

Progress of research of hyperthermia integration with TCM in the treatment of cancer

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With the development of clinical oncotherapies, integrative treatments have generally been recognized by the Oncology Association. Hyperthermia has proven its effectiveness in the treatment of cancer which is different from surgery, radiotherapy, chemotherapy and biotherapy. Besides integration with the above therapies, using this with TCM is a unique approach.

The progress of research of hyperthermia integration with TCM in treating cancer will be presented according to the following six aspects:

1. The advantages of hyperthermia in the treatment of cancer
 2. The advantages of TCM in treating cancer
 3. The advantages of hyperthermia in combination with TCM
 4. An overview of the implementation of hyperthermia integration with TCM in treating cancer in Clifford Hospital
 5. Clinical report of integrative therapy
 6. The future of hyperthermia integration with TCM in treating cancer
1. The advantages of hyperthermia in treating cancer
 - 1.1. Hyperthermia is part of the field of Natural Medicine. It targets cancer cells directly, improves the immune system, induces apoptosis of cancer cells, suppresses the formation of cancer vessels, destroys cancer vessels, and relieves pain caused by cancer. At the same time, hyperthermia has demonstrated no damage to normal tissue.
 - 1.2. Hyperthermia can be utilized in conjunction with other cancer therapies and integrated into a comprehensive anti-cancer protocol.
 - 1.3. Hyperthermia not only enhances the sensitivity to radiotherapy and chemotherapy, but also reduces the side effects, which raises hope for solving of chemo drug resistance.
 - 1.4. Hyperthermia can improve the patient's quality of life and their confidence. It can be used on a long-time period.
 - 1.5. Modern science has contributed to the diverse modalities and methods of hyperthermia.
 - 1.6. Radiofrequency deep localized hyperthermia has broad applications and reliable therapeutic outcomes.
 2. The advantages of TCM treating cancer
 - 2.1. The following are Anti-Cancer Mechanisms of Chinese Medicine: Chinese herbs mentioned below perform different functions in cancer treatment
 - 2.1.1. Antimutagenicity: e.g. Ginseng, Fiveleaf gynostemma herb, green tea, scutellariae barbatae, astragalus, etc.
 - 2.1.2. Direct cytotoxicity: e.g. Oridonin, Ponicidin, Poria, etc.
 - 2.1.3. Inducing cancer cell apoptosis: e.g. Tetrandrine, Berbamine, Rhizoma, etc.
 - 2.1.4. Suppressing proliferation and inducing differentiation: e.g. Epimedium, Tanshinone, Garlicin, etc.
 - 2.1.5. Suppressing the formation of cancer vessels: Coriolus versicolor polysaccharide, Lentinan, Cordyceps sinensis polysaccharide, Chinese thorowax root, Szechuan lovage rhizome, etc.
 - 2.1.6. Influence on membrane protein structure of cancer cells: croton, achyranthis, etc.
 - 2.1.7. Effect of Chinese herbal medicine photosensitizers on cancer: photosensitive and anti-tumorous effect of Coptis, Phellodendri, Sophorae flavescentis, Scutellaria, Fructus, etc. which are able to suppress the vitality and proliferation of cancer cells.
 - 2.1.8. Reversing the effects of multiple drug-resistance to cancer: vincristine, Tetrandrine, Emodine, Cepharanthine, Fructus, etc. These all have reversed the effects of drug-resistance, which improve the sensitivity of cancer cells to chemotherapies while impacting cancer cells.
 - 2.2. Long Term Treatment with Chinese Medicine
 - 2.2.1. Exerting bidirectional regulation of Chinese medicine to eliminate pathogens and strengthen vital Qi. Use Chinese herbal medicine to invigorate to Qi and blood, nourish the

kidneys and liver, balance the Yin and Yang, etc, while at the same time eliminating pathogens. It can decrease the rate of energy loss due to cancer, reduce toxic side effects resulting from radiotherapy and chemotherapy, and improve the body's immunity.

