Original Article

The Effects of Acupuncture on the Insomnia, Anxiety and Depression of Liver Cancer Patients: Pilot study

Chang-Hyeong Lee¹, Byung-Seok Kim¹, Ji-Suk Kim², Hyo-Jung Kwon³, Ae-Ryun Choi⁴, Min-A Kwak⁵, Seung-Mo Kim⁵

¹Department of Internal Medicine, Catholic University of Daegu School of Medicine

²Department of Nursing, College of Nursing, Kyungbuk University

³Department of Acupuncture and Meridian, College of Oriental Medicine, Daegu Haany University

⁴Department of Sasang Constitutional Medicine, College of Oriental Medicine, Daegu Haany University

⁵Department of Internal Medicine, College of Oriental Medicine, Daegu Haany University

Objectives: Most patients who have cancer suffer from anxiety and depression. Because most liver cancer patients have cirrhosis, medication can aggravate their liver function. We need the most effective treatment such that the anxiety and depression can be improved without causing deterioration of liver function. The purpose of this study is to examine the effects of acupuncture on the anxiety and depression of liver cancer patients.

Methods: 8 liver cancer patients who complained of distress were treated by acupuncture three times a week for four weeks (12 times in total). Evaluation of the anxiety, depression and insomnia was measured by NCC (National Cancer Center) score. On visits 1, 4, 7, 10, and 13 we had patients check NCC score after acupuncture treatment. To check deterioration of liver cancer, we checked their abdominal CT, Child-Pugh score and blood test.

Results: After 12 treatments, NCC of the anxiety, depression and insomnia were significantly decreased in all of the patients without causing deterioration of liver function. In particular, symptoms were almost completely improved in 6 patients.

Conclusions: This study suggests that acupuncture treatment will be beneficial for liver cancer patients to reduce anxiety, depression and insomnia. For liver cancer patients with cirrhosis or chronic hepatitis, a large-scale study to confirm efficacy and safety of acupuncture is needed.

Key Words: NCC, insomnia, anxiety, depression, liver cancer

Introduction

Cancer is the commonest cause of death domestically, and despite effective treatment from the development of various treatment modalities, awareness of the quality of life of patients and families is insufficient. Cancer patients are known to complain of three particular symptoms, namely anxiety, depression and insomnia¹⁾. Lately many

studies have been done abroad on the subject of alleviating anxiety, depression and insomnia using various complementary therapies²⁻⁴⁾.

Especially, acupuncture can decrease chemotherapyinduced nausea and post-surgery vomiting^{5,6)}, and is reported to lower the anxiety level of patients⁷⁾. Not only cancer patients, but also patients awaiting other kinds of surgery are known to benefit from acupuncture in reducing anxiety^{8,9)}. According to the

· Received: 25 April 2012 · Revised: 4 June 2012 · Accepted: 7 June 2012

· Correspondence to : Seung-Mo Kim

136 Shinchun-Dong Street, Suseong-Gu, Daegu, 706-828, Korea

Tel: +82-53-770-2111. Fax: +82-53-770-2189. Email: heuwon@hanmail.net

CAM services regulation of Johns Hopkins University anxiety and depression are among symptoms for which acupuncture is efficacious⁷⁾.

Acupuncture stabilized the autonomic nervous system and controls the system of the pituitary gland and adrenal cortex, thereby treating stress-induced anxiety, depression and insomnia 10). In oriental medicine, the text of 『LingShu(靈樞』「CiJieZhenXieLun(刺節 區邪論」¹¹⁾ states "the purpose of using acupuncture is to control qi" and in "SuWen(素問 』「BaoMingQuan-XingLun(寶命全刑論」¹²⁾ is stated "acupuncture treatment is for treating the psyche first" which means acupuncture controls the balance of qi and spirit to affect the body's psychologic activities such as anxiety, depression and insomnia.

Most hepatocellular carcinoma patients, especially those with accompanying hepatocirrhosis, have severe liver function issues, so that the use of medication for the symptoms of anxiety, depression and insomnia is limited. Therefore, a treatment modality for improving anxiety, depression and insomnia without aggravating liver function is called for.

We conducted a pilot study clinical trial of four weeks of acupuncture treatment on patients diagnosed with hepatocellular carcinoma and complaining of anxiety and depression. The trial was done to compare improvement of anxiety, depression and insomnia by acupuncture, and also its effect on liver function and its safety as seen in adverse events. We observed significant results and thereby report the efficacy of acupuncture on anxiety and depression.

