Efficacy of Clotrimazole vs other pharmacological agents for treatment of Oral Candidiasis-A Systematic Review

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ABSTRACT

Aim: To assess the efficacy and safety of topical application of clotrimazole versus others in the treatment of oropharyngeal candidiasis (OPC).

Method: Four electronic databases, registries of ongoing trials, and manual search were used that compared the efficacy of clotrimazole to other antifungal agents in patients who were clinically diagnosed with oral candidiasis up to February 2023. Primary outcomes were clinical response and mycological cure rates. Secondary outcomes include relapse rate, incidence of systemic infections, and compliance. Adverse effects were also evaluated.

Results: 11 RCTs with a total of 1418 patients were included. Our analysis showed no significant difference in clinical response between clotrimazole and all other antifungal agents. However, clotrimazole was less effective in terms of mycologic cure and relapse rate. Analysis showed significant efficacy of fluconazole over clotrimazole.

Conclusion: This systematic review indicated that clotrimazole is less effective than fluconazole effective as other topical therapies in treating OPC. Well-designed high-quality RCT is needed to validate these findings

INTRODUCTION

The opportunistic fungal infection known as "thrush," sometimes known as oral candidiasis, frequently affects the oral mucosa.[1]The most common species being Candida albicans and the other species include Candida tropicalis, Candida glabrata, Candida pseudotropicalis, Candida guilliermondii, Candida parapsilosis, and Candida krusei.[2]**Francois Veilleux**, a pediatrician, first described oral candidiasis in **1838**.

There are several types of oropharyngeal candidiasis which include **acutepseudomembranous, acute atrophic, chronic hyperplastic, chronic atrophic, median rhomboid glossitis, angular cheilitis and many more.**

If oral candidiasis is treated properly and effectively, the prognosis is favourable. Patients who relapse frequently do so as a result of poor adherence to therapy, improper removal, and cleaning of dentures, or an inability to address any underlying or predisposing causes to infection.[6]

Oral Candidiasis can be treated by giving antifungal agents **topically** as well as **systemically**.

Treatment of candidiasis, mucosal or invasive, relies on a limited arsenal of antifungal agents.The paucity of antifungal classes coupled with the shortcomings of the current therapeutic agents hampers the ability to fight fungal infections. The most significant

shortcomings of the available agents are their **suboptimal selectivity, raised toxicity**, and increased likelihood of **developing resistance**.

Topical antifungal treatment is the first-line treatment advised for mild oral candidiasis and when systemic treatment is required, topical therapy should be continued as this lowers the dose and duration that systemic treatment will need to be administered.[8] The systemic adverse effects and drug interactions that occur with the systemic agents do not occur with topical agents.[9]

Topical application to manage OPC minimizes drug interactions and adverse effects known to be associated with systemic antifungal agents; however, limitations exist such as local irritation, unpalatable taste, sugar content especially when used in patients with dental caries or uncontrolled diabetes, and lack of compliance due to the need for frequent administration.

Prevention of superficial oral infections is crucial in order to improve the quality of life as well as to prevent the possible development of systemic fungal infections. Dosage form, side effects, and clinical efficacy vary for each of them. [8]

OBJECTIVE

The aim of this present systematic review is to evaluate the efficacy of clotrimazole as compared with other pharmacological agents i.e., fluconazole, ketoconazole, nystatin, itraconazole and miconazole in the management of oral candidiasis.

MATERIALS AND METHODS

Protocol and registration

The PRISMA (The preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines were followed to report the systematic review. This review had been registered in the International Prospective Register of Systematic Reviews (PROSPERO), Center for Reviews and Dissemination, University of York on 04-02-2023.

Prospero ID:CRD42023396326.

Eligibility Criteria

The search strategy was conducted through PubMed and Google Scholar Which was based on the research question. Is clotrimazole as efficacious as other pharmacological agents like fluconazole, miconazole, itraconazole, nystatin and ketoconazole in treatment of Oral Candidiasis? The search strategy was based on following PICO questions.

Population (P)- Patients with oral candidiasis

Intervention (I)-Clotrimazole used in treating oral candidiasis regardless of dosage regimen.

Comparator (C)-Placebo or other antifungal agents like Fluconazole, Nystatin, Itraconazole, Miconazole, and Ketoconazole.