- 2.2.2. Application of the treatment according to differentiation: Prescription can be individualized based on the patient's immunity.
- 2.2.3. Multiple dosage forms: the delivery method of the medication can be adjusted according to the patient's conditions.
- 2.2.4. Improving and maintaining the patients' quality of life.
- 2.2.5. Low toxicity with no side effects.

2.3. Acupuncture and Moxibustion

- 2.3.1. Acupuncture can modulate the meridians, balance the yin and yang, improve blood circulation, and boost the body's immunity.
- 2.3.2. Acupuncture can also regulate the body's cellular and immune system. It activates the body's immune surveillance system, and delays and inhibits the proliferation of abnormal cells.
- 2.3.3. It can improve the effect of radiotherapy and chemotherapy which include the improvement in bone marrow suppression and reaction in gastrointestinal tract.
- 2.3.4. Acupuncture and moxibustion is effective in alleviating pain.

3. The advantages of hyperthermia in combination with TCM

3.1. Anti-Cancer activity of TCM is increased through the Heating Process

The heating process increases the anti-cancer activity of certain Chinese medicines. e.g. Matrine could improve the therapeutic heating effect of hyperthermia on MA737 mouse mammary carcinoma; it could also induce more cancer cell apoptosis; e.g. Lithospermi preparation A-1 with heating has synergistic and suppressive effects on the growth of ECa109 cells.

3.2. The effect of hyperthermia integration with Chinese Herbal Medicine

A group led by Xie Yiyang applied local hyperthermia with oral Chinese medicine decoction to 162 patients diagnosed with malignant cancer. The results showed that 93.2% of the patients had positive responses to the treatment. Zhang Qinyuan's group used whole body hyperthermia in combination with Chinese medicine on 54 patients with lung cancer. After 4 weeks of treatment, the experimental group demonstrated the best response on KPS, pain relief, focal change, and other aspects.

3.3. Hyperthermia integration with external use Chinese Medicine on malignant cancer

A research group headed by Zhong Dongwei, demonstrated that microwave irradiation can accelerate the penetration and absorption of Chinese medicine by compromising the stability of cellular membrane. Secondly, the effectiveness of Chinese medicine can be increased by the heating process. Mo Dingqun's group reported that patients with hepatic pain could be alleviated by microwave irradiation with TCM patches. 21 patients diagnosed with liver cancer received this treatment, with 11 patients displaying significant pain relief, and 9 patients had good responses to the therapy. The response rate was 100%.

3.4. Hyperthermia with Chinese Medicine injection

Kanglaite Injection(KLT) and hyperthermia: The research done by Deng Fuan studied the clinical efficacy of Kanglaite Injection(KLT) and ultrasound hyperthermia on 30 cases diagnosed with advanced liver cancer. The results suggested that the ratios of cancer pain elimination, symptom alleviation, cancer suppression, and overall survival in the experimental treatment group were significantly higher than in the control group. Compound Kushen Injection and hyperthermia: Gao Zhihong led a study of application of hyperthermia with Compound Kushen Injection on patients with stage III-IV malignant cancers. The results revealed that the experimental group had better responses in early symptom relief, improvement in the quality of life, and pain relief than the group that used Kushen Injection alone. Bolbcstemma Paniculatum preparation and hyperthermia: A study by Han Chengmin confirmed that the combined therapy can increase the inhibitory rate of the cancer cell Tca8113 and suppress the transformation of Tca8113 cell from G1 phase to S phase, resulting in increased cancer cell apoptosis rate and changes in the subcellular structure.

4. An overview of the implementation of hyperthermia integration with TCM in treating cancer in Clifford Hospital

Clifford Hospital is dedicated to the research of nontoxic integrative therapy on cancer. Clifford Hospital highlights the qualities of using TCM in treating different types of the diseases. It has achieved positive outcomes in cancer treatment by incorporating hyperthermia with natural therapies, including oral Chinese medicine, intravenous injection of Chinese herb, external application of Chinese medicine, Chinese medicine enema, acupoint injection, acupuncture, moxibustion, auricular acupoint therapy, compression of acupoint, catgut embedding, tuina massage, cupping, herbal bath, scraping, music therapy, Qigong, medical ozone, and chelation, among others.