Objects and Methods

1. Objects

8 participants who entered for clinical trial recruitment between Sep. 1 and Dec. 31, 2011 (gender ratio 4:4) were enrolled.

Methods

1) Participant Recruitment

Participants were recruited using the internet and posters. Participants either visited the study center or telephoned to schedule an appointment.

2) Inclusion and Exclusion Criteria

Participants who entered for the clinical trial recruitment were enrolled after being explained the purpose, method, anticipated adverse dangers or discomfort, disclosure of personal information, compensation, right to discontinue in the process of the clinical trial, and signing agreement to enter on one's own will. This study was approved by the Institutional Review Board of Daegu Catholic University Hospital.

The inclusion criteria were patients diagnosed with hepatocellular carcinoma complaining of distress, whose National Cancer Center psychologic symptoms score was higher than 4 points on both severity and inconvenience in any one territory of anxiety, depression or insomnia. Other inclusion criteria are Child-Pugh A or B score lower than 9, serum bilirubin level of 3mg dl or lower, AST, ALT 100IU/L or lower, serum creatinine 1.5mg dl or lower, INR 1.5 or lower. The participants had to undergo a washout period starting 3 days prior to the start of the trial to the end, limiting administration of tranquilizers and antidepressants. The participants also had to be able to be tracked any time of the trial, and to follow the standards of limitation.

The exclusion criteria were cases of aggravation of hepatocellular carcinoma such as neutropenia (absolute neutrophil level of 500/ul or lower), platelet count less than 60,000/ul, fever, aggravation of liver function, abdominal aneurysm, sepsis, thrombosis, etc. and other situations judged to be difficult to continue clinical trial by the principal investigator or the person who carried on the trial.

3) Methods

Demographic information, medical history taking by MD or OMD, physical exam (body temperature, blood pressure, pulse, body weight), abdominal CT, Child-Pugh score and pathological examination, and NCC psychologic symptoms score were taken from participants. Participants who were adequate for enrollment were administered 12 sessions of acupuncture treatment and evaluated using the NCC scoring system, Heart Rate Variability, Child-Pugh score and abdominal CT before and after the trial by the investigator.

Acupuncture treatment was done three times per week for four weeks, on 9 acupuncture points: PC6 (single side), SP4(single side), H17(single side), L14 (both sides), LR3 (both sides), HN1, and GV20. 0.25×40mm stainless steel(Dongbang Acupuncture, Korea) needles were used and retained for 25 minutes after insertion.

Evaluation of efficacy was done using the NCC scoring system for psychologic symptoms. The NCC scoring system questionnaire consists of 2 questions each for the 3 symptoms of insomnia, anxiety and depression. Question 1 asks the severity and Question 2 asks the inconvenience caused by the symptom. Each question is answered on a scale of 0 to 10, 0 being 'none at all' or 'does not cause inconvenience at all' and 10 being 'extremely severe' or 'causes extreme inconvenience,' a higher score meaning more severity and inconvenience(1). The person carrying out the trial recorded the result of the NCC questionnaire on visits 1, 4, 7, 10 and 13.

To evaluate the safety of acupuncture treatment, body temperature, blood pressure, pulse, and body weight of the participant were checked at each visit, and Child-Pugh score and biochemistry tests (LFT, CBC, PT/PTT, BUN/Cr, AFP) were done on visits 1, 8, and 14. Abdominal CT was taken on visits 1 and 14, and HRV tests were done on visits 2 and 13. When measuring HRV, external influences were controlled by maintaining a steady indoor temperature

and placing the participant on the back on the bed for ten minutes to adjust to the environment and then connecting the corresponding electrode on both wrists and ankles, carrying out the measurement for five minutes. SA-3000P(Medicore, Korea), a pulse taking instrument for measuring heart rate variability, was used, and the results are shown as Mean HRT, SDNN RMSSD, PSI, ApEn, SRD, TSRD, TP, VLF, LF, HF, LF Norm, HF Norm and LF/HF. Safety evaluation was done by the investigator on every visit from visit 2 to 14, judging from the condition of the participant and looking for signs of adverse events.

Compliance was calculated as an attendance rate of more than 80%; a participant absent for five consecutive appointments was regarded as a drop-out. Occurrence of adverse events were observed on each visit, from visit 2 to visit 14. Participants were told to report any adverse event between visits immediately. Any abnormal condition following acupuncture was to be investigated in relation to the clinical trial and followed up.

