

3.2.1 Basic information statistics of experts

Based on working experience, study field, professional ranks and titles, we chose 13 experts of TCM gynecology, basic theories of Chinese medicine and quality of life, which occupied 53.85%（7/13）, 30.77%（4/13）and 15.38%（2/13）respectively. More than 80% experts have medicine background. The basic information of Delphi experts are shown as Table 3.

3.2.2 Statistic result of expert authority degree coefficient

We calculated expert authority coefficient by expert familiarity and judging criteria[5]. Results showed familiarity with the maximum of 0.7, the minimum of 0.3, and a mean of 0.65, while the expert authority coefficient with the maximum of 0.85, the minimum of 0.55, and a mean of 0.79. It could be explained that Delphi consulting experts participating in this study are more authoritative. The details are shown in Table 4.

3.2.3 The concentrate degree of experts

In the first round of Delphi expert consultation, 13 experts scored the importance of 41 entries. In the second round, 13 of them rated the importance of 38 entries. The importance of entries were scored as 1,

2, 3, 4, and 5 respectively, indicating: very unimportant, unimportant, general, important and very important. By calculating the score ratio, variation coefficient and arithmetic mean of each entry, to show the concentration of expert opinions.

The results of two rounds Delphi expert consultation are shown in Table 8 and 9.

3.2.4 Coordination degree of experts' opinions

The coordination degree of experts' opinions is expressed by calculating the *W* coefficient of two rounds Delphi expert consultations. Coordination degree *W* valued between 0 and 1. The larger the number is, the higher the coordination degree of experts, the number of experts and the number of entries will be. In the first round, W=0.244, whereas W=0.447 in the second, meaning *W* increased. Results are shown in table 5.

3.2.5 An entry filtering result based on boundary value method

In the first round of expert consultation, 13 experts evaluated and recommended the dimensions of the scale, when 71.15% of experts gave the affirmation, and considered the setting of the dimension is reasonable. Three experts disagreed the dimensions of state of social function state and satisfaction, who accounted for 23.08%. No one advised to increase or reduce dimensions. After the team discussion, according to the result of the first round of consultation, we determined the first level of the dimension changing to the name of symptoms, emotion state, social function state and satisfaction, as the number of dimensions requires no increase or decrease, and basic classification is reasonable.

In Delphi expert consultation, the boundary value method was used to filter the entries, and the rules did not meet the entries of two or more boundary values. In the first round, arithmetic mean, variation coefficient and full mark rate was 2.944, 0.454 and 0.120 respectively. Entries would not be deleted when the arithmetic mean of entry importance score of higher than 2.944, the variation coefficient of lower than 0.454, and the full mark rate of above 0.120. Seven entries were removed and four were added in the first round of consultation, then the second round of Delphi expert questionnaire was launched based on first round's result, where symptoms, emotion state, social function state and satisfaction dimensions contained 17, 12, 5 and 4 entries, respectively, with a total of 38 entries.

In the second round, the arithmetic mean, variation coefficient and full mark rate was 3.241, 0.236 and 0.009 respectively. Keeping entries when arithmetic mean of higher than 3.241, the variation coefficient of lower than 0.236, and the full mark rate of higher than 0.009. In the second round, we cut out five entries, with 33 entries remained, where symptoms, emotion state, social function state and satisfaction dimensions contained 13, 11, 5 and 4 entries, respectively. The Delphi method entry filter boundary values are shown in Table 6 and 7. The results of the entries are shown in Table 8 and 9.

3.3 Clinical questionnaire result

All the subjects of this study were from the Gynecological Outpatient Department of Dongzhimen Hospital, Beijing University of Chinese Medicine. With the consent of respondents who meet the inclusion

criteria, respondents filled out questionnaires, and the investigators were able to explain the questionnaire for the respondents. A total of 171 questionnaires were distributed in the clinical survey, where 171 were recovered, 3 were deleted from the survey, thus there were 168 effective questionnaires, with 98.25% effective rate. The questionnaire includes three parts: the basic condition of the patient, the life quality questionnaire of liver depression type infertility, and the Chinese version of Ferti QOL. The basic information of the clinical investigation subjects is shown in Table 10.

