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ORIGINAL ARTICLE

Effects of 3.95 μm infrared moxibustion on cancer-related fatigue: a randomized, controlled trial

Dan Li[1] · Baixiao Zhao[2] · Fengli Jiang[3] · Kaiwen Hu[4] · Li Han[5] · Xiaojun Li[1] · Yi Xu[1] · Yao Lin[2] · Nini Zhangyang[2] · Xingpong Chen[6] · Yifan Wang[7]

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Abstract

Cancer-related fatigue(CRF) is a prevalent and distressing symptom among cancer patients. This study aimed to assess the initial effectiveness and safety of 3.95 μm infrared moxibustion for CRF. A randomized controlled trial was conducted with 65 CRF-diagnosed cancer patients, where the treatment group received 3.95 μm infrared moxibustion on on the ST36 (bilateral), CV4, and CV6 acupoints, each patient underwent 30-minute sessions, with 8 sessions per course and a total of 24 sessions, while the control group received standard care. The study evaluated fatigue and sleep quality using the Piper Fatigue Score (PFS) and the Pittsburgh Sleep Quality Index (PSQI) after the 2nd and 3rd sessions. After the 2nd session, individual fatigue was significantly lower in the infrared moxibustion treatment group than in the control group (6.39 vs. 5.26, $P=0.000$). After the 3rd session, individuals treated with infrared moxibustion had significantly better fatigue and sleep quality than the control group (6.60 vs. 4.63, $P=0.000$), (9.45 vs. 7.84, $P=0.041$). The safety profile of infrared moxibustion was favorable, with only four cases of skin adverse reactions reported. This study suggests that infrared moxibustion is a safe and effective treatment for CRF in Chinese cancer patients. However, further research involving larger and more diverse populations is necessary to validate these findings.

Keywords Cancer-related fatigue · Clinical trial · Infrared · Moxibustion

Introduction

As one of the most common and distressing symptoms in cancer patients, the prevalence of CRF remains high throughout the year. Studies have shown that [1] the prevalence of fatigue in different types of cancer ranges from 50 to 92% and even up to 100%. For instance, a retrospective study of 4067 cancer patients post-treatment reported a fatigue prevalence of 59.60%, making it the most prevalent symptom in this population [2]. Tian [3] investigated the prevalence and influencing factors of CRF in East China and found that 52.07% of 1749 cancer patients experienced significant fatigue, with the severity linked to factors such as cancer stage, sleep quality and functional movement. Despite extensive research on CRF, the medical community often underestimates the negative impact of these symptoms on patients and society. Furthermore, there is a lack of standardized assessment, management and treatment protocols for CRF. Studies have showed that CRF is significantly associated with a lower quality of life [4, 5]in cancer patients, as well as somatic symptoms, anxiety, depression

✉ Baixiao Zhao
baixiao100@vip.sina.com

Dan Li
2274938973@qq.com

1 Department of Traditional Chinese Medicine, Taizhou Hospital of Zhejiang Province Affiliated to Wenzhou Medical University, Taizhou, China

2 School of Acupuncture and Tuina, Beijing University of Traditional Chinese Medicine, Beijing, China

3 Department of Hepatology, Chongqing Traditional Chinese Medicine Hospital, Chongqing University of Traditional Chinese Medicine, Chongqing, China

4 Department of Oncology, Oriental Hospital, Beijing University of Traditional Chinese Medicine, Beijing, China

5 Department of Health Rehabilitation, School of Traditional Chinese Medicine, Beijing University of Traditional Chinese Medicine, Beijing, China

6 School of Traditional Chinese Medicine, Beijing University of Traditional Chinese Medicine, Beijing, China

7 The First Clinical School of Medicine, Beijing University of Traditional Chinese Medicine, Beijing, China

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and comorbidities [6]. In some cases, the severity of fatigue has been identified as a predictor of survival time [7]. Given the complex etiology and pathogenesis of CRF, research on CRF treatment is only in the preliminary stage [8]. Although some non-pharmacological therapies can reduce the clinical symptoms of some CRF patients [9, 10], clear therapeutic interventions are currently lacking.

