

Use of antifungals in the treatment of vulvovaginal candidiasis: an integrative review

Uso dos antifúngicos no tratamento da candidíase vulvovaginal: uma revisão integrativa
Uso de antifúngicos en el tratamiento de la candidiasis vulvovaginal: una revisión integradora

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Abstract

Objective: To identify scientific evidence available in the literature and analyze the action of antifungal drugs used for the treatment of vulvovaginal candidiasis. **Methods:** Integrative literature review conducted in the databases Medline/PubMed, Embase, Web of Science, Cochrane Library, CINAHL, SCOPUS and VHL; with the descriptors "woman", "antifungal agents"; "vulvovaginal candidiasis". **Results:** Ten scientific articles published between 1983 and 2020 were obtained. Of these, four were developed in Iran; followed by Mexico, England, Taiwan, Thailand, Denmark, and the United States. In terms of methodological design, most studies are clinical trials (n=8), and two are cross-sectional studies. Regarding the level of evidence, eight are level II, and only two investigations are level IV. Concerning the antifungal drugs used in the treatment, there was a predominance of clotrimazole (n=4; efficacy ranging from 42.4% to 98.3%), followed by econazole (n=2; efficacy between 39% and 89%), combined or not with another antifungal drug. **Conclusion:** The use of clotrimazole stands out, as it is highly effective in the treatment of vulvovaginal candidiasis. This study contributes to the advancement of knowledge and improvement of the clinical practice of nursing and other health professionals. It is expected that these results will encourage further studies and update clinical practices.

Descriptors: Women; Antifungal Agents; Candidiasis, Vulvovaginal.

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Whats is already known on this?

The scientific literature presents conflicting evidence on the efficacy of antifungal drugs in the treatment of vulvovaginal candidiasis, justifying an integrative review to synthesize and evaluate the available information.

What this study adds?

It contributes with relevant information on the effective use of antifungals in the treatment of vulvovaginal candidiasis, assisting healthcare professionals in choosing the appropriate therapy for this fungal condition.



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Resumo

Objetivo: Identificar evidências científicas disponíveis na literatura e analisar a ação dos antifúngicos utilizados para o tratamento da candidíase vulvovaginal. **Métodos:** Pesquisa de revisão integrativa da literatura conduzida nas bases de dados Medline/PubMed, Embase, Web of Science, Cochrane Library, CINAHL, SCOPUS e BVS; com os descritores "mulher", "agentes antifúngicos"; "candidíase vulvovaginal". **Resultados:** Obtiveram-se dez artigos científicos publicados entre 1983 e 2020. Destes, quatro foram desenvolvidos no Irã; seguidos por México, Inglaterra, Taiwan, Tailândia, Dinamarca e Estados Unidos. A maioria dos estudos são ensaios clínicos (n=8), e dois são estudos transversais. No tocante ao nível de evidência, oito são nível II, e apenas duas investigações são nível IV. Quanto aos antifúngicos utilizados no tratamento, houve predominância do clotrimazol (n=4; eficácia variando de 42,4% a 98,3%), seguido pelo econazol (n=2; eficácia entre 39% a 89%), combinados ou não a outro antifúngico. **Conclusão:** Destaca-se o uso do clotrimazol, pois apresenta alta eficácia no tratamento da candidíase vulvovaginal. Este estudo contribui para o avanço do conhecimento e do aprimoramento da prática clínica da enfermagem e de outros profissionais da saúde. Espera-se que esses resultados incentivem novos estudos e a atualização das práticas clínicas.

Descritores: Mulher. Antifúngicos, Candidíase vulvovaginal

Resumen

Objetivo: Identificar la evidencia científica disponible en la literatura y analizar la acción de los antifúngicos utilizados para el tratamiento de la candidiasis vulvovaginal. **Métodos:** Revisión bibliográfica integradora realizada en las bases de datos Medline/PubMed, Embase, Web of Science, Cochrane Library, CINAHL, SCOPUS y BVS; con los descriptores "woman", "antifungal agents"; "vulvovaginal candidiasis". **Resultados:** Se obtuvieron diez artículos científicos publicados entre 1983 y 2020. De ellos, cuatro se desarrollaron en Irán; seguido de México, Inglaterra, Taiwán, Tailandia, Dinamarca y Estados Unidos. La mayoría son ensayos clínicos (n=8), y dos son estudios transversales. En cuanto al nivel de evidencia, ocho son de nivel II, y sólo dos investigaciones son de nivel IV. En cuanto a los antifúngicos utilizados en el tratamiento, predomina el clotrimazol (n=4; eficacia entre 42,4% y 98,3%), seguido del econazol (n=2; eficacia entre 39% y 89%), combinado o no con otro antifúngico. **Conclusión:** Destaca el uso de clotrimazol, por su alta eficacia en el tratamiento de la candidiasis vulvovaginal. Este estudio contribuye al avance del conocimiento y a la mejora de la práctica clínica de enfermería y otros profesionales sanitarios. Se espera que estos resultados estimulen la realización de nuevos estudios y la actualización de las prácticas clínicas.

