

Extended Abstract 1

Article: Chretien J.H. Efficacy of Undecylenic Acid- Zinc Undecylenate Powder in Culture Positive Tinea Pedis. International Journal of Dermatology. 1980; 19: 51-54.

<http://onlinelibrary.wiley.com.proxy.lib.uwaterloo.ca/doi/10.1111/j.1365-4362.1980.tb01997.x/pdf>

Study Objectives: To reaffirm the efficacy and safety of powder containing 2% undecylenic acid and 20% zinc undecylenate against placebo with a double blinded randomized trial (contrary to previous trials).

Methods:

- Design: Randomized control trial
- Allocation: 151 total patients enrolled based on positive diagnosis and skin scraping. 85 had positive dermatophyte culture and of those 42 assigned to placebo powder and 43 assigned to active powder. Remaining patients split evenly at random.
- Blinding: Double blinded
- Follow up period: at days 7, 14, 21, 28 and 42
- Setting: Single centre, Georgetown University
- Participants: Healthy college students complaining of athletes foot, genders or other information not provided
- Intervention: 2% undecylenic acid/20% zinc undecylenate powder, applied twice daily for 4 weeks
- Outcomes: reversal of pretreatment culture, reversal of KOH preparation, clinical evidence of healing
- Patient follow up: No follow ups exceeding 42 days of trial completion

Main Results:

Trichophyton rubrum or Trichophyton mentagrophytes were isolated in pretreatment from 85 patients. Of these, 88% of those with the active powder had negative cultures at day 28 relative to only 17% negative cultures of placebo at the same time ($P < 0.001$). Fungus was identified with KOH treated skin scrapings in all 151 patients prior to treatment. Of those patients with the active powder 80% were KOH negative at day 28 compared to 49% of those treated with placebo ($P = 0.001$). Erythema and scaling were significantly improved by therapy with active powder as were subjective evaluations of itching and burning. No side effects or adverse events reported.

Conclusions:

2% undecylenic acid/20% zinc undecylenate powder is significantly more effective than placebo in the treatment of tinea pedis. Safety under directed uses does not appear to be a large issue with this formulation.

Comments/Critical Appraisal:

The trial by Chretien et al demonstrated the efficacy of 2% undecylenic acid/20% zinc undecylenate powder as an effective treatment relative to placebo for the treatment of tinea pedis. The efficacy of undecylenic acid has been shown in other trials though they often lacked the benefit of untreated control groups and/or blinding. Patients were advised to wash their feet prior to application and change socks daily. The negative cultures post 4 weeks of identical twice daily treatment showed an 87% success rate with the active powder relative to only 17% with placebo. The KOH skin readings post treatment also showed a significant difference from the control group have negative results in 77% compared to 48%. No adverse effects were noted in either group though the treatment group showed greatly improved symptoms after 4 weeks.

The trial was well constructed and properly controlled however outcome (cure) criteria are difficult to standardize so the study required the use of several outcomes. Half of the outcomes were objective and the other half subjective based on clinical presentation and patient diaries. Internal validity was impacted due to the lack of classification of fungal infection severity and positive cultures were only obtainable in 56% of patient which was common to other trials but had little effect on final results. Administration of medication was not monitored as to ensure proper application or compliance. The classification of patients is not very clear and only described as "otherwise healthy college students" so the external validity can be limited to healthy patients (no age or gender determination). Randomization, blinding, and a placebo control add to the strengths of this article. However, the small sample size and lack of patient differentiation weakens the study though do not seem to impact the results of the trial. The trial dates from the 1980 and does not compare to other agents in its era or to new azole drugs thus no comparative information can be extrapolated. 2% undecylenic acid/20% zinc undecylenate powder which is still a common preparation can provide an adequate treatment option for the majority of patients if first line options are unavailable.

Abstract 2

'Undecylenic acid preparations are used in the treatment of various dermatomycoses, especially [tinea pedis](#). Concentrations of the acid as high as 10%, as well as those of the acid and salt in the compound ointment, may be applied to the skin. The preparations as formulated are usually not irritating to tissue, and sensitization to them is uncommon. It is of undoubted benefit in retarding fungal growth in tinea pedis, but the infection frequently persists despite intensive treatment with preparations of the acid and the [zinc](#) salt. At best, the clinical "cure" rate is ~50%, which is much lower than that obtained with the imidazoles, haloprogin, or [tolnaftate](#). [Efficacy](#) in the treatment of [tinea capitis](#) is marginal, and the drug is no longer used for that purpose. Undecylenic acid preparations also are approved for use in the treatment of diaper rash, [tinea cruris](#), and other minor dermatologic conditions.'

Source:Textbook, Bennet, John E. Goodman & Gilman's The Pharmacological Basis of Therapeutics 12e; Chapter 57. 2011. McGraw-Hill Companies Access Pharmacy:

<http://www.accesspharmacy.com/Content.aspx?searchStr=undecylenic+acids&aid=16678778#1667904>

1

Summary: The author states that up to preparations of 10% undecylenic acid can be used in the treatment of tinea pedis. Undecylenic acid proves to be an effective fungistatic, infections tend to

persist despite intensive treatment with the acid and the zinc salt (astringent). The clinical cure rate is approximately 50% which is much lower when comparing to newer agents like imidazoles, haloprogin or tolnaftate. The drug is no longer used for tinea capitis and is losing popularity in tinea pedis.

Critical appraisal:

The author, John E. Bennett is the chief of the Clinical Mycology Section of the National Institute of Allergy and Infectious Disease where he specializes in cryptococcosis and candidiasis. That being said, his expert opinion in the area of mycology is largely applicable to the treatment of tinea pedis. The reference listed lacks any obvious referencing for claims or statistics but does include an extensive bibliography that likely was. He is an expert on new mycological drugs including azoles and is well positioned to give opinion on that treatment field. The internal and external validity of his statement has not been compromised as it is applicable to the general population. He does not make any specific mention to certain disease states though he discourages its general use compared to newer, more effective agents.