Moxibustion therapy is a crucial element of ancient Chinese medicinal practices and has been employed for generations to combat health deficiencies. By utilizing moxa as a fundamental ingredient, this therapy involves applying heat to specific points on the skin to enhance overall health and prevent diseases. The introduction of the modern infrared moxibustion device marks a significant technological advancement in the medical field, providing a more efficient and controlled treatment method compared to traditional techniques.Research studies have shown that the infrared moxibustion device delivers a consistent source of heat without the issues associated with traditional methods, like incomplete burning and excessive smoke production. This novel approach not only improves safety but also serves as a more eco-friendly option to traditional moxibustion practices. By closely mimicking the infrared wavelengths emitted during traditional moxibustion, the 3.95 μm infrared moxibustion device used in our study effectively overcomes the limitations of conventional methods.Our study aimed to evaluate the effectiveness and safety of 3.95 μm infrared moxibustion for treating Chronic Renal Failure (CRF) in a controlled randomized trial. The main focus of the research was to assess patient fatigue and quality of sleep using the Piper Fatigue Score (PFS) and Pittsburgh Sleep Quality Index (PSQI) after the second and third treatment sessions.

Materials and methods

Patients diagnosed with CRF according to the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) criteria were randomly assigned to a 2-arm randomized controlled trial (RCT) in a 1:1 ratio.

All participants provided written informed consent and met the following criteria: (1) aged 18–80 years; (2) diagnosed with a malignant tumor; (3) meeting the ICD-10 CRF western medicine diagnostic criteria; (4) exhibiting Traditional Chinese Medicine TCM deficiency symptoms; (5) expected survival period of ≥2 months; (6) Piper fatigue scale score of ≥4; (7) demonstrating strong compliance and high cooperation levels.

Participants with incomplete data, pregnant, expected survival of less than 2 months, serious primary illnesses such as cardiovascular and psychiatric diseases, uncooperative and unable to cooperate, having received other physical therapy methods for fatigue, and allergic to infrared light were excluded.

Randomization and blinding

Randomization was conducted using SPSS 22.0 statistical software, and the allocation of patients to treatment and control groups was concealed in opaque sealed envelopes. Patients were then selected in the order of treatment. While maintaining the integrity of the double-blind requirement was challenging given the particularity of moxibustion, our research team ensured scientific rigor by following the principle of ‘three separations’, which involved separating researchers, operators, and statistical analysts.

Study Design

The study consisted of two groups: the treatment group, which received infrared moxibustion, and the control group, which received usual care. The trial flow is illustrated in Fig. 1. In the treatment group, participants underwent 30-minute sessions of infrared moxibustion for 8 sessions, totaling 24 sessions over 3 weeks. Assessment was conducted at the end of the second and third sessions to measure the longevity of the treatment’s effects.

Treatment time and method

Participants in the treatment group underwent sessions with BXM-02 Infrared moxibustion devices (Beijing Deyuan Bohui Technology Tech Co Ltd, Beijing, China) in a designated private room. The Infrared probes were positioned at four specific points - the bilateral ST36, CV4, and CV6 acupoints - approximately 3 cm from the skin surface for a duration of 30 min. Patients in the control group received standard symptomatic nursing care. Each patient underwent a 30-minute treatment session, eight sessions per course, totaling three intervention courses and 24 sessions overall.

Outcome measures

The Piper Fatigue Scale (PFS) was employed in this study to evaluate fatigue levels. The scoring system ranged from 0 to 10, with scores above 6 indicating severe fatigue, scores between 4 and 6 representing moderate fatigue, scores between 1 and 3 reflecting mild fatigue, and a score of 0 indicating no fatigue. The fatigue levels were determined based on the responses to questions 3 to 24. The Pittsburgh Sleep Quality Index (PSQI) was employed to evaluate sleep quality in the past month, with factors such as the use of hypnotic drugs and daytime dysfunction taken into account. Scores on the PSQI ranged from 0 to 3, with higher scores