The following are TCM and Natural Therapies available in Clifford Hospital.

- 4.1. Hyperthermia: We use the Oncoterm EHY-2000 Local Electro-Hyperthermia Machine, NRL-002 Radiofrequency Field Thermo Therapeutic Machine, and Heckel – HT 2000 Infrared Whole Body Hyperthermia Machine.
- 4.2. Oral Chinese medicine: differentiated diagnosis and treatment made in accordance with TCM theory. Patients with cancer who sweat excessively during hyperthermia are considered to have an impairment of the Yin or Qi form heat. In these cases, the treatment should supplement the Qi and balance the Yin with Chinese Medicine Preparation Shengmai Yin, designed by Clifford Hospital.
- 4.3. External application of Chinese medicine, once a day, every 4th hour. It can be used daily during the treatment. The Chinese medicine, which consists primarily of Xiaoliu plaster, Xiaoshui plaster, and Zhitong Ding, is prescribed by senior TCM practitioners based on the patient's condition. These Chinese medicines are used to reduce the size of the cancer, eliminate hydrothorax and ascites or local edema, and control cancer pain.
- 4.4. Chinese Medicine injection: frequently-used Chinese medicine injections include Kanglaite injection, Kangai injection, KkYadanzi Youru and Astragalus Membranaceus injection, etc.
- 4.5. Retention enema: includes Chinese medicine enema and coffee enema
- 4.6. Intracavitary hyperthermal perfusion: Hyperthermia perfusions can be performed to the chest, abdomen and bladder. Small dosages of chemo drugs and sodium bicarbonate are heated before the hyperthermia perfusion.
- 4.7. Acupuncture: Acupuncture is aided by electric acupuncture, infrared irradiation, and so on.
- 4.8. Moxibustion: Lukewarm moxibustion, festering moxibustion, warming acupuncture, herbs - partition moxibustion, and ginger moxibustion, etc.
- 4.9. Acupoint injection: Possesses antiemetic and pain-relieving effects with a longer efficacy than acupuncture.
- 4.10. Acupoint plaster: Medicine such as Pishu, Shenshu, etc. can be plastered on acupoints to increase WBC. Moxibustion and acupoint plaster possess better effects on alleviating patient's bone marrow suppression.
- 4.11. Ozone Therapy: There are different types of ozone therapies in Clifford Hospital, such as EBOO, major and minor hemotherapy, rectal ozone therapy, etc.
- 4.12. Chelation Therapy: It can effectively remove heavy metals from the body.
- 4.13. Herbal fumigation and bath: An ancient and effective external therapy in TCM. It is administered once a day during the treatment stage.
- 4.14. Medical Qigong: Medical qigong, the first mainstream culture in ancient China, which contributed more to society than the four great inventions, is now accepted as a top-rank therapy in Preventive Medicine and Rehabilitative Medicine in a number of countries. Patients at Clifford Hospital practice medical Qigong such as Tai Chi Wu Xing Gong, etc. under the tutoring of qigong practitioners.

5. Clinical report of integrative therapy

5.1. Case 1

Hyperthermia, oral Chinese medicine, western medicine and other treatments

Hyperthermia group: 156 patients, from January, 2008 to December, 2011, radiofrequency deep regional hyperthermia in combination with oral Chinese medicine and western medicine.

Integrative Therapies: Radiofrequency deep localized hyperthermia: 1 hour each time, every other day, 15 treatments per course.

TCM Therapy: oral Chinese medicine, 100ml each time, b.i.d.; prescribed by senior TCM doctors based on the patient's condition.

Western medicine: We used methods with less adverse effects, such as oral chemotherapy, IPT chemotherapy, intra-abdominal hyperthermal chemotherapy, intravesical hyperthermal chemotherapy, etc.

Other treatments: acupuncture and moxibustion, etc.

