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Safety and efficacy of fluoxetine in the treatment of acne excoriée: a double-blind, placebo-controlled study

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Background: Self-inflicted acne excoriée is often observed in patients with compulsive skin picking, posing a challenge for diagnosis and treatment as the exact psychiatric cause remains unknown. Studies have suggested that serotonin reuptake inhibitors such as fluoxetine may help in the management of this condition. The aim of this study was to determine the efficacy and safety profile of fluoxetine in the treatment of acne excoriée and to study the psychological profiles of patients.

Methods: Sixty patients of either sex aged ≥16 years with acne excoriée were assigned to either group A (n = 30), which received oral fluoxetine (F) (20 mg/day) and oral doxycycline (D) (100 mg/day) with topical clindamycin (1%), or group B (n = 30), which received a placebo (P), oral doxycycline (100 mg/day), and topical clindamycin (1%). Patients were evaluated for standardized rating scales and followed up every two weeks for 12 weeks.

Results: Female gender predominance was observed in both groups, with most patients exhibiting anxiety and depression. With each follow-up visit (2nd, 3rd, 4th, and 5th) in both groups (A and B), the mean Acne Excoriée Severity Index (AESI) (91.4% vs. 26.7%), Hamilton Anxiety Rating Scale (HAM-A) (80% vs. 27.7%), Montgomery-Asberg Depression Rating Scale (MADRS) (68.1% vs. 28.2%), Yale-Brown Obsessive-Compulsive Scale (YBOCS) (98.27% vs. 15.63%), PGA (88.47% vs. 31.38%), and visual analogue scale (VAS) (99.17% vs. 37.67%) scores decreased from baseline by the final visit, indicating improved patient conditions. Significant differences were observed between the two groups ($P < 0.001$) in the overall response, indicating that fluoxetine was more efficacious than the control. No remarkable side effects were noted.

Conclusion: Fluoxetine efficiently managed acne excoriée without remarkable side effects.

Keywords: acne vulgaris, fluoxetine, doxycycline

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INTRODUCTION

Acne excoriée is also referred to as compulsive skin picking. Recent studies on community prevalence indicate that acne excoriée is as common as any other psychiatric disorder, with reported global prevalence values ranging from 1.4 to 5.4%, which has contributed to its serious consideration and recognition as a psychiatric disorder in DSM-V (Diagnostic and Statistical Manual of Mental

Disorders, 5th Edition) [1]. Patients affected by this condition suffer from functional disability, which can give rise to medical complications (e.g., infections, severe bleeding, and emotional distress) [2,3].

Clinical evaluation of patients with acne excoriée entails a detailed physical, clinical, and psychiatric examination, promoting an interdisciplinary perspective for its evaluation and management [4]. Approaches to treatment include selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine, sertraline, and paroxetine, along with cognitive behavioral therapy for acceptance-enhanced behavior or habit reversal [5]. Data regarding the efficacy of fluoxetine has been mixed; some studies have demonstrated its effect on one or more assessment scales of compulsive skin picking. In one such study, the fluoxetine group showed significant improvements, but participants responded on only one of the three assessment scales and none experienced full remission [6,7].

Globally, a few studies have demonstrated the efficacy of antidepressants (especially fluoxetine) in treating pathological skin-picking disorder [8,7]. Further, placebo-controlled studies of successful treatment for acne excoriée with SSRIs are limited, especially in India [9]. Hence, this study was undertaken to determine the efficacy and safety profile of fluoxetine in the management of acne excoriée and to analyze the psychological profiles of such patients in India.

MATERIALS AND METHODS

Study design

With the institutional ethics committee approval, this prospective, double-blind, placebo-controlled clinical study was conducted in the Department of Dermatology at a private medical college in Karad (Maharashtra) over a period of two years (2013-15). Informed consent was obtained from all participants and from the parents of patients under 18 years of age.

Selection criteria

Sixty patients of either sex, aged ≥16 years, diagnosed with acne excoriée, having been symptomatic for the past six months with noticeable lesions, and showing clinically significant distress associated with skin picking were included in the study. Patients with cardiovascular, hematological, pancreatic, metabolic, or neurological disorders, those with a history of tuberculosis or a chest X-ray showing evidence of any infective pathology, pregnant and lactating women, and individuals allergic to the study drugs were excluded from the study.

Primary screening

All included patients received a baseline comprehensive psychiatric evaluation using the Acne Excoriée Severity Index (AESI) [10], Hamilton Anxiety Rating Scale (HAM-A) [11], Montgomery-Asberg Depression Rating Scale (MADRS) [12], Yale-Brown Obsessive-Compulsive Scale (YBOCS) [13,14], Visual Analogue Scale (VAS) [15], and Physician Global Assessment (PGA) [16].