Descritores: Mujeres. Antifúngicos. Candidiasis Vulvovaginal

INTRODUCTION

Vulvovaginal candidiasis (VVC) is characterized as an infectious process of the female lower genitourinary tract, caused by different species of candida - such as *Candida albicans*, *glabrata* and *krusei*, the first being the most commonly found, accounting for about 80% of cases. Such fungi compromise women's health and mainly affect the vulva and the vagina.⁽¹⁾

The VVC is a condition frequently observed among users treated in health services, and can be diagnosed based on signs and symptoms, as well as laboratory findings. The latter refers to the use of sterile swabs to collect the sample to be examined in order to characterize the vaginal flora.⁽²⁾

This infection presents characteristic signs and symptoms, such as pruritus, edema, hyperemia in the perineal, perianal and inguinal regions, in addition to vaginal discharge in lumps, similar to "curdled milk". It is noteworthy that symptoms are exacerbated during the premenstrual period, when vaginal acidity increases.⁽³⁾

In the face of the clinical picture of candidiasis, it is necessary to intervene, either by treatment with antifungal drugs or, more recently, by herbal therapy.⁽⁴⁾ Thus, in clinical practice, drugs are still chosen, so that the most used for the treatment of imidazole and triazole agents are fluconazole, miconazole, clotrimazole and ketoconazole, and for polyene agents, nystatin and some formulations containing anthofericin B are more frequently applied.⁽⁵⁾

Still with regard to the treatment of VVC, the abusive use of conventional treatment is understood as a limiting factor, since the drugs are freely available in drugstores, allowing self-medication and the emergence of resistant species through indiscriminate and long-term use.⁽⁶⁾

In this sense, although it is perceived as a notable health problem, being triggered by multiple factors, one must take into account not only the susceptibility of the host, but also the knowledge to carry out a careful evaluation, which includes treatment. Therefore, such measures are considered challenging for nursing professionals who work in the promotion, prevention and screening of this pathology, through cytopathological examination.⁽⁷⁾

In view of the above, it is essential that health professionals, especially nurses, keep up to date with the latest pharmacological approaches available for the treatment of vulvovaginal candidiasis. This continuous updating will enable them to provide patients with accurate guidance and assist them in making informed decisions about treatment. Moreover, constant updating is essential to ensure the quality and effectiveness of the care provided to patients, as well as to maintain the safety and effectiveness of the

treatments used. It is emphasized that there are gaps in the contextualization of the object of this research, important to knowledge, and that need to be addressed.

In this perspective, in view of the construction of the state of the art on VVC, the present study aims to identify scientific evidence available in the literature and analyze in this scientific literature the action of antifungals used for the treatment of VVC.

METHODS

This is an integrative review, structured in six distinct stages: 1) elaboration of the research question; 2) definition of databases and criteria for inclusion and exclusion of studies; 3) definition of the information to be extracted from the selected studies; 4) evaluation of the studies included in the review; 5) interpretation of the results; 6) presentation of the review/synthesis of knowledge.⁽⁸⁾

The study was guided by a protocol prepared by the researchers. The research question was elaborated according to the Population Interest Context (PICO) strategy.⁽⁹⁾ The following structure was considered: P - woman; I - antifungal agents; Co - vulvovaginal candidiasis. Thus, the present question was elaborated: which antifungal agents are used for the treatment of vulvovaginal candidiasis and their efficacy in the treatment of the signs and symptoms of this pathology?

The bibliographic survey was carried out in January 2023, through access to virtual databases: Medical Literature Analysis and Retrieval System Online (MEDLINE), accessed through the PubMed portal; Embase; Web of Science (WOS); Cochrane Library; CINAHL, SCOPUS and LILACS, via the Virtual Health Library (VHL).

The inclusion criteria were: primary article, with quantitative method; sample in human model (i.e., that did not describe the use of these drugs in in vitro research or using mice); published in English, Spanish or Portuguese and available in full. The exclusion criteria were: review studies; short articles; conference abstracts; editorials; theses; dissertations; viewpoints; and essays. There was no time delimitation.

The results were analyzed by two independent authors (KFGM/CDAF) to ensure the quality and validity of the conclusions presented. This means that each author conducted a separate analysis of the data and then compared their results to ensure they reached similar conclusions. This process of double analysis is a common practice in integrative reviews as it helps to minimize errors and increase the reliability of the results presented. In addition, the independent analysis of the authors allows a critical appraisal of the included studies and helps to identify knowledge gaps in the area in question.

