6-1-2021

More than nail deep: The effect of efinaconazole 10% treatment on the quality of life in patients with onychomycosis: A post hoc study

Aditya K. Gupta
University of Toronto Faculty of Medicine

Maanasa Venkataraman
Mediprobe Research Inc.

Emma M. Quinlan
Mediprobe Research Inc.

Madhulika A. Gupta
Schulich School of Medicine & Dentistry, mbgupta@uwo.ca

Naveen Anbalagan
Ortho Dermatologics

See next page for additional authors

Skin Appendage Disorders

Research Article

Skin Appendage Disord 2021;7:272–279
DOI: 10.1159/000514361

Received: October 1, 2020
Accepted: January 11, 2021
Published online: May 19, 2021

More than Nail Deep: The Effect of Efinaconazole 10% Treatment on the Quality of Life in Patients with Onychomycosis: A post hoc Study

Aditya K. Gupta[a, b] Maanasa Venkataraman[b] Emma M. Quinlan[b]
Madhulika A. Gupta[c] Naveen Anbalagan[d] Rachel Lyons[d]

[a]Department of Dermatology, Faculty of Medicine, University of Toronto, Toronto, ON, Canada; [b]Mediprobe Research Inc., London, ON, Canada; [c]Department of Psychiatry, Schulich School of Medicine and Dentistry, University of Western Ontario, London, ON, Canada; [d]Ortho-Dermatologics, Bridgewater, NJ, USA

Keywords
Onychomycosis · Efinaconazole · Quality of life · OnyCOE-t · Questionnaire

Abstract
Introduction: Onychomycosis is a common, difficult-to-treat fungal nail infection. Clinical signs include nail discoloration and thickening, which patients often find embarrassing, causing a negative impact on their quality of life (QOL). ***Methods:*** In this post hoc study, we analyze the effect of efinaconazole 10% solution on a patient's QOL using patient-reported scores from the OnyCOE-t™ questionnaire (appearance, stigma, physical problems, symptom frequency, symptom bothersomeness, treatment satisfaction, and overall problem). Higher scores corresponded to better functioning, thus higher QOL. ***Results:*** Efinaconazole 10% treatment and clinical efficacy were positively correlated with improved QOL in all domains for all groups, except with symptom bothersomeness (how much the onychomycosis symptoms worried or concerned the patient) for female patients <40 years. While still showing improvement in most domains during efficacious treatment, female and younger patients reported lower QOL scores than their male and older counterparts, despite having better clinical outcomes at follow-ups. ***Discussion:*** Female and younger patients appear to be more emotionally bothered by their symptoms, regardless of treatment success or improvement of their nail's appearance, suggesting that onychomycosis is more than nail deep and has a greater psychological effect on these patients. Therefore, younger female patients may require more assurance and mental support.

Introduction

Onychomycosis is a common fungal nail infection affecting both toenails and fingernails. It is a chronic infection which can be difficult to cure; signs include discoloration and thickening of the nail plate. Most patients disguise the abnormal appearance of their nails due to embarrassment and sometimes seek medical help [1–3]. Onychomycosis may cause discomfort and pain, making it difficult to perform basic physical activities such as typing, turning doorknobs, and wearing shoes [1–4]. Therefore, onychomycosis tends to have a noteworthy negative impact on the quality of life (QOL) of patients. QOL de-

karger@karger.com
www.karger.com/sad

Correspondence to:
Aditya K. Gupta, agupta@mediproberesearch.com

Karger

scribes the physical, mental, and social parameters of individuals according to their own perceptions of well-being and how it is affected by a disease and its treatment [4]. Lubeck et al. reported that onychomycosis could have considerable impact on general and mental health, physical appearance, social functioning, and self-confidence [5]. Onychomycosis can lead to restricted social interactions due to embarrassment and low self-esteem [3, 5–8]. The symptoms of onychomycosis and its effect on the appearance of nails are imperative factors of patients' perception of their health [2].

The validated onychomycosis-specific QOL questionnaires that asses patient's QOL include: the international onychomycosis-specific questionnaire, OnyCOE-t™, Dermatology Life Quality Index (DLQI), and NailQOL score [6]. Multiple studies have reported that female patients with onychomycosis have poorer baseline QOL scores than male patients and that successful treatment improves the QOL of all patients [6, 7, 9–13].

Elewski and Tosti published the benefits of efinaconazole 10% topical treatment on the QOL of onychomycosis patients using the OnyCOE-t™ questionnaire, which was designed to measure patient-reported outcomes specifically associated with toenail onychomycosis [2, 14]. Efinaconazole 10% treatment was shown to improve all aspects of QOL compared to vehicle and was more significant in patients who achieved clinical efficacy [2]. We have analyzed the effect of efinaconazole treatment on onychomycosis patients in detail, further stratifying the patient population by age and gender and utilizing the OnyCOE-t™ questionnaire to assess various areas (i.e., domains) of QOL, including appearance, bothersomeness, and stigma.

