Acupuncture Therapy for the Treatment of Myelosuppression after Chemotherapy: A Literature Review over the Past 10 Years

Hongwei Fu 1,2,†, Bo Chen 1,2,†, Shouhai Hong 2, Yi Guo 1,2,*

1 Acupuncture Research Center, Tianjin University of Traditional Chinese Medicine, Tianjin, China
2 Institute of Acupuncture and Massage, Tianjin University of Traditional Chinese Medicine, Tianjin, China

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Abstract
The aim of this study is to review current studies on the effect of acupuncture therapy on bone marrow suppression after chemotherapy. The authors of the present paper have searched related literature over the past 10 years at home and abroad, analyzing the features and the effects of acupuncture therapy (including acupuncture, moxibustion, point injection, point application, etc.) for treating myelosuppression after tumor chemotherapy. We also discuss the year of publication, document type, acupuncture therapy, acupoint selection, and adverse effects with figures. We analyzed 159 articles related to acupuncture therapy from 2004 to 2013, and the analysis revealed that point injection was the most frequently used therapy for clinical applications, and that Zusanli (ST36) was the most frequently used acupoint. The results showed that some problems regarding the design method, acupoint selection, and acupuncture intervention measure existed in those research studies. We hope to provide readers with an overall and objective understanding of acupuncture and moxibustion therapy for treating myelosuppression after tumor chemotherapy.
1. Introduction

Bone marrow suppression is one of the common side effects after antineoplastic chemotherapy, including thrombocytopenia, leukopenia, and lymphopenia [1,2]. For these side effects, existing drug treatments are expensive and the effects remain only for a short period of time. In addition, it can cause rashes, bone pain, fever, and other adverse reactions. It may also increase the damage of bone marrow cells and stimulate certain malignant cell growth, which makes the chemotherapy subject to certain restrictions in the clinical application [3,4]. In recent years, the related clinical trials and preliminary animal studies indicate that acupuncture therapy has a good synergistic effect during chemotherapy, and can effectively alleviate myelosuppression caused by chemotherapy, and the cost of therapy is relatively cheap, having fewer side effects [5]. This paper summarizes the research status of the past 10 years at home and abroad on the impact of acupuncture therapy on bone marrow suppression after chemotherapy, and also analyses the existing problems to provide a valuable reference for further research.

2. Materials and methods

The data were from the online version of China Knowledge Network, Wan Fang Database, Weipu database of Chinese journal, PubMed. (“acupuncture” OR “acupuncture” OR “moxibustion” OR “electro acupuncture” OR “electro-acupuncture” OR “needle” OR “catgut implantation” OR “point injection” OR “point application” OR “cupping”) AND (“bone marrow suppression” OR “myelosuppression” OR “leucopenia”) were retrieved as the medical subject headings from January 2004 to June 2013. Literature inclusion criteria were: (1) treatment with acupuncture therapy (including acupuncture, moxibustion, electro-acupuncture, point injection, acupoint application, etc.); and (2) observation of clinical efficacy and experimental research on bone marrow suppression after chemotherapy. Duplicate documents, repeated documents, and repeated use of published literature in each database were excluded. All articles were assessed by two literature retrieval personnel, respectively, to extract data by the following aspects: the titles of the document, year of publication, document types, acupuncture therapy, acupoint selection, outcome measures, and adverse events; and were entered in an Excel table. In the process of different therapy processes, different appellation were used, such as “medicinal vesication”, “Ginger moxibustion”, “Long snake moxibustion”, etc., which were put under the “moxibustion” statistics; and then analyzed and summarized.

3. Results

3.1. Literature distribution

There were 159 articles by using the above search strategy, which included clinical trials (n = 108), experimental studies (n = 20), reviews (n = 19), meeting abstracts (n = 8), newspapers (n = 3), and a case report (n = 1) (Fig. 1).

There were five foreign literatures: two clinical research literatures, and three reviews comprising 3% of the total literature. There were seven randomized controlled trials and three quasi-randomized controlled trials. Regarding the literature published from 2004 to 2013, the numbers of articles published per year were 12, 16, 21, 15, 14, 13, 21, 13, 19, and 15, respectively, and are displayed in Fig. 2. Further, for a period of 5 years, there was no huge change regarding the literature published.