Treatments	Subjects	CR	PR	NC	PD	Respond rate
Hyperthermia+ TCM	75	5	43	20	7	64.0%
Hyperthermia + TCM + chemo therapy	14	2	9	3	0	78.6%
Hyperthermia + TCM + abdominal cavity perfusion	42	3	23	11	5	61.9%
Hyperthermia + TCM + bladder perfusion	13	1	7	4	1	61.5%
Hyperthermia + TCM + radiotherapy	12	1	8	2	1	75.0%
Total	156	12	90	40	14	65.4%

Control group: 150 patients with advanced malignant cancer, who didn't receive hyperthermia, were randomly selected from January, 2008 to december, 2011

Treatments	Subjects	C R	PR	NC	PD	Respond rate
TCM + chemo therapy	51	4	31	8	8	68.6%
TCM + abdominal cavity perfusion	45	1	18	11	15	42.2%
TCM + bladder perfusion	24	0	12	3	9	50.0%
TCM + radiotherapy	30	1	15	5	9	53.3%
Total	150	6	76	27	41	54.7%

Results: Hyperthermia group: the overall response rate was 65.4% out of 156 patients. While is the control group: the overall response rate was 54.7%. There is statistically significant difference between two groups ($P < 0.05$). There is no statistically differences in adverse effect between the two groups.

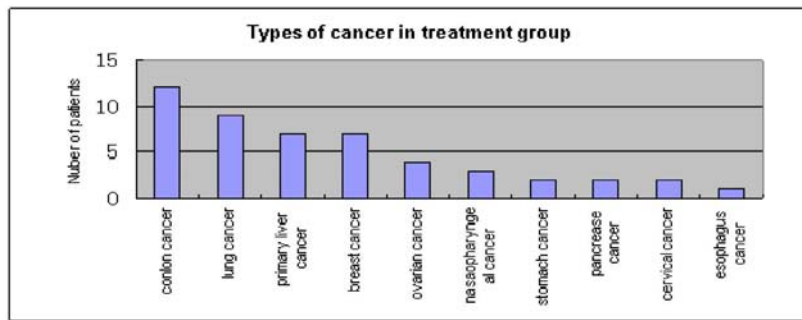
Conclusion: Hyperthermia, in conjunction with TCM and other treatments can significantly improve the therapeutic effects of cancer treatment. Traditional Chinese medicine occupies a unique position in integrative therapies for cancer. The combination of hyperthermia with intra-abdominal and intravesical chemotherapy can produce a synergistic effect. Hyperthermia can improve the quality of life of the patient and does not increase toxic adverse effects from radiochemotherapy.

5.2. Case 1

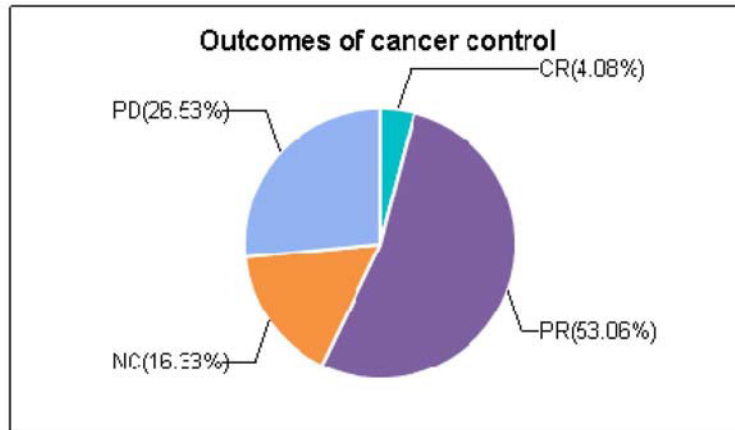
Hyperthermia + oral Chinese medicine + external application of Chinese medicine + other treatments

Participants: 49 cancer patients with chronic pain, and/or pleural or abdominal effusion, 21 males, 28 females, with a mean age of 54.0 ± 7.2 . They received 2 courses of deep regional hyperthermia, Chinese herbal medicine and External application of Chinese medicine.