Methods

This is a post hoc study of results from 2 multicenter, identical, randomized, double-blind, vehicle-controlled, phase 3 studies which evaluated the efficacy of efinaconazole 10% solution in patients with mild to moderate (20–50% clinical involvement) distal lateral subungual onychomycosis (fungal infection of the distal and/or lateral edges of the underside of the nail, indicated by opaque white or yellow colorization in those areas, DLSO) of the target (great) toenail [15]. There were 1,655 patients in total, aged 18–71 years who were randomized (3:1) to efinaconazole 10% solution or vehicle once daily for 48 weeks with a 4-week follow-up period (week 52). Demographic considerations for randomization included age, gender, ethnicity, race, percent of affected toenail, and the number of affected nontarget toenails. Patients with a history of immunosuppression, HIV, uncontrolled diabetes, nondermatophyte or yeast toenail infection, severe moccasin tinea pedis, previous target toenail surgery, or any disease that may have caused toenail abnormalities were excluded [15].

At baseline, there were a total of 1,275 male and 376 female participants in both studies combined. We further divided the patient population into 4 subgroups: males, age <40 years (males <40, $n = 195$); males, age ≥40 years (males ≥40, $n = 1,080$); females, age <40 years (females <40, $n = 52$); and females, age ≥40 years (females ≥40, $n = 324$). In the males <40, males ≥40, females <40, and females ≥40 subgroups, 141, 812, 40, and 243 patients received efinaconazole 10%, and 54, 268, 12, and 81 patients received vehicle, respectively.

The primary efficacy endpoint was complete cure at week 52, defined as 0% clinical involvement of the target toenail plus mycologic cure (negative KOH examination and negative fungal culture of the target toenail sample). Secondary efficacy endpoints included clinical efficacy (<10% clinical involvement of target toenail) at week 52. However, clinical efficacy at week 52 was the primary endpoint for our post hoc study as the visual appearance of the nails is likely to have the greatest effect on patient-reported outcomes. Efficacy analyses were performed using the observed cases (per-protocol) population.

QOL Evaluation

Subjects, whose native language was English, self-administered a validated OnyCOE-t™ QOL questionnaire at baseline (time of enrollment, day 0) and at weeks 24 and 52 (see online suppl. Fig. 1; see www.karger.com/doi/10.1159/000514361 for all online suppl. material). This questionnaire evaluated the following domains:

1. Symptom Frequency: how often patients experienced pain, soreness, redness, etc.
2. Symptom Bothersomeness: how often the aforementioned symptoms worried or concerned them.
3. Appearance Problems: feeling self-conscious or avoiding physical contact with others because of the appearance of their nails, etc.
4. Physical Activity Problem: how problematic it was to perform activities such as swimming and working out.
5. Overall Problems: how much of an overall problem the nail condition was in their life.
6. Stigma: feeling odd or different from others, self-conscious in public, feeling unattractive, etc.
7. Treatment satisfaction: how satisfied patients were with the appearance of their toenails, improvement in the condition of their nails, and the results of the treatment program [14].

All items in the OnyCOE-t™ QOL questionnaire were transformed to a 0–100 scale, with higher scores indicating better functioning (i.e., higher scores equate to a better QOL). Each scale score was calculated as the average of all nonmissing items if at least half of the items making up the scale were nonmissing. The changes in scores from baseline to weeks 24 and 52 were computed for each scale by subtracting baseline scores from scores at weeks 24 and 52. As the survey was distributed to patients randomized in the clinical trials, the response rate was 100%.

Statistical Analysis

For each subgroup, we used 2-sample t tests to determine whether the change in outcome from baseline to week 52 was significant, and a least squares linear regression was run to determine whether the change in clinical efficacy values across the 5 time points (weeks 12, 24, 36, 48, and 52) was significant; a 5% significance level was used.

Table 1. QOL mean domain scores at baseline, week 24, and week 52 for the 4 subgroups – treatment with efinaconazole 10% topical solution