Grouping

The patients were randomized into two groups (groups A and B) using computer-generated sequences. A dermatologist, who was not involved in the study, dispensed the identical containers (Lilly Pharmaceuticals) containing fluoxetine and placebos to the randomly assigned groups. Group A (n = 30) received oral fluoxetine (F) (20 mg/day) and oral doxycycline (D) (100 mg/day) with topical clindamycin (1%), while Group B (n = 30) received the placebo (P), oral doxycycline (100 mg/day), and topical clindamycin (1%).

Post-treatment follow-up

All patients were followed up throughout the course of the treatment by a dermatologist who was blinded to the drugs (every two weeks for 12 weeks) for any adverse drug reactions, particularly those related to psychiatric side effects and drug compliance.

At each visit (five in total), the patients were assessed for efficacy by the AESI, HAM-A, MADRS, YBOCS, VAS, and PGA scales. Clinical screening was performed initially and for follow-up, including a complete medical history, physical examination, complete blood count, biochemical profile, urinalysis, and an electrocardiogram.

Statistical analysis

The statistical data were analyzed using the R version 3.6.0 software. The normality of the data was determined using the Shapiro Wilk test. Continuous variables with normal distribution were presented as mean ± standard deviation and analyzed using the student's unpaired and paired *t*-test. Categorical variables were presented as frequencies and percentages. Qualitative variables were analyzed using the chi-squared test of independence. Data were considered statistically significant when $P \leq 0.05$.

RESULTS

The two groups were comparable in terms of demographic parameters. Table 1 presents the age and gender distribution of the study participants.

No significant difference was observed among the two groups in terms of age and gender ($P > 0.05$). However, the majority of patients in groups A and B were females (86.6% and 66.6%, respectively), indicating female predominance (Table 1).

A minority of patients in groups A and B had neither anxiety nor depression. Nine (30%) patients in Group A and seven (23.33%) in Group B had both anxiety and depression. This demonstrates that most of the patients had at least one apparent psychological comorbidity (Table 2).

No significant difference ($P > 0.05$) was observed in terms of the mean AESI score from baseline until the first visit of the patients during follow-up. However, the mean AESI score kept decreasing in both groups with each subsequent visit. In Group A, the mean AESI score decreased from 65.03 at baseline to 5.60 at the fifth visit, indicating a 91.4% decrease in acne excoriée severity ($P < 0.01$). Similarly, in Group B, the mean AESI score fell from 62.10 at baseline to 45.90 at the fifth visit, indicating a 26.7% decrease in acne excoriée severity. At the end of the study, a significant difference ($P < 0.001$) was observed in the mean AESI score between the two groups (Table 3).

In Group A, the mean MADRS score fell from 8.96 at baseline to 2.86 at the fifth visit, representing a significant decrease (68.1%) in the depression level ($P < 0.01$). Similarly, in Group B, the mean MADRS 9.33 at baseline dropped to 6.70 at the fifth visit, indicating a 28.2 % improvement. A significant difference ($P < 0.001$) was observed in the mean MADRS score between the two groups at the end of the study (Table 3).

The mean HAM-A score fell significantly from 17.20 at baseline to 3.43 at the fifth visit, indicating a decrease in the anxiety level by 80.0% in Group A ($P < 0.01$). Similarly, in Group B, the mean HAM-A score decreased from 15.07 to 10.90, indicating a 27.7% drop in the anxiety level by the end of the study (Table 3). Also, a significant difference ($P < 0.001$) was observed in the mean HAM-A score between the two groups at the final follow-up (Table 3).

The mean YBOCS score in Group A fell from 17.33 at baseline to 0.3 at the final visit, indicating a 98.27% improvement ($P < 0.01$). Similarly, in Group B, the mean YBOCS decreased from 15.63 at baseline to 11.73 at the fifth visit, representing a 24.9% improvement. At the end of the study, a significant difference ($P < 0.001$) was observed in the mean MADRS score between the two groups (Table 4).