Also, to check for aggravation of hepatocellular carcinoma, appearance of hepatic coma, hepatorenal syndrome, hemorrhage from rupture of esophageal and gastric aneurysm, infection/sepsis, spontaneous peritonitis, liver function failure, etc. was checked and recorded. In case of aggravation of hepatocellular carcinoma the investigator was to decide to continue or discontinue the trial and hospitalization.

3. Result Analysis

Statistics were done using ^r atistics Guidelines for Clinical Trials_J CFDA, 2000)¹³⁾ and the statistics program used in this study was PASW(new version of SPSS Win Ver) 18.0. Level of significance was set as p=0.05, and the method of repeated measure single-factor analysis was used to analyze NCC score.

4. Visiting Plan

The visiting plan of participants is shown in Table 1.

Results

1. General Characteristics of Participants

Participants consisted of four male and four female patients. The gender ratio was even, and age was distributed in the range of 47~76 years, the

mean age being 59.75 years. HCC stages were Ⅱ (five participants) > IV ∭ ∍ne participant)(Table 2).

2. Change on NCC psychologic symptoms score

1) Total NCC score

The total NCC score of eight individual participants showed significant improvement following acupuncture

Table 1. Flow Chart

							1							
	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	V14
Items	screening	acup. day1	acup. day2	acup. day3	acup. day4	acup. day5	acup. day6	acup.day7 & exam	acup. day8	acup. day9	acup. day 10	acup. day 11	acup. day 12	final exam
Informed Consent	•													
Inclusion/ xclusion Criteria	•													
History and Physical exam	•													
Body temperature, Blood pressure, Pulse, Body weight	-	•	•	•	-	-	-	-	•	•	•	-	-	•
Child-Pugh score and Blood test	•							-						•
Abdominal CT	•													•
NCC score	•			•			•			•			•	
HRV test		•											-	
Acupuncture		•	•	•	•	•	•	-	•	•	•	•	•	
Evaluation of adverse event		•				•	•	•			-	•	-	•
Evaluation of safety		•	•		•	•	•	•	•		•	•	•	•
Evaluation of aggravation of HCC		•	•	•	•	•	•	•	•	•	•	•	•	•

Table 2. Baseline Characteristics of Patients

Reg. No.	Sex	Age	HCC stage	NCC (screening, total score)	Child-Pugh score
001-001	F	56	I	27	5
001-002	F	58	IVa	18	6
001-003	F	76	${\rm I\hspace{1em}I}$	22	5
001-004	M	69	${\rm I\hspace{1em}I}$	27	5
001-005	F	65	${\rm I\hspace{1em}I}$	38	5
001-006	M	56	${\rm 1\hspace{1em}I}$	54	6
001-007	M	47	${\rm I\hspace{1em}I}$	52	5
001-008	M	51	IVa	59	5

treatment but two cases (001-006, 001-007) ended up with partial NCC scores of more than 4 on each symptom adding up to total NCC score higher than 24, meaning acupuncture alone could not alleviate all symptoms(Tables 3, 5, 6, 7).

Also, the means of total NCC scores on various visits were: 35.88±14.31 on visit 1, 22.88±16.58 on visit 4, 26.25±14.64 on visit 7, 20.12±15.97 on visit 10 and 13.25±15.73 on visit 13, showing general

decrease, and significant improvement(p=0.000) (Table 4, Fig. 1).

2) NCC insomnia score

The NCC scores for insomnia of the eight participants after four weeks generally decreased, and with the exception of three cases(001-003, 001-006, 001-007) the NCC insomnia scores after four weeks of treatment were less than 4, meaning complete

Table 3. Change of Total NCC Score

Reg. No Visit	001-001	001-002	001-003	001-004	001-005	001-006	001-007	001-008
V1	27	18	22	27	38	54	52	49
V4	16	4	17	5	22	42	51	26
V7	35	0	24	23	28	48	37	15
V10	10	0	9	19	37	41	37	8
V13	11	0	7	2	4	31	44	7