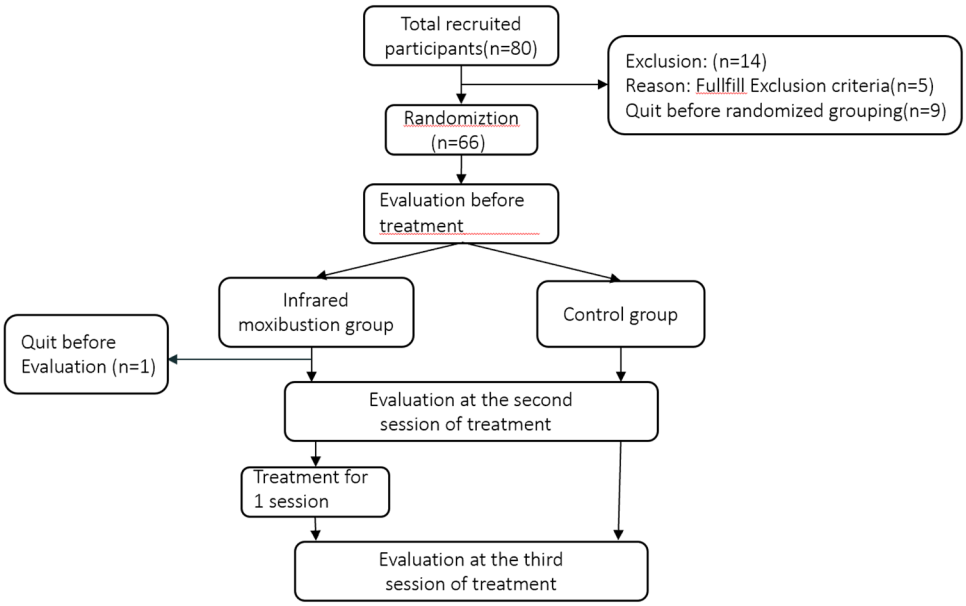

Fig. 1 Flow chart of the study

indicating more severe sleep issues. A total score of 7 or less was considered normal sleep quality, while a score above 7 suggested the presence of a sleep disorder.

Statistical analysis

The sample size calculation was based on both reviewing the relevant literature [11, 12] and our pilot study comparing the FPS scores of the Infrared moxibustion and control groups at Sect. 2 or 3 and Per preliminary data. Considering the dropout rate of 10%, the sample size of each group was 33 cases, and the total sample size was 66 cases. After filling in the questionnaire data into Excel, import it into the SPSS 22.0 software system for statistical analysis, compare the measurement data with the mean ± standard deviation for description, and use the t-test statistics for the measurement data that meet the normal distribution or homogeneity of variance, and do not meet the normal distribution. The rank sum test was used for the data with unequal variance or the chi-square test was used for the count data. $P<0.05$ was regarded as statistically significant for all statistics.

Results

A total of 66 participants were recruited for this study from the outpatient oncology department of the Second Affiliated Hospital of Beijing University of Chinese Medicine between May 2021 and February 2022. The participants were divided into two groups: one receiving conventional symptomatic care (33 participants) and the other receiving the infrared moxibustion method (33 participants). Only one patient (1.52%) dropped out before the second assessment (Fig. 1).

Table 1 General data of the participants

Category	Control group ($N=33$)	Treatment group ($N=32$)	P
Gender			
Male	10(30.30%)	7(21.87%)	0.660
Female	23(69.70%)	25(78.13%)	
Age	66.15 ± 10.54	62.16 ± 4.75	0.058
Cancer type			
Lung cancer	11 (18.75%)	6 (18.75%)	0.25
Bowel cancer	5 (9.38%)	3 (9.38%)	
Liver cancer	0	0	
Stomach cancer	1(3.03%)	0	
Kidney cancer	0	0	
Breast cancer	11 (33.33%)	16 (50%)	
Ovarian cancer	0	4 (12.5%)	
Uterine cancer	2 (6.06%)	0	
Bladder Cancer	2 (6.06%)	0	
Oral Cancer	0	1 (3.125%)	
Pancreatic cancer	1 (3.13%)	1 (3.125%)	
Thyroid cancer	0	0	
Treatment			
Operation	29 (87.88%)	31 (96.88%)	0.952
Chemotherapy	19 (57.58%)	19 (59.38%)	
Radiotherapy	4 (12.12%)	4 (12.5%)	
Target	5 (15.15%)	3 (9.37%)	
Immunity	1 (3.03%)	0	
Endocrine	1 (3.03%)	2 (6.25%)	

Baseline characteristics of the patients

Table 1 shows the baseline data for the 65 participants. The mean age of the patients enrolled was 63.22 years

(range47-85 years); 17 patients (26.15%) were male, whereas 48 patients (73.84%) were female. They were all of Han Chinese ethnicity, all patients were in the survivorship phase after curative cancer treatment. There is no significant statistical difference in the general data among the groups, and they are comparable (Table 1).

