Chinese medicine patterns in patients with post-stroke dementia

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Running Title: Chinese medicine Pattern in post-stroke dementia patients

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Abstract

A stroke often results in post-stroke dementia, a rapid decline in memory and intelligence causing dysfunctions in daily life. The Chinese medicine doctor uses 4 examinations of inspection, listening, smelling, and feeling to determine the Chinese medicine pattern (CMP). Therefore, the purpose of the present study was to investigate the CMP in patients with post-stroke dementia. A total of 101 stroke patients were examined, consistent with the DSM IV diagnostic criteria of the American Psychiatric Association, as well as the National Institute of Neurological Disorders and Stroke-Association International pour Ia Recherche et l'Enseignement en Neurosciences vascular dementia diagnostic criteria of post-stroke dementia. Results: 100 patients (99.0%) were KEDP (kidney essence deficiency pattern, 腎精 虧虛證), 83 patients were (肝陽上亢 ascendant hyperactivity of liver yang pattern, 肝陽上亢證), 83 patients were QBDP (gi-blood deficiency pattern, 氣血虧虛證), 81 patients were SBOCP (static blood obstructing the collaterals pattern, 瘀血阻絡證), 72 patients were BSTRP (bowels stagnation turbidity retention pattern, 腑滯濁留證), 50 patients were FHIEP (fire heat interior excess pattern, 火熱內盛證), and 39 participants (38.6%) were PTOOP (phlegm turbidity obstructing the orifices pattern, 痰濁阻竅證); one to 31 patients have at least 2 CMPs simultaneously. In conclusion, the most CMP is KEDP CMP in the post-stroke dementia patients, and one patient

may have one or at least 2 CMPs simultaneously.

Introduction

Post-stroke dementia is also known as vascular dementia. The main clinical manifestation is a decline in memory and intellectual function, causing dysfunction in daily life (Román, 1993; Tian, 2000). In 1975, Folstein and McHugh developed the Mini-Mental Status Examination (MMSE) scale (Folstein, 1975), including orientation, registration, attention and calculation, recall, language, repetition, complex commands, and other items. The scale of the scores totals 30, and a total score of less than 24 can result in a diagnosis of dementia. Developed in 1993, the Cognitive Abilities Screening Instrument (CASI) can be used to assess early dementia, elderly memory, orientation, and language function. The Clinical Dementia Rating (CDR) can be used to assess patients' daily living functions including memory, orientation, problem-solving skills, community mobility, home hobbies, and self-care ability. The CDR can also be used to indicate the severity, such as 0 (normal), 0.5 (suspected sick), 1 (mild), 2 (moderate), and 3 (severe) dementia (Tian, 2000; Liu, 2005). In the Chinese medicine pattern (CMP) of post-stroke dementia, Tian et al. (1997) developed "The scale for the differentiation of syndromes of vascular dementia, SDSVD," which is divided into 7 categories: KEDP (kidney essence deficiency pattern; 腎精虧虛證), AHLYP (ascendant hyperactivity of liver yang pattern; 肝陽 上亢證), QBDP (qi-blood deficiency pattern; 氣血虧虛證), SBOCP (static blood

obstructing the collaterals pattern; 瘀血阻絡證), BSTRP (bowels stagnation turbidity retention pattern; 腑滯濁留證), FHIEP (fire heat interior excess pattern; 火熱內盛證), and PTOOP (phlegm turbidity obstructing the orifices pattern; 痰濁阻竅證). The total score of each pattern is 30, and a pattern is established when the score ≥ 7 (Tian, 2000). According to the statistics of the Department of Health of Taiwan in 2011, cerebrovascular disease is placed third in the 10 leading causes of death in Taiwan (Department of Health, Executive Yuan, Taiwan, 2011) http://www.doh.gov.tw/CHT2006/DM/DM2_2_p02.aspx?class_no=440&now_fod_lis t_no=11897&level_no=3&doc_no=80725). The results of the study show that

acetylcholine is dysfunctional in dementia after stroke, accompanied by other neurological chemicals such as 5-HT in decreased concentrations (Tian, 2003). However, effective treatment involves few drug options. Most treatment is focused on general prevention, such as control of blood pressure and diabetes (Tian, 2003). Therefore, treatment of dementia after stroke is a critical issue for medical research.