Table 4. Mean Change of Total, Insomnia, Anxiety and Depression NCC

		V1	V4	V7	V10	V13	p-value
NCC (Median±SD)	Total NCC	35.88±14.31	22.88±16.58	26.25±14.64	20.12±15.97	13.25±15.73	p=0.000
NCC (Median±SD)	NCC insomnia	14.38±4.17	9.63±6.02	10.38±4.98	7.38±5.71	5.38±5.55	p=0.000
NCC (Median±SD)	NCC anxiety	11.38±4.37	7.00±5.48	9.13±5.52	7.75±6.23	3.87±4.73	p=0.002
NCC (Median±SD)	NCC depression	10.13±6.66	6.25±6.50	6.75±5.20	5.00±5.45	4.00±5.95	p=0.005

Table 5. Change of Insomnia NCC Score

Reg. No Visit	001-	-001	001-	002	001-	-003	001-	-004	001-	-005	001-	006	001-	007	001-	-008
V1	5	4	6	4	5	6	8	5	8	8	9	9	9	9	10	10
V4	4	3	0	0	4	4	5	0	8	8	7	7	9	9	5	4
V7	5	6	0	0	6	6	5	5	8	6	8	8	6	7	3	4
V10	1	0	0	0	5	4	4	4	6	6	8	7	6	6	1	1
V13	1	1	0	0	5	2	2	0	1	1	6	5	8	8	1	2

Table 6. Change of Anxiety NCC Score

Reg. No Visit	001-	-001	001-	-002	001	-003	001-	-004	001	-005	001-	006	001-	007	001-	-008
V1	6	5	2	2	4	3	6	5	6	6	9	9	9	6	6	6
V4	3	1	2	1	3	2	0	0	3	3	7	7	7	9	3	3
V7	7	7	0	0	3	3	6	5	5	2	8	8	7	7	3	3
V10	3	2	0	0	0	0	6	5	8	7	7	7	7	6	2	2
V13	3	2	0	0	0	0	0	0	1	1	5	5	6	6	1	1

Table 7. Change of	Depression NCC Score
--------------------	----------------------

Reg. No Visit	001-	-001	001-	-002	001-	-003	001-	-004	001-	-005	001-	006	001-	007	001-	-008
V1	4	3	2	2	2	2	2	1	5	5	9	9	10	9	8	8
V4	3	2	1	0	2	2	0	0	0	0	7	7	8	9	4	5
V7	5	5	0	0	3	3	1	1	5	2	8	5	5	5	2	1
V10	2	2	0	0	0	0	0	0	5	5	6	6	6	6	1	1
V13	2	2	0	0	0	0	0	0	0	0	5	5	8	8	1	1

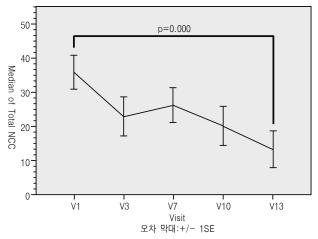


Fig. 1. Mean change of total NCC

improvement of the symptom(Table 5).

The mean NCC insomnia score was 14.38±4.17 on visit 1, 9.63±6.02 on visit 4, 10.38±4.98 on visit 7, 7.38±5.71 on visit 10, and 5.38±5.55 on visit 13, showing overall decrease and statistically significant improvement(p=0.000)(Table 4, Fig. 2).

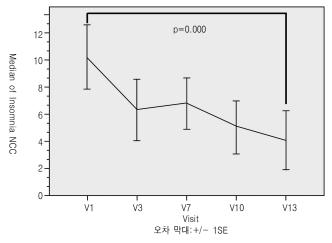


Fig. 2. Mean change of insomnia NCC

3) NCC anxiety score

The NCC scores for anxiety of the eight participants after four weeks generally decreased, and with the exception of two cases (001-006, 001-007) the NCC anxiety scores after four weeks of treatment were less than 4, meaning complete improvement of the symptom(Table 6).

The mean NCC anxiety score was 11.38±4.37 on visit 1, 7.00±5.48 on visit 4, 9.13±5.52 on visit 7, 7.75±6.23 on visit 10, and 3.87±4.73 on visit 13, showing overall decrease and statistically significant improvement(p=0.002)(Table 4, Fig. 3).

4) NCC depression score

The NCC scores for depression of the eight participants after four weeks generally decreased, and with the exception of two cases(001-006, 001-007) the NCC anxiety scores after four weeks of treatment were less than 4, meaning complete improvement of the symptom(Table 7).

The mean NCC anxiety score was 10.13±6.66 on visit 1, 6.25±6.50 on visit 4, 6.75±5.20 on visit 7, 5.00±5.45 on visit 10, and 4.00±5.95 on visit 13, showing overall decrease and statistically significant improvement(p=0.005)(Table 4, Fig. 4).