For the search, controlled descriptors and synonyms were used, as required by each of the databases searched. It is reiterated that for the search carried out in the VHL, in order to identify a greater scope of descriptors, their hierarchical codes were used, accompanied by the truncation symbol.

To systematize the sample collection, the advanced and sensitive search form was used, in order to respect the peculiarities and distinct characteristics of each database. The descriptors were combined with each other with the Boolean OR connector, within each set of terms of the PICO strategy and then crossed with the Boolean AND connector, as shown in the Table. 1.

Table 1. Search strategies and databases. Teresina, Piauí, Brazil, 2023.

BASE	SEARCH ENGINE STRATEGY
<i>Medline via Pubmed</i>	(("Women"[Mesh] OR (Girls) OR (Girl) OR (Woman) OR (Women's Groups) OR (Women Groups) OR (Women's Group)) AND ("Antifungal Agents"[Mesh] OR (Agents, Antifungal) OR (Therapeutic Fungicides) OR (Fungicides, Therapeutic) OR (Antifungal Agent) OR (Agent, Antifungal) OR (Antibiotics, Antifungal) OR (Antifungal Antibiotics))) AND ("Candidiasis, Vulvovaginal"[Mesh] OR (Vulvovaginal Candidiasis) OR (Moniliasis, Vulvovaginal) OR (Vulvovaginal Moniliasis) OR (Genital Vulvovaginal Candidiasis) OR (Candidiasis, Genital Vulvovaginal) OR (Vulvovaginal Candidiasis, Genital) OR (Vaginitis, Monilial) OR (Monilial Vaginitis) OR (Candidiasis, Genital) OR (Genital Candidiasis) OR (Vaginal Yeast Infections) OR (Infection, Vaginal Yeast) OR (Infections, Vaginal Yeast) OR (Yeast Infection, Vaginal) OR (Yeast Infections, Vaginal) OR (Vaginal Yeast Infection))
	"Women"[Mesh] OR (Girls) OR (Girl) OR (Woman) OR (Women's Groups) OR (Women Groups) OR (Women's Group) (Todos os campos) and "Antifungal Agents"[Mesh] OR (Agents, Antifungal) OR (Therapeutic Fungicides) OR (Fungicides, Therapeutic) OR (Antifungal Agent) OR (Agent, Antifungal) OR (Antibiotics, Antifungal) OR (Antifungal Antibiotics) (Todos os campos) and "Candidiasis,

