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Ketoconazole monotherapy for *acanthamoeba* keratitis

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Abstract
In the present study we report good outcome of oral ketoconazole in patients who were laboratory confirmed to be suffering from *Acanthamoeba* keratitis. The drug oral route, convenient frequency of doses, minimal side effects and availability at reasonable price, were important factors for selecting ketoconazole. This study involved 138 patients with chronic keratitis who were seen over a 2-year period. Six (4.3%) of these patients were confirmed to be suffering from *Acanthamoeba* keratitis. Response to ketoconazole was good in four patients at monthly follow up for two years period. Two patients showed initial good ketoconazole response, but had not reported at visits for follow up.

Keywords: ketoconazole, monotherapy, *Acanthamoeba*, keratitis

Introduction
Acanthamoeba keratitis (AK) is defined as infection of the human eye cornea. It is caused by the free-living protozoan *Acanthamoeba.* [1, 2] If AK is not diagnosed promptly and then treated properly, it may lead to blindness. Worldwide, the first cases of AK were reported in 1974 from England [3].
The main risk factors associated with AK are eye trauma and wearing of contact lens [4, 5]. Patients typically suffer from a triad of severe eye pain, photophobia and a unilateral red eye. Laboratory confirmation of AK is usually established 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 [6, 7].
Medical therapy for AK is usually difficult as most cases are treated initially as viral, bacterial or fungal keratitis and this causes significant diagnostic delay.[8] A number of antimicrobial drugs have been recommended for therapy of AK including: ketoconazole, neomycin, chlorhexidine and diamidines [9, 10, 11].
The objective of the present study was to report on the good outcome of oral ketoconazole therapy in patients who suffered from chronic keratitis due to *Acanthamoeba*.

Methods
Over a 2-year period, 138 patients suffering from chronic keratitis (not responding to antibiotics, antiviral or antifungal therapy) were screened for *Acanthamoeba* infection by using direct microscopy and culture methods. The specimens from patients included eye swabs and scrapings from the affected eye.

i) Microscopy
The corneal swab and/or 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 was prepared and examined microscopically for characteristic *Acanthamoeba* trophozoite or cyst stage.

ii) Culture
The corneal swab and/or scraping was suspended in 10 ml of 0.9% NaCL. Most of the supernatant was aspirated and the sediment re-suspended 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. Incubate at 30-35ºC and examine for characteristic *Acanthamoeba* trophozoites daily for up to 14 days.

Ketoconazole Monotherapy Outcome
Patient One
M.M.A., 50-year-old male farmer was complaining of severe eye pain and hyperaemia. Right eye swab proved to be positive for *Acanthamoeba* by culture method. Oral ketoconazole, 200 mg twice per day for two months resulted in complete relief of symptoms and disappearance of hyperaemia.

Patient Two
A.E.I., 55-year-old housewife from was complaining from recurrent eye pain. Left eye swab showed *Acanthamoeba* trophozoites by culture method. Excellent response was observed following oral ketoconazole 200 mg twice per day for one month.

Patient Three
A.I.A., 48-year-old was complaining of severe ocular pain. Left eye swab was positive for *Acanthamoeba* by culture technique. Good response was observed following oral ketoconazole 200 mg twice per day for two months.

Patient Four
A.K.T., 58-year-old female was complaining of impaired vision and eye pain. Left eye swab was positive for *Acanthamoeba* by culture technique. This patient was started

on oral ketoconazole 200 mg twice daily and for two weeks. Her symptoms improved but was rushed to surgical removal of the left eye ball because of sudden severe ocular bleeding.

Patient Five

E.M.N., 32-year-old male was complaining of left eye pain following trauma, left eye swab was positive for *Acanthamoeba* by direct microscopy examination. This patient was started on ketoconazole 200 mg twicw per day. For several days the patient showed marked improvement but he left hospital against medical advice.

Patient Six

H.Z.A., 64-year-old male was complaining of sever eye pain. Right eye scraping was positive for *Acanthamoeba* using culture method. Oral ketoconazole 200 mg twice per day for two months resulted in complete relief of the patient symptoms.

Discussion

Ketoconazole is an imidazole derivative used as broad-spectrum antifungal drug and has proved to be effective against AK [9]. Worldwide there is no consensus as to which antimicrobial agent is optimal for AK therapy [12]. Ketoconazole was given to our patients because of its easy oral administration, convenient frequency of dosages and available at reasonable price. The liver function tests should be normal when starting ketoconazole treatment. Topical use of cationic antiseptics e.g. chlorhexidine is recognized to require hourly applications for extended periods of time [12]. Many studies have suggested that a combination of treatments offers the best chance of management for AK [10, 12]. However, ketoconazole alone (monotherapy) in our patients has proved to be effective.

In conclusion, patients who had chronic keratitis that were documented by laboratory methods to be AK cases, had shown good response to oral ketoconazole therapy. No recurrence of eye symptoms or signs were noted at monthly follow up, for 2 years period.

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