The mean PGA score in Group A fell from 5.2 at baseline to 0.6 at the final follow-up, indicating an 88.47% improvement ($P < 0.01$). Similarly, in

Table 2. Psychological comorbidities (anxiety/depression) of patients in Group A and Group B

Psychological evaluation	Group A (n = 30) N (%)	Group B (n = 30) N (%)
Isolated anxiety	7 (23.33)	6 (20)
Isolated depression	4 (13.33)	4 (13.33)
Anxiety + depression	9 (30)	7 (23.33)
Neither	10 (33.33)	13 (43.33)

Table 1. Comparison of demographic variables among the two groups of patients

Variables	Group A (n = 30)	Group B (n = 30)	*P*
Age (Mean ± SD)	22.77 ± 5.217	21.67 ± 3.790	0.354*
Gender N (%)			
Female	26 (86.6)	20 (66.6)	0.067#
Male	4 (13.4)	10 (33.4)	

*Unpaired t-test; #Chi-squared test

Table 3. Comparison of mean AESI, HAM-A, and MADRS scores among the two groups of patients

	Group A (n=30) (Mean ± SD)	Group B (n=30) (Mean ± SD)	*P**
Mean AESI score			
Baseline	65.033 ± 19.033	62.100 ± 16.035	0.521
First visit	55.233 ± 18.506	60.400 ± 15.730	0.249
Second visit	45.600 ± 17.194	58.033 ± 16.510	0.006
Third visit	32.867 ± 15.620	54.400 ± 16.025	<0.001
Fourth visit	22.300 ± 13.314	50.533 ± 15.613	<0.001
Fifth visit	5.600 ± 3.578	45.933 ± 15.111	<0.001
Mean HAM-A score			
Baseline	17.20 ± 5.18	15.07 ± 3.24	0.0610
First visit	14.60 ± 4.85	13.60 ± 3.09	0.3452
Second visit	11.77 ± 4.26	12.93 ± 2.96	0.2232
Third visit	9.63 ± 3.76	12.13 ± 2.72	0.0045
Fourth visit	6.70 ± 2.72	11.80 ± 3.10	<0.0001
Fifth visit	3.43 ± 2.03	10.90 ± 2.75	<0.0001
Mean MADRS score			
Baseline	8.967 ± 2.697	9.333 ± 2.682	0.6945
First visit	7.433 ± 2.609	8.200 ± 2.325	0.2340
Second visit	6.167 ± 2.198	7.967 ± 2.327	<0.001
Third visit	5.100 ± 1.989	7.400 ± 2.343	<0.001
Fourth visit	4.267 ± 1.780	7.100 ± 2.187	<0.001
Fifth visit	2.867 ± 1.655	6.700 ± 1.896	<0.001

*Paired t-test; AESI: Acne Excoriée Severity Index; HAM-A: Hamilton Anxiety Rating Scale; MADRS: Montgomery-Asberg Depression Rating Scale; SD: standard deviation.

Table 4. Comparison of mean YBOCS, PGA, and VAS scores among the two groups of patients

	Group A (n = 30) (Mean ± SD)	Group B (n = 30) (Mean ± SD)	*P**
Mean YBOCS score			
Baseline	17.333 ± 3.575	15.633 ± 4.895	0.130
First visit	14.567 ± 3.137	14.467 ± 4.826	0.924
Second visit	11.567 ± 3.481	13.833 ± 4.624	0.036
Third visit	8.7 ± 2.793	12.767 ± 4.576	<0.001
Fourth visit	5.567 ± 2.012	12.667 ± 4.381	<0.001
Fifth visit	0.3 ± 1.149	11.733 ± 3.991	<0.0001
Mean PGA score			
Baseline	5.2 ± 0.761	5.1 ± 0.759	0.612
First visit	4.3 ± 0.749	4.7 ± 0.750	0.043
Second visit	3.3 ± 0.749	4.2 ± 0.640	<0.001
Third visit	2.3 ± 0.711	3.9 ± 0.718	<0.001
Fourth visit	1.3 ± 0.556	3.8 ± 0.714	<0.001
Fifth visit	0.6 ± 0.563	3.5 ± 0.730	<0.001
Mean VAS score			
Baseline	100	100	NA
First visit	78.833 ± 7.273	90.667 ± 4.498	<0.0001
Second visit	58.5 ± 10.840	86.833 ± 4.639	<0.0001
Third visit	37.5 ± 13.245	78.167 ± 7.598	<0.0001
Fourth visit	16.333 ± 10.581	71.333 ± 11.366	<0.0001
Fifth visit	0.833 ± 3.733	62.333 ± 12.645	<0.0001

*Paired t-test; PGA: Physician Global Assessment; VAS: Visual Analogue Scale; YBOCS: Yale-Brown Obsessive Compulsive Scale.

Group B, the mean PGA score dropped from 5.1 at baseline to 3.5 at the fifth visit, indicating only a 31.38% improvement. At the end of the study, a significant difference ($P < 0.001$) was observed in the mean PGA score between the two groups (Table 4).