Screening results were integrated for methods of frequency distribution, correlation coefficient, discrete tendency, Kronbach alpha [6] and the correlation coefficient, while eliminating the entries excluded by two methods. Entry B2 was deleted by correlation coefficient method, Kronbach alpha method and factor analysis method, whereas B12, Bl3 were deleted by correlation coefficient method and Kronbach alpha method; E3 was deleted by frequency distribution method, Kronbach alpha method and factor analysis method, so eventually deleting entry B2 "premenstrual pain at two side", B12 "menstrual cycle unstable", Bl3 "less menstrual quantity" and E3 "satisfied with your health", when 29 entries remained, as shown in Table 11.

3.4 The formation of liver depression type infertility quality of life scale

3.4.1 Formation of the scale

This study formed a formal liver depression type infertility quality of life scale based on the result of Delphi expert consultation and clinical questionnaire. The scale includes four dimensions (symptoms, emotion state, social function state and satisfaction), with a total of 29 entries and a VAS score scale, where four dimensions contain 10, 11, 5 and 3 entries respectively. The liver depression type infertility quality of life scale is shown in Appendix 1.

3.4.2 Weight of each dimension and entry

According to the results of the second round of Delphi, this study determined the weight of entries. In the second round, the experts evaluated and scored each dimension and entry according to their importance, scoring 1-5. The higher the score was, the more important the dimension or entry was. In this study, the weight of each dimension and entry was normalized by each expert. According to the statistical calculation, the weight of the symptom dimension is 0.293, of emotional state dimension is 0.270, of social function state dimension is 0.223 and of satisfaction dimension is 0.214. With the total score of 5, the higher the score was, the lower the quality of life it indicated. Entries 25, 27-29 are the reverse ones, and the calculation of the quality of life scores should be calculated with the other entry vectors. Weight of each dimension and entry is shown in Table 12.

3.5 The validity and reliability of the scale

3.5.1 Reliability analysis

This research evaluated the reliability and validity of the scale through clinical questionnaire results, and the reliability mainly used Kronbach alpha method to evaluate internal consistency of scale. We used split-half reliability method to evaluate consistency across entries, and the reliability evaluation result of liver depression type infertility quality of life scale showed that: Kronbach alpha of the whole scale is 0.884, and of dimensions of symptoms, emotion state, social function state and satisfaction are 0.742, 0.947, 0.591 and 0.742 respectively. Kronbach alpha > 0.5 for all dimensions, which shows the scale has good reliability[7]. The scale's split-half reliability is 0.909, indicating that the cross-entries of the scale were consistent. Details are shown in Table 13 and 14.

3.5.2 validity evaluation analysis

Validity measurement mainly used the content validity to evaluate correlation between entries and the whole scale, other entries and related dimensions. We used structure confirmatory factor analysis to evaluate whether the scale is consistent with the theoretical assumptions, and used standard correlation to evaluate the correlation between the scale and results measured by standard scale. Liver depression type infertility quality of life scale validity evaluation results showed that the correlation between each dimension (symptoms, emotion state, social function state and satisfaction) and the total score were 0.619, 0.827, 0.728 and 0.619 respectively. In addition to the satisfaction dimension and whole scale correlation fair to middling, the remaining three dimensions provide good correlation with the whole scale. The evaluation of structural validity of the scale includes seven common factors, and the cumulative variance contribution rate is 66.48%. The factors contained in each dimension are in accordance with the original theoretical conception. As we have the FertiQoL International 2008 as a standard scale[8], correlation of liver depression type infertility quality of life scale and standard scale could be calculated, where the absolute correlation value was 0.792, so liver depression type infertility quality of life scale could be used as an independent tool. The results of structural validity are shown in Table 15-17.

3.5.3 Evaluation results of standard correlation degree

This study selected the FertiQoL international 2008 as the standard scale. Through calculation, the score of liver depression type infertility quality of life scale and the standard scale are under normal distribution. The results showed that Pearson correlation coefficient was -0.792. Correlative coefficient presents negative correlation because scoring methods of two scales are different. By correlation coefficient, we could conclude that the liver depression type infertility quality of life scale could be used independently as an evaluation tool to evaluate liver depression type infertility patients' quality of life.