Changes in fatigue between the groups

Figure 2 shows PFS at baseline, course 2, and course 3 between the infrared moxibustion group (32 patients) and control group (33 patients). At baseline, the PFS was not significantly different between the 2 groups (6.31 ± 1.22 vs. 5.98 ± 1.04, $P = 0.457$). By the middle of treatment (Sect. 2), the PFS was statistically lower in the infrared moxibustion group versus the control group (6.39 ± 0.89 vs. 5.26 ± 0.81, $P = 0.000$). At the end of treatment (Sect. 3), the PFS was much lower in the laser moxibustion group compared with the sham group (6.60 ± 1.04 vs. 4.63 ± 0.84, $P = 0.000$).

Figure 3 shows the PSQI at baseline, course 2, and course 3 between the infrared moxibustion group (32 patients) and control group (33 patients). At baseline, the PSQI was not significantly different between the 2 groups (8.58 ± 3.85 vs. 9.53 ± 5.28, $P = 0.390$). By the middle of treatment (Sect. 2), the PSQI was statistically lower in the infrared moxibustion group versus the control group (9.18 ± 3.82 vs. 8.56 ± 3.953, $P = 0.518$). At the end of treatment (Sect. 3), the PSQI was much lower in the laser moxibustion group compared with the sham group (9.45 ± 3.00 vs. 7.84 ± 3.69, $P = 0.041$).

Assessment of AEs

1) Adverse skin reactions at the treatment site were observed in Four patients within the infrared moxibustion group. These reactions included one case of local skin blistering at the Guan Yuan point and three cases of local skin flushing without itching. In cases where large localized skin blisters appeared, the sterilized needle tip was partially punctured to release the fluid. Following wound healing, other allergic patients were advised to apply local anti-scald cream to prevent burns, with skin reaction.

2) Two patients in the treatment group experienced dry mouth, increased thirst, dry stool, and difficulty sleeping. Patients with dry mouth and dry stool were advised to increase their water intake and consume more fresh fruits and vegetables. Those struggling with sleep were given adjusted treatment times and encouraged to soak their feet and drink milk before bedtime, resulting in significant relief of symptoms.

3) No adverse reactions such as tumor enlargement, metastasis or tumor burden aggravation related to the primary disease occurred in the treatment group.

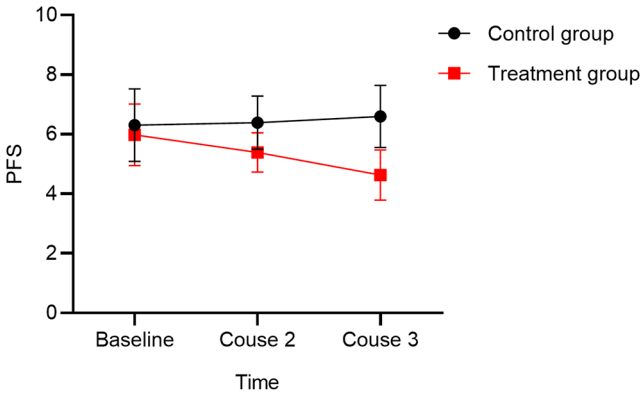

Fig. 2 Comparing Piper fatigue score(PFS) of the infrared moxibustion group (32 patients) and control group (33 patients) at baseline, Sect. 2, Sect. 3 (shown as the mean ± the standard error)

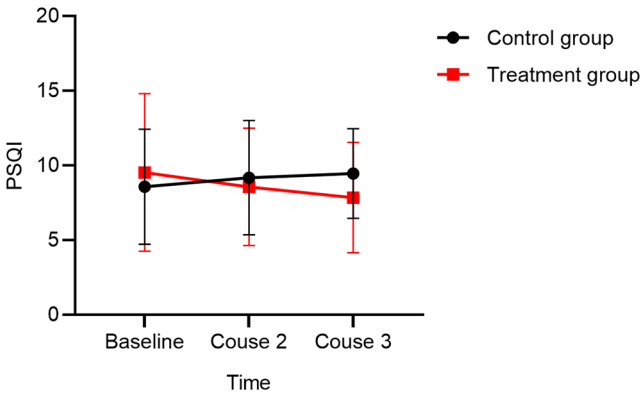

Fig. 3 Comparing PSQI of the infrared moxibustion group (32 patients) and control group (33 patients) at baseline, Sect. 2, Sect. 3 (shown as the mean ± the standard error)