In Group A, the mean VAS score decreased from 100 at baseline to 0.83 at the final visit, indicating a 99.17% improvement. Similarly, in Group B, the mean VAS score dropped from 100 at baseline to 62.33, indicating a 37.67% improvement by the end of the study. At the final follow-up, a significant difference ($P < 0.001$) was observed in the mean VAS score among the two groups (Table 4).

At the fourth visit, no significant change from baseline values was observed in clinical parameters like the electrocardiograms, complete blood count, and total bilirubin, SGPT/SGOT, blood urea, creatinine, sodium, and potassium levels in either group. However, slightly higher levels of complete blood count parameters and abnormal serum sodium and potassium levels were observed in Group A during the fourth follow-up visit, indicating minor side effects of fluoxetine + doxycycline administration.

Additionally, no visible side effects of fluoxetine, clindamycin, and doxycycline were observed among the patients of both the study groups at each visit. Nonetheless, one patient reported diarrhea due to doxycycline administration, though only during the first and second visits.

DISCUSSION

The clinical evaluation of a patient with acne excoriée entails an extensive physical, medical, and psychiatric examination. Individuals with this disorder rarely seek psychiatric medications (e.g., fluoxetine) for their condition due to social embarrassment or the belief that their condition is either untreatable or simply a 'bad habit' [1].

In this prospective study, most of the patients in both groups were young, with the mean age ranging from 21-26 years; females comprised the predominant gender. This is in accordance with previous studies, which suggested that the age of onset for acne excoriée varies substantially; it may occur during adolescence or later at the age of 20-30 years [17,18].

Skin picking disorder can occur with a variety of other disorders, such as depression and anxiety. In this study, some patients had both anxiety and depression as psychological comorbidities. This is in accordance with a study conducted by Flessner and Woods (2006) [19] in which 85.9% of patients had anxiety and 66.3% had depression due to acne excoriée [19]. It is proposed that screening for both acne excoriée as well as its secondary manifestations like anxiety and depression should be done to achieve successful management.

During the second, third, fourth, and fifth follow-up visits, a marked decrease in the AESI score was observed in Group A (91.4%) compared with Group B, indicating the effectiveness of fluoxetine in decreasing the severity of acne excoriée as compared to the placebo ($P < 0.001$). Another study showed similar results with a decrease in the skin-picking severity index due to a lowering of the lesion severity factor and a decreased percentage of lesions ($P = 0.011$) [20].

The mean HAM-A score in this study endured a noticeable decrease in Group A (80%), where patients were administered with fluoxetine ($P < 0.001$). Additionally, the MADRS score in Group A decreased with each follow-up visit as the patients returned to normal conditions from mild depression. Similar observations were made in a comparative study conducted by Çalıkuşu *et al.* (2003) [21] in which HAM-A decreased from the moderate level to the mild level, and an effective reversal of the condition was noted according to the MADRS score in the fluoxetine-administered group ($P = 0.002$).

The YBOCS focuses on skin-picking rather than 'compulsions' or 'obsessions.' A double-blind controlled (fluoxetine vs. placebo) study conducted by Bloch *et al* (2001) [9] showed that eight of the fifteen subjects (53.3%) achieved at least a 30% decrease in the modified YBOCS score by week six [9]. Similar observations were made in this study as a significant decline in the YBOCS score was observed by the fifth week in the fluoxetine-treated group (Group A) as compared to the placebo-controlled group (Group B).

Marked improvements in the VAS and PGA scores in this study support the conclusion that fluoxetine is efficacious in the treatment of patients with acne excoriée. This is in accordance with the results observed in a study conducted by Kim *et al* (2013) [7].

In the present study, the analysis of side-effect reports revealed no significant side effects of fluoxetine and doxycycline. Nonetheless, one patient reported diarrhea due to doxycycline administration only during the first two visits. Contrasting observations were found in another

study wherein out of four patients randomized to fluoxetine, two had no side effects, one had cessation of mild tremors and increased sweating, and one continued to report sexual dysfunction and excessive yawning [9].

Strickland *et al.* (2002) reported that clinicians should consider several possible clinical causes such as anemia, uremia, and hepatic disease for skin picking [22]. However, the clinical screening of the patients in the present study showed no visible difference in the two groups in hemoglobin, complete blood count, total bilirubin, SGPT/SGOT, blood urea, creatinine, serum sodium, and serum potassium levels, and ECGs during the baseline and fifth visits, thus ruling out any possible role of these parameters as the cause of acne excoriée. This study provides evidence that fluoxetine could be useful in the treatment of pathologic skin picking and in improving the psychological profiles of patients.