The purpose of this study was to investigate the CMP in patients with post-stroke dementia. Post-stroke dementia patients were recruited from the department of neurology at China Medical University Hospital, Taichung, Taiwan. Strokes were confirmed using cranial computer tomography (CT) or magnetic resonance imaging (MRI). The dementia patients were screened according to DSM-IV (*Diagnostic and* Statistical Manual of Mental Disorders, 4th edition) (Kong, 2000) and criteria established by NINDS-AIREN (National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherché et l'Enseignement en Neurosciences) (Román, 1993). Stroke data were recorded according to the MMSE, CASI, and CDR scales. In addition, 2 experienced Chinese medicine doctors conducted 4 examinations of Chinese medicine to complete the SDSVD of vascular dementia recordings (Tian, 2000).

Materials and methods

Subjects

A total of 143 stroke patients were enrolled in the neurology clinic at China Medical University Hospital between September 19, 2006, and September 18, 2007. The protocol and the procedures of the study were approved by the institutional review board of China Medical University Hospital, Taichung City, Taiwan (IRB: DMR 95-IRB-111). The procedure of the study was explained to subjects in detail for signed informed consent. The inclusion criteria were as follows: 1) over the age of 40; 2) the stroke was confirmed using CT or MRI examination; 3) stroke was a hemorrhage type or infarction type; 4) the dementia was in agreement with the American Psychiatric Association (1994) DSM-IV diagnostic criteria for vascular dementia (Kong, 2000); and 5) the dementia was also consistent with the

NINDS-ALREN (National Institute of Neurological Disorders and Stroke-Association International pour Ia Recherche et I' Enseignement en Neurosciences) diagnostic criteria for vascular dementia (1993(Román, 1993). Exclusion criteria were 1) transient ischemic attack (TIA); 2) stroke caused by cerebral venous thrombosis; 3) traumatic head injury or head surgical history; 4) combined severe systemic diseases such as uremia, chronic obstructive pulmonary disease and respiratory problems, or heart failure; and 5) disturbance of consciousness, delirium, severe aphasia, or dementia caused by brain degeneration from other brain diseases; and 6) MMSE scores ≥ 24 or CDI scores <1.

The recordings of assessment scale scores

The scores of the MMSE, CASI, and CDR were recorded by an assistant who was experienced and well trained for the aforementioned assessment. Two experienced Chinese medicine doctors recorded the SDSVD of vascular dementia, according to the 4 examinations of Chinese medicine.

Determination of CMP of post-stroke dementia

Determination of CMP of post-stroke dementia was based on Tian et al (2000). The

CMP of post-stroke dementia was divided into KEDP, AHLYP, QBDP, SBOCP,

BSTRP, FHIEP, and PTOOP. The total scores were 30 in each pattern, and the pattern was established when the sum of individual factor scores was \geq 7. The CMP was mild when the scores were between 7 and 14; between 15 and 22 was moderate; and between 23 and 30 was severe.

Statistical Analysis

The CMPs of vascular dementia were presented as a percentage, and mean and standard deviation describes the distribution of SDSVD. Using Pearson's or Spearman's correlation coefficient assessment, the correlation among the scores of CMP for vascular dementia, and MMSE, CASI, and CDR scores. The analysis of variance or Kruskall-Wallis test were used to certify the difference of mild, moderate, and severe patterns in the MMSE, CASI, and CDR scores. The *t* test or Wilcoxon rank-sum assessed the difference between patterns and non-patterns of the MMSE, CASI, and CDR scores. The test or Wilcoxon rank-sum assessed the difference between patterns and non-patterns of the MMSE, CASI, and CDR scores. The chi-square test or Fisher's exact test assessed the various patterns, non-patterns, or patterns with mild severity of dementia. When the type I error of this study is set at 0.05, whereas the type II error is set at 0.2, the power of this study must be confirmed to be 0.8. Assuming that the purpose of this study was to evaluate the difference between patterns (non-patterns) and scale scores of MMSE,

