

Original Article

The effect of itraconazole pulse therapy on quality of life in Pakistani patients of disto-lateral subungual onychomycosis

Shahbaz Aman, Talat M. Akbar, Ijaz Hussain, Muhammad Jahangir, Tahir S. Haroon
Department of Dermatology, King Edward Medical College/Mayo Hospital, Lahore, Pakistan

Abstract *Background* Distal and lateral subungual onychomycosis (DLSO) is the most common clinical type of onychomycosis. The disease causes little physical handicap but it has a devastating effect on quality of life (QOL) particularly in our set up.

Objective The purpose of the study was to assess the effect of itraconazole pulse therapy on quality of life in Pakistani patients with DLSO.

Methods Sixty-two patients, 47 males and 15 females suffering from DLSO, age range 19 to 55 years, who were themselves able to understand and fill the questionnaire related with general and disease-specific QOL in English or Urdu version, were enrolled in the study. The total score ranged from 0-60. The higher the score, the greater was the impact on QOL. The patients were subjected to itraconazole pulse therapy and each pulse consisted of 200 mg twice a day for 7 days, followed by a drug-free interval of three weeks. Two pulses were given for fingernail onychomycosis and three pulses for toenail infection. The pre- and post-trial data was analyzed before and after therapy in 46 finger- and 16 toenail cases of DLSO.

Results The disease caused psychosocial problems (92%), economic problems in treatment (89.4%), difficulty in cutting nails (62.9%), physical contact problems with hands (60.8%), discomfort in wearing shoes and walking (56.2%), pain (33.8%), disturbance of work with hands (30.4%) and affected performance in sports (22.5%). After itraconazole pulse therapy, these problems decreased to 12.9%, 14.5%, 6.45%, 6.4%, 12.5%, 4.8%, 6.45% and 3.2%, respectively. The mean pretreatment score in patients with finger- and toenail disease was 32 ± 3.4 and 29 ± 4.5 , respectively. The score dropped to 4.3 ± 5.4 and 4.4 ± 5.6 ($P < 0.05$) after itraconazole therapy at last follow-up 32 weeks and 48 weeks for finger- and toenail disease, respectively. Fingernail disease has affected QOL more than toenail disease and longer duration of disease, greater involvement of individual nails and greater number of nails involved was also associated with more serious impact on QOL. Females were found to be more psychologically upset than males.

Conclusion Itraconazole pulse therapy significantly improves the QOL in disto-lateral subungual onychomycosis of both finger- and toenails in our patients.

Key words

Onychomycosis, quality of life, itraconazole

Introduction

Onychomycosis is the major cause of nail disease in which the affected nails become

discolored, thickened and friable.¹ Distal and lateral subungual onychomycosis (DLSO) is the most common clinical type of onychomycosis.^{2,3} This is a chronic disease which can have a severe impact on patient's physical and psychological well-being.⁴ It can limit the mobility and affect peripheral circulation. The disease may also precipitate recurrent thrombophlebitis

Address for correspondence

Dr. Shahbaz Aman,
2-C Hearn Road, Islampura,
Lahore, Pakistan
Ph # 92 42 7226045
Email: shahbazaman@mayoderm.org.pk

and cellulitis in the legs.⁴ The disease is resistant to topical treatment and to achieve resolution, an effective oral anti-fungal therapy is essential.⁵ Owing to its broad-spectrum keratophilic nature and long tissue half-life, itraconazole is a widely used oral antimycotic in onychomycosis. Various studies show an intermittent pulse therapy of itraconazole for onychomycosis to be effective.^{5,6}

Quality of life (QOL) is defined as capacity to perform the daily activities appropriate to person's age and major social role.⁷ The role could be paid employment, schooling, house work or self care. Several indices are available in the form of questionnaires to measure the extent of disability caused by skin diseases.⁷ Due to protracted course of illness, the patients with onychomycosis are bothered in numerous ways e.g. nail discoloration, disfigurement, pain and embarrassment.^{4,8-10} The psychosocial consequences are probably more common than the physical.⁴

The present study "Quality of life in disto-lateral onychomycosis: pre- and post-itraconazole therapy" was conducted to quantify the level of handicap experienced by Pakistani patients with DLSO before and after itraconazole pulse therapy.

