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STUDY ON ANALYSIS OF SIGNIFICANCE OF SYMPTOM-TREATMENT METHOD COMBINATION†

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Abstract. Treatment method refers to a principle or method for treating diseases in Traditional Korean Medicine(TKM). As doctors determine the ideal treatment for a patient's disease or symptom, they are also able to prescribe effective treatment means for the diseases or symptom such as medicinal materials, prescription, acupuncture and moxibustion. Therefore, if significant symptom-treatment method combinations are found from literature or database, proper treatment means for the patient's diseases or symptom may be presented to TKM doctors and enhanced treatment accuracy and efficiency can be expected. This study aims to analyze the relation between symptom and treatment method by interpreting hypotheses through null hypotheses to find significant symptom-treatment method combinations. This combinations suggested in this study will be compared with TKM experts analysis result to find an objective analysis method and eventually apply the method to medical big data, e.g., a huge amount of literature or treatment records.

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1. Introduction

TKM has developed over a long period of time, and its theory and clinical experiences have been recorded in many books. In the past, to employ the accumulated medical knowledge efficiently there were efforts to publish books that comprehensively contains the contents of different books such as 'Donguibogam'. Recently efforts are made include building, saving and using medical knowledge as a database or ontology by using advanced IT technology(see [1]). One of the

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efforts is to study how to build a TKM ontology by the Information Development Group of Korea Institute of Oriental Medicine in the field of TKM(see [2]). The definition of Ontology is an explicit formal specification of a shared conceptualization(see [3]) and the advantage of ontology is sharing knowledge and implementing flexible connection with existing knowledge and additional knowledge by defining the relation between terms in a format that a computer can understand(see [4]). The TKM ontology is composed of diseases, medicinal material, prescription, acupuncture and moxibustion, physiology and pathology. Data for diseases include treatment depending on diseases, involved symptoms, methods of treatment, related medicinal materials, etiological causes, mechanisms, and prognoses. Treatment method among the aforementioned elements refers to principles or methods for treating diseases in TKM so that doctors can determine the ideal treatment for a patient's disease or symptom to enable them to determine efficient treatment means, for example, medicinal material, prescription, acupuncture and moxibustion. Therefore, if significant symptom-treatment method combinations are found from literature or database, proper treatment means for the patient's diseases or symptom may be presented to TKM doctors and enhanced treatment accuracy and efficiency can be expected. This study aims to analyze the relation between symptom and treatment method by interpreting hypotheses through null hypotheses to find significant symptom-treatment method combinations. This combinations suggested in this study will be compared with TKM expert′s analysis result to find an objective analysis method and eventually apply the method to medical big data, e.g., a huge amount of literature or treatment records.

2. Main subject

A disease ontology which is one of the TKM ontologies built by the Korea Institute of Oriental Medicine is built based on the contents of textbooks for 5 internal medicines used as a textbook in Korea's TKM universities(see [5, 6, 7, 8, 9]). The disease information described in the 5 internal medicine textbooks is generally composed of treatment depending on diseases, involved symptoms, treatment, efficient medicinal material, etiological causes, mechanisms, and prognoses. Therefore, the ontology also include information of treatment groups and involved system groups depending on each disease. In general, one disease has 4 to 5 treatments and about 10 involved symptoms. There are combinations of a single symptom-single treatment, directly related in the TKM theory among the treatment groups and the involved symptom groups, and some combinations are not related. Although it is necessary to examine not only the symptoms but also the patient's complex situation comprehensively to determine accurate treatment methods, it is possible to find treatment method combinations for each general symptom based on the TKM theory. For example, the disease 'cold caused by wind and cold pathogens' in the lung system textbook is similar to the common cold in western medicine. The exemplary involved symptoms in 'cold

caused by wind and cold pathogens' include aversion to cold, mild fever, sneeze, secretion of clear tears, itchy throat, cough, absence of sweating, headache disorder, increased volume of urine and excretion of diluted urine. The recommended treatment method for this is disperse wind, dissipate cold, release the exterior, and diffuse the lung. Thirty-six symptom-treatment combinations by $\binom{9}{1} \times \binom{4}{1}$ are found from the involved symptom groups and the treatment groups, where $\binom{n}{k} = \frac{n!}{(n-k)!k!}$. Significant combinations based on the TKM theory among them are dissipate cold-aversion to cold, release the exterior-absence of sweating, diffuse the lung-sneeze, and diffuse the lung-cough. These are suggested TKM experts opinions since there have been studies to analyze symptom and treatment terms to find and use significant symptom-treatment method combinations(see [10]). In prior studies, the relation between symptom and treatment method is based on the TKM theory by a plurality of TKM experts for analysis to account for disciplinary specialty, which is enabled through expert's manual work. As a result, it is hard to expand the output into an objective method an a TKM expert's analysis is needed for analyzation of the contents in a new book. Therefore, it is hard to apply it to analyzing big medical data, such as treatment records. In this study, hypothesis interpretation is used instead of TKM experts for each related symptom to establish the following null hypothesis and to derive results.