CASI, and CDR, assumption has (or none) certain pattern the MMSE, CASI or CDR scale scores of the standardized differences (standardized effect size) was 0.65 (difference between the 2 groups of 2 points, standard deviation is assumed to be 3), if this study to be able to detect this difference, has or none certain pattern would require 45 respondents, respectively (Hulley, 2001). Assuming there are age, gender, or other variables causing the interference effect, then statistical models must be used to control this interference effect, the number of samples must be increased by 10% for diagnosis, and the total sample would be 50 people. Therefore, this study scheduled for 100 dementia patients should generate adequate statistical power to detect this effect.

Result

Basic characteristic data

A total of 101 (52 women, 49 men) stroke patients were examined, and their MMSE scores were ≤ 23 and SDR ≥ 1 , which are consistent with the criteria of DSM-IV (Kong, 2000) and NINDS-AIREN (Román, 1993). The age ranged from 42 to 100 years (mean \pm standard deviation; 75.4 \pm 9.4 years). The education ranged from 0 to 16 years (mean 5.3 \pm 3.9 years) (Table 1).

CMP of post-stroke dementia, and the relationship of the severity between CMP and non-CMP in the 101 post-stroke dementia patients

Of the 101 post-stroke dementia patients, 100 patients (99.0%) had KEDP, 83 patients (82.2%) had AHLYP, 83 patients (82.2%) had QBDP, 81 patients (80.2%) had SBOCP, 72 patients (71.3%) had BSTRP, 50 patients had FHIEP, and 39 patients (38.6%) had PTOOP (Table 2).

The CDR scores for the non-QBDP patients were less than those for the QBDP patients (p < .05), whereas there was no significant difference in the MMSE and CASI scores between non-QBDP and QBDP patients with post-stroke dementia (both p > .05; Table 3). The score of CDR, MMSE, and CASI were not significantly different between non-KEDP and KEDP, between non-AHLYP and AHLYP, between

non-SBOCP and SBOCP, between non-BSTRP and BSTRP, between non-FHIEP and FHIEP, and between non-PTOOP and PPTOOP for patients with post-stroke dementia (all p > .05; Table 3).

The CMPs combined in the 101 post-stroke dementia patients

Table 4 shows that 2 patients (1.2%) had 2 CMPs combined, 10 patients (9.9%) had 3 CMPs combined, 21 patients (20.8%) had 4 CMPs combined, 31 patients (30.7%) had 5 CMPs combined, 24 patients (23.8%) had 6 CMPs combined, and 13 patients (12.9%) had 7 CMPs combined, for all of the 101 patients with post-stroke dementia (Table 4).