Patients and methods

This was a questionnaire-based study. The study protocol and questions were approved by the Institutional Review Board Committee (IRBC). The study was carried out at the Department of Dermatology, King Edward Medical

College/Mayo Hospital, Lahore during the period from June, 1996 to December, 1998. A full medical history and clinical assessment of onychomycosis with informed consent was taken. Sixty seven patients of either sex but of more than 18 years of age with disto-lateral subungual onychomycosis of finger- and/or toenails who could themselves complete the questionnaire in English or Urdu (National language in Pakistan) version were enrolled in the screening period. Mycologically confirmed (positive microscopy plus fungal culture) cases were included in the study. Those patients were excluded who had involvement of the proximal region of the nail plate i.e. nail matrix or had psoriasis, dermatitis of nail fold, diabetes, peripheral vascular disease/arterial insufficiency and severe general underlying disease. Those patients were also excluded who used oral anti-fungal therapy within 2 months prior to screening while topical anti-fungal therapy was stopped at screening. The subjects who were receiving concurrent rifampicin, phenytoin, digoxin, oral anticoagulants, cyclosporin, astemizole, terfenadine, midazolam, cisapride or history of drug allergy or hypersensitivity to an azole antifungal drug were also excluded. Pregnant and lactating females, patients with abnormal liver functions and immunosuppression, either by disease or treatment-induced or patients with evidence of bacterial paronychia were omitted, too.

The patients who fulfilled the inclusion and exclusion criteria were subjected to itraconazole pulse therapy, 200 mg twice a day for 7 days, followed by a drug-free

interval of three weeks. Two pulses were given for fingernail and three pulses for toenail onychomycosis. Patients were followed up to six months after stopping the 2-pulses in fingernails and 9 months after stopping the 3-pulses in toenails, respectively. No antimycotic therapy was allowed during the follow-up period. The patients were evaluated for QOL at 0 and 32 weeks for fingernails while 0 and 48 weeks for toenails.

All the patients were instructed to fill a health related quality of life (HRQOL) questionnaire (**Table 1**) that included general and disease-specific items measuring the impact of disease on daily activities, appearance and problems associated with this infection at base-line and last follow-up (32 & 48 weeks) after treatment in finger- and toenail infection, respectively. The questionnaire consisted of 15-questions covering 7 different domains of QOL e.g. psychosocial and feelings (Q1-5), socio-economic aspect (Q6), psychological (Q7-8, 12-13), leisure activities/sports (Q9), physical (Q10-11), personal relationship (Q14a) and daily activities (Q14b,-15b). The patients were asked to score, on a scale from 0 to 4, for each of 15 questions, how they felt their lives have been affected by the disease. The response for each question could be 0= not at all, 1= yes, but not bothersome, 2= yes, somewhat bothersome, 3= yes, a lot bothersome, 4= yes, extremely bothersome. The total score ranged from 0 to 60 for all the items of questionnaire. The higher the scores, the poorer was the quality of life.

Table 1 Health related quality of life questionnaire used in the study

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1. People find it unpleasant to look at my nails.
 2. (a) I feel uncomfortable by shaking hands because of my nail problem.
(b) I feel disheartened because of my nail problem.
 3. I am embarrassed when going out to eat or to a party.
 4. I have to explain to others what is wrong with my nails.
 5. Others are afraid of catching mycosis from me.
 6. It costs a lot of money to treat my nail disease.
 7. I tend to hide my nails.
 8. I worry that my nail problem is contagious.
 9. I am limited in my performance when doing sports activities due to nail problem.
 10. I have pain in my fingers/toes and nails.
 11. I have difficulty in cutting my nails.
 12. I feel, I will never manage to get rid of my nail problem.
 13. I can't forget that I have this nail problem.
 14. (a) I feel that people avoid physical contact with me because of my nail problem.
(b) I can't wear shoes, due to my nail problem.
 15. (a) I find it difficult to work with my hands.
(b) I limit my walking, I do because of my nail problem.
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Patients were followed-up after pulse treatment and no antimycotic therapy was allowed during the follow-up period. Nail dust samples were also taken for microscopy and fungal culture. Final evaluation at 32 weeks for fingernail and 48 weeks for toenail infection (last follow-up) was done by analyzing the data collected and marked by the patients themselves. Paired and unpaired student t test was used for comparison between males and females pre- and post-treatment scores for finger- and toenail patients, respectively. A *p* value of <0.05 was considered significant.

Results

Of 67 enrolled patients, there were two delayed exclusions and three were lost to follow up, so there were 62 evaluable patients. Of 62 patients, 47 were males and 15 females (mean age 27.6 years, range 19-55 years). Fingernails were affected in 46 cases whereas 16 had toenail infection. Fifty-one patients had dermatophyte onychomycosis while 11 were suffering from candida onychomycosis.