Web of Science	<i>Vulvovaginal</i> [Mesh] OR (<i>Vulvovaginal Candidiasis</i>) OR (<i>moniliasic, Vulvovaginal</i>) OR (<i>Vulvovaginal moniliasic</i>) OR (<i>Genital Vulvovaginal Candidiasis</i>) OR (<i>Candidiasis, Genital Vulvovaginal</i>) OR (<i>Vulvovaginal Candidiasis, Genital</i>) OR (<i>Vaginitis, monilia</i>) OR (<i>monilia Vaginitis</i>) OR (<i>Candidiasis, Genital</i>) OR (<i>Genital Candidiasis</i>) OR (<i>Vaginal Yeast Infections</i>) OR (<i>Infection, Vaginal Yeast</i>) OR (<i>Infections, Vaginal Yeast</i>) OR (<i>Yeast Infection, Vaginal</i>) OR (<i>Yeast Infections, Vaginal</i>) OR (<i>Vaginal Yeast Infection</i>) (Todos os campos)
SCOPUS	(ALL ("Women" [mesh] OR (girls) OR (girl) OR (woman) OR ("Women's Groups") OR ("Women Groups") OR ("Women's Group")) AND ALL ("Antifungal Agents" [mesh] OR ("Agents, Antifungal") OR ("Therapeutic Fungicides") OR ("Fungicides, Therapeutic") OR ("Antifungal Agent") OR ("Agent, Antifungal") OR ("Antibiotics, Antifungal") OR ("Antifungal Antibiotics")) AND ALL ("Candidiasis, Vulvovaginal" [mesh] OR ("Vulvovaginal Candidiasis") OR ("Moniliasis, Vulvovaginal") OR ("Vulvovaginal Moniliasis") OR ("Genital Vulvovaginal Candidiasis") OR ("Candidiasis, Genital Vulvovaginal") OR ("Vulvovaginal Candidiasis, Genital") OR ("Vaginitis, Monilial") OR ("Monilial Vaginitis") OR ("Candidiasis, Genital") OR ("Genital Candidiasis") OR ("Vaginal Yeast Infections") OR ("Infection, Vaginal Yeast") OR ("Infections, Vaginal Yeast") OR ("Yeast Infection, Vaginal") OR ("Yeast Infections, Vaginal") OR ("Vaginal Yeast Infection"))))
EMBASE	'female'/exp OR (females) OR (woman) OR (women) AND 'antifungal agent'/exp OR (anti fungal) OR (anti fungal drug) OR (anti-fungal) OR (antibiotics, antifungal) OR (antifungal) OR (antifungal agents) OR (antifungal drug) OR (antifungal, topical) OR (antifungals) OR (antifungals, ophthalmic) OR (antifungals, topical) OR (antifungus agent) OR (antimycotic) OR (antimycotic agent) OR (antimycotic drug) OR (fungistatic agent) OR (fungostatic agent) OR (mycostatic agent) OR (topical antifungal) OR (topical antifungal agent) OR (topical antifunga) AND 'vagina candidiasis'/exp OR (Candida vaginitis) OR (candidiasis vaginalis) OR (candidiasis, vaginal) OR (candidiasis, vulvovaginal) OR (vaginal candidiasis) OR (vulvovaginal candidiasis)
LILACS (via VHL)*	(mh: mulheres OR (mulheres) OR (women) OR (mujeres) OR (meninas) OR (mulher) OR mh:m01.975*) AND (mh: antifúngicos OR (antifúngicos) OR ("Antifungal Agents") OR (antifúngicos) OR ("Agente Antifúngico") OR ("Agente Antimicótico") OR ("Agentes Antifúngicos") OR ("Agentes Antimicóticos") OR ("Antibióticos Antifúngicos") OR (antifúngico) OR (antimicótico) OR (antimicóticos) OR ("Fungicidas Terapêuticos") OR ("Fármaco Antifúngico") OR ("Medicamento Antifúngico") OR ("Medicamento Antimicótico") OR mh:d27.505.954.122.136*) AND (mh: "Candidíase Vulvovaginal" OR ("Candidíase Vulvovaginal") OR ("Candidiasis, Vulvovaginal") OR ("Candidiasis Vulvovaginal") OR ("Candidíase Genital") OR ("Candidíase Genital Vulvovaginal") OR ("Candidíases Genitais") OR ("Infecções Vaginais por Leveduras") OR ("Monilíase Vaginal") OR ("Monilíase Vulvovaginal") OR ("Vaginite Monilial") OR ("Vaginite por Monília") OR mh: c01.150.703.160.190* OR mh: c12.050.351.500.894.906.820.500* OR mh: c12.050.351.500.944.902.737.500* OR mh: c12.100.250.894.906.820.500* OR mh: c12.100.250.944.902.737.500*) AND (db:("LILACS"))
CINAHL	(MH "Women+")
	(MH "Antifungal Agents+")
	(MM "Candidiasis, Vulvovaginal")
	S1 AND S2 AND S3
Cochrane Library	#1 MeSH descriptor: [Women] explode all trees
	#2 MeSH descriptor: [Antifungal Agents] explode all trees
	#3 MeSH descriptor: [Candidiasis, Vulvovaginal] explode all trees
	#1 AND #2 AND #3

Legend: *Search by category of the term
Source: authors (2023).

To ensure access to the content in its entirety, the articles were accessed through the journal portal of the Coordination for the Improvement of Higher Education Personnel (CAPES), in an area with Internet Protocol (IP) recognized by the Federal University of Piau.

The studies found were imported into the Endnote Web bibliographic reference management software to exclude duplicates. Then, the Rayyan QCRI⁽¹⁰⁾ application was used to read titles and abstracts,

