

**The Immune Regulating Effect of Hyperthermia in
Combination with TCM on Cancer Patients**

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ABSTRACT

In recent years, as the development of integrative cancer treatments, hyperthermia and Traditional Chinese Medicine (TCM) have become significant methods of treating cancer, and the immune regulating effects of them have attracted more and more attentions. In this text, depending on the clinical research data of Clifford Hospital from 2009 to 2013, research progress of hyperthermia in the world, and research achievements of TCM, we discussed the immune regulating effect of hyperthermia in combination with TCM on cancer patients, and its potentiality in anticancer treatments.

1. Introduction

As heating and temperature detecting techniques have continuously improved, hyperthermia has become another significant method of treating cancer after surgery, radiotherapy, and chemotherapy. Research showed that killing cancer cells did not only depend on extrinsic sources of treatment, but also depend on the immunity of the body itself. With the rise of importance of hyperthermia in cancer treatments, the immune regulating effect of hyperthermia has gained more and more attentions. TCM is an important method for treating cancer in China. Immune regulating effect is the biggest advantage and feature of TCM in treating cancer. The main advantages of immune regulating of TCM are: improving the internal environment of human body, especially the microenvironment; helping patients to survive with tumor; and preventing the metastasis and recurrence. These features are consistent with the trends of cancer treatment in recent years, which are changing the focus from purely killing cancer cells to interfering the microenvironment of their occurrence and progress, with the treatment strategy of targeting the cancerous microenvironment. Hyperthermia and TCM are both important methods of integrative cancer treatments. So far there are many experimental and clinical research on the immune effect of hyperthermia and TCM on cancer patients. In the past clinical practice at Clifford Hospital, we have focused on the non-toxic integrative cancer treatments, and the combination of hyperthermia and TCM has obtained definite curative effects. We will discuss the role of the immune regulating effect of hyperthermia in combination with TCM on cancer patients based on the review of our clinical data and the study progress of other reported research.

2. Immunological effect of hyperthermia

2.1 Induction of anticancer immunity of local hyperthermia

In the process of local hyperthermia, after treatments on primary focus, doctors found that not only the primary focus disappeared or reduced, but also metastases did; or after treatments on metastases, primary focus also appeared or reduced. This is called the abscopal effect of cancer hyperthermia. We recognized that the immunological effect induced by hyperthermia had significant influence on the reduction of the size of primary tumor and metastatic of site. The anticancer immunity which were induced by local hyperthermia included the reinforcement of immunological effect of NK cells, T-lymphocytes and macrophages.

Hu Yongcheng, et al. found that the activity of NK cells increased in mice with transplanted tumor after hyperthermia, and the speed of growth and size of the primary tumor decreased, and the occurrence of lung metastasis decreased^[1].

Kubista, et al. applied hyperthermia to treat osteosarcoma and chondrosarcoma. They found that, after applying hyperthermia, anticancer activity induced by NK cell increased, and the nonspecific immunity NK cell played an important role in controlling the growth of cancer, killing cancer cells in the circulation, and preventing and reducing hematogenous dissemination^[2].

2.2 Cancer hyperthermia and immunostimulation

In 1969, Strauss indicated that the decomposed product of cancer cell degeneration and necrosis was absorbed by the body after hyperthermia, which stimulated the immune system to generate anticancer immunity as a kind of antigen. Researchers in China applied hyperthermia on mice with transplanted tumors in their lower limbs, and found that: in the 43°C and 45°C groups, lung metastases were reduced, and the activity of NK cells was raised; in the 47°C group, because the temperature was too high, some lower limbs fell off, lung metastases were more than those in 43°C and 45°C groups, and NK cell activity was not raised at all. This phenomenon proved the importance of necrosis and decomposition products in increasing the immunity of the body.

Wu Yu, et al. applied radiofrequency ablation in treating lung cancer. They detected lymphocytes, and found that after treatments, the cellular immune function of patients was stimulated. Luo Baoming, et al. concluded in their research that radiofrequency ablation could improve the immunosuppression state of liver cancer patients at certain levels^[3,4].

2.3 Immunological reaction induced by non-specific inflammatory reaction

Local hyperthermia is a kind of physical injury factor, which can cause non-specific inflammatory reactions. Inflammatory reactions can induce immunological reactions by dissolvable cell factors such as IL-1.