The mean pretreatment score in patients with finger- and toenail disease was 32 ± 3.4 and 29 ± 4.5 , respectively. The score dropped to 4.3 ± 5.4 and 4.4 ± 5.6 ($p < 0.05$) after itraconazole therapy at final evaluation. **Figures 1 and 2** show the mean pre- and post-treatment score in individual questions in finger- and toenail disease. The problems noted at baseline were psychosocial problems (92%), economic problems in treatment (89.4%), difficulty in cutting nails (62.9%), physical contact problems with hands (60.8%), discomfort in wearing shoes and walking (56.2%), pain (33.8%), disturbance of work with hands (30.4%) and affected performance in sports (22.5%). After pulse therapy these problems decreased to 12.9%, 14.5%, 8%, 6.4%, 12.5%, 4.8% and 3.2%, respectively (**Figure 1 and 2**). The patients suffering physical handicap in daily routine work were house- hold females (n=8), farmers (n=2), gardeners (n=2), teachers (n=1) and tailors (n=1). The psychosocial problems like more self-consciousness, embarrassment and avoidance of social interaction with close relatives and friends

were noted due to unsightly ugly appearance of diseased nails.

The pretreatment mean score in females (34 ± 3.2) was higher than males (30 ± 3.9) and they were found to be more psychologically upset. There was no difference between the pretreatment scores of married and unmarried patients and different age groups but patients with disease of more than 6 months duration were seen to be more psychologically disturbed as compared with patients of disease with short duration. It was also noted that the greater involvement of individual nails and the more number of nails involved were associated with more negative impact on QOL. Fingernail disease was found to have much more impact on QOL than toenail disease. The mean pretreatment score for pain in females was higher than males ($p < 0.05$). At the last follow-up, after the therapy, patients reported fewer problems including embarrassment or self-consciousness, the desire to keep their nails concealed and avoidance of contact by others.

Discussion

Onychomycosis is a public health concern causing cosmetic and functional disability.^{4,9,11} Both finger- and toenail disease can cause pain, psychosocial distress and has the potential to be a continuous source of infection for others.^{14,11} Fingernail disease may cause difficulty in manipulation and deterioration in fine touch sensitivity while toenail infection may lead to difficulty in walking, wearing shoes and sustained standing.^{14,11,12} Psychosocial

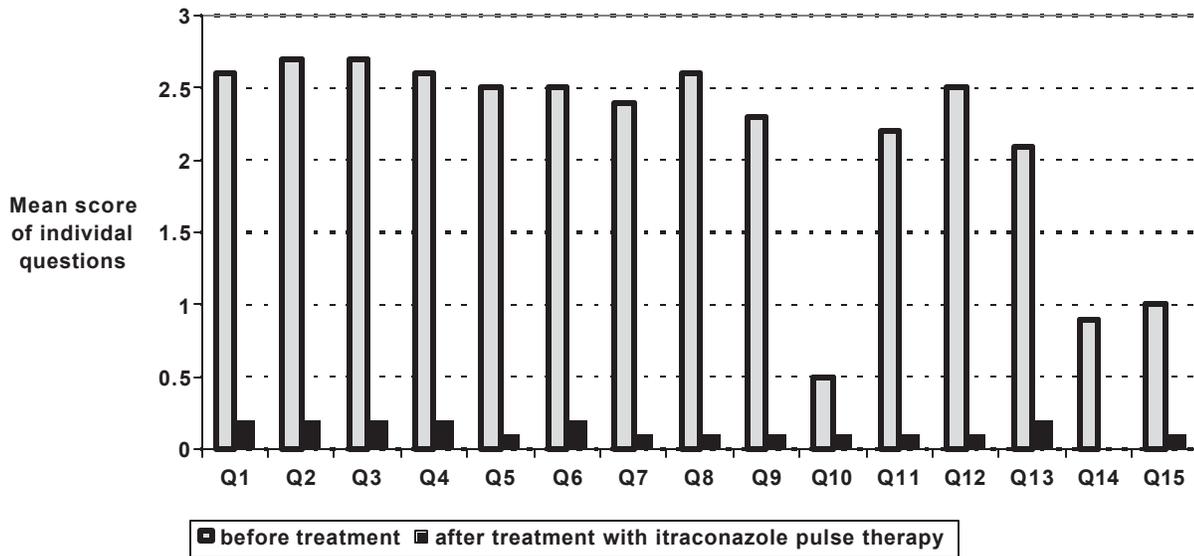


Figure 1 Question response in fingernail infection (n=46)