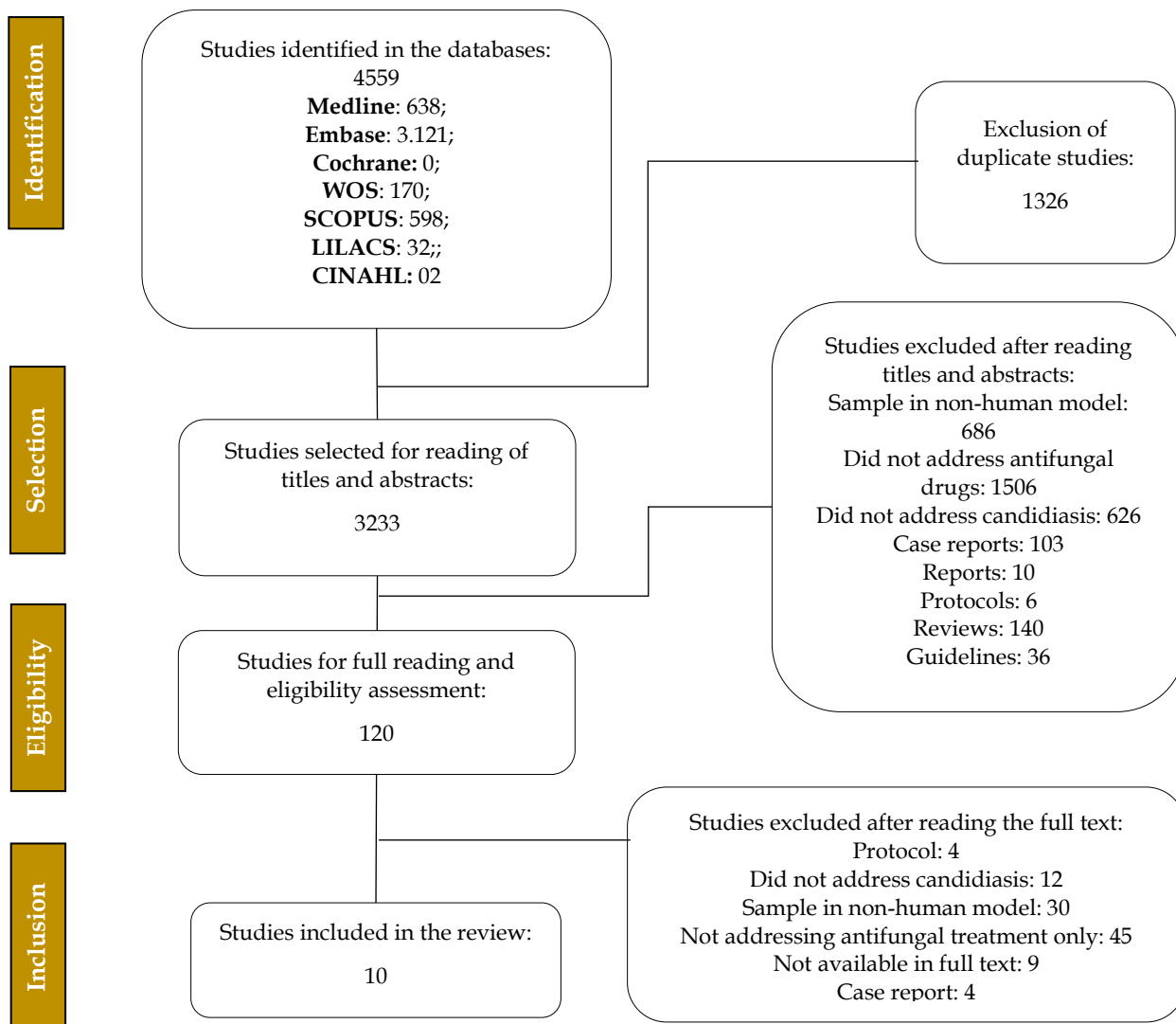
excluding those that did not answer the research question, and the selection of articles that would fit for reading in their entirety.

For the extraction and synthesis of information from the selected studies, the form of the Red de Enfermería en Salud Ocupacional (RedENSO Internacional) was adapted.⁽¹¹⁾ The following information were extracted: year of publication; country; study design; study objective; level of evidence.

The level of evidence was determined by the following classification: level I – meta-analysis of randomized controlled studies; level II – experimental study; level III – quasi-experimental study; level IV – descriptive/non-experimental study or with a qualitative approach; level V – case report or experience; level VI – consensus and expert opinion.⁽¹²⁾

A total of 4,559 publications were identified and, after applying the inclusion and exclusion criteria, 10 articles were selected for the final sample of this review. For the selection of publications, the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) were followed⁽¹³⁾, presented in Figure 1.

Figure 1. Flowchart of selection of primary studies, based on the PRISMA recommendation. Teresina, Piauí, Brazil, 2023.



Source: authors (2023).

As this is an integrative review, the research was not submitted to the Research Ethics Committee, but the ideas of the authors of the publications used in the development of this study were maintained. The critical analysis and qualitative synthesis of the selected studies were performed descriptively.

RESULTS

The 10 articles selected for the final sample of this study were published between 1983 and 2020. Of these, four were developed in Iran, the others were produced in Mexico, England, Taiwan, Thailand, Denmark, and the United States. Regarding the methodological design, most studies are clinical trials (n=8), and two are cross-sectional studies.

Thus, regarding the level of evidence, eight studies are level II, and only two investigations are level IV. Regarding the antifungal drugs used in the treatment, there was a predominance of clotrimazole (n=4), followed by econazole (n=2), combined or not with another antifungal drug. A summary of the studies is presented in Table 2.

Table 2. Articles selected for composition of the final sample. Teresina, Piauí, Brazil, 2023.

