

Radiodermatitis in the Field of Traditional Persian Medicine; A Narrative Review

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ABSTRACT

Background: Radiotherapy comprises one of the treatment modalities offered in the treatment of various types of cancer. Acute radiation-induced dermatitis is a common complication of radiotherapy. Interestingly, manifestations consistent with radiodermatitis have been reported in the literature of Traditional Persian Medicine (TPM). The purpose of this narrative review was to achieve an adaptive understanding of radiodermatitis from the perspective of TPM and semiotics.

Method: In this review, all new studies pertaining to radiodermatitis performed according to TPM theories were reviewed along with all TPM references. The Scopus, PubMed, Cochrane Library, Embase, Google Scholar, ISI Web of Science, SID, and Magiran databases were scanned with the terms 'radiodermatitis' or 'radiation dermatitis' or 'radiation burn' or 'radiation-induced skin burning' or 'radiation-induced dermatitis' and 'Persian medicine.' All articles published until the end of February 2021 were included.

Results: Similarities were found between the findings of three novel TPM research articles and the texts of 36 TPM reference books. Evidence was found in favor of some consistence between thermal and chemical burns in TPM and radiodermatitis in modern medicine, although the precise equivalent for radiodermatitis in TPM could not be delineated.

Conclusion: According to the clinical manifestations and pathophysiology of radiodermatitis described in modern medicine, it seems that radiodermatitis can be considered as a compound disease similar to *Ihrāq*.

KEYWORDS

Radiodermatitis, Persian Medicine, Cancer, Radiotherapy.

Introduction

Cancer represents one of the most challenging health problems in both developed and developing countries and is responsible for an immense rate of mortality worldwide. Various treatments such as surgery, chemotherapy, and radiotherapy can be used to treat different types of cancer [1, 2]. Radiotherapy is currently used in many cases of breast cancer as part of standard adjuvant therapy to minimize local recurrence and improve patient survival [3-5]. Nowadays, despite improvements in radiotherapy techniques, acute and chronic skin reactions remain common side effects of ionizing radiotherapy. The severity of radiodermatitis is related to various factors such as the patient's age, the presence of underlying diseases (e.g., diabetes), obesity, breast size, genetic factors, radiation dose, radiation duration, radiotherapy technique, and the area of skin being treated [3, 6, 7]. Acute dermatologic complications from radiotherapy may range from simple erythema and discoloration to edema, wet desquamation, bleeding, and necrosis [8, 9].

In Traditional Persian Medicine (TPM), such skin changes have been referred to using terms such as '*Ihrāq*' or 'burn', and several treatment options have been described, one of which is topical therapy [10, 11]. It goes without saying that in the TPM literature, no equivalent is found for radiodermatitis because ionizing radiation is required to cause this complication. Nonetheless, understanding the similarity of its signs and symptoms with what TPM scholars have described as *Ihrāq* can play an important role in treating and preventing this complication in cancer patients. By adapting our understanding on this condition, a wide range of valuable herbal medicines and natural and traditional products can be introduced, each of which may prove useful in the prevention and treatment of radiodermatitis [12]. Hence, the aim of this narrative review was to achieve an adaptive understanding of radiodermatitis from the perspective of TPM and semiotics.

Methods

This study was a narrative review of the most important sources of TPM and modern medicine. For this purpose, 36 TPM reference books published between the 4th and 13th centuries AH were accessed from the National Library of Iran (appendix 1). We also searched the Scopus, PubMed, Cochrane Library, Embase, Google Scholar, and ISI Web of Science databases, along with two modern Persian databases (SID & Magiran). The following terms together with their Persian equivalents were used in our search strategy: 'radiodermatitis' or 'radiation dermatitis' or 'radiation burn' or 'radiation-induced skin burning' or 'radiation-induced dermatitis' and 'Persian medicine.'

All peer-reviewed English and Persian articles (original articles, reviews, case studies, and letters to the editor) published until the end of February 2021 were included in our study. We excluded articles that had no full text available or did not match our search topic. First, the title and abstract of each article was read by the first two authors; then, in the absence of the above exclusion criteria, the entire article was studied by the third and fourth authors. If all criteria were not met, the article would be removed from the study. Secondary articles were found by scanning the references of the primary manuscripts (snowball method). For the study of the TPM texts, all books published by great TPM scholars in different centuries available in the form of microfilms, electronic files, or hard copies were evaluated and the important findings were recorded. Findings from both the traditional literature and novel databases were independently reviewed by two authors and, in the case of discrepancy, discussed collectively among all authors.