Other changes (Table 8)

1) HRV

No change of HRV between visits 2 and 13 was observed in any patient.

2) Aggravation of HCC

No aggravation of laboratory results occurred during the trial period, such as Child-Pugh score, LFT, bilirubin, INR, etc. on all patients. Also, no aggravation of liver cirrhosis or major complications (hepatic coma, hepatorenal syndrome, esophageal/gastric aneurysm rupture, infection/sepsis, spontaneous peritonitis) happened, and the abdominal CT taken before and after the trial period showed no aggravation of HCC in any patient.

3) Adverse event

Hemorrhage from gastric ulcer happened with one participant and was treated with hospitalization. The hemorrhage was ruled out as not related to acupuncture clinical trial and the participant continued acupuncture treatment and was also completely recovered from hemorrhagic gastric ulcer.

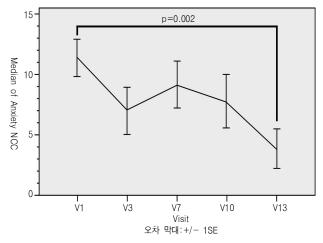


Fig. 3. Mean change of anxiety NCC

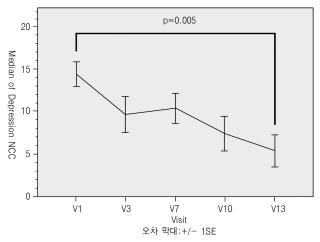


Fig. 4. Mean change of depression NCC3

Discussion

As conventional medicine advances, the techniques of treating cancer develop quickly and the survival rate of cancer patients is growing, thus emphasizing the need for understanding of cancer patients' psychological problems and improvement of quality of life. Compared with normal people, cancer patients show a high rate of somatization, depression, anxiety and animosity, and a low rate of self-esteem and quality of life, which indicates the need for understanding and solving the psychological problems of patients undergoing cancer treatment, and especially to improve the quality of life, resolution of psychological problems and pain control are reported to be most important ^{14,15)}.

Therefore, many studies have been done lately on CAM to treat the side effects related to cancer^{2-4, 16-20)}. Johns Hopkins University offers CAM service with guidelines for acupuncture treatment. They have made manuals for cancer side effects for which acupuncture is efficacious such as pain, nausea, vomiting, fatigue, insomnia, anxiety, depression, etc⁷). They have also suggested that cancer patients, with side effects from treatment such as nausea, vomiting or with symptoms of post-operative pain, cancerous pain, chemotherapy-

induced leukopenia, fatigue, xerostomia, depression, anxiety or insomnia, can benefit from acupuncture treatment ¹⁶⁻²⁰.

Domestically, study of traditional medicine treatment for cancer is limited to herbal medicine, and the few acupuncture studies are focused only on animal studies of pharmacopuncture or bee venom²¹. However, rigorous clinical trials on the effect of acupuncture on anxiety, depression and mental stress are under way and provide evidence for treating symptoms of anxiety, depression and insomnia²²⁻²⁸.

Also, in 『LingShu』「JiuZhenShiErPian(九鍼十二 篇」¹¹⁾ the meridian is expressed as "the place where spirit comes and goes" explaining the intricate relationship between the meridian and the functions of spirit. In 『SuWen』「ZhenJie(鍼解」¹²⁾ is stated that "controlling spirit moves qi" emphasizing the role of mind-healing, and in 『LingShu』「LuoShi(絡始」¹¹⁾ it tells to "move the spirit" meaning spiritual healing can cure mental diseases such as anxiety, depression and insomnia caused by one's spiritual instability. Also in 『LingShu』「CiJieZhenXieLun」¹¹⁾ acupuncture is said to "control qi" and in 『SuWen』「BaoMing-QuanXingLun」¹²⁾ to treat with acupuncture "one has first to treat the spirit" which means acupuncture balances qiand controls the spirit to influence one's

mental activity.

As the majority of hepatocellular carcinoma patients also have liver cirrhosis and impaired liver function, and use of medication to treat symptoms of anxiety, depression and insomnia is limited for fear that it should progress liver dysfunction. Therefore a treatment to improve anxiety, depression and insomnia without aggravating liver disease is in much need.

To clinically prove the efficacy of acupuncture as a way of improving anxiety, depression and the quality of life of patients undergoing HCC treatment, we carried out a pilot study seeking to establish the foundation for a later, larger sample size trial.