Morita, et al. observed that hyperthermia could increase lymphocyte infiltration (LI) in parts of the tumor of patients with esophagus cancer. The five year survival rates of patients with LI (++) , LI (+) and LI (-) were 75.5%, 46.1% and 27.8%^[5].

2.4 Heat shock protein (HSP) and tumor immunity

Due to the effectiveness of some physical and chemical factors (such as viral infection, anoxia, heavy metal ions, ultraviolet ray exposure, etc.), organism cells can activate HSP gene, and selectively compose a group of highly conservative protein, which is HSP. In recent years, we found that HSP participated in specific anticancer immunological reaction of the human body, and that the expression quantity of HSP was closely related to the immunogenicity of tumor. The effectiveness of HSP in immune response has drawn wide attention of researchers^[6,7].

Menoret, et al. recognized that after being heated, cancer cells could generate HSP, which could stimulate immune system of the body, improve immunity, and cause specific immunological reactions to the tumor^[8].

Schueller, et al. found that the expression of HSP70 and HSP90 of liver cancer cells could be reinforced after hyperthermia, which could improve immunity against hepatic cellular cancer^[9].

3. TCM and immunity

3.1 Effectiveness of TCM in tumor microenvironment

In the opinion of TCM, the occurrence of cancer is due to the functional disorder of Zang-Fu organs. Under multiple inductions of internal and external factors, the generation of etiological factors causes the disorder of Qi and blood, and Yin and Yang, in combination with the accumulation of pathological factors such as sputum, blood stasis, wetness, and hotness, breakage of the internal balance of the human body, which causes infernal circle process, and generates an internal environment that promotes the occurrence and progress of cancer. This is consistent with the recognition of tumor microenvironment. Zhou Zhongying, a famous physician of TCM and a master of traditional medicine, considers that in the multiple effectiveness of internal and external factors, a kind of pathogenic factor is generated based on the disorder of organ disorder, which is a specific causative agent of the occurrence and progress of cancer^[10].

3.2 Vital Qi in TCM and immunity

Vital Qi in TCM was called “Zhen Qi” (genuine Qi) in ancient times. It originated from the simple materialism and spontaneous dialectics thought in ancient time of China. Vital Qi is the material foundation of the human body that fights against pathogenic factors. It includes the functions and activities of YING (nutritive Qi or blood circulating in meridian), WEI(protective Qi), meridian

Qi, blood · JING (essence), spirit, JIN(lighter and clearer fluids), YE(fluids with heavier and thicker nature), Zang-fu Organs, and meridians. Vital Qi exists in either inside or outside the vessels, and runs all over the body. It has the functions of protecting the human body from pathogen, self recovery, and balance regulating^[11].

An Hui College of Chinese Medicine applied Jianpi Yiqi Decoction to 42 patients. After treatments, the T cell ratio, lymphocyte transformation rate, and number of immunoglobulin were raised. Bao Suzhen, et al used Shiquan Dabu Decoction to treat mice with liver cancer. They observed that both the T cell transformation rate and the number of neutrophilic leukocyte, the activator of NK cell, were significantly increased^[12].

Zheng Wangqiao, et al. found that after treatments of Shenqi Fuzheng Injection, the thymus index and spleen index of mice with liver cancer after chemotherapy were both higher than the control group ($P < 0.05$); the IL-2 level in blood serum of mice in the treatment group was significantly higher than the control group, and TNF- α in the treatment group was lower than that in the control group ($P < 0.05$)^[13]. Chinese formulated products Kang Lai Te Injection and Huang Qi Injection are both representatives of the methods of “supplementing Qi and nourishing Yin” and “benefiting vital energy and strengthening body resistance”.

3.3 Types and examples of immune effectiveness of TCM

According to modern pharmacology research of Chinese medicine in the recent 50 years, many kinds of Chinese medicine have different levels of immune effectiveness in the human body, which can be divided into 4 types^[14]:

3.3.1 Herbs with effectiveness on abnormal immunological reaction (allergy)

folium Perillae, radix saposhnikoviae, radix bupleuri, herba schizonepetae, herba ephedrae, rhizoma atractylodis, dryopteris crassirhizoma Nakai, fructus xanthii, fructus kochiae, cortex dictamni, radix et rhizoma rhei, cortex phellodendri, and feculae bombycis.

