

Treatment of perniosis with oral tadalafil, pentoxifylline or prednisolone A therapeutic comparative study

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Abstract:

Background: perniosis is a common dermatological problem. Different modalities of treatment are available with conflicting results and no single effective therapy is universally accepted.

Objective: To evaluate the effectiveness of oral tadalafil and compare it with pentoxifylline or prednisolone in treatment of perniosis

Patients and methods: This was a therapeutic comparative trial conducted in the department of Dermatology, Baghdad Teaching hospital, Baghdad, Iraq between November 2011 and March 2014.

Fifty eight patients with perniosis were enrolled in this study, and divided into 3 groups. Group (A) comprised 19 patients who received oral tadalafil (5 mg once daily); group (B) comprised 18 patients who received pentoxifylline tablet (400 mg three times daily) and group (C) included 21 patients who received prednisolone 15 mg twice daily. The treatment duration was 2 weeks. All patients did not receive any treatment before the study. A severity score was proposed taken in consideration the number of finger/ toes, type of lesion, coldness, cyanosis and itching

Results: Forty seven patients completed the study. Their ages ranged from 13-43 with a mean \pm SD of 22.38 \pm 6.99 years. Thirty three patients were females (70.21%) and 14 were males (29.79%).

The percentage of improvement was 50.65, 44.16 and 31.51% for the groups A, B and C respectively.

Conclusion: Tadalafil has a superior effect over pentoxifylline. The latter has a better effect than prednisolone.

Key words: Tadalafil, pentoxifylline, prednisolone, perniosis, chilblains.

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Introduction:

Perniosis (chilblains) is a localized disease which presents as inflammatory, erythematous or purple, intensely pruritic or painful acral lesions. It is seen in susceptible individuals after prolonged exposure to nonfreezing cold temperatures and damp conditions (1, 2).

Typically there is severe localized cold erythema and swelling, but in severe cases, blistering and ulceration may develop (3). Local remedies are of little help, but many systemic agents had been used in the treatment of perniosis (3).

Tadalafil is a long-acting, highly specific phosphodiesterase type 5 (PDE-5) inhibitor. Like other PDE-5 inhibitors, tadalafil slows the metabolism of cyclic guanosine monophosphate, which acts as the second messenger for most of the vasoactive properties of nitric oxide and the natriuretic peptides. It has been used for erectile dysfunction, pulmonary hypertension and benign prostatic hyperplasia (4)

Pentoxifylline increases fibrinolysis, decreasing blood viscosity, increasing red cell deformity and inhibiting platelet aggregation. It is used to reduce symptoms of ischaemia in patients with occlusive arterial disease, and a number of studies indicate it may be beneficial with or without concurrent

compression in the treatment of chronic venous leg ulcers (5) prednisolone was used for chilblain lupus erythematosus (3). The aim of the present study is to evaluate the effectiveness of tadalafil in the treatment of perniosis, in comparison with pentoxifylline and prednisolone.

Patients and methods:

This was a therapeutic comparative study. A total of 58 patients with perniosis were seen between November 2011 and March 2014 in the department of Dermatology and Venereology, Baghdad Teaching Hospital, Baghdad, Iraq. A detailed history was taken from each patient regarding age, gender, occupation, duration of attack, history of previous attacks, symptoms of the lesions, family history, medical history, and previous treatment modalities. All patients did not receive any medical treatment before recruitment in the study. Full clinical examination was carried out to assess the morphology, distribution and extent of the lesions, and to look for any other associated skin and systemic diseases. Pregnant patients, those with cardiovascular diseases, children <12 years, patients with connective tissue diseases, those on antiplatelets, aspirin, and immunosuppressive therapy were excluded from the study.

A formal consent was obtained from each patients after explanation of the nature of the disease, course, follow up and

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prognosis and the possible side effects of therapy.

The patients were divided into 3 groups. Group (A) included 19 patients who received tadalafil in a dose of 5 mg once daily. Tadalafil was manufactured by Ajanta, India with a trade name (Apcalis 10 mg). In group (B), 18 patients were included who received pentoxifylline tablets in a dose of 400 mg thrice daily. It was made by Bahri pharmaceuticals, Syria with a trade name (tronteral). Group (C) included 21 patients who received oral prednisolone 15 mg twice daily. It was made by Nineveh Drug Industries, Iraq.

The duration of treatment was two weeks

The patients were seen at the end of treatment period and every two weeks for a four weeks follow up to assess the clinical response, side effects and relapse.

The severity of the disease before and after treatment was graded using an innovative scoring system which was proposed by the author taken in consideration the number of fingers/toes, type of the lesions and the presence of coldness, cyanosis or itching. Table- 1.

Table-1: severity scoring of perniosis lesions

Score	I	II	III
No. of fingers/ toes	< 5	5-10	>10
Type of lesion	patches	Patches/plaques	Bullae or ulcers
coldness	feet	hands	Hands and feet
cyanosis	feet	hands	Hands and feet
Itching	feet	hands	Hands and feet

The total score of severity of the lesions ranged from 2-15. The minimal score 2 stands for patches lesions involving < 5 fingers / toes with absence of coldness, cyanosis or itching.

Descriptive and analytic statistics were carried out by using graph pad software. Paired t test was used to compare results within each group. ANOVA test was used to compare the results among the 3 groups. P-value of less than 0.05 was considered significant.