Outcome (O)-Clinical response, remission of lesion.

Main Outcome:

- Clinical response- relief in symptoms like burning sensation, and discomfort.
- Reduction in clinical signs (size and severity) of lesion. Remission of lesion.

Measure of effect- Follow up should be done in 2weeks.

SEARCH STRATEGY

The literature search was carried out through PubMed, Google Scholar, Medline, Web of Science and Cochrane Library databases from 1978 - 2023for the studies regarding the evaluation of efficacy and safety of Clotrimazole intervention in the management of Oral Candidiasis.

The search was restricted to the studies published in English language from 1978 to 2023. The search included the terms to define population as “Oral Candidiasis’’ and “Oral Candidosis”,‘‘candidiasis” OR ‘‘candidiosis” OR ‘‘oral candidiasis” OR ‘‘oral candidiases”

OR ‘‘oropharyngeal candidiasis” OR ‘‘thrush” OR ‘‘candida stomatitis” OR ‘‘prosthetic stomatitis” OR ‘‘candida mucositis” OR ‘‘oral moniliasis” OR ‘‘rhomboid glossitis”) AND ‘‘clotrimazole” AND (‘‘randomized controlled trial” OR ‘‘controlled clinical trial” OR ‘‘randomized controlled study” OR ‘‘RCT”). Other sources were used to search for more studies, which include registries of ongoing trials: clinicaltrial.gov, controlled-trial.com, centerwatch.com, and world health organization portal. A hand search was conducted by checking the reference lists of articles retrieved.

STUDY SELECTION

Identification

All studies were extracted by electronic and manual search. Database search was performed by two independent reviewers and the articles were first selected by reading the title and abstracts. The duplicate search was removed.

Screening

As the database search was done independently by two reviewers, the articles were excluded based on the following criteria.

- Retrospective studies, review articles, case reports, case series, case-control studies.
- Letter to the editor, opinion articles, book chapters, conference abstracts and meetings, duplicate publications, in vitro studies.
- Non-human studies; studies not published in English and studies published prior to 1978.
- Animal studies and unpublished articles were excluded.

Eligibility criteria of the included studies

The full text of selected studies was evaluated and assessed individually by the two investigators, had there been any disagreement between the two, the reviewers discussed the study and reached the conclusion.

The studies were included based on the following criteria:

1. **Type of studies**-Randomized controlled trials to assess the beneficial effects of treatment.
2. **Publishing date**-1st January 1978 to 5th February 2023

Inclusion criteria

- Patients diagnosed with Oral Candidiasis.
- Male and female both genders are included.

Data Extraction

The data extraction and validity assessment of all selected studies that met the inclusion criteria was done by reading the material and methods and the result section of the individual study. Data was extracted focusing on following details.