Abstract 3

Smith E, et al. Topical Undecylenic Acid In Tinea Pedis: A New Look. International Journal of Dermatology. 1977; 16: 52-56 <http://onlinelibrary.wiley.com/doi/10.1111/j.1365-4362.1977.tb00741.x/pdf>

Study Objectives: To determine the efficacy of 2 undecylenic acid powder preparations as compared to a talc vehicle or no treatment for dermatophytosis of the feet.

Methods:

- Design: Randomized control trial
- Allocation: 104 patients with clinical evidence of tinea pedis confirmed with KOH preparations stratified according to age, duration and severity of infection. Subjects were then randomized to 4 groups: 2% undecylenic acid/20% zinc undecylenate, lower strength active powder, talc powder, no treatment
- Blinding: Double blinded
- Follow up period: at weeks 2, 4, and 6. Patients reported 5 days/week for medication application
- Setting: Single centre, University of Mexico
- Participants: Students or staff of University of Mexico with clinically confirmed tinea pedis
- Intervention: 2% undecylenic acid/20% zinc undecylenate, lower strength active powder, talc powder, no treatment. Medication groups received treatment once daily 5 days a week.
- Outcomes: Clinical and mycological clearing
- Patient follow up: No follow ups exceeding 42 days of trial initiation

Main Results:

Table 2. Results of Final Evaluation After 6 Weeks' Treatment*

Group	Medication	Total no. subjects	No. subjects clinically & mycologically clear	No. improved & mycologically clear	No. improved but mycologically positive	No. unimproved whether mycologically positive or negative
1	New undecylenic acid powder	27	16	9	0	2
2	Old undecylenic acid powder	30	14	9	4	3
3	Talc	23	1	0	1	21
4	No treatment	22	2	1	5	14

* The number of subjects clinically and mycologically clear in Groups 1 and 2 is significantly greater than that in control Groups 3 and 4 ($P < 0.001$).

Conclusion:

Undecylenic acid and its zinc salt are relatively safe and effective in the management of dermatophytosis in the feet.

Comments/Critical Appraisal:

This is another study taking a more in depth look at the effectiveness of undecylenic acid that builds on previous studies lacking control groups and blinding. Patients were stratified into groups based on age, duration of infection and severity (4 point scale). The preparation of undecylenic acid was 2%/20% zinc salt which at the time was the newest formulation. A lesser strength was used in the other active group. The analysis here showed that significantly better results in both clinical and mycological improvements relative to talc treatment and placebo. As with most other trials, patients were advised to wash their feet prior to treatment and wear fresh socks. One striking statistic was the improved statistic of the no treatment group over the talc group. The explanation offered was the potential difference in adherence to non-pharmacological measures. Ultimately there were no significant differences in the undecylenic acid preparation groups (53%, 47%) as they both showed significant improvement compared to the other groups.

The trial was well structured in its patient allotment with the stratification though the trial itself was subject to clinician bias as it was only single blinded. The patient size was rather small but the results correlate well with other similar trials, though they had their own pitfalls. Some interesting things to point out of the trial that affect its internal validity is the treatment regimen being only once daily and only 5 days a week contrast to typical twice daily therapy. This could largely explain the seemingly low 53% cure rate (7% other groups) compared to other similar trials. Though the investigators went to great measures to ensure compliance and consistency by monitoring patient dose administration which many other trials failed to do. Externally there is limited data on the stratification but given the nature of other similar studies the results can applied to the general population. Other benefits of the study include

randomization and the inclusion of a broader age range unlike other college studies based exclusively on students. Several patients however did drop out, mostly from the non-medicated groups due to worsening conditions and only 2 patients from the treatment group due to the development of an erythematous pruritic eruption.

Abstract 4

Source: Mayo Clinic disease state review: <http://www.mayoclinic.com/health/athletes-foot/DS00317>
Accessed July 11, 2012

Summary: The clinical summary provided by the Mayo Clinic failed to even mention undecylinic acid as a potential option for athlete's foot. Despite the fact undecylinic acid is still available as an OTC option, the summary cited numerous of current treatment guidelines that all failed to list it as a relevant treatment option. Lack of efficacy or cost effectiveness compared to newer agents is likely the reason given the clinical data.

Critical Appraisal: The Mayo Clinic is a renowned authority on healthcare and consistently bases its recommendations with appropriate evidence. Many disease specific experts place their input and add credibility to recommendations. The references listed are current with many dating from the 2010. The objectives of the article are clearly made with an extensive overall summary describing the pathology, diagnosis and treatment of tinea pedis.

Abstract 5

Source: Tinea Pedis, Courtney M Robbins, MD <http://emedicine.medscape.com/article/1091684-medication#1> Accessed July 11, 2012

Summary: The clinical summary provided by Medscape also failed to mention undecylinic as relative treatment option for the treatment of tinea pedis. Despite the fact undecylinic acid is still available as an OTC option, the summary cited numerous of current treatment guidelines that all failed to list it as a relevant treatment option. Lack of efficacy or cost effectiveness compared to newer agents is likely the reason given the clinical data.

Critical Appraisal: Medscape is a renowned authority on healthcare and consistently bases its recommendations with appropriate evidence. Many disease specific experts place their input and add credibility to recommendations. The references listed are current with many dating from the 1990s and 2000s with comparative efficacy to newer agents. The objectives of the article are clearly made with an extensive overall summary describing the pathology, diagnosis and treatment of tinea pedis.