3.3.2 Herbs with promotion of immunity

radix astragali, ganoderma, radix ginseng, rhizoma atractylodis macrocephalae, semen coicis, caulis spatholobi, radix rehmanniae recens, radices paeoniae alba, equus asinus Linnaeus, cornu cervi pantotrichum, herba cistanchis, herba epimedii, semen cuscutae, radix morindae officinalis, radix glehniae, radix ophiopogonis, fructus schisandrae chinensis, cordyceps sinensis Sacc., tremella fuciformis Berk., lycium chinense Mill., radix polygoni multiflori, polyporus umbellatus(Pers.) fries, garlic, spreading hedyotis herb, herba houttuyniae, radix salviae miltiorrhizae, rhizoma Chuanxiong, flos carthami, radix scutellariae, and rhizoma coptidis.

3.3.3 Herbs with immunodepressive effect

radix puerariae, forsythia suspensa Vahl, flos lonicerae, herba agastachis, herba eupatorii, folium isatidis, radix isatidis, herba houttuyniae, flos chrysanthemi indici, herba taraxaci, herba artemisiae scopariae, herba andrographitis, radix gentianae, fructus gardeniae, herba leonuri, cortex moutan, tripterygium wilfordii, and camptothecin.

3.3.4 Herbs with immune regulating effect

many herbs have biphasic modulation effect on immunity, such as radix astragali, radix saposhnikoviae, rhizoma atractylodis macrocephalae, radix glycyrrhizae, radix bupleuri, rhizoma atractylodis, radix pseudostellariae, radix acanthopanacis senticosi, herba artemisiae annuae, herba andrographitis, spreading hedyotis herb, Tripterygium wilfordii, and tripterygium hypoglaucum hutch.

4. Acupuncture and immunity

With the development of modern acupuncture, the research of the effect and mechanism of acupuncture on immunity have attracted more and more attention. A lot of research materials have

shown that acupuncture can change the specific and non-specific immunity of the body, significantly affect immunocyte and immunological molecule, and play a positive role in preventing and treating allergic disorders, infections, inflammatory diseases, and cancer. This effect has the characteristics of entirety and bidirectionality^[15].

Chen Liangliang, et al. applied acupuncture in combination with chemotherapy in treating 50 cases with middle and advanced staged lung cancer. Acupoints: Dayuan, Zusanli, Neiguan; with herbal point application on the acupoints of Dazhui and Feishu. The results showed that while relieving the symptoms of patients with lung cancer, the treatments could raise the low lymphocyte conversion ratio, and recover the activity of NK cells without obvious side effects. This kind of immune regulating effect of acupuncture has parallel relation with the improvement of clinical therapeutic effect^[16].

Zhao Changlin, et al did research of acupuncture on the acupoints of Zusanli, Sanyinjiao, Neiguan, Shang Juxu, Hegu, Taixi, Taichong, Yinlingquan, and Yanglingquan, with moxibustion on the acupoints of Shenque, Guanyuan, Qihai, and Zusanli. The results showed that after treatments, the number of T-lymphocyte subsets (CD3, CD4, and CD8) in the peripheral blood of patients with colon cancer and liver metastases was significantly increased^[17].

Sun Hua reported that acupuncture had a depressant effect on the accentuation of humoral immunity in patients with rheumatoid arthritis. It could lower the level of IgG, IgA, and IgM, or make them return to normal; it could also raise complement C3 and decrease the level of immune complex^[18].

5. Clinical research data of Clifford Hospital

5.1 Effect of immunity of local hyperthermia in combination with TCM treating patients with middle and advanced staged colorectal cancer

Patient resource: inpatients of Clifford Hospital from April, 2011 to April, 2012 diagnosed with middle and advanced staged colorectal cancer.

Observation index: numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells.

60 cases with middle and advanced staged colorectal cancer were divided into 3 groups randomly. There were 20 cases in hyperthermia + TCM group, accepting Oncothermia in combination with TCM. Hyperthermia was applied 3 times a week, and orally taken herbal decoction was applied one dose per day, with the treatments for 2 months. There were 20 cases in hyperthermia group, accepting Oncothermia alone, 3 times a week, with the treatment for 2 months. There were 20 cases in TCM group, accepting herbal decoction alone, one dose per day, with the treatment for 2 months. Along with hyperthermia and TCM, all 3 groups accepted routine symptomatic supportive treatments, and there were no significant differences of symptomatic supportive treatments, age, gender, stage, and numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells among the 3 groups.