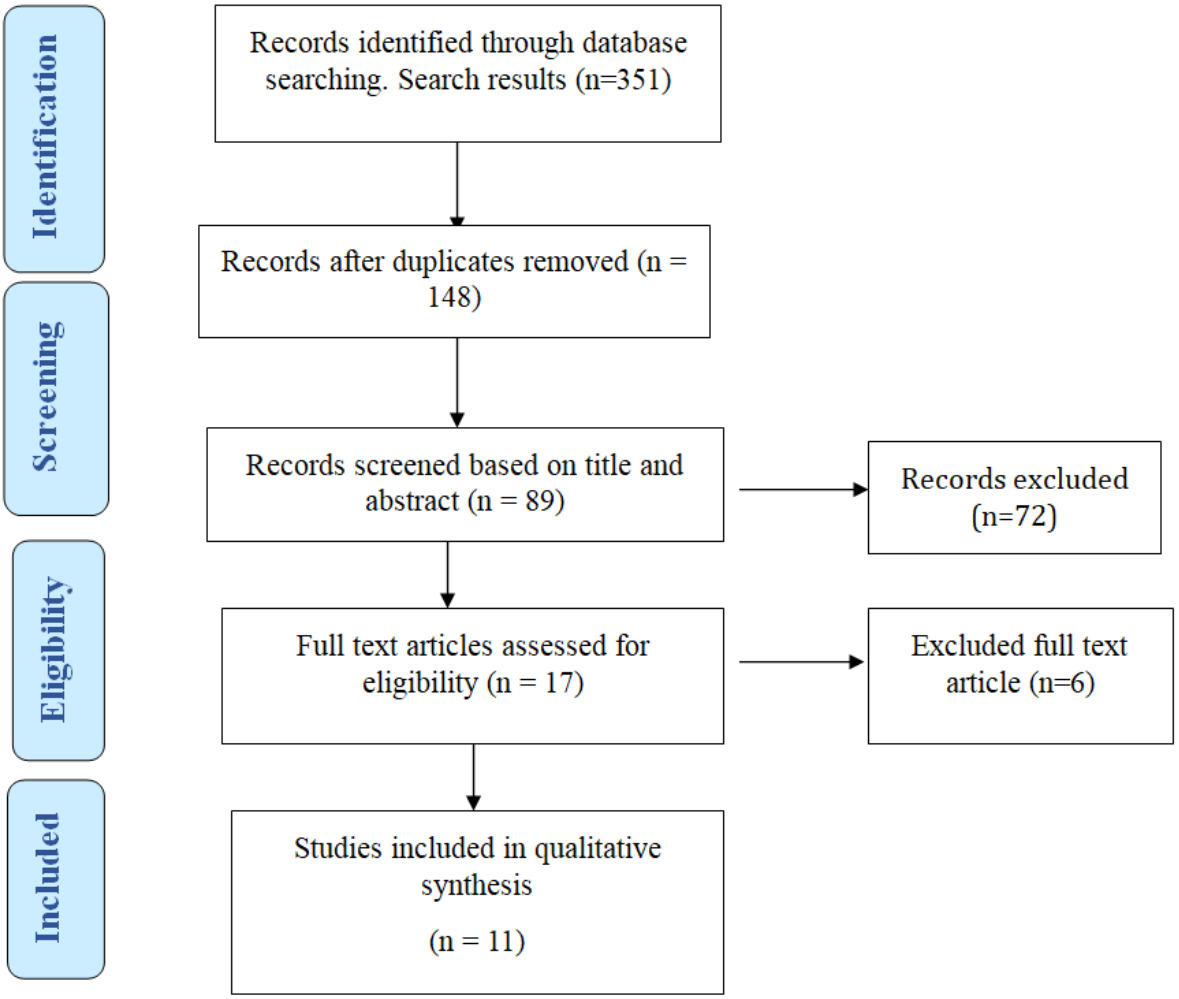
- For each included trial, the year of publication, author of study, country of origin.
- Study population
- Sample size and number of groups.
- Inclusion and exclusion criteria

Details on the intervention and control; the reported outcomes and its assessment methods.

RISK OF BIAS IN INDIVIDUAL STUDIES

The risk of bias in each included study was evaluated independently using Revised Cochrane risk-of-bias tool for randomized trials (RoB2.0) 2018. The 2 authors assessed 5 domains for individually randomized trials are:
1) Bias arising from the randomization process.
2) Bias due to deviation from intended intervention.
3) Bias due to missing outcome data.
4) Bias in measuring the outcome.
5) Bias in the selection of reported results. (Table 3)

Prisma flow diagram



RESULT

Study selection

A total of 351 articles were obtained from the electronic search, which it was cross-checked by another examiner to remove the duplicate articles. 203 articles were removed after a duplicate examination. 148 articles were reviewed for title and abstract, after which 59 articles were excluded as they were in other language, 89 articles were excluded as they were review articles and case reports, and 17 articles were examined based on the research question. 11 articles that matched the PICO format of the review were included for qualitative analysis.

Study characteristics

An examination of full text of 17 potential reports resulted in 11 studies being included (11,12,13,14,15,16,17,18,19,20,21) with a total participant of 1418.
All studies examined the role of Clotrimazole and other pharmacological agents like fluconazole, miconazole, itraconazole, nystatin.

Study design

All 11 studies included in the review were Randomized controlled trial. All studies were parallel arm group.

Participants

The participants of the study consisted of both genders from 3 years to 80 years. Participants suffered from Oral candidiasis. Many of the studies did not provide more specific about context of intervention.

