Comparison of Skin Erythema and Melanin Level in Sulfur Mustard Induced Chronic Skin Lesions and Normal Skin

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Abstract

Background: Sulfur mustard gas is a chemical agent that has been used in many wars, especially in Iran-Iraq war. This chemical agent affects many organs including lungs, eyes and skin, causing numerous acute and chronic lesions including erythema and hyperpigmentation, respectively. This study was conducted to evaluate erythema and melanin in subjects with a history of exposure to sulfur mustard.

Methods: This case-control study was done on 309 subjects. They were divided into four groups: sulfur mustard-exposed patients with skin lesions (n=87), sulfur mustard-exposed cases without current skin lesions (n=71), non sulfur mustard-exposed patients with dermatitis (n=78) and normal controls (n=74). Erythema and melanin were measured in 4 areas (forehead, suprasternal, palm and back of hands) by Mexameter MX18 (Courage-Khazaka, Germany).

Results: Erythema was significantly lower in suprasternal and palmar aspect of hands in sulfur mustard-exposed patients with dermatitis ($P<0.05$) while there was no significant difference in other areas. In terms of melanin, there was a significant difference in the dorsal aspect of hands in all four groups ($P<0.05$), where patients with dermatitis (both sulfur mustard exposed and normal population) had higher levels of melanin, probably due to pruritus in such areas. Forehead melanin of the normal population was also significantly lower than other three groups ($P<0.05$) while there was no significant difference between the melanin level of sulfur mustard exposed subjects (with or without dermatitis) and patients with dermatitis.

Conclusion: Sulfur mustard contact can affect erythema and melanin content of the skin. *(Iran J Dermatol 2008;11: 151-154)*

Keywords: skin erythema, skin melanin, sulfur mustard

Introduction

Skin, according to its expansion, is the most vulnerable organ to damage when exposed to sulfur mustard (a blistering agent).[1] This agent reacts with skin proteins and degrades the structure of both cells and underlying extracellular matrix and also causes severe inflammation of the skin causing erythema, itching and vesicles in its acute phase and xerosis and itching in the chronic phase. Altered pigmentation often manifests as a late complication.[2,3,4]

Khateri S et al. reported skin lesions in 24.5% of 34000 Iranian mustard agent victims. Xerosis and pruritus are the main complaints of patients suffering from skin lesions.[5] Moreover, there are many other patients who refer to dermatology clinics complaining of xerosis and itching without any documented exposure to sulfur mustard. Hence, an objective method seemed necessary to distinguish veterans from normal population with xerosis. In this study, we measured some biophysical characteristics of skin (skin erythema and melanin) in patients who had a history of contact with sulfur mustard.

Materials and Methods

This case-control study was conducted on 87 sulfur mustard-exposed patients with current skin

lesions, 71 sulfur mustard-exposed cases without current skin lesions, 78 non sulfur mustard-exposed participants with various forms of dermatitis and 74 normal controls. All subjects were males and age-matched.

Skin type, xerosis, lichenification, post lesional pigmentation and cherry angioma were evaluated by a dermatologist, and then the biophysical characteristics of the skin were measured at four clinically normal-appearing locations of the body skin, i.e. the forehead, suprasternal, and palmar and dorsal aspects of hands using the following noninvasive biophysical methods. Before the measurements were taken, participants were asked not to use any kind of cream on mentioned areas and were acclimatized to a room temperature of 20°C with a relative humidity of 35% for 15 minutes. They had their last hygiene toilet not less than 3 hours before the measurements.

Erythema and melanin were measured using Mexameter MX18 (Courage & Khazaka electronic GmbH, Germany), a narrow-band simple reflectance meter.

The collected data were analyzed with SPSS-13 software using independent t-test, analysis of variance (ANOVA) and Kruskal-Wallis test. This study was approved by the ethics committee of our university and was performed according to the Declaration of Helsinki Principles. All of the participants were instructed about the study and an informed consent was obtained from each one.