Years	Country	Design	Objective	Level of evidence	Outcome
2017 ⁽¹⁴⁾	Mexico	Clinical Trial	To evaluate the efficacy and tolerability of <i>A. pichinchensis</i> extract (intravaginal administration) in patients with vulvovaginal candidiasis	Level II	The experimental treatment, made with the extract of <i>A. pichinchensis</i> was able to significantly (73.3%) reduce the signs and symptoms of vulvovaginal candidiasis. Clotrimazole, in turn, reduced by 81.7% - (administered over six days). (administered over six days).
2018 ⁽¹⁵⁾	Iran	Clinical Trial	To compare the efficacy of <i>Anethum graveolens</i> L. (dill) vaginal cream with clotrimazole 1% vaginal cream for treating vulvovaginal candidiasis.	Level II	The highest rate of efficacy in the recovery of signs and symptoms belonged to the group that used Clotrimazole (98.3%).
2020 ⁽¹⁶⁾	Iran	Clinical Trial	To determine if the use of the vaginal tablet which contains <i>Rosa damascena</i> , <i>Punica granatum</i> L. (Punicaceae), <i>Quercus infectoria</i> Oliv, <i>Myrtus communis</i> L. (Myrtaceae) and <i>Nardostachys jatamansi</i> (Caprifoliaceae) could alleviate the symptoms of vulvovaginal candidiasis.	Level II	All clinical symptoms presented by the study participants improved with the use of the vaginal tablet (<i>Punica granatum</i> L + <i>Quercus infectoria</i> Oliv. + <i>Myrtus communis</i> L. + <i>Nardostachys jatamansi</i>), for three days. The clinical cure rate in the control group (63.045%) was significantly higher than in the placebo group.
2020 ⁽¹⁷⁾	Thailand	Clinical Trial	To compare the clinical and laboratory cure rate of <i>dequalinium chloride</i> with that of clotrimazole in Thai women who had vulvovaginal candidiasis.	Level II	All participants had moderate to very high satisfaction and tolerability with both treatment regimens. However, patients using Clotrimazole (42.4%) were found to have greater microscopic improvement than those using <i>dequalinium chloride</i> - (used for six days)
2020 ⁽¹⁸⁾	Iran	Clinical Trial	Comparing standard outpatient treatment using clotrimazole, with chamomile extract cream.	Level II	By means of the chi-square test, there was an association between the use of Clotrimazole and chamomile extract cream for the improvement of symptoms such as: discharge, itching, burning and "strawberry neck" (p<0.001) (administered for five days).
2006 ⁽¹⁹⁾	Taiwan	Clinical Trial	To evaluate the efficacy, acceptability, and safety of treatment with single-dose vaginal tablets of sertaconazole (500 mg)	Level II	The sample was divided into two groups: group A received vaginal Sertaconazole and group B, Econazole - for three days.

			compared with conventional treatment with 3-dose vaginal tablet of econazole (150 mg) for vulvovaginal candidiasis.		Those patients in group A had a better response to signs and symptoms (95%), while group B had only a 39% success rate.
2004 ⁽²⁰⁾	United States	Clinical Trial	To evaluate the clinical and mycological efficacy of weekly treatment with fluconazole compared to placebo in reducing the frequency of clinical episodes of recurrent vulvovaginal candidiasis.	Level II	There was no statistically significant difference in the cultures between the fluconazole (90.8%) and placebo patients. However, six months later, patients receiving placebo were found to have a significantly higher rate of clinical recurrence compared to those receiving fluconazole - (given in three doses every 72 hours).
1991 ⁽²¹⁾	India	Cross-sectional	To evaluate and compare the combination of oral and vaginal treatment medications for vaginal candidiasis.	Level IV	There was significant improvement in symptoms in all patients of the 3 groups investigated, with the combination of therapies (oral ketoconazole + vaginal miconazole - 98%) giving the best results. (Group 1 received ketoconazole for 5 days, group 2 used miconazole for 14 days and group 3 used the combination of drugs for 14 days).
1985 ⁽²²⁾	Denmark	Cross-sectional	To examine the efficacy of tioconazole for the treatment of patients with vaginal candidiasis.	Level IV	At the first assessment, after one week of Tioconazole use, only 3 of 28 patients had a positive vaginal culture for <i>C. albicans</i> , resulting in a mycologic cure rate of 89.3%. At the second and third assessment (2 and 4 weeks after treatment initiation), the mycologic cure rates were 88.5% and 78.6% respectively - (administered for three days).
1983 ⁽²³⁾	England	Single blind clinical trial	To compare the efficacy of these two antifungal agents (econazole and clotrimazole) in the treatment of vaginal candidiasis.	Level II	All signs and symptoms were resolved in both treatment groups (Clotrimazole 97% and Econazole 89%). With the exception of one patient, from the clotrimazole group, who encountered difficulty in using the medication, causing a break in treatment - (use for three days).

Source: authors (2023).