TABLE 1: Study Table Representing Characteristics Of The Included Studies

Ref no.	Author/Year/Country	Journal	Study design	Age of included patients	Sample size	Control	Intervention
11	Jagat Reddy RC, Jeelani S, Duraiselvi P, Kandasamy M, Kumar GS, Pandian RA. 2017/ India	Journal of International Society of Preventive and Community Dentistry	Comparative Study	Patient over age 18 years	180 patients	Clotrimazole mouth paint 3 times a day for 2 weeks	Fluconazole suspension in form of a mouth rinse 3 times a day for 2 weeks.
12	AA Sholapurkar, KM Pai,S Rao 2009/India	Australian Dental Journal	Randomized controlled trial	Age at least 18 years.	89 patients (42 women and 47 men)	Clotrimazole mouth paint 1% is prescribed the commercially available mouth paint. Patients were advised to apply the mouth paint to affected areas with the index finger thrice daily for two weeks.	Fluconazole suspension of 2 mg/mlin distilled water was prepared by a hospital pharmacist. Each patient was instructed to rinse 5 ml of the solution for 2–3 minutes and then swallow. Mouth rinse was used 3 times daily for two weeks.
13	Charles H Kirkpatrick 1978/ England	The New England Journal Of	Randomized double-blind,	Patient over age 18 years	20 patients	A troche containing 10 mg of	A troche containing 10 mg of

		Medicine	placebo controlled clinical trial.			clotrimazole was given five times a day for a period of two weeks. The troches were retained in the mouth and dissolved in 15 to 30 minutes; saliva was swallowed.	placebo 5 times a day for two weeks. The placebo was retained in the mouth and dissolved in 15 to 30 minutes; saliva was swallowed.
14	Vincent Pons, Greenspan Deborah 1993/USA	J of Acquired Immune deficiency Syndromes	Randomized, single-blind, multicenter study design.	Patient over age 18 years	334 patients	Clotrimazole 10mg troche 5times a day for 2weeks	Fluconazole 100mg capsule 1 time a day for 2 weeks.
15	SUSAN L. KOLETAR, JANE A. RUSSELL, ROBERT J. FASS, AND JOSEPH F. PLOUFFE 1990/ Ohio	Antimicrobial Agents Chemotherapy	Randomized controlled trial.	Not Mentioned	39 patients	Clotrimazole 10mg troche 5times a day for 2weeks	Fluconazole 100mg capsule 1 time a day for 2 weeks.
16	Redding SW, Farinacci GC, Smith JA, Fothergill AW, Rinaldi MG. 1992.	Special Care in Dentistry	Randomized controlled trial	Not mentioned	24 HIV patients with thrush.	Clotrimazole troche 10mg 5 times per day for 2weeks.	Fluconazole 100mg tablets once daily for 2 weeks.
17	Vazquez Jose A et al 2010/ Ohio	HIV Clinical Trials	Randomized, Comparative, Double-Blind, Double Dummy, Multicenter Trial	Patient above 18years of age	578 patients	The Clotrimazole troche was given as a lozenge to be gradually dissolved in the mouth five times each	After the initial dosage of CT or placebo troche, Miconazole Buccal Tab (MBT) was administered in the morning to

						day.	the canine fossa depression of the upper gum, superolateral to the canine tooth. It was switched out for a fresh tablet after at least 6 hours. During 30 seconds, mild pressure was given to the upper lip to help the MBT adhere to the gum. Patients could eat, drink, and chew after application at any point during the experiment.
18	Patricia A. Murray, Susan L Koletar, Irma Mallegoh Jane Wu,Bruce L. Moskovitz 1997/Ohio	Clinical Therapeutics	Multicenter, open label,third party trial	Patient above 13 years of age	162 patients	Clotrimazole 10mg troche 5times a day for 2weeks	Itraconazole oral solution 200mg 1 time daily for 2weeks
19	Linpiyawan R, Jittreprasert K, Sivayathorn A 2000/ Thailand	International Journal of Dermatology	Clinical trial	Not mentioned	29 patients	Clotrimazole 10mg 5times a day for 1 week	Itraconazole oral solution (100mg/10 ml) twice a day for 1 week.
20	Myles E. Gombert, Lorraine duBouchet, Taryn M. Aulicino, Khalid M. H. Butt 1987/ New York	JAMA	Randomized Controlled Trial (Open Study)	Not mentioned	62 patients	Clotrimazole was administered as 10-mg lozenges,	Nystatin 15ml oral suspension (1,00,000U/ml) 6 times daily.

						three times daily.	
21	James Ruskin et al 1992 USA	Oral Surg Oral Med Oral Pathol	Randomized clinical trial	>3 years of age	34 patients	Clotrimazole 10mg dissolved on tongue 5 times daily.	Nystatin 5ml suspension, swished in mouth for 1 minute and swallowed 4 times daily.