5.1.1 Changes of numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells in 3 groups after treatments

Table 1 Changes of numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells in 3 groups after treatments ($\bar{x} \pm S$, %)

Groups	n	CD3 ⁺		CD4 ⁺		CD8 ⁺		NK	
		before	after	before	after	before	after	before	after
		treatments	treatments	treatments	treatments	treatments	treatments	treatments	treatments
Hyperthermia + TCM group	20	31.20±5.	54.96±11.	24.18±2.1	39.96±3.0	40.08±5.3	30.97±2.4	16.14±1.5	26.37±1.0
	38		21*▲	7	5*▲	3	1*▲	2	6*▲
hyperthermia group	20	34.11±4.	47.31±3.2	23.94±3.0	34.10±2.9	41.26±4.6	36.22±2.6	15.29±1.5	20.18±1.5
	26		5*	1	7*	3	4*	4	3*
TCM group	20	32.42±4.	45.63±5.3	24.67±3.3	33.97±3.0	40.66±5.0	37.52±3.0	16.37±2.0	21.06±2.1
	03		3*	1	4*	2	1*	3	2*

* $P < 0.05$, after treatments, there were statistical differences of numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells among the 3 groups.

▲ $P < 0.05$, after treatments, the numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells in hyperthermia + TCM group were statistically different from those in the other two groups.

5.1.2 Conclusions

This research showed that hyperthermia in combination with TCM could improve the immune function of patients diagnosed with middle and advanced staged colorectal cancer, and its therapeutic effect was better than hyperthermia alone or TCM alone ($P < 0.05$). Both hyperthermia alone and TCM alone could improve the immune functions of patients with middle and advanced staged colorectal cancer, but there was no significant difference between the improvements (the numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells after treatments) of the two groups ($P > 0.05$).

5.2 Effect of immunity of local hyperthermia in combination with Kang Lai Te Injection on patients with advanced cancer

Patient resource: inpatients of Clifford Hospital from July, 2011 to July, 2012 with advanced cancer.

Observation index: numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells.

45 patients with advanced cancer (8 patients with gastric cancer, 12 with colon cancer, 6 with lung cancer, 12 with breast cancer, and 7 with liver cancer) were divided into 3 groups randomly. There were 15 patients in hyperthermia + Kang Lai Te Injection group, accepting Oncothermia in combination with Kang Lai Te Injection treatments. Oncothermia was applied 3 times a week, with the treatment for 2 months. Kang Lai Te injection (Approval Number Z10970091) was applied 200mL per time through i.v., once per day, with 21 days as a course. After an interval of 3 ~ 5 days, the second course was applied. 2 courses of Kang Lai Te Injection were applied in total. There were 15 patients in hyperthermia group, accepting Oncothermia alone, 3 times a week, with the treatment for 2 months. There were 15 patients in Kang Lai Te Injection group, accepting Kang Lai Te Injection (Approval Number Z10970091) alone, 200mL per time through i.v., once per day, with 21 days as a course. After an interval of 3 ~ 5 days, the second course was applied. 2 courses of Kang Lai Te Injection were applied in total. Along with hyperthermia and Kang Lai Te Injection, all 3 groups accepted routine symptomatic supportive treatments, and there were no significant differences of symptomatic supportive treatments, age, gender, stage, and numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells among 3 groups.

5.2.1 Changes of numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells in 3 groups after treatments

Table 2 Changes of numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells in 3 groups after treatments ($\bar{x} \pm S, \%$)

Groups	n	CD3 ⁺		CD4 ⁺		CD8 ⁺		NK	
		before treatments	after treatments	before treatments	after treatments	before treatments	after treatments	before treatments	after treatments
Hyperthermia + Kang Lai Te Injection group	15	36.53±4.2	56.49±7.92	37.48±8.17	52.07±8.05	33.08±5.16	22.14±7.52*	15.14±6.84	25.47±5.91*▲
hyperthermia group	15	35.22±4.8	45.73±4.12	36.15±2.02	47.10±3.15	31.75±3.63	25.64±4.79*	16.13±3.26	21.15±2.93*
Kang Lai Te Injection group	15	37.64±3.0	46.91±2.33	34.43±4.13	44.96±7.62	33.17±9.02	23.68±8.72*	13.05±4.03	19.61±4.26*

* $P < 0.05$, after treatments, there were statistical differences of numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells among the 3 groups.

▲ $P < 0.05$, after treatments, the numbers of CD3⁺, CD4⁺, and NK cells in hyperthermia + Kang Lai Te Injection group were statistically different from those in the other two groups.