DISCUSSION

The results of this review indicated a low number of articles addressing antifungal drugs and their efficacy in the treatment of VVC, especially when it comes to tests performed in women, since an expressive number of productions were observed that portray the use of these drugs in in vitro research or using mice. This preference, in addition to ethical precepts, will be due to the need for azole drugs to be tested at pH 7.0, when the pH levels found in women with *Candida vaginitis* is 4.5.⁽²⁴⁾

Regarding the period of the publications included in the final sample of this research, it was verified from the oldest to the most recent articles. It is understood, therefore, that both science and popular wisdom have always sought experimentation, mainly to discover the pharmacological properties of substances.⁽²⁵⁾

With respect to the countries of development of the articles that constituted the final sample, it is evident that Asia, through Iran, has been prominent in research on antifungals for the treatment of VVC. In an integrative review developed by Brazilian researchers, in which 12 articles were analyzed, it was shown that 41.7% of the analyzed productions also had Iran as their country of origin.⁽²⁶⁾

The clinical trial, observed in most of the articles evaluated, also constituted a significant amount in a similar study.⁽²⁷⁾ Thus, the level of evidence of the articles found, classified in greater quantity at level II⁽¹²⁾, points to the presence of robust evidence.

The outcome found was distributed in the following thematic category: Treatment applied to vulvovaginal candidiasis.

Treatment applied to vulvovaginal candidiasis

The treatment of VVC using drugs aims to improve the patient's symptoms and can be prescribed orally or topically. Azoles are the standard choice for VVC, as they contribute to symptom relief and make cultures negative in 80% to 90% of women who complete treatment.⁽²⁸⁾

In this perspective, among the articles that made up the final sample of the investigation on screen, the following antifungal drugs were used: vaginal sertaconazole, econazole, fluconazole, oral ketoconazole, vaginal miconazole, tioconazole, vaginal tablet based on *Punica granatum L* + *Quercus infectoria Oliv.* + *Myrtus communis L.* + *Nardostachys jatamansi*, *dequaline chloride*, chamomile extract cream, *A. pichinchensis* extract, and, prominently, clotrimazole was used in most of the articles analyzed.

In view of this scenario, in a clinical trial developed in Taiwan, for different groups, vaginal sertaconazole and econazole were used for three days. It was therefore found that for the variables negative bacilloscopy for *C. albicans*, the global assessment of the disease, its complete cure or improvement of clinical symptoms (individual or general), the sertaconazole proved superior in the treatment of the women in the sample.⁽¹⁹⁾

The above information confirms that sertaconazole has mucoadhesive properties that prolong the duration of the medication in the vaginal mucosa. Thus, this antifungal provides an efficient treatment due to its ability to disperse in the vagina, thus conferring effective coating property.⁽²⁹⁾

In turn, in a study conducted in the United States with patients who received fluconazole and placebo tablets, it was observed that there was no statistically significant difference in cultures between patients who used fluconazole and those who used placebo. However, with the follow-up of six months after taking the drugs, there was clinical recurrence in a shorter time in those women who received the placebo, with records that, about four months after taking the drug, they presented the symptomatology again.⁽²⁰⁾

When addressing the treatment of VVC, the Brazilian Ministry of Health presents the use of miconazole 2% cream or nystatin 100,000 IU as the first option, and fluconazole, in a single dose of 150mg, as a second treatment option or in cases of complicated or recurrent VVC.⁽³⁰⁾ However, currently, the rampant use of fluconazole has been a problem due to the expressive resistance of fungi, which makes the treatment of the infection extremely difficult.⁽³¹⁾

Regarding the resistance of strains, especially to fluconazole, there is a relationship with the increased expression of the ERG11 gene and protein efflux pumps, and not with the duration of treatment. In Brazil, the test that provides resistance or susceptibility patterns as a result is called antifungigram, so that in this country the recommended sensitivity tests are the diffusion disk and the CECOM disk, as well as the agar microdilution test by ETEST, all with reading after 24 hours.⁽³²⁾

The aforementioned review found that fluconazole, the second-choice medication in Brazil, also has a limited effect on commensal biofilms. In this sense, it would not act as effectively with *C. albicans* fungi, since they can remain within the biofilm, which would explain its recurrence, since, when released, they can cause new infections and decrease the effectiveness of antifungal agents.⁽³²⁾

In this sense, with the recurrence and resistance of cases involving the *Candida* fungus strain, alternative treatments involving the use of plant species have been used. Essential oils extracted from plants, for example, have shown antifungal potential against the *C. albicans* species. Among them, *Melaleuca alternifolia* Cheel, *Origanum vulgare L.*, *Cymbopogon nardus* and *Cuminum cyminum* stand out.⁽³³⁾