Table 2: Tabular Representation of Results of all Included Studies

Ref No	Results
11	For group I patients, the fungal eradication was 89.5%, whereas for group II patients, the fungal eradication was 86.7%. No significant results were obtained while comparing the mycological eradiation in patients of the two study groups.
12	Those who received fluconazole had a higher likelihood of continuing to be disease-free during the 15-day follow-up than individuals who received clotrimazole. The mean candidal colony numbers before to treatment did not statistically differ significantly between the two groups. However, when mean candida colony counts were assessed following therapy, there was no statistically significant distinction between the two groups. There was no statistically significant difference between the two groups, nevertheless, according to an intergroup comparison that took the mycological eradication into account.
13	In all 10 patients who received clotrimazole, symptoms and mucosal lesions significantly improved, and in nine patients, cultures of mucosal scrapings and potassium hydroxide preparations revealed no signs of candidiasis. Only one of the 10 patients who received a placebo, however, experienced any improvement.When compared to the group that received placebo, the clinical outcome in the clotrimazole-treated group was considerably better (P 0.001). There were no reported medication side effects. After the trial's blind phase, 15 patients received clotrimazole patches as part of an open trial. It was observed that one to three troches per day were sufficient to maintain remissions. The author concluded that the treatment for persistent oral candidiasis, clotrimazole, is quite successful.
14	Both therapies were clinically successful; patients who received clotrimazole either recovered completely or showed improvement. By the end of treatment, fluconazole (65% vs. 48%) outperformed clotrimazole in eliminating candida from the oral flora (p=0.005).Also, patients who received fluconazole had a higher likelihood of continuing to be symptom-free throughout the second week of follow-up (82.3 versus 50%) (p 0.001). By the post-therapy visit in week four, this difference was no longer perceptible. Fluconazole temporarily gave a longer disease-free condition and was just as effective as clotrimazole in the treatment of oral candidiasis.
15	Clinical resolution rates were 100% and 65%, respectively, among the 36 evaluable cases (P=0.018).The rates of mycological eradication were, respectively, 75% and 20% (P=0.004). Patients who received fluconazole had a higher chance of being disease-free during follow-up than patients who received clotrimazole (P=0.014 at 2 weeks). After the conclusion of therapy, prolonged clinical responses related to mycological eradication (P=0.043). According to this study, fluconazole proved superior to clotrimazole troches in treating oral candidiasis in HIV-positive patients. Although earlier trials had not demonstrated such a relationship, prolonged clinical responses after 14 days of therapy were associated, at least in part, with greater mycological eradication. Fluconazole may have had better compliance and tolerance, which may have contributed to some of its