4. Discussion

4.1 Insufficiency of Expert coordination of Delphi method

In this study, the coordination degree of the first round Delphi expert consultation was 0.244, and the second round was 0.447, higher than the former. Firstly, the condition of fewer Delphi experts participated but more entries, leads to that the experts' coordination degree in two rounds of consultations is low. Secondly, in the Delphi method, for the experts invited from different fields (clinical or scientific research quality of life, TCM gynecology and TCM basic theory research), the focuses of different experts point to the different focuses. The third reason is that coordination degrees in two rounds of Delphi expert consultations are low.

Experts' coordination degree coefficient W is between 0 and 1. The higher the value is, the higher the coordinate degree it indicates, which generally fluctuates at about 0.5, but numerically mainly depends on the number of experts and the number of entries.

4.2 Quantity and quality of experts is insufficient in Delphi method

In Delphi expert consultation, where less experts focusing on quality of life from the perspective of Chinese medicine research, meanwhile understanding clinical quality of life, so according to factors such as work experience, research and professional titles, we only chose experts studying the basic theory of TCM, TCM gynecology and quality of life, with a total of 13. Therefore, Delphi expert consultation result of this study has limitations.

4.3 Inadequate survey site

The type of traditional Chinese medicine liver depression patients with infertility is based on the characteristics of TCM syndrome differentiation and treatment, and a large number of Chinese medicine terminology is reflected in the questionnaire, therefore the chosen objects are all came from Gynecology Outpatient Department of Dongzhimen Hospital, Beijing University of Chinese Medicine while other areas failed to be involved. This study also has some limitations in sample selection.

4.4 Limitative range of application

According to its TCM characteristics, infertility is mainly divided into the liver, kidney, blood stasis and phlegm syndrome, which liver depression syndrome is the most common type. Liver depression is different from other types of infertility patients' syndromes. Therefore, this is only suitable for liver depression type infertility patients, and could not be used on other type infertility patients.

4.5 The scale lacking reactivity evaluation and retest reliability

Due to the clinical questionnaire survey carried out in outpatients, this study time is uncertain to the patients, and since the limitation of time, we failed to do the secondary clinical questionnaire survey to patients, therefore this study failed to evaluate scale response and retest reliability.

5. Conclusion

Based on liver depression infertility and women's quality of life research as well as investigation data from experts and patients, the quality of life scale of Chinese medicine liver depression type infertility was developed by literature research, Delphi method and clinical questionnaire, with good reliability and validity of the scale evaluated. It could be used as a tool for efficacy judgment tool or quality of life evaluation in Chinese medicine treatment or intervention for patients with liver depression infertility. So that it could help improve the quality of life of liver depression type infertile women.

6. Abbreviations

FertiQOL	Fertility quality of life Tool
QOL	Quality of life
SAS	Self—Rating Anxiety Scale
SCL-90	Self—Report Symptom Inventory, Symptom Check—List90
SDS	Self-rating depression scale
TCM	Traditional Chinese Medicine

7. Declarations

7.1 Ethics approval and consent to participate

Participants were informed about the study objective by information on the questionnaire. There was an announcement at the beginning of the questionnaire to ensure all the participants are voluntary.

7.2 Consent for publication

Not applicable.

7.3 Availability of data and material

All data generated or analysed during this study are included in this published article (supplementary files).

7.4 Competing interests

The authors declare that they have no competing interests.

7.5 Funding

No funding was obtained for this study.

7.6 Authors' contributions

Ying was the main leader who was in charge of the main execution of the research and wrote the main part of the paper. Chang and Xuan translated the paper into English. Mengpei, Zhiheng, Haoxiang, Xiaomei, Jie and Kaini distributed questionnaires and combed data. Wentao supervised and instructed the study. All authors read and approved the final manuscript.

7.7 Acknowledgements

Not applicable.

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Tables

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