Results

Three hundred and ten participants were included in the study: 87 (%28.1) sulfur mustard-exposed patients with current skin lesions (group 1), 71 (%22.9) sulfur mustard-exposed cases without current skin lesions (group 2), 78 (%25.2) non sulfur mustard-exposed patients with dermatitis (group 3) and 74 (%23.8) normal controls (group 4). All of them were males with a mean age of 44.0 ± 6.7, 41.9 ± 5.9, 43.8 ± 9.3 and 44.8 ± 8.9, respectively, which were not significantly different (P=0.146). Sixty-seven (77%) patients in group 1 and 45 (63.4%) patients in group 2 recalled initial skin lesions including erythema, edema, and vesicles with an itching and burning sensation a few minutes to several hours after they had come in contact with sulfur mustard.

The frequency of skin types and skin lesions including xerosis, lichenification, post-lesional hyperpigmentation and cherry angioma are highlighted in table-1. There was no significant discrepancy in skin types between groups. Diffused cherry angioma, unlike local cherry angioma, was significantly more frequent in sulfur mustard-exposed participants (P=0.047).

Xerosis, post-lesional hyperpigmentation and lichenification were significantly more common in dermatitis patients with skin lesions either due to sulfur mustard or else (P<0.05).

Skin erythema and melanin were measured in subjects in four anatomically different areas including forehead, suprasternal, and palmar and dorsal aspects of hands. (Figure-1)

Erythema was significantly lower in suprasternal and palmar aspect of hands in veterans with dermatitis (P<0.05) while there was no significant difference in other areas. In terms of melanin, there was a significant difference in the dorsal aspect of hands in all four groups (P<0.05), where patients with dermatitis (both sulfur mustard-exposed and non-exposed) had higher levels of melanin. Forehead melanin of the normal population was also significantly lower than other three groups

Table 1: *Fitzpatrick skin types and skin lesions four groups of participants.*

		Sulfur mustard exposed with skin lesion (%)	Sulfur mustard exposed without current skin lesion (%)	Non sulfur mustard-exposed patients with dermatitis (%)	Normal population (%)	P-Value
Fitzpark skin type	I	1.1	1.4	0	0	.408
	II	2.3	0	1.3	0	
	III	26.4	23.9	30.8	37.8	
	IV	64.4	73.2	62.8	60.8	
	V	5.7	1.4	5.1	1.4	
Xerosis	Yes	80.5	18.3	73.1	0	<.001
	No	19.5	81.7	26.9	100	
Post lesional hyperpigmentation	Yes	82.8	4.2	53.8	0	<.001
	No	17.2	95.8	46.2	100	
Lichenification	Yes	66.7	1.4	15.4	0	<.001
	No	33.3	98.6	84.6	100	
Cherry angioma	Diffuse	4.6	1.4	0	0	.201
	Local	6.9	12.7	9.0	4.1	
	No	88.5	85.9	91.0	95.9	

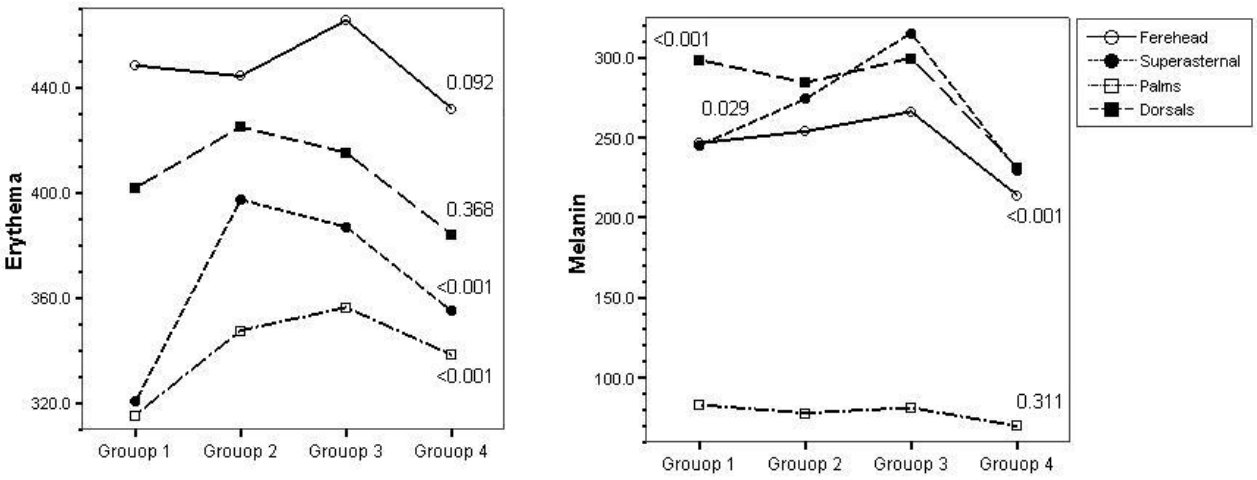

Figure 1: *Skin biophysical characteristics in four groups. Group 1: sulfur mustard exposed patients with skin lesions (n = 87); Group 2: sulfur mustard exposed patients without current skin lesions (n = 71); Group 3: dermatitis patients without exposure to sulfur mustard (n = 78); Group 4: Normal controls (n = 74)*

