Treatment of perniosis with oral pentoxyfylline in comparison with oral prednisolone plus topical clobetasol ointment in Iraqi patients

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ABSTRACT

الأهداف: تقييم مدى فعالية وأمان عقار البنتوكسيفيلين في علاج مرض الشرث بالمقارنة مع عقار البردنزولون مع مرهم الكلوبيتاسول.

الطريقة: أُجريت دراسة مقارنة مفتوحة لـ40 مريضاً خلال الفترة مابين يناير 2008م وحتى مارس 2008م، في قسم الأمراض الجلدية – مستشفى بغداد التعليمي – بغداد – العراق. تم تقسيم المرضى بشكل عشوائي إلى مجموعتين بناء على نوع العلاج المعطى. تلقت المجموعة (أ) عقار البردنزولون بمقدارها (0.5mg/kg) بجرعتين مقسومتين مع مرهم الكلوبيتاسول لمدة أسبوعين. المجموعة (ب) تلقت عقار البنتوكسيفيلين بجرعة مقدارها (1200mg) يوميا مقسمة إلى ثلاث جرعات لمدة أسبوعين أيضا. تم اخذ التاريخ المرضي، وأُجري فحص سريري للمرض لجمع معلومات عن كل ما يتعلق بالمرض.

النتائج: تراوحت أعمار المرضى مابين 5–60 عاماً، بمعدل (22SD±6.2) عاماً، وكانت نسبة الإناث للذكور 3.5:1. لم يتلقى أي من المرضى علاج قبل هذه الدراسة. في المجموعة (أ) 11 مريضا أكملوا العلاج، 3 (27.2%) منهم اظهروا استجابة جيدة للعلاج، حيث اختفت آفات المرض وزالت أعراضه خلال أسبوعين. أما في المجموعة (ب) فقد أكمل 9 مرضى العلاج، واظهر 5 منهم (55.5%) استجابة جيدة حيث اختفت آفات المرض وزالت أعراضه خلال اسبوعين.

خاتمة: تبين أن عقار البنتوكسيفيلين فعال وآمن في علاج مرض الشرث، كما أنه ذو فعالية أعلى من عقار البردنزولون ومرهم الكلوبيتاسول معاً، ($p<0.05$).

Objective: To evaluate the effectiveness and safety of pentoxyfylline in treatment of perniosis in comparison with prednisolone plus topical clobetasol ointment.

Methods: This is an open comparative therapeutic trial conducted in the Department of Dermatology, Baghdad Teaching Hospital, Baghdad, Iraq between January and March 2008. Forty patients with perniosis were enrolled in this study, and divided randomly into 2 equal groups, according to the sort of treatment. Group A comprised patients who received oral prednisolone (0.5 mg/kg) in 2 divided doses, and topical clobetasol ointment for 2 weeks. Group B comprised patients who received pentoxyfylline tablet (1200 mg /day) in 3 divided doses for 2 weeks. Detailed history and full clinical examination were carried out for each case, regarding all relevant points related to the disease.

Results: The age of patients ranged from 5-60 mean±SD (22±6.2) years, with 31 females and 9 males with a female to male ratio of 3.5:1. All patients did not receive any treatment before the study. In group A, 11 patients completed the treatment course, and only 3 (27.2%) patients showed good improvement and complete cure after 2 weeks. In group B, 9 patients completed the regime, and 5 (55.5%) patients showed good improvement, in which symptoms disappeared and lesions resolved after 2 weeks.

Conclusion: Pentoxyfylline was shown to be an effective and safe drug for treatment of perniosis, and superior to oral plus topical glucocorticoids ($p<0.05$).

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Perniosis (chilblains) is a common dermatological problem. The condition results from abnormal reaction to cold.[1] Thus, it is seen during the cold months of winter.[2,3] In people with poor peripheral circulation, even moderate exposure to cold may trigger the onset of perniosis.[4,5] It occurs chiefly on the hands, feet, ears, and face, especially in children.[6,7] Patients are usually unaware of the injury at first, but later burning, itching, and redness call their attention.[5] Typically, there is severe localized cold erythema and swelling, but in severe cases, blistering and ulceration may develop.[5] Sometimes the condition show a familial tendency.[2] The main histological features include, dermal papillary edema, and marked perivascular lymphoid infiltrate.[8,9] The treatment depend mainly on the protection of the affected parts against further exposure to cold. Local remedies are of little help, but many systemic agents had been used in the treatment of perniosis.[5] Pentoxyfylline is a vasodilator agent that increases the blood flow to the skin, rather than muscles. It has been used for therapy of many skin vascular diseases, such as venous leg ulcers.[10] Also, prednisolone and topical clobetasol are widely used for their anti-inflammatory and immunosuppressive properties.[10] The aim of the present study is to evaluate the effectiveness and safety of pentoxyfylline in the treatment of perniosis, in comparison with prednisolone plus clobetasol.