3.2. The frequency of various acupuncture therapy

Analysis of the 159 articles related to acupuncture therapy from 2004 to 2013 showed that the application of different acupuncture therapies was followed by point injection 78 times, moxibustion 36 times, acupuncture 29 times, acupoint application six times, electroacupuncture five times, and catgut implantation one time (Fig. 3). It may be concluded that point injection is the most frequently used therapy for clinical application.

3.3. Acupoint selection

Acupuncture points in the order of high to low frequency in application were Zusanli (ST36) 106 times, followed distantly by Geshu (BL17) 32 times, Shenshu (BL23) 25 times, Dazhui (DU14) 24 times, Xuehai (SP10) 17 times, Pishu (BL20) 16 times, Sanyinjiao (SP6) 14 times, and Guanyuan (RN4) eight times (Fig. 4). In conclusion, the points of the Stomach Meridian of Foot-Yangming, the Spleen Meridian of Foot-Taiyin, and the Bladder Meridian of Foot-Taiyang were mostly selected.

3.4. Reported adverse effects

There were a total of 51 pieces among 108 clinical research articles which observed the adverse reactions of acupuncture therapy; among which adverse reactions were mentioned in nine pieces. The main reactions were pain, soreness, numbness, palpitation, dizziness, and allergies. There is one article which mentioned that adverse effects were due to the sham acupuncture needle forgotten to be taken out from a control group of patients, and the remaining 41 references reported no adverse reactions.

Figure 1 Number of different document types in 159 articles.
3.5. Commonly used acupuncture therapy

Through the summary and analysis of the existing literature, the following will be the three most commonly used acupuncture therapies in the treatment of bone marrow suppression after chemotherapy.

3.6. Point injection

In recent years, there are an increased number of reports of point injection in the treatment of myelosuppression. Point injection has many advantages, such as using small dose, easy to operate, microintervention, easily accepted by patients, and so on. Summarizing previous research, the major medications of the injection were dexamethasone, Shenfu injection, Huangqi injection, and rhG-CSF. And Zusanli is mostly selected for point injection. Modern studies suggest that acupoint injection has the characteristics of acupuncture combined with injection of drugs [6]. It can effectively alleviate myelosuppression caused by chemotherapy drugs, stimulating the bone marrow hematopoietic function, enhancing the role of peripheral blood leukocytes. Some scholars speculate that the mechanism of elevated white blood cells may be related to improvement of T-cell immune function and may reduce the phagocytosis of white blood cells [7]. At present, the mechanism involved has not been well established because researchers have concentrated mainly on clinical curative observations. Further research is therefore needed to strengthen work into mechanism of action and, moreover, to improve the quality of clinical research and optimization selection of acupoint and drugs. However, the positive curative effect explores the regularity and clarifies its internal mechanism. The aim of this study is to better promote the clinical practice and applicability in the field.

3.7. Acupuncture and moxibustion therapy

The clinical application frequency of acupuncture and moxibustion therapy is second only to point injection and both are often used together. Animal experiments and clinical experiments indicated that acupuncture and moxibustion have played a positive role on reducing the side effects of chemotherapy, protecting the hemogram, strengthening bone marrow hematopoietic function, and improving patients' immunity. It can increase the number of peripheral white blood cells and bone marrow nucleated cell count, increase the phagocytosis, has a lasting effect with less adverse effects, and is worthwhile for spreading in clinical practice [8,9]. The mechanism of acupuncture treatment of bone marrow suppression after chemotherapy focuses on the following several aspects: (1) acupuncture and moxibustion can enhance the DNA repair function of bone marrow cells, which will help hematopoietic cell proliferation and differentiation [10]. (2) Acupuncture and moxibustion can promote stromal cell membrane on the release of cytokines, microvascular damage repair, bone marrow hematopoietic stem cell proliferation, and energy increase, and thus improve the damaged hematopoietic microenvironment [11]. (3) Acupuncture and moxibustion can increase the activity of serum colony-stimulating factor, prompting hematopoietic stem/progenitor cell proliferation as soon as possible [12]. In conclusion, the present study focuses on the mechanism of bone marrow cells expressing the protein molecule, and whether they relate to the regulation of other biologically active substances has not yet been fully understood. In addition, some clinical studies have found that moxibustion is superior to acupuncture therapy in the fight against bone marrow suppression [13]. However, the research on the regularity of effectiveness is still inadequate and still needs further investigation.