(P<0.05). However, there was no significant difference between the melanin level of sulfur mustard-exposed subjects (with or without dermatitis) and patients with dermatitis.

Discussion

Sulfur mustard [bis(2-chloroethyl)sulphide; SM] is a leading blistering agent and one of the major chemical warfare agents used during World War I.[4,6] It highly affects eyes, skin and the respiratory system locally. Absorption of large amounts of SM can damage rapidly proliferating cells of the bone marrow and may result in both short-term and long-term impairment of the immune system.[7-9]

The SM agent damages the structure of skin cells and underlying extracellular matrix and by release of cytokines, including IL-1-beta, IL-6, IL-8 and tumor necrosis factor alpha, results in severe inflammation of the skin.[10] After exposure, the skin lesions begin after a latent period of about 4-6 hours. Itching, burning, and erythema appear initially. When exposed to low doses for a short period of time, these symptoms and signs may heal without blister formation, but hyperpigmentation usually follows after the erythema.[11] There may also be hypopigmentation due to melanocyte destruction.[12] At higher doses, vesicle formation at the periphery of the erythematous area may first appear which merge into bullae. Blisters tend to form within 24 hours of exposure, but sometimes appear later; they generally concentrate in warm moist areas such as the groin and axilla. Lesions tend to heal slowly, and often ulcerate and vesicate repeatedly.[11]

More than 100,000 Iranians were exposed to sulfur mustard during the Iran and Iraq war and one-third of them are still suffering from chronic effects.[4]

Balali-Mood evaluated a group of Iranian veterans injured by mustard gas during the Iran–Iraq was two years after the exposure. Skin pigmentation disorders were seen in 41% of them.[13]

In another study conducted by Balali-Mood et al. on 40 sulfur mustard-exposed victims who were injured 16-20 years ago, skin xerosis of the lower extremities was reported as the most prominent skin lesion.[5]

Fekri and Janghorbani found a significant association between SM exposure and late cutaneous lesions such as dry skin, hyper- and hypopigmentation, local hair loss, eczema and chronic urticaria.[14]

Regular patient follow-ups suggest that, except for dry skin and its associated itching sensation, most skin complications generally improve in the course of time. Dry skin and itching tend to intensify as patients become older and are regarded as the principal late skin complaints of these patients.[15,16] The results of our study also illustrated significantly higher incidence of post-lesional hyperpigmentation in patients with dermatitis (with or without sulfur mustard exposure) which is strongly associated with pruritus. Therefore, the main cause of higher melanin level in subjects with dermatitis (either sulfur mustard exposed or non-exposed) seems to be hyperpigmentation due to pruritus.

Injuries that result in erythema and edema without vesicle formation are almost always followed by complete healing and no residual effects.[15,16] Our results also showed no significant difference in skin erythema.

Diffuse cherry angiomas were demonstrated in previous surveys.[17] Balali-Mood et al. recorded cherry angiomas in 37.5% of SM-exposed Iranian veterans 16 to 20 years after exposure. 5 In another study, Firooz et al. also reported a higher prevalence of cherry angiomas (a mean of 18) in patients who had developed skin blistering after contact with SM. Most of the lesions were detected at the sites of healed blisters on trunk, arms and face.[18]

Moradi and Aghaei found a mean of 13.4 cherry angiomas in 36% of SM-exposed patients.[19] The frequencies of multiple cherry angiomas in these two studies are roughly estimated to be higher than the frequency expected in the normal population. In our study, diffuse cherry angioma, unlike local cherry angioma, were significantly more frequent in sulfur mustard exposed group (P=0.047).

In conclusion, authors believe that sulfur mustard agent can affect biophysical characteristics of the skin, particularly melanin, due to pruritus as one of the main complaints of veterans even several years after exposure.

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