

## ***Acanthamoeba* keratitis in Sudan: outcome of ketoconazole treatment in six patients.**

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### **Abstract**

In an exploration of the acanthamoebic aetiology of chronic keratitis cases (not responding to antibiotics, antiviral or antifungal therapy), 138 Sudanese patients were seen over a 2-year period at two teaching eye hospitals in Khartoum State. Six (4.3%) of these patients were found to be suffering from *Acanthamoeba* keratitis. The present study focuses on the good outcome of oral ketoconazole in four patients at 18 months follow up period. The drug oral route, convenient frequency of doses, minimal side effects and availability at reasonable price favour ketoconazole therapy.



### **Introduction:**

*Acanthamoeba* keratitis (AK) is infection of the human eye cornea by the free-living protozoan *Acanthamoeba*<sup>1,2</sup>. AK is a recognized cause of blindness in man. The first cases of AK were reported in 1974<sup>3</sup>. The main risk factors associated with AK are eye trauma and contact lens wear<sup>4,5</sup>. Patients typically suffer from a triad of severe ocular pain, photophobia and a unilateral red eye. Laboratory confirmation of AK is usually made by microscopy examination of wet mounts of a corneal swab/scraping or by culture of the same type of specimens in non-nutrient agar seeded with *Escherichia coli* bacteria<sup>6,7</sup>.

Medical therapy for AK is usually difficult as many cases are treated initially as viral, bacterial or fungal keratitis and this causes significant diagnostic delay<sup>8</sup>. Medical therapy for AK is usually difficult as many cases are treated initially as viral, bacterial or fungal keratitis and this causes significant diagnostic delay<sup>8</sup>.

A number of antimicrobial agents have been recommended for therapy of AK including: ketoconazole, neomycin, chlorhexidine and diamidines<sup>9,10,11</sup>.

We assume that AK in Sudan has not been previously documented<sup>12,13</sup>. The objective of the present study was to report on the good outcome of oral ketoconazole therapy in six Sudanese patients.

### **Subjects and Methods:**

Over a 2-year period (2003-2005), 138 patients suffering from chronic keratitis (not responding to antibiotics, antiviral or antifungal therapy) were seen at Khartoum Eye Hospital and El Walidain Eye Hospital, Omdurman. Direct microscopy and culture methods were used for diagnosis of *Acanthamoeba* infection. Specimens included eye swabs and scrapings (when indicated) from the affected eye.

#### **Microscopy:**

The corneal swab/scraping was suspended in 10 ml of 0.9% NaCl, centrifuged at a medium speed (4000 rpm) for five minutes. Most of the supernatant was aspirated and a smear from the sediment is prepared and examined microscopically.

Characteristic *Acanthamoeba* trophozoite or cyst stage could be seen.

#### **Culture:**

The corneal swab/scraping was suspended in 10 ml of 0.9% NaCl. Most of the supernatant was aspirated and the sediment resuspended in the remaining fluid. Using a sterile Pasteur pipette two or three drops of the suspension was placed in the center of the agar plate seeded with *E. coli* bacteria, incubated at 30-35°C and examined for characteristic *Acanthamoeba* trophozoites daily for up to 14 days.

### **Results and outcome of ketoconazole treatment:**

#### **Case One**

M.M.A., 50-years-old male Sudanese farmer from Bara (Northern Kordofan State), seen at El Walidain Eye Hospital, Omdurman (Fig. 1), complaining of severe eye pain and hyperaemia. Right eye swab was positive for *Acanthamoeba*

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by culture method. Oral ketoconazole, 200 mg b.d. for two months resulted in complete relief of symptoms and disappearance of hyperaemia (Fig. 2).

Fig 1. Case one; corneal scar and hyperaemia are evident in the right affected eye. Compare with normal left eye.



Fig2. Case one, two weeks following start of oral ketoconazole therapy, hyperaemia diappeared. Four weeks later pain in the eye completely relieved.



#### Case Two

A.E.I., 55-years-old female Sudanese housewife from Al Aylafon (Khartoum State), seen at Khartoum Eye Hospital, complaining, recurrent eye pain. Left eye swab was positive for *Acanthamoeba* by culture method. Good response was observed following oral ketoconazole 200 mg b.d. for one month.

#### Case Three

A.I.A., 48-years-old Sudanese farmer from Bara (Northern Kordofan State), seen at El Walidain Eye Hospital, Omdurman, complaining of severe ocular pain. Left eye swab was positive for *Acanthamoeba* by culture method. Good response was observed following oral ketoconazole for two months.

#### Case Four

A.K.T., 58-years-old female Sudanese housewife living in Khartoum (originally from Wao, Bahr Elgazal State), seen at Khartoum Eye Hospital, complaining of impaired vision and eye pain. Left eye swab was positive for *Acanthamoeba* by culture method. This patient was started on oral ketoconazole 200 mg b.d. and

for two weeks her symptoms improved but was rushed to surgical enucleation of the left eye ball because of sudden severe ocular bleeding.