Extracting data

The symptom-treatment method combination data are extracted from the disease-involved symptom group-treatment group data of the ontology built by the Korea Institute of Oriental Medicine. For example, 'cold caused by wind and cold pathogens' has involved symptoms of aversion to cold, mild fever, sneeze, secretion of clear tears, itchy throat, cough, absence of sweating, headache disorder, increased volume of urine and excretion of diluted urine, and is treated through disperse wind, dissipate cold, release the exterior, and diffuse the lung. Therefore, 36 symptom-treatment combinations are extracted, including aversion to cold-disperse wind, aversion to cold-dissipate cold, aversion to cold-release the exterior, aversion to cold-diffuse the lung, mild fever-disperse wind, mild fever-dissipate cold, mild fever-release the exterior, and mild fever-diffuse the lung. In this way, 9458 combinations were extracted from 834 diseases in the TKM ontology. The symptom-treatment method combinations of which the number of appearances was categorically small were considered not ideal in terms of generalization for this study. As a result, the combinations of which the number of appearances in the extraction was smaller than 10 were not analyzed but 1860 combinations of which the number of appearances was not smaller than 10 were analyzed.

Assumption

It was assumed that combinations which have been usually described together in literature are related more than other combinations, in order to find significant symptom-treatment method combinations. However, because exemplary symptoms like simple pain can appear and be described regardless of the type of diseases, the standard of frequent appearances about individual symptoms may be different. Therefore, the assumption was that treatment method combinations of which the number of appearances was greater than other treatment method combinations for a symptom is more significant in order to apply a standard fit for each system.

1) Establishing a null hypothesis

A null hypothesis (H_0) and an alternative hypothesis(H_A) were established as described below in order to find symptom-treatment method combinations with higher relation for each symptom. If the number of appearances of the treatment method combinations for a symptom is defined as P_n, respectively,

H_0 : All P_n's are equal.

H_A: All P_n's are not equal.

2) Interpreting null hypothesis (interpret p-value)

The p-value interpretation was used to interpret the null hypothesis, and the significance level was set as $\alpha = 0.05$ (see [11]).

3) Data structure and interpretation process

If only one symptom-treatment method combination is higher in terms of the number of combinations than other symptom-treatment method combinations according to symptom as shown in Fig.1, there can be cases that all combinations other than one can be greater in terms of the number of combinations as shown in Fig.2.

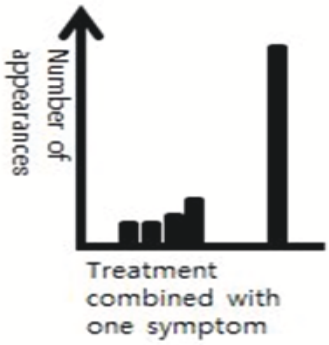

FIGURE 1. Number of appearances

Just one symptom-treatment combination has many appearances(see Figure 1).

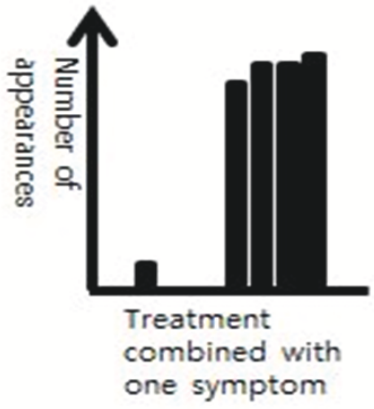

FIGURE 2. Number of appearances

Just one symptom-treatment combination has the smaller number of appearances(see Figure 2).

Therefore, p-value interpretation was repeated. Because the p-value smaller than 0.05 at the significance level 0.05 is thought that the number of appearances for each treatment is not equal, combinations with the smaller number of appearances exist with the combinations with the greater number of appearances. In this case, if there is one combination with the smaller number of appearances to remove the combination with the smallest number of appearances after the first p-value interpretation and then to conduct p-value interpretation again, the value will become at least 0.05. If the number is 2 to remove 2 combinations with the smallest number of appearances and then to conduct p-value interpretation again, the value will become at least 0.05. For example, if the number of appearances of treatments a, b, c, d and e combined with a symptom is 30, 29, 3, 2 and 1, respectively, the first p-value is smaller than 0.05. The p-value after removing e and d subsequently is also smaller than 0.05, and the p-value just for a and b after removing c will become at least 0.05. Therefore, treatments a and b were derived in the aforementioned way, of which the number of appearances was greater than other treatments. The following flow chart illustrates this method.