After deleting duplicates and removing inconsistent articles, 10 articles from the international databases were screened, though no relevant papers were found in the Iranian databases. Among the 10 papers, three were eligible for inclusion, all being experimental clinical studies. Out of 36 TPM books reviewed, only 19 met the necessary criteria for inclusion in the study. It should be noted that no review studies in this field were found in the international databases.

Results

Radiodermatitis in Modern Medicine

Radiotherapy fulfils a crucial role in the treatment of cancer in modern medicine. Recent studies have shown that about two-thirds of cancer patients receive radiotherapy, and among them, over 95% show the signs and symptoms of radiodermatitis [2, 13]. As one of the predominant complications of cancer treatment, radiodermatitis asserts different effects on the patient, including reduced quality of life and delays in radiotherapy [14]. Despite the range of manifestations and consequences of this complication, a proven treatment is yet to be available, with a supportive role mostly being offered through the application of a range of treatment modalities [15]. This is while there has been a great deal of interest in using traditional, complementary, and alternative therapies in various topical or systemic forms for treating this challenging condition [16].

Mechanism

Inflammation and oxidative stress have been introduced in novel medicine as the two most important mechanisms through which radiodermatitis occurs [14]. Through the interaction of these two factors, different skin reactions occur, classified as mild to severe acute or chronic reactions. In mild cases, erythema or desquamation is seen, while in severe cases, bleeding and necrosis occur in the skin. Various intrinsic (e.g., radiation sensitivity) and extrinsic

(e.g., radiation intensity) factors can affect the severity of radiodermatitis [15, 17].

Novel Findings

In the study of Hemmati et al., the positive effect of oral Curcumin on preventing radiodermatitis in a six-week radiotherapy course was recorded in comparison with a control group. In this article, the anti-inflammatory effects of turmeric in TPM and the exact correspondence between radiodermatitis and the condition and treatment described in TPM being mentioned [18, 19].

In the second article, which examined the effect of the alcoholic extract of *Adiantum capillus-veneris* on chronic wound healing, the therapeutic effects of TPM in the field of medicinal plants were explored. Accordingly, the preventive effects of this medicinal plant against fibroblast damage induced by free oxygen radicals were noted [20]. This anti-inflammatory effect has also been emphasized in the books of TPM [21].

The third and final article investigated the preventive effect of *Aloe vera* against radiodermatitis in a randomized clinical trial. In this study, the effect of this plant on increasing skin moisture and the theory of TPM regarding its use in the treatment of traumatic dermatitis were mentioned. The researchers demonstrated a significant effect of the topical use of the mentioned agent among cancer patients [22], which is in line with the recommendations provided in historic TPM sources [11].

Radiodermatitis in Traditional Persian Medicine

In TPM, diseases are divided into two general categories: singular diseases and compound diseases. When more than three types of singular diseases [*Máráz-e mofrád*] prevail simultaneously, a compound disease [*Máráz-e morákkáb*] occurs [23]. Due to the fact that radiotherapy was not performed in the past, an exact equivalent for the term 'radiodermatitis' is not available in the historic sources of TPM. However, considering the clinical manifestations and pathophysiology of radiodermatitis, it seems that it can be considered as a compound disease that is suddenly caused by an extrinsic factor [24]. This is such that ionizing rays of radiation (an extrinsic factor) cause organ detachment [*Táfároq-e áazā*] and dystemperament [*Sūe mizāj*], followed by swelling in the organ exposed to the radiation, with the manifestations varying according to the intensity and duration of contact with the radiation. In TPM, burns give rise to manifestations such as erythema [*Homrát*], blisters [*Náfāt*], burning pain [*Vájá*], and swelling [*Āmās*] [10].

Also, according to the severity of manifestations in TPM, burns can be divided into three types: without blisters, with blisters, and wounds that are difficult to heal [11]. In terms of the cause of burns, TPM recognizes seven categories: burns due to fire, burns from hot oil, burns from boiling water, burns from lightning, sunburns, chemical burns, and traditional depilatory burns [10, 24].