Methods. This is an open-comparative therapeutic trial. A total of 40 patients with perniosis were seen between January to March 2008 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, family history, and history of previous attacks, smoking, medical history, and previous treatment modalities. All patients did not receive any medical remedies before the start of the study. Full clinical examination was carried out to assess the distribution and extent of the lesions, and to see if there is any other associated skin and systemic diseases. Pregnant patients and those with cardiovascular diseases, and children <12 years were excluded the study. Also, any patients with known connective tissue diseases such as systemic sclerosis, systemic lupus erythematosus, and those with Raynaud's phenomenon were excluded from this study. In addition to that, patient on systemic medications such as antiplatelets, aspirin, antiepileptic, and immunosuppressive therapy was also excluded. We obtained a formal consent after a full explanation of the nature of the disease, course, methods of treatment, follow-up, and prognosis. The Scientific Committee of the Scientific Council of Dermatology and Venereology, Iraqi Board for Medical Specializations approved the ethical approval.

Patients were divided randomly into 2 equal groups depending on the type of treatment. Each group consisted of 20 patients. Group A were patients who received an oral prednisolone in a dose of 0.5 mg/kg in 2 divided doses, and topical clobetasol ointment for 2 weeks. Prednisolone used in this study was manufactured by Ninivea Drug Industries, Iraq. Group B were patients who received pentoxyfylline tablets in a dose of 1200 mg/day, in 3 divided doses for 2 weeks. The Medical Bahri Company in Syria, manufactured the drugs. Patients in both groups were asked to protect themselves from further cold exposure. The patients were clinically evaluated after 2 weeks, to assess the clinical response to treatment, and record any side effects. The patients who showed good response after 2 weeks, were asked to stop therapy and keep on regular follow up every 2 weeks, while patients with no response after 2 weeks were switched to another treatment.

Statistical analysis was carried out by using unpaired t-test to compare both groups of treatment. The probability value of less than 0.05 was considered significant. Pentoxyfylline was found to be statistically significantly better, than the oral prednisolone plus topical clobetasol ointment (p<0.05).

Results. A total of 40 patients were assessed and treated. Their ages ranged from 5-60 years with a mean±SD of 22 ± 6.2 years. They comprised 31 females and 9 males, with a female to male ratio of 3.5:1 (**Table 1**). Shows the location of lesions in patients with perniosis. Regarding response to treatment, the patients were seen after 2 weeks, and were assessed clinically and the results were as follows: Group A: 11 patients completed the 2 weeks treatment course, and only 3 (27.2%) showed good improvement, in which their symptoms disappeared and lesions resolved after 2 weeks. Patients who responded to therapy were asked to stop therapy and keep on regular protective measures and followed up for another 2 weeks for further assessment and no recurrence were detected during follow up. Group B: 9 patients completed the 2 weeks treatment course, and 5 (55.5%) patients showed good improvement in which symptoms disappeared and lesions resolved after

Table 1 - Showing the location of lesions in patients with perniosis (N=40).

Site of lesion	No. of patients	(%)
Toes	16	(40)
Fingers	9	(22)
Heels	10	(25)
Toes and fingers	11	(27)
Nose	1	(2.5)

2 weeks. Patients with improvement, were asked to stop the therapy and keep on the similar manner of group A. No side effects were recorded in all patients.

Discussion. Perniosis is a common skin problem. The condition results from abnormal reaction to cold.[1] There are many drugs used for treatment of perniosis, but none of them is uniformly effective.[5] Pentoxyfylline is a vasodilator agent that increases the blood flow to the skin, rather than muscles. It has been used for treatment of many skin vascular diseases, for instance, venous leg ulcers.[10] In the present study, pentoxyfylline is shown to be effective and safe drug in the treatment of perniosis. Response rate was 55% after 2 weeks of treatment, in which there was symptomatic relief and resolution of the lesions. The mechanism of action may be attributed to its vasodilator action,[10] and increasing the red blood cell deformability,[2] thus increasing the blood flow and tissue oxygenation, since perniosis is the result of abnormal vascular response to cold and tissue ischemia.[5] No side effects were recorded in all patients. The results achieved with pentoxyfylline were comparable to those achieved with oral nifedipine.[11] Prednisolone and clobetasol ointment are glucocorticoids that are widely used in dermatological practice for anti-inflammatory and immunosuppressive properties.[10] In this study, these agent had been shown to be an effective anti-inflammatory agent in the treatment of perniosis. Only 27.2% of treated patients showed good response after 2 weeks of treatment. The action is probably attributed to the anti-inflammatory effects, since perniosis manifests perivascular inflammatory infiltrate and dermal edema. The small number of patients and short duration of follow up period is due to the outbreak of this disease in Iraq, which occurs only during cold months (December to March). Therefore, long-term follow up is difficult to obtain.

In conclusion, pentoxyfylline is shown to be effective and safe drug for treatment of perniosis and it is superior to oral and topical glucocorticoids.

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