3.8. Acupoint application

The existing experimental studies have shown that combining the pharmacological action of Chinese medicine and the provocation in the body point, point application is a distinct method of Chinese medicine [14]. To a certain extent, it can alleviate the decline of interleukin-2 in the mice serum caused by cyclophosphamide (CTX), upregulate interleukin-6 level, and regulate the body immunity. It can reduce repeated chemotherapy damage in bone marrow,
promote bone marrow cell maturation, stimulate the bone marrow hematopoietic system, and increase peripheral white blood cells. Other studies indicate that point application can effectively improve a patient’s immune function and the level of peripheral white blood cells, preventing the decline of leucocyte, and greatly improve clinical symptoms [15]. Point sticking therapy is easy to operate and accepted by patients. There is no unified formula of point application ointment, so it is difficult to compare the curative effect of different therapy processes.

4. Discussion

Current clinical studies of acupuncture therapy on myelosuppression after chemotherapy are still few and insufficient, and there are still some design defects. Previous studies have demonstrated that the main problems are incomplete research reporting. The lack of detailed description of random method, statistical analysis method, adverse reactions, and follow-up impacts test repeatability. In addition, some studies showed lack of combined standards regarding inclusion criteria and thus the baseline is not at the same level. For example, the research objectives of some articles are included in mixed tumor types, and are rarely used alone regarding a certain type of cancer as the research objective. The design of experiments is given priority in small sample clinical observations and there is a lack of multicenter large sample random clinical trials. The clinical design of the only seven randomized controlled trials also has certain flaws, such as lack of description regarding the random method and allocation concealment, lack of blinding intervention, which will result in the occurrence of bias test results, reducing the authenticity and reliability of the findings. Thus, it is very important for the treatment of bone marrow suppression to improve the quality of clinical research and optimize the design of acupuncture therapy.

The mechanism of action of acupuncture therapy used in the treatment of myelosuppression after chemotherapy is complex and not well understood. For example, the analysis of single therapy with too many confounding factors, such as acupuncture combined with moxibustion, and acupoint injection combined with acupuncture, is not sufficient. Moreover, the acupuncture literature on point positioning, needle selection, acupuncture methods, needle depth, Deqi, etc., and other details include lack of explanation, which will affect the effectiveness and safety of acupuncture therapy. Currently, acupuncture therapy for myelosuppression is mostly limited to observations of certain relevant clinical indicators, such as white blood cell and platelet counts, leukocyte common antigen content, and interleukin-2 levels. These indicators are carried on the preliminary exploration from the individual single index to lack of systematic, comprehensive, and deep research. However, the mechanism of action of acupuncture intervention in the treatment of myelosuppression is not well understood. What affects the pathway? What is its biological mechanism? These fundamental questions still remain to be studied further.

Acupuncture points of strengthening spleen and replenishing Qi in treating bone marrow suppression were often chosen. We found that acupuncture and moxibustion treatment of myelosuppression with optional Zusanli (ST36) is the most frequently used method. Zusanli (ST36) is the He-sea point of Stomach Meridian, curing viscera diseases by the point. Stomach Meridian is abundant in Qi and blood. The stomach is the reservoir for food and drink. The spleen's meridians connect with the stomach, with which they are internally—externally related. Zusanli can regulate spleen and stomach, strengthen the middle warmer and benefit the vital energy, strengthen body resistance and eliminate evil, which is the important point of health preservation [16]. It is proved that Zusanli stimulates the influence of nerve—humoral immunity and can effectively improve the body’s red blood cells, white cells, and immunoglobulin level, and therefore affects cellular immunity and enhances the body’s immune function [17,18]. However, researchers differ on acupoint selection and acupuncture point number in the use of acupuncture and moxibustion prescription. There is no comprehensive understanding of the function of specific acupoints and therefore affects the repeatability of clinical trials. In this regard, it is difficult to compare the curative effects of different therapies.

Overall, this review summarizes the research situation of the relevant documents on acupuncture therapy and demonstrates that acupuncture is considered by many to be acceptable and effective on bone marrow suppression after chemotherapy. However, many detailed mechanisms cannot be addressed in the presenting studies. This will result in a significant reduction in long-term bone marrow suppression toxicity and increase living quality of carcinoma patients. Future studies should concentrate on mechanisms for bone marrow suppression that could make results more convincing. The application of acupuncture
therapy should also be tested widely in cancer diagnostic groups.

Disclosure statement

The authors declare that they have no conflicts of interest and no financial interests related to the material of this manuscript.

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References