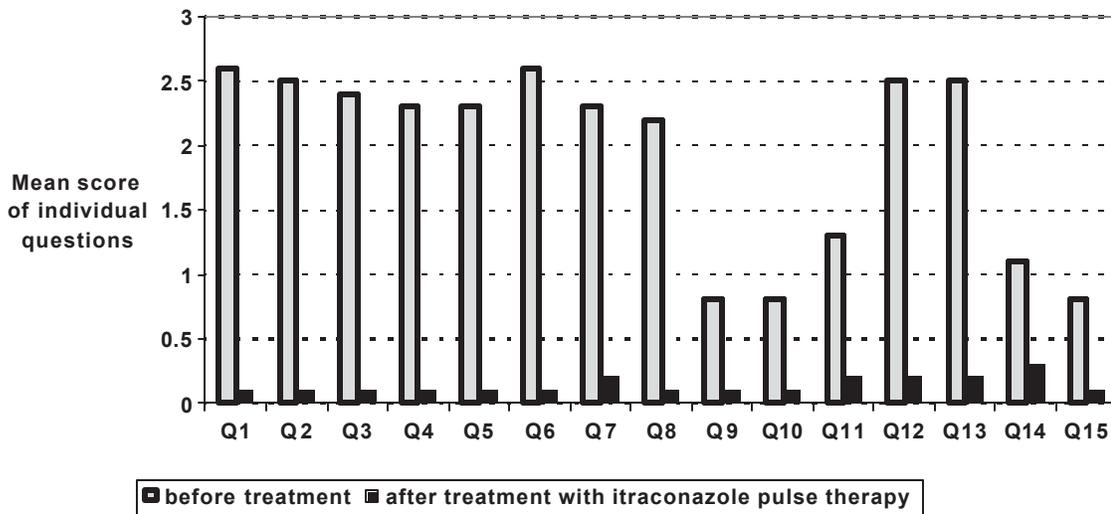


Figure 2 Question response in toenail infection (n=16)

limitations result from reactions of relatives, friends and others to the visible impairment in affected nails.⁸ Therefore, medically confirmed onychomycosis should be treated.

The disease specific questionnaire was used in 62 confirmed cases of DLSO to highlight specific areas of their life affected by disease. The variables that

influence the QOL include physical (mobility, pain, sexual), role (daily activities, work), mental (anxiety, depression & attention) and social (leisure activities) parameters.^{17,13,14} The mean pretreatment score in patients with finger- and toenail disease was higher before pulse therapy which dropped significantly ($p < 0.05$) after itraconazole therapy at last follow-up. The difference between mean

pretreatment score for females and males was statistically significant ($p < 0.05$).

The present study showed that the disease had affected quality of life via social and mental stigma and disrupted daily activities similar to other studies.^{9,11,12} Our study also revealed that DLSO leads to more self-consciousness and embarrassment in persons similar to most of other studies.^{9,15-17} Physical activities such as sports and house-hold work were affected little as compared to psychosocial impact similar to other studies. Most of the patients in the study also reported that the disease lead to some problems associated with physical contact with life partner or other relatives. The physical appearance was an important determinant in our study. The effect of disease is more on psychosocial than physical functioning similar to other reported data.^{4,10,12} The data indicate that female patients doing house-hold work or males associated with fine technical work reported mild to moderate pain. Fingernail disease was found to have much impact on QOL than toenail disease because of cosmetic considerations or technical work done with the fingers than toes.^{4,12}

The present study confirmed the psychological and physical effects of the disease on quality of life and the use of itraconazole pulse therapy resulted in superior patient outcomes regarding disease and quality of life. Patients reported satisfaction with the treatment program was significantly higher.

In the end, dermatologists should be alert to the negative impact of disease and

should try effective remedy for this problem. Patients with high score may also benefit from counseling and/or contact with psychologist, so that appropriate psychological intervention can be made in addition to drug treatment.

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Editor's note

From the October-December, 2004 issue of JPAD, the 'QUIZ' section has been replaced by 'PHOTODERMDIAGNOSIS' section and it is edited by Dr. Amor Khachemoune, MD. The manuscripts should be submitted to:

Dr. Amor Khachemoune, MD. 1440 Beacon St # 508, Brookline MA 02445, USA.

E-mail: amork@pol.net.