	Males <40				Males ≥40				Females <40				Females ≥40			
	B	W24	W52	ΔB → ΔV	B	W24	W52	ΔB → ΔV	B	W24	W52	ΔB → ΔV	B	W24	W52	ΔB → ΔV
Symptom frequency	56.6	83.2	85.4	ns	56.2	82.0	82.4	***	50.1	77.1	76.7	ns	50.9	79.4	82.0	ns
Symptom bothersomeness	66.6	89.4	89.5	ns	72.5	89.0	88.4	**	60.2	83.0	78.9	ns	62.3	85.7	88.3	ns
Physical activity problems	63.1	81.8	86.8	ns	71.2	85.8	87.6	ns	51.4	72.4	81.3	ns	59.8	79.2	82.6	ns
Appearance problems	55.1	77.8	83.8	ns	63.3	82.2	84.8	*	44.1	68.9	77.4	*	50.4	74.5	79.5	*
Overall problems	36.0	65.1	75.0	ns	52.9	73.0	77.4	*	25.3	54.4	70.2	ns	33.6	61.2	69.6	*
Stigma	66.3	76.6	78.3	*	73.2	80.9	81.3	*	60.0	71.3	75.4	ns	66.0	76.1	80.8	ns
Treatment satisfaction		74.2	78.6	**		69.5	68.9	***		73.3	73.8	*		77.1	77.9	***

$p < 0.001$ for all week 52 values compared to baseline for all subgroups and domains, except for symptom bothersomeness and stigma in females <40. B, baseline; W24, week 24; W52, week 52; ΔB → ΔV, change from baseline values in efinaconazole 10% group compared to that in the vehicle group; ns, not significant; QOL, quality of life. *** $p < 0.001$. ** $p < 0.01$. * $p < 0.05$.

If results from the 2-sample *t* test (QOL domains) and linear regression (clinical efficacy) were significant ($p < 0.05$), their β coefficients were used to estimate the absolute QOL scores or clinical efficacy rates at 3 other time points (underlined) to achieve a total of 8 time points required for correlation tests (week 12, 18, 24, 30, 36, 42, 48, and 52). Tests of correlation were then performed for clinical efficacy and QOL scores at the respective time points.

Results

Baseline QOL mean domain scores for all 4 subgroups treated with efinaconazole 10% were lowest in the overall problem domain (i.e., patients rated their QOL in this domain poorly), ranging from 25.3 for females <40 to 52.9 for males ≥40 (Table 1; Fig. 1a). A similar trend was observed at baseline in vehicle-treated patients with mean overall problem domain scores ranging from 21.2 for females <40 to 49.8 years for males ≥40 (Table 2). Baseline QOL mean domain scores in the efinaconazole 10%-treated groups were highest in symptom bothersomeness for males and females <40 (66.6 and 60.2, respectively) and in stigma for males and females ≥40 (73.2 and 66.0, respectively) (Fig. 1b, c; Table 1). Subgroups in the vehicle-treated cohort also reported the highest baseline QOL mean domain scores in symptom bothersomeness (females <40, 67.0) and stigma (males <40, 73.9; males ≥40, 72.8; and females ≥40, 62.5) (Table 2).

Impact of Efinaconazole on QOL Domains in the Four Subgroups

In general, efinaconazole 10% was more effective than vehicle in improving QOL mean domain scores for all subgroups (Tables 1, 2). In males ≥40, treatment with efinaconazole 10% was statistically more effective than vehicle in improving QOL mean domain scores in all domains, except for physical activity problems. In females ≥40, treatment with efinaconazole 10% was statistically more effective than vehicle in improving appearance problems ($p = 0.032$), overall problem ($p = 0.017$), and treatment satisfaction ($p < 0.001$). In males <40, efinaconazole 10% solution was statistically more effective than vehicle in improving stigma ($p = 0.019$) and treatment satisfaction ($p = 0.003$), whereas in females <40, the same was true for appearance problems ($p = 0.015$) and treatment satisfaction ($p = 0.013$) (Tables 1, 2).

The lowest improvement in the QOL mean scores from baseline to week 52 was seen in the stigma domain, ranging from 7.6 to 16.8 in the efinaconazole 10%-treated cohort and 2.9–8.4 in the vehicle-treated cohort (Fig. 1c). The greatest improvement in the mean QOL scores from