A total of eight patients diagnosed with HCC and complaining of distress(scoring more than 4 on any one area of anxiety, depression or insomnia in the NCC evaluation of psychological symptoms) participated in the study. The acupuncture treatment was administered three times a week for four weeks, 12 sessions. Nine acupuncture points were used: single-sided PC6, SP4, HT7, both-sided L14, LR3, and HN1 and GV20. 0.25×40mm stainless steel(Dongbang Acupuncture, Korea) needles were inserted in the acupuncture points and retained for 25 minutes before removal. During the four weeks of acupuncture treatment on the eight patients NCC evaluation for psychological symptoms was done on visits 1, 4, 7, 10, and 13.

For the selection of acupuncture points the study of Kang *et al*²⁹. on anxiety and depression suggests use of frequently used acupuncture points such as PC6, SP4, HT7, LI4, LR3 and GV20. HN1 was added from the extra-meridian points for the calming effect. In recent studies PC6, SP4, HT7, LI4 and LR3 are reported to inhibit the acceleration of sympathetic nerves in a mentally stressful situation^{22-24,28}. Also, the 'four gates' points, namely both LI4 and LR3, are clinically used in a variety of conditions, and thought to be efficacious by the study of Lee et al. and other literature^{30,31}, for use in stress-related symptoms by regulating the flow of blood and qi.

The NCC evaluation questionnaire for psychological symptoms used in this study lets patients self-report the severity of insomnia, anxiety, and depression symptoms in the past week and the toll they had on everyday life. There are two questions for each of the three symptoms, namely insomnia, anxiety and depression. Question 1 asks the severity of the symptom and question 2 asks the impediment of the symptom. Each question scores the answer in a scale of 0 to 10, 0 being 'not at all' and 'causes no inconvenience,' and 10 being 'excruciatingly severe' and 'causes excruciating inconvenience.' When one or more symptom scores more than 4 on both question 1 (severity) and question 2(impediment), it is suggested to seek help from a mental health professional. An additional question at the end asks if the patient 'wants professional medical help for the symptom,' to grasp the patients' desire for professional intervention¹⁾.

The mean total NCC scores as a result of 4 weeks of treatment were: 35.88±14.31, 22.88±16.58, 26.25± 14.64, 20.12±15.97, and 13.25±15.73. The mean NCC scores for insomnia were: 14.38±4.17, 9.63±6.02, 10.38±4.98, 7.38±5.71, and 5.38±5.55. The mean NCC scores for anxiety were: 11.38±4.37, 7.00±5.48, 9.13± 5.52, 7.75±6.23, and 3.87±4.73. The mean NCC scores for depression were: 10.13±6.66, 6.25±6.50, 6.75±5.20, 5.00 ± 5.45 , and 4.00 ± 5.95 . They showed overall decrease(Table 3). Total NCC(p=0.000), NCC for insomnia(p=0.000), NCC for anxiety(p=0.002), and NCC for depression(p=0.005) were statistically significantly improved. The individual analysis of the result of the eight participants also show significant improvement of NCC scores following acupuncture treatment(Tables 3, 5, 6, 7, Fig. 1, 2, 3, 4).

But in two cases(001-006, 001-007) the total NCC score, NCC score for insomnia, NCC score for anxiety and NCC score for depression decreased but the last NCC scores for each symptoms were higher than 4, indicating acupuncture treatment could not cure the symptoms(Tables 3, 5, 6, 7).

In one case hemorrhage from gastric ulcer occurred resulting in hospitalization, but hemorrhage was deemed not to be related to acupuncture, and the patient continued participation in the clinical trial.

In this study we administered acupuncture on patients with HCC as well as liver cirrhosis that makes it difficult to use medication for symptoms of anxiety, depression and insomnia, and observed improvement of NCC scores in all eight participants, and in six participants acupuncture alone almost cured the symptoms. We did not encounter any complications of acupuncture treatment or aggravation of liver cirrhosis, HCC or liver dysfunction. There were no direct adverse events following acupuncture such as subcutaneous bleeding. All eight participants completed the clinical trial safely.

The significance of this study was to suggest an alternative to medication for improving the insomnia, anxiety, and depression that can be harmful to HCC patients because antidepressants or sedatives can aggravate liver disease. Four weeks of acupuncture treatment remarkably improved symptoms of insomnia, anxiety and depression and did not cause aggravation of liver function or complication of liver cirrhosis. Acupuncture is thought to be a safe and efficacious treatment for HCC patient accompanied by liver cirrhosis.