Discussion

Our results indicated that 100 patients were KEDP (99.0%); 83 patients were both AHLYP and QBDP (82.2%), 81 patients were SBOCP (80.2%), 72 patients were BSTRP (71.3%), 50 patients were FHIEP (49.5%), and 39 patients were PTOOP (38.6%) for all of the 101 post-stroke dementia patients. These results suggest that KEDP is closely related to post-stroke dementia. Traditional Chinese medicine considers that the kidney dominates human birth, growth, aging, and death, which is the base of bone, store essence and the root of innate. The kidney is also considered to dominate human minds (Yin, 1997). Clinical AHLYP leads to the primary symptoms of dizziness, tinnitus, distending pain in the head and eye, vexation, and irritation (Yao, 2002). These symptoms are similar to hypertension or sudden elevation of blood pressure, easily leading to arteriosclerosis, thus causing the clinical manifestations of cerebral ischemia or stroke (Huang, 2002). This study showed that QBDP was a critical factor in post-stroke dementia. Several studies have shown that the pathogenesis of vascular dementia should focus on the elderly and feeble, occur in stroke, and lesions in the brain (Zhang, 1999). This study showed that the CDR scores of non-QBDP patients were lower than those for QBDP patients. Because dementia is a slow progressive disease, similar to the aging, that is a main cause of QBDP. Another study suggested that etiology and pathogenesis of vascular dementia includes static blood stagnation and marrow deficiency. The performance of both deficiency and stasis, but stasis based (Wang, 2001). Li indicated that the patterns of elderly people with vascular dementia can be broadly divided into "qi deficiency with blood stasis," "kidney liver yin deficiency," and "spleen deficiency and turbidity obstruction" (Li, 1994). The results indicated that the CDR scores of non-QBDP were lower than those of the QBDP. The other patterns with or without were not significantly different in the severity of the MMSE, CASI, and CDR, indicating that QBDP may play an essential role in post-stroke dementia, but the etiology requires

further study in future.

In addition, our results indicated that 2 patients had 2 CMPs combined, 10 patients had 3 CMPs combined, 21 patients had 4 CMPs combined, 31 patients had 5 CMPs combined, 24 patients had 6 CMPs combined, and 13 patients had 7 CMPs combined for the 101 patients with post-stroke dementia. These results are in favorable agreement with the theory of traditionary Chinese medicine (TCM), stating that one patient may have one or at least 2 CMPs simultaneously. These results are also consistent with our previous studies showing that patients in the acute stroke stage, including the infarction type and hemorrhagic type, has one or at least 2 CMPs simultaneously (Liu, 2006; Tang, 2006). Therefore, clinical manifestations involve many varieties in patients with post-stroke dementia.

In conclusion, most of the CMP is KEDP CMP in the post-stroke dementia, and one patient may have one or at least 2 CMPs simultaneously. The relationship between CMPs and clinical severity is not prominent.

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Item	M& F	М	F
No (%)	101 (100)	49(48.5)	52(51.5)
Age (years)	75.4±9.4	73.8±10.6	76.9±8.0
Education (years)	5.3±3.9	7.1±3.6	3.6±3.4
MMSE	14.5±5.5	15.6±5.8	13.5±5.0
CASI	44.0±17.2	46.6±18.0	41.6±16.1
CDR	1.2±0.4	1.1±0.3	1.3±0.5

Table 1. Basic characteristic data in 101 patients with post-stroke dementia

Mean ± standard deviation; M: male; F: female; M&F: male plus female; MMSE: Mini Mental State Exam; CASI: Cognitive Abilites Screening Instrument; CDR: Clinical Dementia Rating.

pattern	no	yes	mild	moderate	severe
KEDP	1(1.0%)	100(99.0%)	3(3.0%)	77(77.0%)	20(20.0%)
AHLYP	18(17.8%)	83(82.2%)	47(56.6%)	34(41.0%)	2(2.4%)
QBDP	18(17.8%)	83(82.2%)	69(83.1%)	14(16.9%)	0(0.0%)
SBOCP	20(19.8%)	81(80.2%)	51(63.0%)	29(35.8%)	1(1.2%)
BSTRP	29(28.7%)	72(71.3%)	51(70.8%)	20(27.8%)	1(1.4%)
FHIEP	51(50.5%)	50(49.5%)	48(96.0%)	2(4.0%)	0(0.0%)
РТООР	62(61.4%)	39(38.6%)	33(84.6%)	6(15.4%)	0(0.0%)

Table 2. The number of individual Chinese medicine pattern in 101 patients with post-stroke dementia