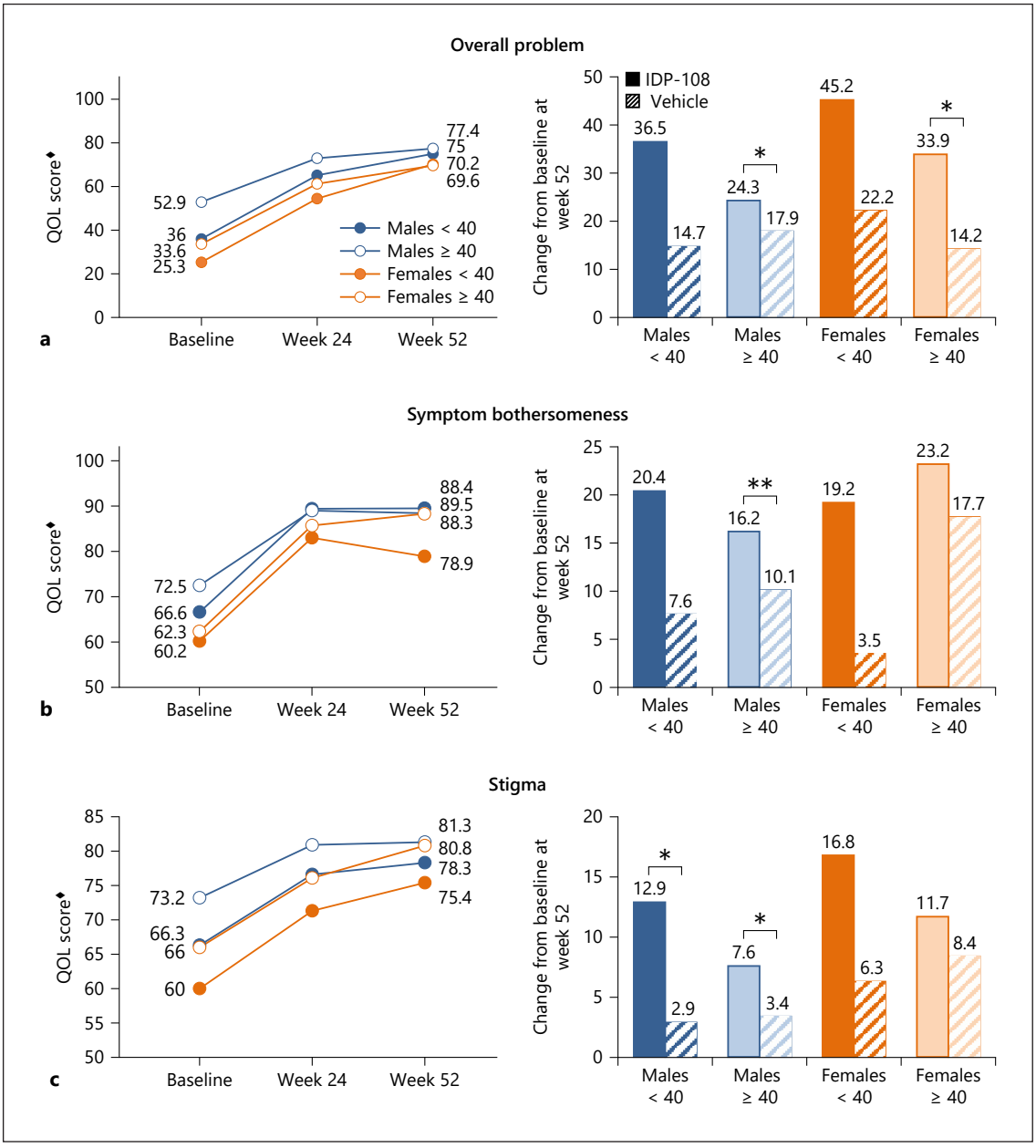

Fig. 1. Effect of treatment on symptom bothersomeness, stigma, and treatment satisfaction in patients. Left, QOL mean domain score at baseline, week 24, and week 52 with efinaconazole 10% topical solution. Right, change from baseline at week 52 with efinaconazole 10% topical solution and vehicle for all the subgroups for the domains. **a** Symptom bothersomeness . **b** Stigma. **c** Treatment satisfaction. ◆Higher score means better functioning; *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$. QOL, quality of life.

baseline was seen in the treatment satisfaction domain: 68.9–78.6 for the efinaconazole 10% cohort and 38.0–50.7 for the vehicle-treated cohort (Fig. 2a).

Aside from treatment satisfaction, the appearance problem domain had the most subgroups which experienced a significant difference between the efinaconazole 10%- and vehicle-treated groups, with the patients of the same sex sharing similar QOL scores despite variances in age (males < and ≥ 40 = 83.8 and 84.8, respectively; females < and ≥ 40 = 77.4 and 79.5, respectively) (Fig. 2b).

