

• Review

Post-hematopoietic stem cell transplantation in patients with hematologic disorders: Chinese herbal medicine for an unmet need

Tom Fleischer¹, Tung-Ti Chang^{2,3,4}, Hung-Rong Yen^{2,3,5,6}

1. Graduate Institute of Chinese Medicine, College of Chinese Medicine, China Medical University, Taichung 40402, Taiwan, China
2. Department of Chinese Medicine, China Medical University Hospital, Taichung, Taiwan 40447, China
3. School of Chinese Medicine, China Medical University, Taichung, Taiwan 40402, China
4. School of Post-baccalaureate Chinese Medicine, China Medical University, Taichung 40402, Taiwan, China
5. Research Center for Chinese Medicine & Acupuncture, China Medical University, Taichung 40402, Taiwan, China
6. Research Center for Traditional Chinese Medicine, Department of Medical Research, China Medical University Hospital, Taichung 40402, Taiwan, China

ABSTRACT

While much progress has been made in the field of hematopoietic stem cell transplantation (HSCT), headway in the promotion of recovery following this procedure has been limited. Data regarding the potential of Chinese herbal medicine (CHM) for patients with hematologic disorders who received HSCT are gradually increasing; however, these data are mostly in Chinese. Therefore, we set out to summarize the existing data. We searched PubMed, the Cochrane Library and the China National Knowledge Infrastructure and retrieved 9 clinical studies related to this group of patients, in whom CHM was used as an intervention. Of the 9 papers, 6 were published by the same group of researchers. The focus of the reviewed studies was heterogeneous, and the objectives varied widely. With the exception of one randomized control trial, all of the studies were retrospective and observational; the median number of patients was 11.5, with the largest study containing 104 patients. CHM treatment was largely divided into two stages: (1) pre-HSCT, which was initiated as soon as conditioning chemotherapy was administered and aimed to counterbalance the adverse effects of these potent agents; (2) post-HSCT, which began immediately after transplantation and was intended to promote engraftment, control graft-versus-host disease and prolong survival. In addition, the 9 Chinese materia medica most commonly prescribed (appearing in four studies) were: Shengdihuang (*Rehmannia glutinosa*), Baizhu (*Atractylodes macrocephala*), Renshen (*Panax ginseng*), Dangshen (*Codonopsis pilosula*), Maimendong (*Ophiopogon japonicus*), Danggui (*Angelica sinensis*), Taizhishen (*Pseudostellaria heterophylla*), Huangqi (*Astragalus membranaceus*) and Ejiao (*Equus asinus*).

Keywords: hematologic diseases; hematologic disorder; hematopoietic stem cells; Chinese herbal medicine; hematopoietic stem cell transplantation; review

Citation: Fleischer T, Chang TT, Yen HR. Post-hematopoietic stem cell transplantation in patients with hematologic disorders: Chinese herbal medicine for an unmet need. *J Integr Med.* 2016; 14(5): 322–335.

[http://dx.doi.org/10.1016/S2095-4964\(16\)60270-4](http://dx.doi.org/10.1016/S2095-4964(16)60270-4)

Received May 2, 2016; accepted July 4, 2016.

Correspondence: Hung-Rong Yen, MD, PhD; E-mail: hungrongyen@gmail.com

1 Introduction

For high-risk and relapsed patients, hematopoietic stem cell transplantation (HSCT) has been increasingly indicated as a standard treatment for many hematologic conditions. However, the prognosis following this therapy is still poor. Although 70% of post-HSCT relapsed acute myeloid leukemia (AML) and acute lymphocytic leukemia (ALL) patients achieve complete remission (commonly defined as a blast count <5%), the eventual median overall survival (OS) might not reach one year^[1]. One large study examining more than 2 000 AML or ALL relapse and refractory patients showed that the 3-year post-HSCT OS rates were 19% and 16%, respectively^[2]. Other than relapse, opportunistic infections can account for more than 10% of mortality in post-HSCT patients^[3]. Due to a compromised immune response, patients are susceptible to bacterial, fungal and viral infections during different stages following transplantation^[4]. Additionally, graft-versus-host disease (GVHD) continues to pose a threat to HSCT patients. Despite our growing understanding of GVHD, up to 80% and 34% of patients still experience GVHD in its acute or chronic forms; this has a detrimental impact on the quality of life and is linked to one-fourth of all deaths associated with transplantation^[3,5].

