

# Sildenafil is an Effective Therapy for Treatment of Chilblain in Female Patients with Bacteriological Study of Ulcerative Lesions

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## Abstract

**Background:** Chilblains, also called pernio or perniosis, are localized, tender, inflammatory, erythematous, often itchy lesions, which may blistered or ulcerated, caused by continued exposure to cold above the freezing point. More commonly seen in children, women and persons with low body mass index, with a genetic predisposition. Many prophylactic measures are used, and therapeutic remedies for the treatment of developed chilblains, like nifedipine, diltiazem, nicotinic acid derivatives, tamoxifen and minoxidil topically.

**Objectives:** The aim of the present study was to evaluate the effectiveness of sildenafil in the treatment of chilblains in female patients.

**Patients and methods:** Sixty five female patients with chilblain were seen in a private clinic in Kalar city, Al-Sulaimania Province, Iraq, for the period from the first of October 2014 to the thirty of September 2016, their ages ranged from 10-25 years (mean 16±8). The disease was diagnosed clinically and the patients were evaluated for different data, and identification of bacteria which complicate some patients with ulcerative lesions and all patients treated by sildenafil tablet (50mg, once daily after meal), for 7-10 days and assisted clinically (subjectively) for resolution of the disease.

**Results:** Sixty patients (92.3%) out of (65) studied patients shows complete clearance of the disease clinically within 7-10 days of sildenafil treatment (50mg, tablet, once daily orally after meal). Five patients (7.7%) shows partial improvement of the disease with persistence of the signs and symptoms. *Staphylococcus aureus* was isolated from 20(30.76%) patients. Ten patients (15.4%) developed flushing and hotness of the face with nasal stiffness and 5 patients (7.7%) developing gastric upset.

**Conclusion:** It was concluded that sildenafil was an effective therapy for the treatment of chilblain in female patients, although it was associated with some side effects.

**Key words:** Chilblain, nifedipine, diltiazem, sildenafil, flushing

## INTRODUCTION

Chilblains, also called pernio or perniosis, are localized, tender, inflammatory, erythematous, often itchy lesions, which may be blistered or ulcerated, caused by continued exposure to cold below the freezing point.<sup>[1,2]</sup> Dampness and wind that increase thermal conductivity and convection play a part, absolute temperature is less important than the cooling of nonadapted tissue and the condition shows a genetic predisposition.<sup>[1]</sup> Chilblains

have been described most often in temperate regions, where winters are occasionally cold and damp, and are seen less often in very cold climates, where well-heated houses and warm clothing are available. Both acrocynosis and chilblains appear to be more common in children, women, and persons with low body mass index, pregnancy may have a beneficial effect on chilblain.<sup>[3]</sup> Immunohistochemistry revealed increase in nerve bundles in the papillary dermis.<sup>[4]</sup> However,

chilblains do not always occur at the time of maximum cold.<sup>[5]</sup>

Chilblains develop acutely as a single or multiple, burning, erythematous, or purplish swellings. Patients may complain of itching, burning, or pain, in severe cases blisters, pustules and ulceration may occur. Characteristic locations include the proximal fingers and toes, planter surfaces of the toes, heels, noses and ears, but other sites like calves and thighs can be affected.<sup>[1,6-8]</sup> Lesions usually resolved in 1-3 weeks, but may become chronic in elderly people with venous stasis.<sup>[9]</sup> Tight garments such as gloves, stockings and shoes are especially to be avoided in cases in which, there is also peripheral vascular diseases.<sup>[1,10]</sup> Chilblains can be idiopathic (spontaneous and unrelated to an other diseases), but may also be a manifestation of another serious medical condition that need investigations, e.g. systemic lupus erythematosus.<sup>[1,9]</sup> Idiopathic perniosis is characterized histologically by edema of the papillary dermis and the presence of superficial and deep perivascular lymphocytic infiltrates, necrotic keratinocytes and lymphocytic vasculitis also have been reported.<sup>[1,6,11,12]</sup>

The most important point in the management of chilblains is prophylaxis, through the use of adequate, loose, insulating clothing and appropriate warm housing and workplace. Maintaining the blood circulation by avoiding immobility is also helpful, a short course of ultraviolet light therapy at the beginning of winter is recommended, avoid rapid changes in temperature, soaking in warm water with Epson salts for 15-20 minutes, 3-4 times a day and avoid very hot water.<sup>[1,6,13]</sup> Once chilblains occur, treatment is symptomatic with rest, warmth and topical antipruritics (topical steroid creams), calcium channel-inhibiting drugs may be effective in the treatment of sever recurrent perniosis (e.g. nifedipine), diltiazem, nicotinic acid derivatives, tamoxifen and minoxidil topically as a vasodilator may also be used,<sup>[14-17]</sup> In cases of crippling severity, thyrocalcitonin and heamodilution may be helpful.<sup>[1]</sup> Sildenafil is one member of phosphodiesterase type-5 (PDE5) inhibitors, which hydrolyses cyclic guanylate monophosphate specifically to 5 guanylate monophosphate, promoting corporal vascular relaxation and penile erection in response to sexual stimulation. Oral PDE5 inhibitors have afforded effective and well tolerated treatment for erectile dysfunction. PDE5 have a potential benefits in divers non-sexual applications, including, cardiovascular, pulmonary, cutaneous, gastrointestinal, neurological and reproductive disorders.<sup>[18]</sup> Sildenafil is used in the treatment of Raynaud's phenomenon resistant to vasodilator therapy in dose of (50mg) twice daily for one month.<sup>[19]</sup> The aim

of the present study was to evaluate the effectiveness of sildenafil in the treatment of chilblains in female patients.