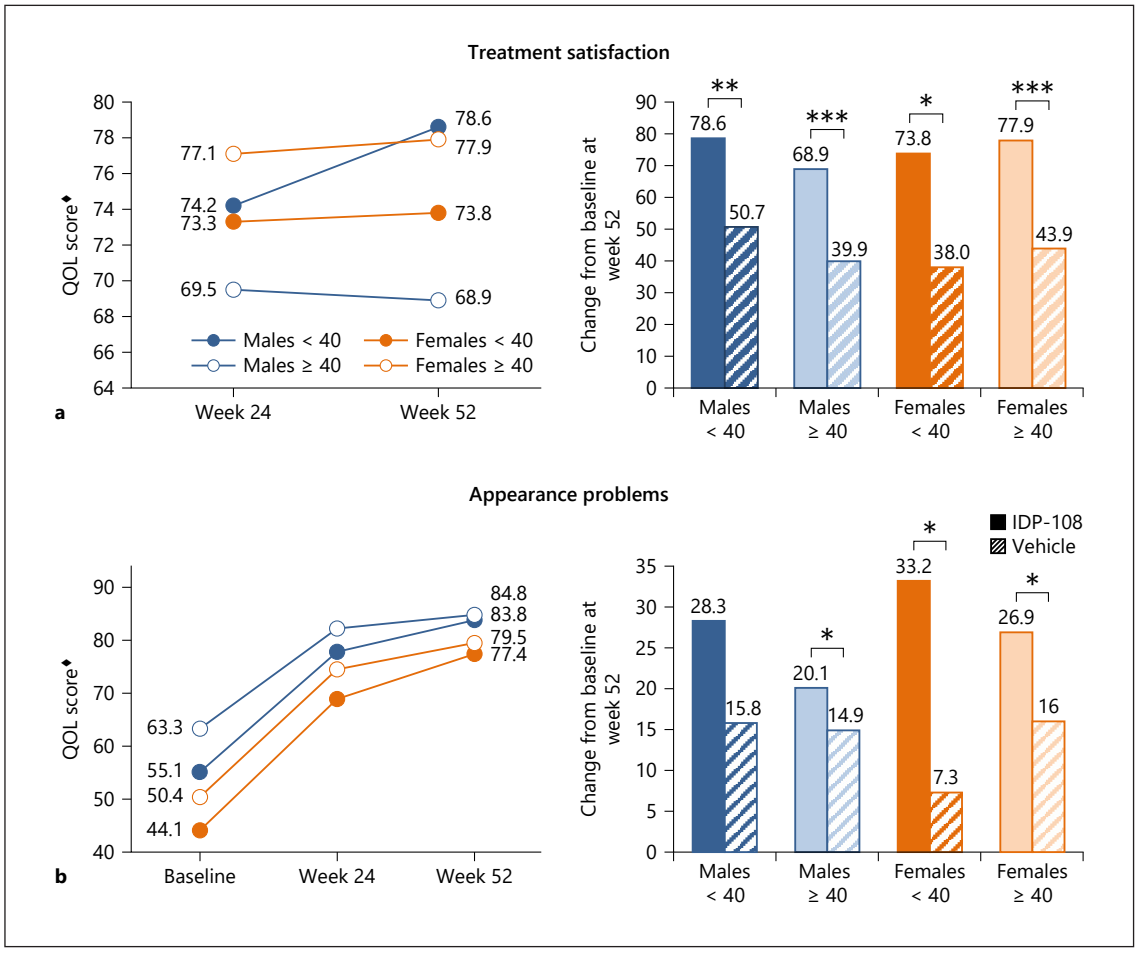

Fig. 2. Effect of treatment on overall problem and appearance problems in patients. Left, QOL mean domain score at baseline, week 24, and week 52 with efinaconazole 10% topical solution; right, change from baseline at week 52 with efinaconazole 10% topical solution and vehicle for all the subgroups for the domains. **a** Overall problem. **b** Appearance problems. •Higher score means better functioning; *, $p < 0.05$. QOL, quality of life.

Table 2. QOL mean domain scores at baseline, week 24, and week 52 for the 4 subgroups – vehicle

	Males <40			Males ≥40			Females <40			Females ≥40		
	B	W24	W52	B	W24	W52	B	W24	W52	B	W24	W52
Symptom frequency	58.4	77.7	79.8	57.2	77.6	72.7	59.8	70.7	67.6	46.1	70.4	69.3
Symptom bothersomeness	72.7	86.7	85.4	71.6	85.3	81.1	67.0	78.5	72.0	56.3	74.8	74.4
Physical activity problems	68.6	82.9	78.7	67.3	80.3	80.0	58.4	68.3	68.8	52.0	67.1	65.5
Appearance problems	56.3	76.3	74.7	61.5	77.5	77.2	45.9	64.8	61.6	47.2	62.7	62.7
Overall problems	42.4	66.7	56.0	49.8	67.7	67.4	21.2	37.0	48.1	35.3	51.0	47.9
Stigma	73.9	80.5	78.6	72.8	77.5	76.5	52.6	64.3	66.7	62.5	73.1	72.1
Treatment satisfaction		53.4	50.7		51.5	39.9		61.1	38		62.7	43.9

B, baseline; W24, week 24; W52, week 52; QOL, quality of life.