4) The incidence of adverse reactions in the IR group was 12.5%, and no serious adverse reactions occurred in both groups.

Discussion

The purpose of this study was to evaluate the efficacy and safety of infrared moxibustion in patients with CRF.

CRF is the most common and distressing symptom among cancer patients. The incidence of fatigue is high, reaching 25–99% in oncology patients after treatments such as surgery, radiotherapy and chemotherapy [13, 14]. CRF takes a significant toll on patients. According to a survey, fatigue affects the normal life of 91% of cancer patients, forcing 88% of patients to change their lifestyle and causing 75% of patients to make adjustments to their work [15]. Moreover, CRF is associated with negative emotions like anxiety depression, impacting patients' overall well-being and confidence in battling cancer [16]. Addressing CRF is crucial for enhancing patients' quality of life and extending

their survival. Despite numerous international clinical trials, a safe and effective treatment for CRF remains elusive [17].

Moxibustion activates receptors in superficial areas of the body and increases the internal energy of the body [18]. It acts on deep tissues and mediates the capillary network to produce extensive thermal effects, accelerating the body's circulation and metabolism [19]. Additionally, moxibustion activates active substances such as heat shock proteins, stimulating the body's neurological and humoral immune functions [20]. It is also effective in reducing the toxic side effects of surgery, radiotherapy, and chemotherapy [21], improving clinical symptoms, immune function, and the quality of life for cancer patients [22, 23]. Widely used in the treatment of CRF due to its effectiveness, convenience, safety and economy. Scholars agree [24] that the key efficacy factors of moxibustion are light radiation and thermal stimulation, with pharmacological effects playing an auxiliary role. Infrared moxibustion can partially replace the physical effects of moxibustion [25], but its therapeutic effects on CRF have been underreported, hindering the advancement of modern medical technology and the exploration of moxibustion's mechanism of action. And infrared moxibustion treatment was found to be safe, with no significant adverse events reported. The results of this study indicate that 3.95 μm infrared moxibustion could be a safe and effective non-pharmacological approach for managing CRF, aligning with findings from previous clinical studies.

Inflammatory factor imbalance and circadian rhythm disturbances are associated with the development of CRF [26, 27]. Pro-inflammatory factors such as interleukin-6 (IL-6), C-reactive protein (CRP), interleukin-1β (IL-1β), tumor necrosis factor-a (TNF-a), and others can trigger central fatigue through various mechanisms including anemia, fever, depression, and cachexia [28]. A retrospective study of 1312 chemotherapy patients identified over 20 cytokines associated with CRF, with anthracycline chemotherapy patients showing significant associations with transforming growth factor-β (TGF-β), soluble tumor necrosis factor receptor 2 (sTNF-R2), and interleukin-1RA (IL-1 RA) [29]. Research [30] also indicates that sleep disturbances can impact inflammation and lead to fatigue, with factors like difficulty falling asleep, frequent awakening, poor sleep quality, and sleepiness being linked to CRF. Studies have shown a positive correlation between fatigue and sleep duration, number of awakenings, total sleep time, and a negative correlation with sleep efficiency [31]. Furthermore, longer latency to fall asleep in breast cancer patients was associated with more nighttime awakenings and increased severity of CRF symptoms [32]. Circadian rhythms play a role in regulating sleep duration, and phototherapy can influence the suprachiasmatic nucleus's function to synchronize with the body's circadian rhythm [33]. In addition, infrared light also exhibits a beneficial anti-inflammatory effect. This suggests that the combined light radiation and thermal effects of infrared moxibustion may be crucial initiating factors for the overall effectiveness of moxibustion.