Mechanism in Traditional Persian Medicine

The references of modern medicine regard radiodermatitis as the consequence of ionizing radiation, which directly or indirectly (through the production of oxygen radicals) exerts damage to DNA [14]. Given that the clinical manifestations of radiodermatitis are similar to those described in TPM (burning, swelling, blistering, and redness), it may be possible to consider radiodermatitis equivalent to *Ihrāq*, classifying it among the burns caused by chemicals and heat [6, 10, 11].

Traditional Persian Medicine Findings

Due to the fact that in the process of radiotherapy, inflammatory factors and cytokines such as interferon-1 and tumor necrosis factor- α (TNF- α) are released and give rise to inflammatory and symptoms such as burning, pain, and itching, it may be possible to trace the role of the bile humor in this process [25]. In our examination of other skin diseases mentioned in the historic TPM books, we found no other conditions that correlate with radiodermatitis (Table 1).

Table 1. Characteristics of selected skin lesions according to Traditional Persian Medicine (TPM) and modern

medicine

Skin lesion in TPM	Latin equivalent	Humor(s) involved	Characteristics in modern medicine
<i>Jomrá</i>	Carbuncle	Coarse bile humor with blood humor	Accumulation of several interconnected infectious follicular abscesses; deep and highly painful
<i>Jāversiyá</i>	Miliary	Dilute bile humor with phlegm humor	Clear or red papules that develop due to obstruction of the sweat gland ducts
<i>Sherā</i>	Urticaria	Blood humor with phlegm humor	Red or pink plaques that are edematous (non-pitting); may be surrounded by a white to pink halo
<i>Homrá</i>	Erysipelas	Pure bile humor or bile humor mixed with blood humor	a type of acute inflammatory cellulitis that affects the dermis and upper subcutaneous tissue and has a distinct margin
<i>Feleghmūnī</i>	Phlegmona	Blood humor	Inflammation of the subcutaneous tissue that has an infectious or non-infectious cause

Discussion

The current study examines and compares radiodermatitis in modern medicine and TPM and summarizes the evidence that exists in both sources. During radiotherapy, when the cells are destroyed, an inflammatory response is triggered [26]. Inflammation is a complex biological response of the vasculature to harmful stimuli, such as pathogens and damaged or stimulated cells. In fact, inflammation is a protective effort by the body, aiming to eliminate harmful stimuli while initiating the healing process [27]. The inflammatory response involves various systems, including the local vasculature, the immune system, and various cells within the damaged tissue [28]. In radiotherapy, skin erythema is caused by dilation of the dermal capillaries, while edema, pruritus, and burning of the skin occur secondary to the permanent destruction of sebaceous glands and sweat glands after several sessions of radiotherapy [29]. Burning, pruritus, and pain also begin with the release of mediators such as histamine, serotonin, and prostaglandins [30]. Therefore, it seems that this study confirms the anti-inflammatory effects of traditional treatment modalities for burns caused by chemicals and heat, which are emphasized in the books of TPM scholars.

As mentioned in the explanation of radiodermatitis in TPM, symptoms such as redness, burning, pain, and blisters are similar to those seen in hot burns and swellings, especially inflammation caused by bile humor [24]. These types of swelling can be treated using cooling agents and humidifying agents [21]. In TPM, the treatment of burns is topical, delivered across two steps. The first is cooling, which works to balance and eliminate heat damage and is effective in preventing the formation of blisters at the burn site. The second step is only considered if blisters form, in which case the use of drying agents with a moderate temperament in heat and cold is recommended [11, 24]. These findings could lead to the introduction of new therapies with herbal or natural products, minimizing the incidence of radiodermatitis [12].

Conclusion

The findings of the present study facilitate a better understanding of radiodermatitis from the perspective of TPM. Radiotherapy was not performed in the past and the exact equivalent for radiodermatitis is not included in the TPM texts. However, considering the clinical manifestations and pathophysiology of radiodermatitis described in modern medicine, it seems that radiodermatitis can be considered as a compound disease similar to *Ihrāq*, occurring due to external traumas such as heat.

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