#### Case Five

E.M.N., 32-years-old male Sudanese shepherd from Elkawah (White Nile State), seen at Khartoum Eye Hospital complaining of left eye pain following trauma, left eye swab was positive for *Acanthamoeba* by direct microscopy. This patient was started on ketoconazole.

200 mg b.d. and for several days he showed improvement but he left hospital against medical advice.

#### Case Six

H.Z.A., 64-years-old male Sudanese farmer living in Khartoum (originally from Dongola), seen at El Walidain. Eye hospital, Omdurman, complaining of sever eye pain. Right eye scraping was positive for *Acanthamoeba* by culture method. Oral ketoconazole 200 mg b.d. for two months resulted in complete relief of his symptoms.

#### Discussion:

Ketoconazole is an imidazole derivative used as broad-spectrum antifungal agent and has proved to be effective against AK<sup>9</sup>. There is no consensus as to which antimicrobial agent is optimal for AK therapy<sup>(14)</sup>. Ketoconazole was given to our patients because of its easy oral administration, convenient frequency of doses and availability at reasonable price. The liver function tests should be normal at the start of treatment. Topical use of cationic antiseptics e.g. chlorhexidine is known to require hourly applications for extended periods of time<sup>15</sup>. Most of our patients came from rural areas and compliance to therapy can not be ensured.

Many studies have suggested that a combination of treatments offers the best chance of management for AK<sup>10,14,16</sup>. In our patients meticulous eye hygiene was maintained by repeated saline cleansing while on ketoconazole therapy.

In conclusion, six Sudanese patients who had chronic keratitis were documented by laboratory methods to be AK cases. Good response to oral ketoconazole therapy was observed. At 18 months follow up period, four patients remain symptoms and signs free.

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**References**

1. Marcano G. *Acanthamoeba* as agent of disease in humans. Clin Microbiol Rev 2003; 16: 273-307.
2. Walker CW. *Acanthamoeba*: ecology, pathogenicity and laboratory detection. Br J Biomed Sci. 1996; 53: 146-151.
3. Nagington J, Jones BR, Steel AD. Amoebic infection of the eye. Lancet. 1974; 2: 1537-1540.
4. Radford CS, Minassian DC, Dart JK. *Acanthamoeba* keratitis in England and Wales: incidence, outcome and risk factors. Br J Ophthalmol. 2002; 86: 536-542.
5. Seal DV and Hay J. Risk factors for *Acanthamoeba* keratitis. BMJ. 1995; 311: 808.
6. Baharathi MJ, Ram KR, Vasu S, Menakshi PR. Aetiological diagnosis of microbial keratitis in south India: a study of 1618 cases. Indian J Med Microbiol. 2002; 20: 19-24.
7. Deng XG, Li JC, Zhu L. Laboratory diagnosis of *Acanthamoeba* keratitis. Zhongguo Ji Sheng Za Zhi (China). 2000; 18: 301-304
8. Claerhout I and Keystyn PH. *Acanthamoeba* keratitis: a review. Bull Soc Belgium Ophthalmol. 1999; 274: 71-82.
9. Ishibashi Y. Oral itraconazole and topical miconazole for *Acanthamoeba* keratitis. Am J Ophthalmol. 1990; 109: 121-126.
10. Hargrave SL, Maculley JP, Husseni Z. Results of a trial of combined propamidine isethionate and neomycin therapy for *Acanthamoeba* keratitis. Ophthalmology. 1999; 106: 952- 957.
11. Ogbunude PO and Asiri SA. In vitro effect of diamidines on intracellular polyamines of *Acanthamoeba polyphaga* Drugs Exp Clin Res. 2001; 27: 127-133.
12. Haroun SH. Prevalence and causes of blindness in Khartoum State: a population based study. MD Thesis, Dept. of Ophthalmology, University of Khartoum, 2000.
13. El-Khidir MS. Contact lens wear: experience in Sudan. MD Thesis, Dept of Ophthalmology, University of Khartoum, 2003.
14. Driebe WT, Stern GA, Epestein RJ, Visvesvara GS. *Acanthamoeba* keratitis: potential role for topical clotrimazole in combination chemotherapy. Arch Ophthalmol. 1988; 106: 12.
15. Radford CWF, Lehman OJ, Dart JK. *Acanthamoeba* keratitis: multicenter survey in England 1992-96. Br J Ophthalmol. 1998; 82: 1387-1392.
16. Auran JD, Starr MB, Jakobie FA. *Acanthamoeba* Keratitis: a review of literature. Cornea. 1987; 6: 2-26.