No: non-Chinese medicine pattern with the score < 7; yes: the scores \geq 7; mild: the scores \geq 7~14; moderate: the scores \geq 15~22; severe: the scores \geq 23~30 KEDP: kidney essence deficiency pattern; AHLYP: ascendant hyperactivity of liver yang pattern;QBDP: qi-blood deficiency pattern;SBOCP: static blood obstructing the collaterals pattern;BSTRP: bowels stagnation turbidity retention pattern;FHIEP: fire heat interior excess pattern; PTOOP: phlegm turbidity obstructing the orifices pattern.

pattern		MMSE(0~30)	CASI(0~100)	CDR(0~3)
KEDP	no (1)	4	8	1
	yes (100)	14.6±5.4	44.4±16.9	1.2±0.4
AHLYP	no (18)	12.6±5.9	39.7±20.2	1.1±0.3
	yes (83)	15.0±5.4	44.9±16.4	1.2±0.4
QBDP	no (18)	15.1±6.4	48.1±19.0	1.1±0.2
	yes (83)	14.4±5.3	43.1±16.7	1.2±0.4*
SBOCP	no (20)	13.2±5.1	40.0±16.8	1.3±0.4
	yes (81)	14.9±5.6	45.0±17.2	1.2±0.4
BSTRP	no (29)	15.4±6.1	48.3±18.3	1.1±0.4
	yes (72)	14.2±5.2	42.3±16.5	1.2±0.4
FHIEP	no (51)	15.0±5.5	15.1±16.9	1.2±0.4
	yes (50)	14.0±5.5	42.9±17.5	1.2±0.4
PTOOP	no (62)	14.5±5.0	46.1±15.1	1.2±0.4
	yes (39)	14.6±6.3	40.6±19.8	1.2±0.4

Table 3. Relationship between patterns and severity of dementia in the 101 post-stroke dementias

Mean ± standard deviation; MMSE: Mini Mental State Exam; CASI: Cognitive Abilites Screening Instrument; CDR: Clinical Dementia Rating; KEDP: kidney essence deficiency pattern; AHLYP: ascendant hyperactivity of liver yang pattern; QBDP: qi-blood deficiency pattern; SBOCP: static blood obstructing the collaterals pattern; BSTRP: bowels stagnation turbidity retention pattern; FHIEP: fire heat interior excess pattern; PTOOP: phlegm turbidity obstructing the orifices pattern; no: without pattern; yes: with pattern; *p<0.05: compare with no.