The immediate ‘aplastic phase’ following HSCT usually normalizes relatively quickly, and the neutrophil count may recover within 2 to 4 weeks. However, other cell compartments may require several months to return to normal levels, and B cells, representing humoral immunity, may require up to 2 years^[6]. Prognostic measures related to immune reconstitution have been accumulating over the years. Thymic T cell receptor excision circle has been used to measure thymic recovery post-HSCT and allows for the assessment of mature T cell populations in patients^[7]. Another example is the advancement in the measurement of minimal residual disease, which is used primarily as a prognostic tool for relapse and allows physicians to assess patients’ immune reconstitution^[8].

The vulnerability of the immune system following HSCT has motivated researchers to find ways to aid immune reconstitution. Several experimental methods are being developed to isolate and manipulate certain subtypes of donor T cells, which are then transfused into patients^[9,10]. The goal of these is to aid the patients’ weakened immune systems and ward off opportunistic infections while maintaining GVHD at a reasonable level. Different approaches that are currently being researched include the infusion of regulatory T cells, which prevent GVHD while not interfering with the beneficial effects of graft versus leukemia (GVL)^[11,12]. Other approaches include the administration of specific cytokines that are known to

induce the proliferation of key cells in the line of defense, such as natural killer (NK) cells and CD8⁺ T cells^[6,13].

However, these methods are still in the early stages of research and do not quicken immune reconstitution *per se*. To date, the only standardized post-transplant treatment administered to quicken immune reconstitution is granulocyte colony-stimulating factors. Drugs, such as filgrastim and pegfilgrastim, are commonly used to manage chemotherapy-induced neutropenia, from which HSCT patients may suffer^[14]. In light of the above, it is clear that there is a need to develop interventions that actively help post-HSCT patients cope with the natural recuperation process of transplantation as well as decrease the odds of relapse.

Many Chinese *materia medica* (CMM) formulations are believed to exert different types of influences on the immune system, both quickening and restraining. These influences may be beneficial to post-HSCT patients in different ways. For example, both *in vitro* and *in vivo* studies have demonstrated that some commonly used herbs, such as Renshen (*Panax ginseng*), Huangqi (*Astragalus membranaceus*), Danggui (*Angelica sinensis*) and Dihuang (*Rehmannia glutinosa*), may promote the activation of CD34⁺ hematopoietic cells and related growth factors through various pathways^[15–37]. The constituents of Danggui have also been shown to enhance hematopoiesis directly and indirectly by stimulating macrophages, fibroblasts and lymphocytes in the hematopoietic inductive microenvironment^[37]. Conversely, Renshen, Shaoyao (*Paeonia lactiflora*) and Gancao (*Glycyrrhiza glabra*) have been shown to activate and increase the numbers of T-regulatory cells, possibly counteracting the sometimes detrimental complications of GVHD^[38–42]. While current data are limited to these few herbs from the CMM, there is no reason to assume that they are the only CMM preparations beneficial to post-HSCT patients. Moreover, the effects of the above studies relate to mechanisms of recuperation in post-HSCT conditions and may thus address some immune system complications that these patients face.

Because no standard treatment has been established that improves the health or quality of life for post-HSCT patients, we sought to understand better the potential role that Chinese herbal medicine (CHM) might have. Unfortunately, there is a lack of high-quality prospective clinical trials to date. Therefore, we conducted this review to summarize the currently research on CHM for post-HSCT patients.

2 Review

2.1 Inclusion and exclusion criteria

Eligible studies included all instances where CHM was used in a clinical setting to treat patients with hematologic

Download English Version:

<https://daneshyari.com/en/article/8693339>

Download Persian Version:

<https://daneshyari.com/article/8693339>

[Daneshyari.com](https://daneshyari.com)