The limitations of this study were the small sample size and the short period of follow-up. Furthermore, doses of fluoxetine were not titrated according to the severity of acne excoriée, which sets the scope for future studies. Larger double-blind studies are necessary to assess which individuals are more likely to respond better to fluoxetine (categorization of patients according to age), as well as the relative long-term effectiveness of fluoxetine and the efficacy of other serotonin reuptake inhibitors or treatment approaches.

CONCLUSION

Fluoxetine was found to be efficacious and safe in the management of acne excoriée as it decreased the associated anxiety and depression without leaving any side effects. The decrements in AESI, HAM-A, MADRS, and YBOCS scores supported this conclusion, along with marked improvements in the VAS and PGA values.

Conflict of interest: None declared.

REFERENCES

1. Grant JE, Odlaug BL, Chamberlain SR, et al. Skin picking disorder. Am J Psychiatry. 2012;169(11):1143-9.
2. Arnold LM, Auchenbach MB, McElroy SL. Psychogenic excoriation: clinical features, proposed diagnostic criteria, epidemiology and approaches to treatment. CNS Drugs. 2001;15(5):351-9.
3. Hayes SL, Storch EA, Berlanga L. Skin picking behaviors: An examination of the prevalence and severity in a community sample. J Anxiety Disord. 2009;23(3):314-9.
4. Schumer MC, Bartley CA, Bloch MH. Systematic review of pharmacological and behavioral treatments for skin picking disorder. J Clin Psychopharmacol. 2016;36(2):147-52.
5. Guest PC, Knowles MR, Molon-Noblot S, et al. Mechanisms of action of the antidepressant fluoxetine and the substance P antagonist L-000760735 are associated with altered neurofilaments and synaptic remodeling. Brain Res. 2004;1002(1-2):1-10.
6. Grant JE, Stein DJ, Woods DW, et al (Eds). Trichotillomania, skin picking, and other body-focused repetitive behaviors. Washington DC: American Psychiatric Publishing Inc; 2012.
7. Kim DI, Garrison RC, Thompson G. A near fatal case of pathological skin picking. Am J Case Rep .2013; 14:284.
8. Del Rosso JQ. Oral doxycycline in the management of acne vulgaris: current perspectives on clinical use and recent findings with a new double-scored small tablet formulation. J Clin Aesthet Dermatol. 2015;8(5):19-26.
9. Bloch MR, Elliott M, Thompson H, Koran LM. Fluoxetine in pathologic skin-picking: open-label and double-blind results. Psychosomatics. 2001;42(4):314-9.
10. Arbabi M, Farnia V, Balighi K, et al. Efficacy of citalopram in treatment of pathological skin picking: a randomized double-blind placebo-controlled trial. Acta Med Iran. 2008; 46(5):367-72.
11. Hamilton M. The assessment of anxiety states by rating. Br J Med Psychol. 1959; 32(1):50-5.
12. Montgomery SA, Åsberg M. A new depression scale designed to be sensitive to change. Br J Psychiatry. 1979; 134:382-9.
13. Goodman WK, Price LH, Rasmussen SA, et al. The yale-brown obsessive-compulsive scale. I. development, use, and reliability. Arch Gen Psychiatry. 1989;46(11):1006-11.
14. Goodman WK, Price LH, Rasmussen SA, et al. The yale-brown obsessive-compulsive scale II validity. Arch Gen Psychiatry. 1989;46(11):1012-6.
15. Aitken RC. Measurement of feelings using visual analogue scales. Proc R Soc Med. 1969; 62(10):989-93.
16. Freedman JD, Gottlieb AB, Lizzul PF. Physician performance measurement: tiered networks and dermatology (an opportunity and a challenge). J Am Acad Dermatol. 2011;64(6):1164-9.
17. Collier CN, Harper JC, Cafardi JA, et al. The prevalence of acne in adults 20 years and older. J Am Acad Dermatol. 2008;58(1):56-9.
18. Keuthen NJ, Koran LM, Aboujaoude E, et al. The prevalence of pathologic skin picking in US adults. Compr Psychiatry. 2010;51(2):183-6.
19. Flessner CA, Woods DW. Phenomenological characteristics, social problems, and the economic impact associated with chronic skin picking. Behav Modif.2006; 30(6):944-63.

20. Christensen RC. Olanzapine augmentation of fluoxetine in the treatment of pathological skin picking. Can J Psychiat. 2004;49(11):788.
21. Çalıkuşu C, Yücel B, Polat A, Baykal C. The relation of psychogenic excoriation with psychiatric disorders: a comparative study. Compr Psychiatry. 2003; 44(3):256-61.
22. Strickland P, Rostron E, Haddad P, et al. Assessing and managing compulsive scratching in schizophrenia with chronic renal failure. Can J Psychiatry. 2002; 47(5):484-5.