Finding combinations of which the relative number of appearances is more than others(see Figure 3).

Results

As a result, 1589 symptom-treatment method combinations were obtained. Table 1 illustrates comparison of the result of this study with the analysis result by TKM experts for each number of appearances.

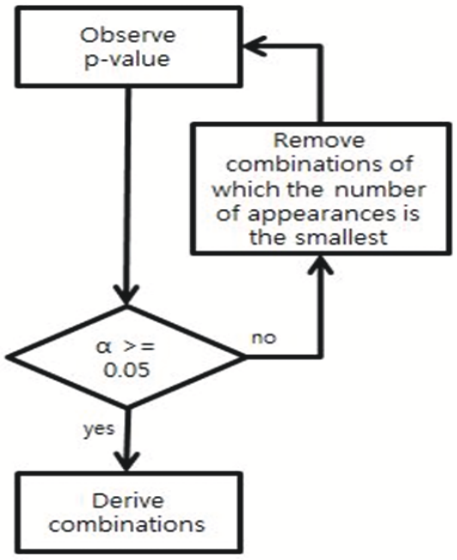

FIGURE 3. Flow chart

Table 1. Comparison of the result of this study with expert's analysis result

Number of appearances	Number of combinations in ontology	Number of significant combinations in result of this study	Number of combinations with result of this study inconsistent with expert's analysis result	Number of combinations with result of this study inconsistent expert's analysis result	Consistency of result of this study with expert's analysis result
10 or greater	1860	1589	690	898	43.45%
20 or greater	575	519	277	242	53.37%
30 or greater	160	123	75	48	60.98%
40 or greater	72	64	45	19	70.10 %
50 or greater	63	57	39	18	68.42%
60 or greater	12	9	8	1	88.89%
66 or greater	9	6	6	0	100%

Table 2 and Table 3 illustrates combinations of which the number of appearances is at least 40 among combinations determined significant in the result of this study.

Table 2. Combinations of which the number of appearances

Symptom	Treatment	Number of appearances	Expert's analysis result
expectoration of fishy odor phlegm	activate blood	58	significant
expectoration of fishy odor phlegm	resolve stasis	58	insignificant
amnesia disorder	activate blood	58	significant
amnesia disorder	resolve stasis	58	insignificant
bluish black lower palpebral(eyelid)	activate blood	58	insignificant
bluish black lower palpebral(eyelid)	resolve stasis	58	significant
high fever	clear heat	74	significant
high fever	detoxify	74	significant
dry mouth with urge to cough but no urge to drink	activate blood	58	insignificant
dry mouth with urge to cough but no urge to drink	resolve stasis	58	insignificant
deviated mouth and tongue	activate blood	63	significant
deviated mouth and tongue	resolve stasis	58	significant
skin roughening and thickening	activate blood	59	significant
skin roughening and thickening	resolve stasis	58	significant
black stool	resolve stasis	118	significant
black stool	activate blood	116	significant
headache disorder	activate blood	58	significant
headache disorder	resolve stasis	58	significant
chronic headache	activate blood	58	insignificant
chronic headache	resolve stasis	58	insignificant
headache with scorching heat-like pain	activate blood	58	insignificant
headache with scorching heat-like pain	resolve stasis	58	insignificant
fixed spot headache	activate blood	58	significant
fixed spot headache	resolve stasis	58	significant
tenesmus	clear heat	47	insignificant
pale complexion	replenish qi	52	significant
vomiting in the morning of food eaten in the evening	harmonize the stomach	56	significant
vomiting in the morning of food eaten in the evening	downbear counterflow	54	significant
hemiplegia	activate blood	73	significant
hemiplegia	resolve stasis	58	significant
rigidity and fullness in the abdomen	resolve stasis	60	significant
rigidity and fullness in the abdomen	activate blood	58	insignificant
abdominal pain	clear heat	65	insignificant
abdominal pain	detocify	54	insignificant