The present study has several limitations. Firstly, the short duration of treatment in this study was due to trial time and site, constraints, leading to a lack of follow-up observation on late clinical outcomes. Secondly, the study included CRF patients with fatigue from 12 different tumor types, predominantly breast cancer, resulting in a relatively complex distribution of disease types. Future trials could consider focusing on CRF patients with a single disease type to enhance the scientific validity of the trial results. Thirdly, the absence of a sham infrared moxibustion group as a control made it challenging to assess the placebo effect of infrared moxibustion for CRF. Lastly, the safety evaluation of this study lacked quantitative evaluation indexes, potentially introducing bias. For future clinical trials, quantitative indicators such as body temperature, heart rate, blood pressure, pulse, and routine liver and kidney function tests can be utilized to evaluate the safety of the experiment.

Author contributions Dan Li: Study design, quality control of data and algorithms, data analysis and interpretation, article preparation, article editing, and article review. Kaiwen Hu: Data analysis and interpretation, article editing, and article review. Li Han: Data acquisition and article preparation. Yao Lin: Statistical analysis and article preparation. Fengli Jiang: Data acquisition and article preparation. Yini Zhangyang: Data acquisition and article preparation. Xingpong Chen: Data acquisition and article preparation. Yifan Wang: Data acquisition and article preparation. Baixiao Zhao: Study design and article concepts, study design, data analysis and interpretation, article editing, and article review. Dan Li and Baixiao Zhao are responsible for the overall content of the article.

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Declarations

Ethical approval This study followed the human guidelines of the Helsinki Declaration and the Tokyo Declaration, and was approved by the Clinical Research Ethics Committee of Dongfang Hospital, Beijing University of Traditional Chinese Medicine, with informed consent.

Competing interests We have no conflicts of interest to disclose.