Patterns combined	No. (%)	MMSE	CASI	CDR
Two patterns	2(100%)			
KEDP-FHIEP	2(100.0%)	16.5±4.9	55.0±21.2	1.0±0.0
Three patterns	10(100%)			
KEDP-BSTRP-QBDP	2(20.0%)	12.5±7.8	34.5±6.4	1.0±0.0
KEDP-SBOCP-BSTRP	1(10.0%)	11	48	1
KEDP-SBOCP-QBDP	1(10.0%)	5	17	1
KEDP-SBOCP-FHIEP	2(20.0%)	20.0±1.4	67.5±6.4	1.0±0.0
KEDP-SBOCP-AHLYP	1(10.0%)	9	26	1
KEDP-AHLYP-QBDP	2(20.0%)	18.0±1.4	54.0±5.7	1.0±0.0
PTOOP-SBOCP-BSTRP	1(10.0%)	4	8	1
Four patterns	21(100%)			
KEDP-PTOOP-BSTRP-QBDP	3(14.3%)	11.0±7.0	34.3±27.5	1.0±0.0
KEDP-PTOOP-SBOCP-AHLYP	2(9.5%)	22.5±0.7	66.0±1.4	1.0±0.0
KEDP-SBOCP-AHLYP-QBDP	5(23.8%)	16.8±3.9	51.4±11.7	1.0±0.0
KEDP-SBOCP-AHLYP-BSTRP	2(9.5%)	16.0±7.1	45.0±17.0	1.5±0.7
KEDP-SBOCP-BSTRP-QBDP	2(9.5%)	13.0±7.1	34.0±22.6	1.0±0.0
KEDP-SBOCP-AHLYP-FHIEP	2(9.5%)	12.0±9.9	43.0±21.2	1.0±0.0
KEDP-AHLYP-BSTRP-QDP	2(9.5%)	10.5±0.7	28.0±1.4	2.0±0.0
KEDP-AHLYP-FHIEP-BSTRP	1(4.8%)	10	30	1
KEDP-AHLYP-FHIEP-QBDP	1(4.8%)	5	18	1
KEDP-FHIEP-BSTRP-QBDP	1(4.8%)	11	23	2
Five patterns	31(100%)			
KEDP-PTOOP-AHLYP-BSTRP-QBDP	2(6.5%)	18.0±5.7	52.0±22.6	1.5±0.7
KEDP-PTOOP-SBOCP-AHLYP-BSTR	2(6.5%)	17.0+7.1	54 0+22 6	1.0+0.0
Р	2(0.3%)	17.0±7.1	J4.0±22.0	1.0±0.0
KEDP-PTOOP-SBOCP-AHLYP-QDP	3(9.7%)	12.3±8.4	38.7±20.2	1.7±0.6
KEDP-PTOOP-SBOCP-BSTRP-QDP	1(3.2%)	12	33	1
KEDP-SBOCP-AHLYP-FHIEP-QDP	8(25.8%)	16.1±5.7	50.9±20.7	1.3±0.5
KEDP-SBOCP-AHLYP-BSTRP-QBDP	11(35.5%)	15.3±4.4	49.2±12.9	1.2±0.4
KEDP-SBOCP-AHLYP-FHIEP-BSTRP	1(3.2%)	8	34	1
KEDP-SBOCP-FHIEP-BSTRP-QDP	1(3.2%)	8	46	2
KEDP-AHLYP-FHIEP-BSTRP-QDP	2(6.5%)	13.0±7.1	50.5±7.8	1.0±0.0
Six patterns	24(100%)			

Table 4. CMP combined in the 101 post-stroke dementia patients

KEDP-SBOCP-AHLYP-FHIEP-BSTRP	12(50,00())	15 9 2 4	49.4 10.4	12.05	
-QBDP	12(50.0%)	15.8±5.4	48.4±10.4	1.3±0.5	
KEDP-PTOOP-SBOCP-AHLYP-BSTR	7(20,20()	10.2.2.2	477169	11.04	
P-QBDP	7(29.2%)	18.3±3.3	4/./±10.8	1.1±0.4	
KEDP-PTOOP-AHLYP-FHIEP-BSTRP	2(9,20/)	14.0±0.0	38.5±9.2	1.5±0.7	
-QBDP	2(8.3%)				
KEDP-PTOOP-SBOCP-AHLYP-FHIEP	1(4 20/)	21	60	1	
-QBDP	1(4.2%)	21	60	1	
KEDP-PTOOP-SBOCP-AHLYP-FHIEP	1(4 20/)	21	50	1	
-BSTRP	1(4.2%)	21	39	1	
KEDP-PTOOP-SBOCP-FHIEP-BSTRP-	1(4, 204)	10	55	1	
QBDP	1(4.2%)	19	55	1	
Seven patterns	13(100%)				
KEDP-PTOOP-SBOCP-AHLYP-FHIEP	12	115.00	30.3±18.0	1.3±0.5	
-BSTRP-QDP	13	11.5±6.2			

Mean ± standard deviation; MMSE: Mini Mental State Exam; CASI: Cognitive Abilites Screening Instrument; CDR: Clinical Dementia Rating; No: number of patient; KEDP: kidney essence deficiency pattern; AHLYP: ascendant hyperactivity of liver yang pattern; QBDP: qi-blood deficiency pattern; SBOCP: static blood obstructing the collaterals pattern; BSTRP: bowels stagnation turbidity retention pattern; FHIEP: fire heat interior excess pattern; PTOOP: phlegm turbidity obstructing the orifices pattern.