5.2.2 Conclusions

This research showed that hyperthermia in combination with Kang Lai Te Injection could improve the immune function of patients with advanced cancer, and its therapeutic effect was better than hyperthermia alone or Kang Lai Te Injection alone ($P < 0.05$). Both hyperthermia alone and Kang Lai Te Injection alone could improve the immune functions of patients with advanced cancer, but there was no significant difference between the improvements (the numbers of CD3⁺, CD4⁺, and NK cells after treatments) of the two groups ($P > 0.05$). In addition, there was no statistical difference among the numbers of CD8⁺ of the 3 groups after treatments ($P > 0.05$).

5.3 Effect of immunity of local hyperthermia in combination with Huang Qi Injection on patients with middle and advanced staged liver cancer

Patient resource: inpatient of Clifford Hospital from January, 2009 to May, 2010 diagnosed with middle and advanced staged liver cancer.

Observation index: numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells.

90 patients with middle and advanced staged liver cancer were divided into 3 groups randomly. There were 30 patients in hyperthermia + Huang Qi Injection group, accepting Oncothermia in combination with Huang Qi Injection treatments. Oncothermia was applied 3 times a week, with the treatment for 2 months. Huang Qi Injection (Approval Number Z51021776, with effective constituent of *radix astragali* 2g) was applied 20mL per time through i.v., once per day, with 20 days as a course. After an interval of 3~5 days, the second course was applied. 2 courses of Huang Qi Injection were applied in total. There were 30 patients in hyperthermia group, accepting Oncothermia alone, 3 times a week, with the treatment for 2 months. There were 30 patients in Huang Qi Injection group, accepting Huang Qi Injection (Approval Number Z51021776, with effective constituent of *radix astragali* 2g) alone, 20mL per time through i.v., once per day, with 20 days as a course. After intervals of 3~5 days, the second course was applied. 2 courses of Huang Qi Injection were applied in total. Along with hyperthermia and Huangqi Injection, all 3 groups accepted routine symptomatic supportive treatments, and there were no significant differences of symptomatic supportive treatments, age, gender, stage, and numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells among the 3 groups.

5.3.1 Changes of numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells in 3 groups after treatments

Table 3 Changes of numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells in 3 groups after treatments ($\bar{x} \pm S, \%$)

Groups	n	CD3 ⁺		CD4 ⁺		CD8 ⁺		NK	
		before treatments	after treatments	before treatments	after treatments	before treatments	after treatments	before treatments	after treatments
Hyperthermia + Huang Qi Injection group	30	47.63±5.17	59.08±6.98*▲	30.61±5.47	42.67±6.56*▲	28.79±4.66	24.64±5.30*	22.70±6.84	32.28±6.40*▲
hyperthermia group	30	44.82±7.83	51.73±6.74*	29.51±3.47	33.27±5.61*	29.08±6.43	26.01±5.07*	19.28±7.32	26.39±6.07*
Huang Qi Injection group	30	45.74±6.02	50.92±8.32*	27.60±7.81	34.06±6.69*	29.85±7.12	27.08±4.80	20.53±8.31	25.08±7.16*

* $P < 0.05$, after treatments, there were statistical differences of numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells among the 3 groups.

▲ $P < 0.05$, after treatments, the numbers of CD3⁺, CD4⁺, and NK cells in hyperthermia + Huang Qi Injection group were statistically different from those in the other two groups.

5.3.2 Conclusions

This research showed that hyperthermia in combination with Huang Qi Injection could improve the immune function of patients with middle and advanced staged liver cancer, and its therapeutic

effect was better than hyperthermia alone or Huang Qi Injection alone ($P < 0.05$). Both hyperthermia alone and Huang Qi Injection alone could improve the immune functions of patients with advanced cancer, but there was no significant difference between the improvements (the numbers of CD3⁺, CD4⁺, and NK cells after treatments) of the two groups ($P > 0.05$). In addition, there was no statistical difference among the numbers of CD8⁺ of the 3 groups after treatments ($P > 0.05$).

5.4 Effect of immunity of local hyperthermia in combination with acupuncture on patients with cancer after chemotherapy

Patient resource: inpatient of Clifford Hospital from October, 2012 to October, 2013 with cancer after chemotherapy.

Observation index: numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells.