References

1. Lancker AV, Velghe A, Hecke AV et al (2014) Prevalence of symptoms in older cancer patients receiving palliative care: a systematic review and meta-analysis. J Pain Symptom Manage 47(1):90–104
2. Reilly CM, Bruner DW, Sandra AM et al (2013) Mitchella literature synthesis of symptom prevalence and severity in persons receiving active cancer treatment. Support Care Cancer 21(6):1525–1550
3. Tian L, Lin L, Li HL et al (2016) Prevalence and Associated factors of Cancer-related fatigue among Cancer patients in Eastern China. Oncologist 21(11):1349–1354
4. Andreas C, Christiana K (2016) Cancer related fatigue and quality of life in patients with advanced prostate Cancer undergoing chemotherapy. Biomed Res Int 2016:1–11
5. Corbett T, Groarke A, Walsh JC, McGuire BE (2016) Cancer-related fatigue in posttreatment cancer survivors: application of the common sense model of illness representations. BMC Cancer 16(1):919–936
6. Johns SA, Brown LF, Beck-Coon K et al (2016) Randomized controlled pilot trial of mindfulness-based stress reduction compared to psychoeducational support for persistently fatigued breast and colorectal cancer survivors. Support Care Cancer 24(10):4085–4096
7. Lacourt TE, Kavelaars A, Ohanian M et al (2018) Patient–reported fatigue before treatment is prognostic of survival in patients with acute myeloid leukemia. Oncotarget 9(58):31244–31252
8. Saligan LN, Olson K, Filler K et al (2015) The biology of cancer-related fatigue: a review of the literature. Support Care Cancer 23(8):2461–2478
9. Al Maqbali M, Hughes C, Dunwoody L et al (2019) Exercise interventions to manage fatigue in women with gynecologic cancer: a systematic review. Oncol Nurs Forum 46(1):71–82
10. Nna B, Mm A, Mss A (2021) Effects of massage therapy on cancer-related fatigue: a systematic review. Enfermeria Clin 31(S5):S692–S696
11. Kyungsun H, Mikyung K, Eun-Jung K et al (2021) Moxibustion for treating cancer-related fatigue: a multicenter, assessor-blinded, randomized controlled clinical trial. Cancer Med 10(14):4721–4733
12. Lee S, Jerng U, Liu Y et al (2014) The effectiveness and safety of moxibustion for treating cancer-related fatigue: a systematic review and meta-analyses. Support Care Cancer 22(5):1429–1440
13. AlFayyad I, Al-Tannir M, Yaqub M et al (2020) Clinically significant fatigue in adult leukemia patients: prevalence, predictors, and impact on quality of life. Cureus 12(12):e12245–e12245
14. Taro U, Daisuke I, Yoichi S et al (2022) Comorbid insomnia among breast cancer survivors and its prediction using machine learning: a nationwide study in Japan. Jpn J Clin Oncol 52(1):39–46
15. Yeo S, Lee J, Kim K et al (2021) Depression, rather than cancer-related fatigue or insomnia, decreased the quality of life of cancer patients. Cancer Res Treat 53(3):641–649
16. Ying H, Chen L (2019) Effect of gratitude intervention on cancer-related fatigue and negative emotion for patients with advanced lung cancer. J Nurs Rehabilitation 18(3):9–1317
17. Pearson EJM, Morris ME, di Stefano M et al (2018) Interventions for cancer-related fatigue: a scoping review. Eur J Cancer Care (Engl) 27(1):1–13
18. Xu HQ, Zhang HR, Gu YH (2014) Progress of research on prevention and treatment of sports fatigue with moxibustion therapy. Acupunct Res 39(2):169–173
19. Li Y, Yang J, Gui L et al (2019) Effect of moxibustion on long term memory in vascular dementia model rates. World J Acupunct Moxibustion 29(1):63–68
20. Yu J, Peng H, Lin Y et al (2013) Effect of moxibustion treatment on cell apoptosis and expressions of heat shock protein and second mitochondrial activator of caspase in the acute gastric mucosal lesion of rats. J Tradit Chin Med 33(2):258–261
21. Zhang HW, Lin ZX, Cheng F et al (2018) Moxibustion for alleviating side effects of chemotherapy or radiotherapy in people with cancer. Cochrane Database Syst Reviews 11(11):CD010559
22. Han Y, Zhang H, Liang X et al (2015) Effects of moxibustion for immune function in malignant tumor. J Changchun Univ Chin Med 31(1):87–89
23. Zhang M, Ling G, Wang L et al (2018) Effect of scar-producing moxibustion at the acupoints Zusanli(ST 36) and Feishu(BL 13) on neutrophil-to-lymphocyte ratio and quality of life in patients with non-small-cell lung cancer: a randomized, controlled trial. J Tradit Chin Med 38(3):439–446
24. Zhao L, Shen X (2013) Chemical and physical characteristics of Moxibustion. Curr Res Acupunct 1(5):109–127
25. Lin L, Cheng K, Tan MT et al (2019) Comparison of the effects of 10.6-μm infrared laser and traditional moxibustion in the treatment of knee osteoarthritis. Lasers Med Sci 35(4):823–832
26. Yang S, Chu S, Gao Y, Ai Q, Chen N (2019) A narrative review of cancer-related fatigue (crf) and its possible pathogenesis. Cells 8(7):738
27. Echchikhi Y, Abbassi SE, Touil A et al (2017) Sleep disorders and Sleep Quality in Moroccan adult patients with Cancer during treatment. J Cancer Sci Therapy 09(9):637–643
28. Bower JE, Lamkin DM (2013) Inflammation and cancer-related fatigue: mechanisms, contributing factors, and treatment implications. Brain Behav Immun 30(Suppl):S48–S57
29. Eyob T, Ng T, Chan R et al (2016) Impact of chemotherapy on cancer-related fatigue and cytokines in 1312 patients: a systematic review of quantitative studies. Curr Opin Support Palliat Care 10(2):165–179
30. Irwin MR, Opp MR (2017) Sleep Health: reciprocal regulation of Sleep and Innate Immunity. Neuropsychopharmacology 42(1):129–155
31. Berger AM, Matthews EE, Kenkel AM (2017) Management of sleep-wake disturbances comorbid with cancer. Oncology 31(8):610–617
32. Bower JE, Ganz PA, Irwin MR et al (2011) Inflammation and behavioral symptoms after breast cancer treatment: do fatigue, depression, and sleep disturbance share a common underlying mechanism? J Clin Oncol 29(26):3517
33. Emanuel H, Revana A, Te T et al (2021) 830 combined phototherapy and melatonin for treatment of circadian rhythm disorder in a patient with cornelia de lange syndrome. Sleep 44(Supplement2):A323–A324