Conclusion

In this pilot clinical trial, acupuncture remarkably improved symptoms of insomnia, anxiety and depression in HCC patients with liver cirrhosis, without causing side effects of aggravation of HCC. With this result we think it necessary to carry out further larger sample sized RCT to verify the efficacy and safety of acupuncture for insomnia, anxiety and depression of liver disease patients who have limitations on using medication.

Acknowledgements

This study was funded by Comprehensive Integrative Medicine Institute (CIMI) in 2011.

References

- 1. National Cancer Center. Development of recommendations for distress management toward improvement of quality of life in cancer patients. Seoul: The Ministry of Health-Welfare. 2009: 5-13, 44-105.
- 2. Mehling WE, Jacobs B, Acree M, Wilson L, Bostrom A, West J, et al. Symptom management with massage and acupuncture in postoperative cancer patients: a randomized controlled trial. J Pain Symptom Manage. 2008; 33(3):98-102.
- 3. Spence DW, Kayumov L, Chen A, Lowe A, Jain U, Katzman MA, et al. Acupuncture increases nocturnal melatonin secretion and reduces insomnia and anxiety: a preliminary report. J Neuropsychiatry Clin Neurosci. 2004;16(1):19-28.
- 4. Weidong Lu, Elizabeth DC, Anne DG, David SR. The value of acupuncture in cancer care. Hematology/Oncology clinics of North America. 2008:22(4):1-13.
- 5. Ezzo J, Vickers A, Rechardson MA, Allen C, Dibble SL, Issel B, et al. Acupuncture-point stimulation for chemotherapy-induced nausea and vomiting. J Clin Oncol. 2005;23(28):7188-98.
- 6. Lee A, Done ML. The use of nonpharmacologic techniques to prevent postoperative nausea and vomiting: a meta-analysis. Anesth Analg. 1999; 88(6):1362-9.
- 7. Lorenzo, Cohen, Maurie, Markman. Integrative Oncology: Incorporating Complementary Medicine into Conventional Cancer Care. Seoul:Epublic

- Korea. 2010:170-297.
- Wang SM, Gaal D, Maranets I, Caldwell-Andrews A, Kain ZN, Acupress and preoperative parental anxiety: a pilot study. Anesth Analg. 2005;101: 666-9.
- Wang SM, Peloquin C, Kain ZN, The use of auricular acupuncture to reduce preoperative anxiety. Anesth Analg. 2001;93:1178-80.
- Filshie J, White A. Medical Acupuncture: a Western Scientific Approach. Seoul: Korean Society of Chuna Manual Medicine for Spine &Nerves. 1999:241-2, 250-2.
- 11. Hong WS. Elaborated The Emperor Inner Scripture Young-chu(靈樞 Seoul:Publish part of Oriental Medicine Research. 1985:12, 68, 73, 159, 213, 316.
- 12. Hong WS. Elaborated The Emperor Inner Scripture So-mun (素問 Seoul:Publish part of Oriental Medicine Research. 1981:95, 97, 193, 273-4, 282, 303.
- Korea Food & Drug Administration. Clinical trial statistics guideline. Seoul: Korea Food & Drug Administration. 2000:1-54.
- Mishel MH, Sorenson DS. Uncertainty in gynecological cancer: a test of the mediating functions of mastery and coping. Nurs Res. 1991;40:167-71.
- Lee SW, Lee EO, Huh DS, Noh KH, Kim HS, Kim SR, et al. The Study on the Medical and Nursing Service Needs of Terminal Cancer Patients and Their Caregivers. Journal of Korean Academy of Nursing. 1998;28(4):958-69.
- Shen J, Wenger N, Glaspy J, Hays RD, Albert PS, Choi C, et al. Electroacupuncture for control of myeloablative chemotherapy-induced emesis: A randomized controlled trial. JAMA. 2000;284(21): 2755-61.
- 17. Walker G, de Valois B, Davies R, Young T, Maher J. Ear acupuncture for hot flushes--the