	greater efficacy.
16	When compared to clotrimazole patches, fluconazole pills provided a more effective clinical cure. Fluconazole tablets also had lower rates of colonization at the conclusion of therapy and relapse at days 28 and 42 than clotrimazole troches did. These variations were not statistically significant, though. When compared to clotrimazole, fluconazole had better patient compliance. Statistics showed that this difference was significant. Patients with HIV infection can effectively cure thrush with fluconazole pills and clotrimazole troches.
17	Clinical cure at the test of cure (TOC) visit (days 17–22) in the populations treated with intent to treat (ITT) and treated per protocol (PP) were the co-primary efficacy objectives. The outcomes were Clinical cure rates for patients receiving MBT treatment at the TOC visit were statistically comparable to those for patients receiving CT treatment in both the ITT (61% vs 65%) and PP (68% vs 74%) populations. Safety, tolerability, and secondary outcomes were comparable across treatment groups. The study found that the therapy of OPC in individuals who were HIV-positive was demonstrated in this major trial to be noninferior to CT given five times daily.MBT provides a convenient once-daily topical treatment alternative for OPC that is efficient, secure, and well-tolerated.
18	Itraconazole significantly outperformed clotrimazole in terms of the proportion of patients having negative cultures at the end of treatment (60% vs. 32%, respectively). Significantly more patients receiving itraconazole (53%) than clotrimazole (30%) achieved a negative culture plus clinical response, and the results were similar in the subset of patients with HIV/AIDS. Many reported side effects for both medications involved the gastrointestinal system, and both medications were well tolerated. For the treatment of oral candidiasis in immunocompromised patients, including those with HIV/AIDS, once daily itraconazole oral solution administration for 14 days is effective and well tolerated.
19	Throughout follow-up and via treatment, the clinical severity levels of all patients gradually decreased, although there was no statistically significant difference between the groups. By the conclusion of the first week of treatment, 73.3% of clotrimazole patients and 66.7% of itraconazole patients had reached a clinical cure.At week 2, two of 12 patients receiving itraconazole and five of 13 patients receiving clotrimazole both experienced relapses (P = 0.31).At week 4, there were five relapses in the clotrimazole group out of eight patients and three out of nine in the itraconazole group (P = 0.347).
20	In the patients under study, both regimens were 100 percent successful in preventing the onset of thrush.Negative effects were rarely observed in any group (one case of mild nausea in the clotrimazole group and three cases in the nystatin group). Before completing 60 days of treatment, one patient from the clotrimazole group and eight patients from the nystatin group voluntarily withdrew (P =0.002). The taste of the medications or an inability to follow the protocol were cited as reasons for discontinuation. In the preventive doses used in this trial, the cost of clotrimazole troches was roughly $1/10^{th}$ that of nystatin oral suspension. Compared to nystatin oral suspension, clotrimazole troches are more efficient, more affordable, and simpler to administer on one's own.
21	Nystatin and clotrimazole are equally effective for oropharyngeal candidiasis prophylaxis in orthotopic liver transplant patients.

TABLE 3: Tabular Representation for Risk of Bias Assessment of The Included Studies

Ref no.	Author/Year/ Country	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Overall risk of Bias Judgement
11	Jagat Reddy RC et al 2017/India	Low risk	Some concern	Low risk	Low risk	Some concern	Low risk
12	AA Sholapurkar 2009/ India	Low risk	Low risk	Low risk	Low Risk	Low risk	Low Risk
13	Charles H Kirkpatrick 1978/ England	Some concern	Some concern	Some concern	Low risk	Low risk	Some concern
14	Vincent Pons, Greenspan Deborah 1993/USA	Some concern	Low risk	Low risk	Some concern	Low risk	Low risk
15	SUSAN L. KOLETAR, JANE A. RUSSELL, ROBERT J. FASS, AND JOSEPH F. PLOUFFE 1990/ Ohio	Some concern	Low risk	Low risk	Some concern	Some concern	Some concern
16	Redding SW, Farinacci GC, Smith JA, Fothergill AW, Rinaldi MG. 1992	Low risk	Some concern	Some concern	Low risk	Low risk	Low risk
17	Vazquez Jose A et al 2010/ Ohio	Low risk	Some concern	Low risk	Low Risk	Some concern	Low Risk
18	Patricia A. Murray, Susan L Koletar, Irma Mallegoh Jane Wu,Bruce L. Moskovitz 1997/Ohio	Some concern	Some concern	Low risk	High Risk	Low risk	High Risk
19	Linpiyawan R, Jittreprasert K, Sivayathorn A 2000/ Thailand	Some concern	Some concern	Low risk	High Risk	High Risk	High Risk
20	Myles E. Gombert, Lorraine duBouchet, Taryn M. Aulicino, Khalid M. H. Butt 1987/ New York	Low risk	Low risk	Some concern	Some concern	Low risk	Low risk
21	James Ruskin et al 1992 USA	Some concern	Some concern	Low risk	Low risk	Low risk	Low risk

DISCUSSION

To our knowledge, this is the first systematic review exclusively and comprehensively analysing the literature on the efficacy and safety of clotrimazole in the treatment of Oral Candidiasis in various patient populations. Although other systematic reviews in the treatment of Oral Candidiasis have been previously published, these either addressed other antifungal agents (Lyu et al., 2016; Zhang et al., 2016) or specific patient populations

including patients with denture stomatitis, HIV, and cancer (Emami et al., 2014; Pienaar et al., 2010; Worthington et al., 2010).