Table 3. Combinations of which the number of appearances

Symptom	Treatment	Number of appearances	Expert's analysis result
stiff tongue and sluggish speech	activate blood	44	significant
impatient innate nature and emotion	activate blood	58	insignificant
impatient innate nature and emotion	resolve stasis	58	insignificant
distending pain in the lower abdomen	activate blood	58	insignificant
distending pain in the lower abdomen	resolve stasis	58	significant
decreased volume of urine	clear heat	41	significant
and excretion of reddish urine	clear heat	41	significant
delirious speech	clear heat	51	significant
insomnia disorder	activate blood	58	insignificant
insomnia disorder	resolve stasis	58	insignificant
stabbing pain in the heart and chest	activate blood	58	significant
tinnitus disorder	enrich yin	44	significant
suppressed essence-spirit	activate blood	58	insignificant
suppressed essence-spirit	resolve stasis	58	significant
vomiting in the evening of food eaten in the morning	harmonize the stomach	56	significant
vomiting in the evening of food eaten in the morning	downbear coutnerflow	54	significant
vomiting in the evening of food eaten eaten in the morning, vomiting in the morning of food in the evening	harmonize the stomach	53	significant
vomiting in the evening of food eaten eaten in the morning, vomiting in the morning of food in the evening	downbear coutnerflow	51	significant
hematemesis of red blood	stop bleeding	43	significant
hematemesis of red blood	cool the blood	40	significant
awl stabbing-like pain	activate blood	58	significant
awl stabbing-like pain	resolve stasis	58	significant
fixed pain	activate blood	58	significant
fixed pain	resolve stasis	58	significant
half-body numbness	activate blood	73	significant
half-body numbness	resolve stasis	58	significant
static spot of the skin	activate blood	58	significant
static spot of the skin	resolve stasis	58	significant
scorching heat anal pain	clear heat	50	significant
stuffiness and oppression in the chest and stomach	harmonize the stomach	47	significant

3. Conclusions

This study aims to analyze the relation between symptom and treatment method in a mathematical method to derive significant symptom-treatment method combinations and to compare them with analysis results by TKM experts and eventually suggest an objective analysis method applicable to other data. Treatment method refers to a principle or method for treating diseases.

Determining treatment method contributes to determining effective treatment means including medicinal material, prescription, acupuncture and moxibustion. Therefore, significant symptom-treatment method combination data can be used for treating target diseases. For example, it can be applied to treatment support systems developed for TKM doctors by recommending prescriptions or treatment means ideal for patient's symptom and giving the doctors a consideration for various treatment methods. Another exemplary application is to automatically find and suggest articles for medicinal materials effective for the patient's symptom. Also, in self-health control programs for the general public it is applicable to suggest TKM treatment effective for symptoms throughout the user's daily life.

In this study, 1589 symptom-treatment method combinations were obtained. This result implies the number of appearances is greater than other treatment method combinations. Therefore, according to the assumption in this study that the greater number of appearances is more significant, 1589 symptom-treatment method combinations are thought as significant symptom-treatment method combinations. According to prior studies, 787 symptom-treatment method combinations are considered significant by TKM experts. The concordance rate of the result of this study and the result of TKM expert's analysis increases as the number of appearances increase, and the symptom-treatment method combinations is expected to be selectively used in consideration of accuracy and convenience depending on the purpose of use. Synonyms for symptom or treatment method terms were not provided, and may have limited the result of this study. Further study is required for a method of finding significant combinations among combinations which appear less than 10 times, not examined in this study, or a method of finding α proper for the features of TKM or using the result of this study.

References

1. H.C. Jang, J.H. Kim, S.K. Kim, C. Kim, S.H. Bae, A.N. Kim, D.M. Eum, M.Y. Song, Ontology for Medicinal Materials Based on Traditional Korean Medicine, Bioinformatics (2010), 2359-2360
2. H.C. Jang, Ontology-based Traditional Korean Medicine Knowledge Framework(K13090), Korea Institute of Oriental Medicine, Daejeon, 2013
3. T.R. Gruber, A Translation Approach to Portable Ontology Specifications, Knowledge Acquisition 5(2)(1993), 199-220
4. S.K. Kim, Y.T. Oh, A.N. Kim, J.Y. Kim, S.J. Yea, C. Kim, et al, Mobile Application for Supporting Medical Treatment in Korean Medicine, Korean Journal of Oriental Physiology & Pathology 26(6)(2012), 834-841
5. Joint Text Compilation Committee for Korean internal medicine(Liver), Korean internal medicine(Liver), Institute of Oriental Medicine, Seoul, 2001
6. Joint Text Compilation Committee for Korean internal medicine(Heart), Korean internal medicine(Heart), Gunja Publishing Ltd., Seoul, 2008
7. Joint Text Compilation Committee for Korean internal medicine(Spleen), Korean internal medicine(Spleen), Gunja Publishing Ltd., Seoul, 2009

8. Joint Text Compilation Committee for Korean internal medicine(Lung), Korean internal medicine(Lung), Nado Publishing Ltd., Seoul, 2007
9. Park HG compilation, Korean internal medicine (Kidney), Sungbo Publishing Ltd., Seoul, 2006
10. Y.T. Oh, A.N. Kim, S.K. Kim, J.S. Seo, H.C. Jang, Study on Systematizing the Combination of Method of Treatment and Symptoms Using the Basic Traditional Medicine Theory, Korean Journal of Oriental Physiology & Pathology 27(4)(2013), 383-390
11. H.Y. Lee, Prof. Lee's Statistics(3rd), Chungram Publishing Ltd., Seoul, 2000

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