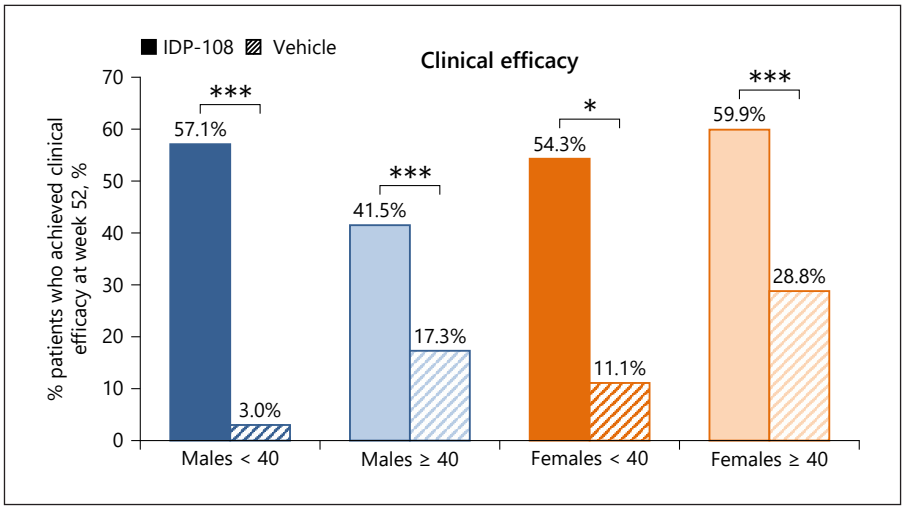

Fig. 3. Clinical efficacy of the 4 subgroups at week 52 with efinaconazole 10% treatment and vehicle. *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$.

Clinical Efficacy

Clinical efficacy was achieved in the efinaconazole 10% treatment group by 57.1, 41.5, 54.3, and 59.9% of males <40, males ≥40, females <40, and females ≥40, respectively. Similarly, at week 52, clinical efficacy was achieved in the vehicle-treated group by 3.0, 17.3, 11.1, and 28.8% of males <40, males ≥40, females <40, and females ≥40, respectively. Females ≥40 had the highest clinical efficacy with both treatment and vehicle. Conversely, males ≥40 had the lowest clinical efficacy with efinaconazole 10% treatment and males <40 had the lowest clinical efficacy with vehicle (Fig. 3).

Correlation between Clinical Efficacy and QOL Domains

The correlation between clinical efficacy and QOL mean domain scores was significant with efinaconazole 10% for all the domains for females ≥40 and males < and ≥40. The correlation between clinical efficacy and QOL mean domain scores was significant with efinaconazole in all the domains, except symptom bothersomeness in the subgroups, females <40 (Table 3).

Discussion

Once daily topical efinaconazole 10% solution was effective in improving QOL scores in all domains, in all 4 subgroups, similar to previous reports (Table 1) [2, 16, 17]. There was significant correlation between higher clinical efficacy and a greater improvement in QOL mean domain scores for most of the domains in all the subgroups with efinaconazole treatment (Table 3). However, the correlation did not extend between subgroups as female patients generally reported lower QOL scores than their male counterparts throughout the study, despite experiencing higher efficacy outcomes at the end of treatment (Table 1; Fig. 1–3). This finding is similar to previous reports where female patients had worse QOL outcomes compared to male patients, even at the end of successful therapy [6, 7, 9–13, 16, 17]. Males also reported higher overall QOL mean scores at baseline, indicating that males are less affected by onychomycosis than female patients, regardless of treatment status (Table 1; Fig. 1–3).

Treatment with efinaconazole did not seem to have an effect on how disease symptoms affected female patients <40 years emotionally (symptom bothersomeness, $p = 0.109$) (Table 1). Female patients <40 years treated with efinaconazole 10% solution had the second-highest clinical efficacy rate yet reported being most bothered by their symptoms at the end of efinaconazole treatment (Fig. 1b, 3). This is despite the fact that patients in this group reported improvements in their nail's appearance and reduction in the overall problem their condition caused them (Fig. 1a, 2b). In other words, these patients appeared to concur with their physicians (who clinically evaluated them) that their nails were improving visually, yet their onychomycosis symptoms (though reduced) still emotionally affected them. These results further support our conclusion that young female patients feel worse about having onychomycosis than male patients, regardless of objective improvements in their condition. Therefore, it is important to initiate treatment early in this population.

Treatment satisfaction was the single domain that demonstrated a significant difference between treatment and vehicle for all 4 subgroups. We observed a correlation

Table 3. Correlation results between clinical efficacy and the QOL domains over time for the 4 subgroups