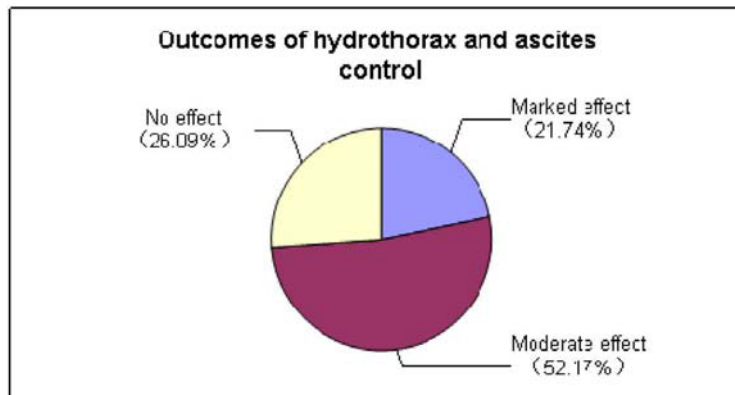
Among these patients, 23 cases had pleural or abdominal effusion; 37 cases had chronic pain.



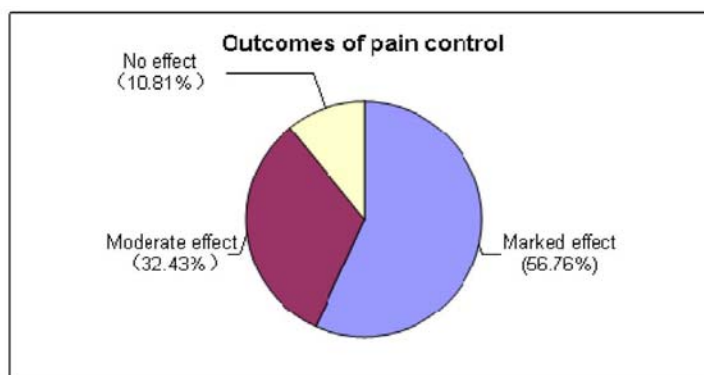
Results: cancer control: the overall response rate was 57.14%.



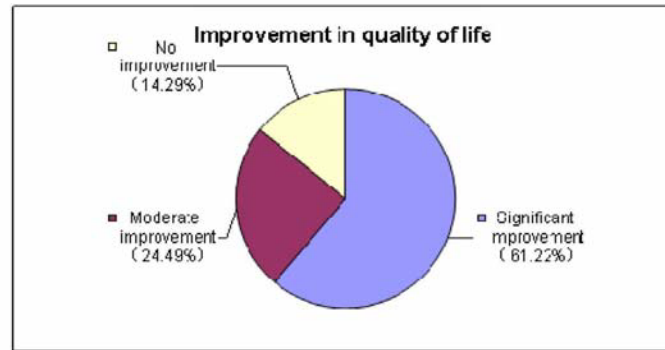
- Ascites and hydrothorax control: The overall response rate was 73.91%



- Pain control: The overall response rate was 89.2%



- Improvement in quality of life: The overall response rate was 85.7%



Conclusion: Hyperthermia along with internal and external use of Chinese medicine can: effectively control the progress of cancer, possess favorable efficacy on the control the pleural and abdominal effusion, effectively control pain and improve quality of life.

6. The outlook on hyperthermia integration with TCM in treating cancer

The integration of hyperthermia and TCM possesses unique advantages in treating cancer. Clinical trials have demonstrated that patients had good responses when they received the integration of hyperthermia and TCM. The above therapies not only improved the immune function of the body and relieved the patients' symptoms, but also extended patients' life spans and improved their quality of life. TCM nourishes the Yin and Qi of the kidney, compensates for the depletion of the Yin caused by sweating during hyperthermia sessions. With the continuous development of biological mechanisms of anticancer medicine in hot environments and the impact of basic research on cancer cell, hyperthermia, in combination with TCM, will be utilized more extensively as a form of anti-cancer treatment.

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