Results:

Forty seven patients completed the study. Their ages ranged from 13-43 with a mean ± SD of 22.38 ±6.99 years. Thirty three patients were females (70.21%) and 14 were males (29.79%).

The distribution of lesions was shown in Table-2.

The severity score of lesions and response to treatment after 2weeks of treatment is as follows:

Group A: Fifteen patients completed the treatment. The mean severity score before treatment was 10.13 ± 2.17 and became 5 ±1.93. P-value < 0.0001. The percentage of improvement is 50.65%. Fig. 1

Group B: Thirteen patients completed the treatment. The mean severity score before treatment was 9.92 ±1.98 and became 5.54 ±1.45. P-value < 0.0001. The percentage of improvement is 44.16%. Fig. 2

Group C: Nineteen patients completed the treatment. The mean severity score before treatment was 9.68± 2.52 and became 6.63 ±2.14. P-value <0.0001. The percentage of improvement is 31.51%. Fig.3

Using ANOVA test to compare the results among the three groups, revealed a significant difference, p- value = 0.004. The group A showed a better response.

At the end of treatment, patients were asked to keep on protective measures to avoid coldness.

At 4 weeks of follow up, all patients maintained their response and no exacerbation of lesions was noted.

No side effects were reported in all three groups, apart from mild headache in the first few days detected in 6 (40%) patients in group A that did not necessitate cessation of therapy.

Table- 2. The distribution of lesions

Site	No .of patients	%
toes	22	46.8
fingers	10	21.27
Toes and fingers	15	31.91

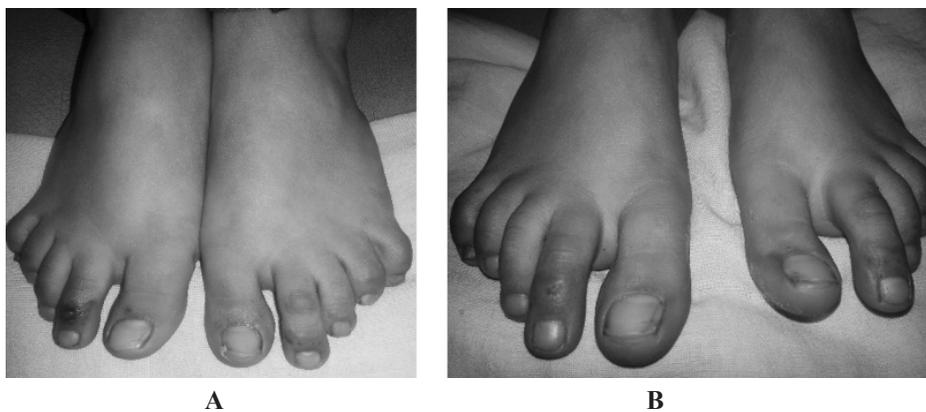


Fig. 1: A twenty year old female with perniosis
(A) Before treatment the score was 11.
(B) After treatment with tadalafil, the score became 4.



A



B

Fig. 2: A twenty one year old female with perniosis

(A) Before treatment. The score was 7

(B) After two weeks of treatment with Pentoxifylline the score became 4



A



B

Fig. 3: A twenty four year old female with perniosis

(A) Before treatment the score was 6

(B) After two weeks of treatment with Prednisolone the score became 3

Discussion:

Perniosis is still frequently encountered throughout the winter season in the setting of socioeconomic conditions predisposing to prolonged cold exposure. Lesions begin in fall or winter and disappear in spring or early summer. Common features leading

to diagnosis of chilblains include a history of exposure to cold, usually for recreational or occupational purposes, along with presence of painful or itchy erythematous skin lesions affecting distal extremities, especially the digits and a self-limiting course (6, 7)

The treatment of perniosis remains unsatisfactory (8). Treatment options included potent topical steroids and, in the most severe instances, prevention with the calcium channel blocker nifedipine (9, 10) Pentoxifyllin and prednisolone (11)

Tadalafil has been used successfully for Raynaud's phenomenon resistant to vasodilator therapy (12). This means that it has a powerful effect on circulation of the acral parts which are the sites of predilection of perniosis. The prolonged half-life of tadalafil makes it ideally suited for daily dosing and attainment of steady-state serum levels for up to 36 hours after dosing (13, 14). To the best of our knowledge tadalafil was not used previously in the treatment of perniosis.

Tadalafil resulted in a better response than pentoxifylline and prednisolone. It has comparable effect to nifedipine (8). It is assumed to be safe in young age group who are free from cardiovascular problems. There are a mild and transient side effects when compared with other systemic remedies for example nifedipine which frequently result in hypotension and headache that may eventually limits its use because of intolerance. It was given once daily versus nifedipine which has to be administered three times daily, the former has better compliance.

The response rate of patients receiving pentoxifylline was slightly lower than that of a previous study using the same drug with the same duration (11). This could be explained by the difference in the method of grading of severity.

The present study introduced a new objective method that covers all the disease aspects in terms of extension and severity. It has not mentioned before and we expect that the results are more conclusive than previous studies

Authors' contribution:

Prof. Khalifa E. Sharquie: Design of the study and critical revision

Assistant prof. Husam Ali Salman: Data collection, analysis, interpretation, writing and critical revision.

Prof. Adil A. Noiami: Manuscript draft, revision and preparation of drugs

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