Domain	Males <40	Males ≥40	Females <40	Females ≥40
Symptom frequency	$r_T = 0.79$ $p = 0.006$	$r_T = 0.71$ $p = 0.014$	$r_T = 0.64$ $p = 0.031$	$r_T = 0.79$ $p = 0.006$
Symptom bothersomeness	$r_T = 0.71$ $p = 0.014$	$r_T = 0.64$ $p = 0.031$	$r_T = 0.50$ $p = 0.109$	$r_T = 0.79$ $p = 0.006$
Physical activities problems	$r_T = 0.86$ $p = 0.002$	$r_T = 0.79$ $p = 0.006$	$r_T = 0.93$ $p < 0.001$	$r_T = 0.79$ $p = 0.006$
Appearance problems	$r_T = 0.86$ $p = 0.002$	$r_T = 0.79$ $p = 0.006$	$r_T = 0.86$ $p = 0.002$	$r_T = 0.79$ $p = 0.006$
Overall problem	$r_T = 0.86$ $p = 0.002$	$r_T = 0.79$ $p = 0.006$	$r_T = 0.93$ $p < 0.001$	$r_T = 0.86$ $p = 0.002$
Stigma	$r_T = 0.79$ $p = 0.006$	$r_T = 0.79$ $p = 0.006$	$r_T = 0.86$ $p = 0.002$	$r_T = 0.93$ $p < 0.001$

r_T, Kendall's tau correlation coefficient; p, p value; QOL, quality of life.

between treatment satisfaction and clinical efficacy, with subgroups that had better clinical efficacy reporting higher mean QOL scores at the end of treatment, and vice versa (Fig. 2a, 3). Additionally, we observed that the mean QOL scores for treatment satisfaction decreased over time for all patients treated with vehicle and for male patients ≥40 years treated with efinaconazole 10%, who achieved the lowest clinical efficacy (Tables 1, 2; Fig. 3). Essentially, patients who observed their treatment working were more satisfied with said treatment. The same was observed in the study by Drake et al., where subject treatment satisfaction correlated with better QOL outcomes and higher clinical efficacy [13].

There was not much of an improvement for any subgroup in the stigma domain at the end of efinaconazole treatment (Fig. 1c). Our findings align with a recent systematic review of the literature by Gupta et al., which reported that social stigma was the only onychomycosis measure that had less improvement over time, with only 40% of reported outcomes showing significance [1]. In our study, male patients in either age group felt less stigmatized throughout the study than female ones. It appears that women were more embarrassed about their diseased nails than men, regardless of disease outcome, which is in accordance with the literature [6, 7, 9–13, 16]. Furthermore, younger patients are more stigmatized by onychomycosis than older patients of the same gender throughout treatment (Tables 1, 2; Fig. 1c). Similar findings were observed in a population study by Szepietowski et al., which reported that age negatively correlated with stigmatization [18].

Patients of either gender aged 40 years and above reported significant improvement in their opinion on the overall problems that they faced due to their nail condition with treatment compared to vehicle (Fig. 1a). This may be attributed to the fact that patients <40 years consider onychomycosis to be a higher overall burden (physical, psychological, and social) than patients ≥40 years, which is demonstrated by their low domain scores at baseline (Tables 1, 2). Younger patients seemed to be more psychologically affected by onychomycosis, and their QOL is not impacted as much with successful treatment compared to older patients.

Onychomycosis has a significant psychosocial impact on patients and negatively affects QOL. Younger patients and female patients appear to be more psychologically affected by their condition, regardless of treatment efficacy, though they acknowledge the benefits of treatment. Therefore, for these patients, the effects of onychomycosis run deeper than the nail. Patients in those demographics may require more emotional support and reassurance when managing their onychomycosis.

Limitations

The clinical efficacy rates are based on the target great toenail, whereas the patients' perspective on their QOL related to their onychomycosis and its treatment is likely influenced by the status of all affected nails, not just the target toenail. Therefore, some bias when comparing the clinical efficacy rates and the QOL questionnaire results may have occurred.

While the exclusion criteria for this study included diseases which might cause toenail abnormalities, un-

controlled diabetes mellitus, immunosuppression, and other comorbidities were not part of the exclusion criteria or randomization scheme, and thus may have biased the results. Other patient factors such as socioeconomic status were not considered in the original randomization scheme, and thus may influence the patients' responses to the QOL questionnaire. That being said, the OnyCOE-t™ QOL questionnaire is mostly targeted toward patients' QOL in direct relationship to their onychomycosis.

Conclusion

All patients, regardless of age and gender, were more satisfied with efinaconazole treatment and had better QOL scores if they received successful treatment. Thus, receiving effective onychomycosis treatment not only improves nail health but the overall mental health as well. Assessment of health-related QOL measurements in routine clinical activities offers a patient-centered approach to the treatment of onychomycosis and aids in the development of guidelines for wholesome patient care, which involves both dermatologic and holistic aspects.

Statement of Ethics

This post hoc study analyzes data from clinical trials performed by another group. For those trials, all patients provided written informed consent. The clinical trials were conducted in accordance with the ethical principles specified in the Declaration of Helsinki and in compliance with requirements of local regulatory committees.

Conflict of Interest Statement

A.K.G. is an advisor to Moberg Pharma, Bausch Health (Canada), and Ortho Dermatologics and an investigator for Bausch Health (Canada). M.V. and E.M.Q. are employed by Dr. Gupta at Mediprobe Research Inc. M.A.G. has no conflicts of interest to declare. N.A. and L.R. are employed by Ortho Dermatologics.