## PATIENTS AND METHODS

Sixty five female patients with chilblain (perniosis) were seen in a private clinic in Kalar City – Al-Sulaimania Province, Iraq, for the period from first of October 2014 to the thirty of September 2016. Their ages ranged from (10-25) years with a mean age of (16±8) years, all patients were females, because males were excluded from the study due to sexual excitation in males. The disease was diagnosed clinically, and all patients were attended the clinic during the winter time, where the temperature around zero C°. They were fully interrogated regarding the age, job and outdoor working, exposure to cold weather and damping, humidity, previous history of the same disease and therapy used, family history of the same condition and personal and family history of other medical disease, like systemic lupus erythematosus, systemic sclerosis, Raynaud's phenomenon and disease and hypercrioglobulinema, to be excluded from the study, so all patients had idiopathic chilblains. Clinically patients had either bullous, erosive and ulcerative lesions, or only erythema and swelling with sever itching. Some patients with ulcerative lesions developed secondary bacterial infection, and swabs were taken from them, and cultured on different culture media and submitted to a serial of different biochemical tests for diagnosis of type of bacteria which cause infection. All patients were treated by sildenafil tablets (50mg once daily orally after meal) for 7-10 days, and those with bacterial infection were treated by cefexem 400mg daily, orally for 7 days, and all patients were assisted clinically after the course of treatment, to evaluate the response of the disease to the therapy, i.e. the evaluation was subjective according to the clinical assessment by the dermatologist and patients satisfaction. If the lesions and symptoms were disappeared, means the response was complete, and if some signs and symptoms were persisted, the response was partial.

## RESULTS

The study revealed that the patients had an idiopathic chilblain (i.e. non of them had medical disease associated with chilblain), with clinical features consisting of erythema, swelling of the fingers and toes in 40 (61.54%) patients (figure-1), and some patients 25 (38.46%) had bullea, erosions and ulcerations, associated with sever itching and burning sensation (figure-3) and 20 (30.76%) patients of those with ulcerative lesions developed secondary bacterial infections. Sixty patients (92.3%) out of (65) patients,

shows complete clearance of the disease, within 7-10 days of treatment with sildenafil (50mg tablet once daily orally) (figure-2,4) and (5) patients (7.7%) shows partial improvement with persistence of erythema, swelling, itching, burning sensation and sometimes erosions and ulcerations. Bacteriological study of those with secondary bacterial infections, only staphylococcus aureus was isolated. Ten patients (15.4%) developed flushing and hotness of the face with nasal stiffness and (5) patients (7.7%) developed gastric upset.



**Figure 1:** Chilblain of feet with erythema and swelling before treatment.



**Figure 2:** Patient in figure-1 after treatment with sildenafil.



**Figure 3:** Chilblain of foot with erosive, bullous and ulcerative lesions with infection, before treatment with sildenafil and cefexem.



**Figure 4:** Patient in figure-3 after treatment with sildenafil and cefexem.

Table shows Clinico - soscio-demographic information of the patients

| Total No | Patients with swelling, edema, erythema |       | Patients with erosions and ulceration |       | Complete clearance |      | Partial improvement |     | Side effects |      | Bacterial infections |       |
|----------|---|-------|---------------------------------------|-------|--------------------|------|---------------------|-----|--------------|------|----------------------|-------|
|          | No                                      | %     | No                                    | %     | No                 | %    | No                  | %   | No           | %    | No                   | %     |
| 65       | 40                                      | 61.54 | 25                                    | 38.46 | 60                 | 92.3 | 5                   | 7.7 | 15           | 23.1 | 20                   | 30.76 |

## DISCUSSION

We Chilblains were a relatively common skin disease in countries with cold winter, and more common in

females than males, specially in teen ager groups, most probably due to hormonal changes at menarche ages of female patients. Also the disease was most commonly seen in outdoor workers, due to excessive exposure to

cold weather and in those with genetic predisposition to develop the disease. Regarding the age and gender the study was concordant with other study.<sup>[1,10]</sup> Regarding the study there was a limited number of studies in which sildenafil used to treat patients with chilblains, although sildenafil was used as trial in the treatment of Raynaud's phenomenon and disease, which were resistant to vasodilator therapy and giving a good results and satisfaction by the patients using this drug.<sup>[26]</sup> Chilblains were caused by exposure to cold around freezing point, which cause vasoconstriction of peripheral blood vessels and appearance of signs and symptoms of the disease and the disease resolute spontaneously with in (1-3)weeks with discontinuation of exposure to cold, so the use of therapy was to control the disease in presence of exposure to cold and the mode of action of sildenafil was most probably through vasodilatation of the peripheral circulation and improvement of perfusion, which result in improvement of chilblains and resolution of signs and symptoms.<sup>[25]</sup> *Staphylococcus aureus* was the only bacteria isolated from the lesions with bacterial infection, most probably due to the *staphylococcus aureus* carrier state in a bout (35%) of general population, the results was concordant with other studies.<sup>(1)</sup> Because the effects of sildenafil were not restricted to the skin and may result in some troublesome side effects, but it appears in this study to be an effective therapy in chilblains with cure rate of (92.3%). In comparison with other drugs used in treatment of chilblain,<sup>[21-24]</sup> like nifedipine, diltiazem, tamoxifen, and nicotinic acid, in which response of the disease ranging from 50-85%, sildenafil appears to be more effective, specially for severe and resistant cases and those with erosions and ulcerations. Conclusions: It was concluded that sildenafil was a good therapy for treatment of severe and resistant cases of chilblains, although may be associated with some side effects.

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