It included 11 randomized trials that tested 4 different antifungal drugs:

1. Fluconazole (R. C. Jagat Reddy, S. Jeelani1, P. Duraiselvi, M. Kandasamy, G. Suresh Kumar, R. AzhalVel Pandian 2017), (AA Sholapurkar, KM Pai, S Rao 2009), (CHARLES H. KIRKPATRICK, DAVID W. ALLING, 1978), (Vincent Pons, Deborah Greenspan, Michael Debruin 1993), (SUSAN L. KOLETAR, JANE A. RUSSELL, ROBERT J. FASS, JOSEPH F. PLOUFFE 1990) and (Redding SW et al 1992)

2. Miconazole (Vazquez JA, Patton LL, Epstein JB, Ramlachan P, Mitha I, Noveljic Z, Fourie J, Conway B, Lalla RV, Barasch A, Attali P. 2010)

3. Itraconazole (Patricia A. Murray, Susan L Koletar, Irma Mallegoh Jane Wu, Bruce L. Moskovitz,1997), (RumpaLinpiyawan, Kitti Jittreprasert, ApichatiSivayathorn,2000)

4. Nystatin (Myles E. Gombert, Lorraine duBouchet, Taryn M. Aulicino, Khalid M. H. Butt, 1987), (James D. Ruskin, R. Patrick Wood, Michael R. Bailey, Cherie K. Whitmore, Byers W. Shaw, Omaha, Nebr., Tex. 1992)

1. Clotrimazole: Clotrimazole has been successfully used as treatment and prophylaxis of oropharyngeal candidiasis in immunosuppressed patients.It is rapidly absorbed when taken orally, yet it remains unsuitable for systemic treatment because of enzyme induction and accelerated metabolism in the liver. Clotrimazole inhibits the demethylation of lanosterol and ergosterol, which results in fungal growth inhibition.[21]

A topical antifungal called clotrimazole blocks the formation of ergosterol in the fungal cell membrane. It is fungistatic. It is produced as a cream, solution, or oral or vaginal troche, and has the advantage of having anti-candidal and anti-staphylococcal properties.

2. Fluconazole: An effective and targeted inhibitor of fungal enzymes, fluconazole prevents the production of ergosterol, a crucial component of the plasma cell membrane. As a result, it interferes with the development of cell walls, causing leakage of cellular contents and cell death. The gastrointestinal system effectively absorbs it, and the plasma levels are over 90% of those attained with intravenous dosing.

Reddy JC et al 2017 Conducted a study to evaluate the effectiveness of fluconazole and clotrimazole in the treatment of patients withoral candidiasis. In results, groupI patients showed fungal eradication of 89.5%, whereas group II patients showed fungal eradication of 86.7%. The study concluded thatapproximately similar effectiveness in terms of treatment was noted with fluconazole and clotrimazole in treating patients with candidiasis.

Sholapurkar AA 2009 Conducted this study compares the efficacy offluconazole mouth rinse and clotrimazole mouth paint inthe management of oral candidiasis. There was no statistically significant difference between the two groups, nevertheless, according to an intergroup comparison that took the mycological eradication into account.

According tothe study done by**Charles H Kirkpatrick 1978**,it was observed that 1-3 troches per day were sufficient to maintain remissions. The author concluded that the treatment for persistent oral candidiasis, clotrimazole, is quite successful.

Pons, Vincent 1993 carried out a study to assess the toxicity and clinical effectiveness of oral fluconazole and clotrimazole troches. Both therapies were clinically successful; patients who received clotrimazole either recovered completely or showed improvement. By the post-therapy visit in week four, this difference was no longer perceptible.Fluconazole temporarily gave a longer disease-free condition and was just as effective as clotrimazole in the treatment of oral candidiasis.

Susan Koletar et al 1990 evaluated the effectiveness (clinical and mycological) and tolerance to clotrimazole troches with that of fluconazole in the treatment of oropharyngeal candidiasis in people with human immunodeficiency virus infection (HIV). According to this study, fluconazole proved superior to clotrimazole troches in treating oral candidiasis in HIV-

positive patients.Fluconazole may have had better compliance and tolerance, which may have contributed to some of its greater efficacy.