Funding Sources

Funding was provided by Ortho Dermatologics.

Author Contributions

A.K.G. conceptualized the paper, analyzed the data, and authored and edited the manuscript. M.V. performed the literature search, analyzed the data, and authored the manuscript. E.M.Q. analyzed the data, and authored and edited the manuscript. M.A.G. provided scientific expertise and reviewed the manuscript. N.A. and L.R. provided the data, performed the statistical analysis, analyzed the data, and reviewed the manuscript.

References

1 Gupta AK, Mays RR. The impact of onychomycosis on quality of life: a systematic review of the available literature. Skin Appendage Disord. 2018;4(4):208–16.
2 Tosti A, Elewski BE. Treatment of onychomycosis with efinaconazole 10% topical solution and quality of life. J Clin Aesthet Dermatol. 2014 Nov;7(11):25–30.
3 Chacon A, Franca K, Fernandez A, Nouri K. Psychosocial impact of onychomycosis: A review. Int J Dermatol. 2013;52(11):1300–7.
4 Lubeck DP. Measuring health-related quality of life in onychomycosis. J Am Acad Dermatol. 1998 May;38(5 Pt 3):S64–8.
5 Lubeck DP, Patrick DL, McNulty P, Fifer SK, Birnbaum J. Quality of life of persons with onychomycosis. Qual Life Res. 1993 Oct;2(5):341–8.
6 Stewart CR, Algu L, Kamran R, Leveille CF, Abid K, Rae C, et al. Impact of onychomycosis and treatment on patient reported quality of life outcomes: a systematic review. J Am Acad Dermatol. 2020 Jun 2.
7 Drake LA, Scher RK, Smith EB, Faich GA, Smith SL, Hong JJ, et al. Effect of onychomycosis on quality of life. J Am Acad Dermatol. 1998 May;38(5 Pt 1):702–4.
8 Firooz A, Khamesipour A, Dowlati Y. Itraconazole pulse therapy improves the quality of life of patients with toenail onychomycosis. J Dermatolog Treat. 2003 Jun;14(2):95–8.
9 Schein JR, Gause D, Stier DM, Lubeck DP, Bates MM, Fisk R. Onychomycosis. Baseline results of an observational study. J Am Podiatr Med Assoc. 1997 Nov;87(11):512–9.
10 Lubeck DP, Schein JR, Gause D, Prebil LA, Potter LP. Health-related quality of life in patients with toenail onychomycosis: data from a 9-month observational study. JCOM. 1999 Sep;6(8).
11 Szepietowski JC, Reich A, Pacan P, Garlowska E, Baran E; Polish Onychomycosis Study Group. Evaluation of quality of life in patients with toenail onychomycosis by Polish version of an international onychomycosis-specific questionnaire. J Eur Acad Dermatol Venereol. 2007 Apr;21(4):491–6.
12 Milobratović D, Janković S, Vukičević J, Marinković J, Janković J, Railić Z. Quality of life in patients with toenail onychomycosis. Mycoses. 2013 Sep;56(5):543–51.
13 Drake LA, Patrick DL, Fleckman P, Andr J, Baran R, Haneke E, et al. The impact of onychomycosis on quality of life: development of an international onychomycosis-specific questionnaire to measure patient quality of life. J Am Acad Dermatol. 1999 Aug;41(2 Pt 1):189–96.
14 Potter LP, Mathias SD, Raut M, Kianifard F, Tavakkol A. The OnyCOE-t questionnaire: responsiveness and clinical meaningfulness of a patient-reported outcomes questionnaire for toenail onychomycosis. Health Qual Life Outcomes. 2006 Aug 15;4:50.
15 Elewski BE, Rich P, Pollak R, Pariser DM, Watanabe S, Senda H, et al. Efinaconazole 10% solution in the treatment of toenail onychomycosis: Two phase III multicenter, randomized, double-blind studies. J Am Acad Dermatol. 2013 Apr;68(4):600–8.
16 Del Rosso JQ. Onychomycosis of toenails and post-hoc analyses with efinaconazole 10% solution once-daily treatment: impact of disease severity and other concomitant associated factors on selection of therapy and therapeutic outcomes. J Clin Aesthet Dermatol. 2016 Feb;9(2):42–7.
17 Rosen T. Evaluation of gender as a clinically relevant outcome variable in the treatment of onychomycosis with efinaconazole topical solution 10. Cutis. 2015 Sep;96(3):197–201.
18 Szepietowski JC, Reich A; National Quality of Life in Dermatology Group. Stigmatisation in onychomycosis patients: a population-based study. Mycoses. 2009 Jul;52(4):343–9.