60 patients with cancer after chemotherapy were divided into 3 groups randomly. There were 20 patients in hyperthermia + acupuncture group, accepting Oncothermia in combination with acupuncture treatments. Oncothermia was applied 3 times a week, with the treatment for 2 months. Acupuncture was applied once per day, with acupoints being selected based on differentiation of symptoms and signs, with 10 days as a course. There was an interval of 2~3 days after every course. 4 courses of acupuncture were applied in total. There were 20 patients in hyperthermia group, accepting Oncothermia alone, 3 times a week, with the treatment for 2 months. There were 20 patients in acupuncture group, accepting acupuncture alone, once per day, with acupoints being selected based on the differentiation of symptoms and signs, with 10 days as a course. There was an interval of 2~3 days after each course. 4 courses of acupuncture were applied in total. Along with hyperthermia and acupuncture, all 3 groups accepted routine symptomatic supportive treatments, and there were no significant differences of symptomatic supportive treatments, age, gender, stage, and numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells among the 3 groups.

5.4.1 Changes of numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells in 3 groups after treatments

Table 4 Changes of numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells in 3 groups after treatments ($\bar{x} \pm S, \%$)

Groups	n	CD3 ⁺		CD4 ⁺		CD8 ⁺		NK	
		before treatments	after treatments	before treatments	after treatments	before treatments	after treatments	before treatments	after treatments
Hyperthermia + acupuncture group	20	52.63±3.	62.42±4.08	32.76±3.	40.67±5.21	24.81±3.	21.76±4	19.90±8.	30.74±8.9
	28		*▲	54	*▲	07	.29*	65	7*▲
hyperthermia group	20	50.74±6.	55.38±5.93	31.40±4.	34.48±4.75	25.03±4.	23.84±3	17.96±8.	23.49±7.9
	23		*	31	*	28	.76	34	4*
acupuncture group	20	51.49±4.	55.72±5.04	33.67±4.	36.94±3.86	24.87±3.	23.39±3	18.59±6.	24.03±7.6
	32		*	28	*	27	.84	69	0*

* $P < 0.05$, after treatments, there were statistical differences of numbers of CD3⁺, CD4⁺, CD8⁺, and NK cells among the 3 groups.

▲ $P < 0.05$, after treatments, the numbers of CD3⁺, CD4⁺, and NK cells in hyperthermia + acupuncture group were statistically different from those in the other two groups.

5.4.2 Conclusions

This research showed that hyperthermia in combination with acupuncture could improve the immune function of patients with cancer after chemotherapy, and its therapeutic effect was better than hyperthermia alone or acupuncture alone ($P < 0.05$). Both hyperthermia alone and acupuncture alone could improve the immune functions of patients with advanced cancer, but there was no significant difference between the improvements (the numbers of CD3⁺, CD4⁺, and NK cells after treatments) of the two groups ($P > 0.05$). In addition, there was no statistical difference among the numbers of CD8⁺ of 3 groups after treatments ($P > 0.05$), and there was no statistical

difference of the numbers of CD8⁺ in both hyperthermia group and acupuncture group after treatments comparing to those before treatments($P > 0.05$).

6. Effect of immunity of hyperthermia in combination with TCM in patients

According to the research data and reports mentioned above, in the clinical observations of Clifford Hospital, both hyperthermia and TCM treatment alone can improve the immunity of patients, which is also consistent with the reported clinical research progression. In addition, hyperthermia in combination with TCM (orally taken herbal decoction), anticancer Chinese formulated products (injection), and acupuncture all have positive immune regulating effects; and combined application has better therapeutic effects than applications of hyperthermia or TCM treatment alone. Based on this, we recommended this integrative treatment to other patients who didn't participate in our clinical research, and obtained positive therapeutic effect. In the future, we plan to do further research with bigger sample sized, stricter, double-blinded, randomized, and controlled trials, in order to obtain more clinical observations about immune regulating effect of hyperthermia in combination with TCM.

7. Prospects

Both hyperthermia and TCM have positive effects of immunity on cancer patients, and they play important roles in anticancer treatments. It is improved in both laboratory research and clinical research. The immune regulating effect of hyperthermia and TCM applied alone is widely admitted. According to clinical research in recent years at Clifford Hospital, as treatments which can improve immunity of patients, hyperthermia and TCM (herbs, Chinese formulated products, and acupuncture) have synergistic effect when applied in combination, and have great potentials in anticancer treatments.

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