Redding SW1992 Conducted study to compare efficacy between fluconazole tablets and clotrimazole troches for management of oral thrush in HIV infection. When compared to clotrimazole patches, fluconazole pills provided a more effective clinical cure. Fluconazole tablets also had lower rates of colonization at the conclusion of therapy and relapse at days 28 and 42 than clotrimazole troches did.

3. Miconazole: An antifungal drug with imidazole structure, miconazole also exhibits anti-candidal and anti-staphylococcal effects. It can be applied to the treatment of angular cheilitis, just like clotrimazole. Miconazole comes in gel (Zeasorb-AF), cream, ointment, and lacquer forms for the treatment of oral candidiasis.

Vazquez et al 2010 This study's goal was to compare the effectiveness and safety of miconazole 50 mg buccal tab-let (MBT) once daily versus CT given five times daily for treating OPC in individuals who were HIV-positive. The study found that the therapy of OPC in individuals who were HIV-positive was demonstrated in this major trial to be noninferior to CT given five times daily.MBT provides a convenient once-daily topical treatment alternative for OPC that is efficient, secure, and well-tolerated.

4. Itraconazole: Itraconazole is useful in the salvage therapy of immunocompromised patients with fluconazole-resistant candidosis because it has a larger spectrum of activity than fluconazole. Itraconazole, a lipophilic triazole, has response rates of 64–80% and is particularly effective in treating fluconazole-resistant candidal strains like C. krusei or C. glabrata.

Murray PA et al 1997 They evaluated the effectiveness and safety of itraconazole oral solution (200 mg once daily) and clotrimazole troches (10 mg five times daily) in a group of immunosuppressed individuals. Itraconazole significantly outperformed clotrimazole in terms of the proportion of patients having negative cultures at the end of treatment (60% vs. 32%, respectively). Significantly more patients receiving itraconazole (53%) than clotrimazole (30%) achieved a negative culture plus clinical response, and the results were similar in the subset of patients with HIV/AIDS.

Linpiyawan R, Jittreprasert K, Sivayathorn A. 2000compared the effectiveness and safety of itraconazole oral solution and clotrimazole troche in treating oropharyngeal candidiasis in AIDS patients. By the conclusion of the first week of treatment, 73.3% of clotrimazole patients and 66.7% of itraconazole patients had reached a clinical cure. The author concluded that itraconazole oral solution and clotrimazole troche were both reliable and secure treatments for oral candidosis in AIDS patients. The relapse rates did not differ statistically.

5. Nystatin: One of the most popular topical antifungals is nystatin, a polyene antifungal agent.It comes in a variety of forms, including an oral solution of 50% sucrose, a vaginal pill, a cream, an ointment, and a lozenge (pastille).

Myles E Gombert 1987compared the efficiency of nystatin oral suspension and clotrimazole troches in the treatment of oropharyngeal candidiasis. Compared to nystatin oral suspension, clotrimazole troches are more efficient, more affordable, and simpler to administer on one's own.

Ruskin JD 1992 This research was done to compare the prevalence of oropharyngeal candidiasis in liver transplant recipients who had received prophylactic treatment with either clotrimazole troches or nystatin liquid. The author concluded that nystatin and clotrimazole are equally effective for oropharyngeal candidiasis prophylaxis in orthotopic liver transplant patients.

CONCLUSION

In conclusion, clotrimazole is a useful medication for treating OPC. Our investigation revealed no discernible difference between clotrimazole and any other antifungal medications in terms of clinical response. Clotrimazole, however, performed less well in terms of mycologic cure and relapse rate. Notably, there were no differences in clinical response, microbiologic cure, or relapse when clotrimazole was exclusively compared to other topical antifungal drugs. Fluconazole is more effective than placebo, but clotrimazole is less effective. As a result, when fluconazole is unavailable or inappropriate, clotrimazole represents a significant alternative treatment option for OPC. Due to the requirement for numerous daily administrations, compliance with clotrimazole remains a significant challenge. To support these findings, high-quality randomised controlled trials are required.

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