- perceptions of women with breast cancer. Complement Ther Clin Pract. 2007;13(4):250-7.
- Chen C, Zhang Z, Li H, Tan Z, Lu Y, Huang Z. Electroacupuncture on Zusangli (ST36) to reduce chemotherapy induced toxicity. Xin Zhong Yi (New Journal of Traditional Chinese Medicine). 2004;36(3):46-7.
- Molassiotis A, Sylt P, Diggins H. The management of cancer-related fatigue after chemotherapy with acupuncture and acupressure: A randomised controlled trial. Complement Ther Med. 2007;15 (4):228-37.
- Blom M, Lundeberg T. Long-term follow-up of patients treated with acupuncture for xerostomia and the influence of additional treatment. Oral Dis. 2000;6(1):15?24.
- Nam DW, Lee JD, Choi DY. Study Trends on Acupuncture Treatment of Cancer. The Journal of Korean Acupuncture & Moxibustion Society. 2007;24(1):209-16.
- Kang MS, Kim LH. The Effect of Mental Stress Stimulation and Acupuncture at Shinmun (HT7) on Heart Rate Variability. Journal of Oriental Neuropsychiatry. 2009;20(1):165-76.
- Park EY, Jang JA, Kim HJ, Han HJ, An TH, Kim JW, et al. Effects of LI4, Liv3 Acupuncture for Mental Stress on Short-term Analysis of Heart Rate Variability. Journal of Oriental Neuropsychiatry. 2010;21(4):163-73.
- Kim JS, Hwang W, Bae KT, Nam SS, Kim YS. Effect of Acupuncture for Mental Stress on Short-term Analysis of Heart Rate Variability (HRV). The Journal of Korean Acupuncture & Moxibustion Society. 2004;21(5):227-40.
- Jung IC, Lee SR, Park YC, Hong KE, Lee YG, Kang WC, et al. The Effect of Sa-am Acupuncture Simjeongkyeok Treatment for Major Symptom of Hwa-byung. Journal of Oriental Neuropsychiatry. 2008;19(1):1-18.

- 26. Sohn IC. Effect of acupuncture applied to Naegwan (PC6) and Joksamni (ST36) on the fullness of epigastrium or epigastric pain. The Korean Journal of Meridian & Acupoint. 2006; 23(1):111-9.
- 27. Choi WJ, Lee SG, Park KM. A Study on the Relationship with Acupuncture Stimulation and Stress Using Heart Rate Variability. Journal of Oriental Neuropsychiatry. 2004;15(1):197-210.
- 28. Park SU, Jung WS, Moon SK, Park JM, Ko CM, Cho KH, et al. Effects of Acupuncture on Autonomic Nervous System in Normal Subjects under Mental Stress. Journal Korean Oriental

- Med. 2008;29(2):107-15.
- 29. Kang HC, Lee SG. The Trends in Clinical Trials about Effects of Acupuncture on Anxiety, Depression and Mental Stress-In Medline, Pubmedcentral & Oriental Medicine Journal since 2004. Journal of Oriental Neuropsychiatry. 2009; 20(4):137-48.
- 30. Lee JS, Ko HK, Keum CH, The Evidence and Clinical Meaning of Sakwan acupuncture points. The Journal of Korean Acupuncture & Moxibustion Society. 1992;9(1):109-17.
- 31. Choi YT. Determined Acupuncture. Seoul:Haeng Lim. 1974:228-9.

Attachment

NCC psychological symptoms score assessment

The followings are the main psychological problems which cancer patients suffer from during the process of cancer treatment. Please answer every question based on the past week.

1-1. How n	nuch severe	was your ins	omnia degi	ee during the	last week?					
not at all						completely	severe			
0	1	2	3	4	5	6	7	8	9	10
1-2. How n	nuch did tha	t insomnia di	srupt your	everyday life?	?					
not at all						completely	severe			
0	1	2	3	4	5	6	7	8	9	10
2-1. How n	nuch severe	was your an	riety degree	during the la	st week?					
not at all						completely	severe	ı		
0	1	2	3	4	5	6	7	8	9	10
2-2. How n	nuch did tha	t anxiety disi	upt your ev	eryday life?						
not at all						completely	severe			
0	1	2	3	4	5	6	7	8	9	10
3-1. How n	nuch severe	was your dep	pression de	gree during th	e last week?					
not at all						completely	severe	ı		
0	1	2	3	4	5	6	7	8	9	10
3-2. How n	nuch did tha	t depression	disrupt you	r everyday life	e?					
not at all						completely	severe			
0	1	2	3	4	5	6	7	8	9	10
4. Check(\	/) each sym	ptom for whi	ch youdesi	e to get treatm	nent from sp	ecialists.				
	□ inso	mnia			□ anxiety			d	epression	