Furthermore, in a study conducted in India, the sample was divided into three groups. Group 1 received ketoconazole for five days; group 2 used miconazole for 14 days; and group 3 made combined use of drugs for 14 days. At the end, it was found that there was a significant improvement in symptoms in all patients in the three groups investigated, with emphasis on the one in which there was a combination of medications.⁽²¹⁾ This fact is justified because, by associating appropriate drugs, they may be more effective, since there is a tendency for species to depend on higher concentrations of antifungals.⁽³⁴⁾

In Denmark, the efficacy of tioconazole in the treatment of VVC was examined. The results showed a mycological cure rate of 89.3%. At the second and third evaluation (2 and 4 weeks after treatment initiation), the mycological cure rates were 88.5% and 78.6%, respectively.⁽²²⁾

In an investigation carried out on swab samples obtained from Iranian women with symptoms of VVC, strains of *Candida albicans*, *glabrata*, *parapsilosis*, *krusei* and *tropicalis* were isolated, and some antifungal drugs were tested, including tioconazole, which also proved effective in treating most of the isolated *Candida* species.⁽³⁵⁾

When using a vaginal tablet based on *Punica granatum L*, *Quercus infectoria Oliv.*, *Myrtus communis L.* and *Nardostachys jatamansi*, called "Ward" in the research, it was obtained that all the clinical symptoms presented by the study participants had improved (A10).⁽¹⁶⁾ Among the articles analyzed, only this one presented the activity of natural compounds in the treatment of VVC.

In this sense, there is currently a search for new active compounds that have fungicidal action, since, in addition to fungal inhibition, they have the advantage of being renewable sources, found abundantly in nature, in addition to having versatile applications. To this end, as well as in the aforementioned study, it is verified the use, mainly of *Punica granatum* (pomegranate), with pharmaceutical formulation of ethanolic, methanolic and aqueous extract of the bark and root.⁽³⁶⁾

The results of this research showed that clotrimazole alone⁽¹⁵⁾ – or compared to other substances such as *A. pichinchensis* extract⁽¹⁴⁾, *dequalinium chloride*⁽¹⁷⁾, chamomile extract cream⁽¹⁸⁾ and econazole⁽²³⁾ – is effective in the treatment of VVC, and was the most widely used drug among the studies found.

The orientation of the use of clotrimazole (CTZ) is in line with the treatment applied in Brazil, whose first option involves miconazole in 2% cream or nystatin 100,000 IU of single application, vaginally.⁽³⁰⁾ This degree of choice in some countries may be related to the better tolerability and reduced adverse effects of clotrimazole when compared to other azoles.

In addition, CTZ has a difference in cell viability, so that the drug can be protected inside the cells, which may indicate that there should be control over the sale of this drug. In addition, the potential to reduce the possible toxic effects of its molecules may suggest that this antifungal drug is a promising alternative to others.⁽³⁷⁾

In view of this information, it is important to know the treatment of VVC, beyond caring. This care, in turn, also involves nursing, which is fundamental in the promotion, prevention and treatment of candidiasis, whether recurrent or not. In addition, through multi-professional work, nursing can also assist in the early and accurate diagnosis of VVC, as well as the monitoring of appropriate treatment.

Regarding the prescription by the nurse, in a documentary analysis of ethnomedical nature, three subtypes of autonomy were made explicit for this activity in Primary Health Care (PHC), being the third subtype characterized by the independence of the nurse regarding the diagnosis and medical prescription. The protocols that involve this practice are: Child Nutrition; AIDPI Protocol; Prenatal and HIV/AIDS; Hepatitis and other STIs.⁽³⁸⁾

In a scoping review on the contributions of advanced nursing practices in PHC, it was found that, among the care practices, this professional category prescribes drugs for parasitosis, dermatitis, mycoses, sexually transmitted infections and during prenatal care, guided by pre-established protocols.⁽³⁹⁾

Thus, health professionals should follow protocols and not choose treatment individually. In this sense, when there is a divergence between the results of the research and the protocols, as verified in this study, it is understood that it is necessary to update the protocol and not to adopt other forms of prescriptions.

Finally, the development of this research presented as a limitation the low number of scientific publications developed on antifungals and their effectiveness in the treatment of VVC. Studies involving the theme were identified, however, most articles did not have the human model as a sample. In addition, it is worth mentioning the prioritization of articles in English, Spanish and Portuguese, so that articles that were not in these languages were not eligible to integrate the sample and, therefore, were not retrieved. However, it is emphasized that the authors, during the evaluation of the articles obtained, were judicious regarding their evaluation and inclusion in this study.

It is pointed out as a gap in knowledge the geographical scope of the studies, since all the articles were developed in foreign countries, which demonstrates how fragile the production of laboratory research, especially clinical trials, involving the theme of this research in countries like Brazil has been.

This study contributes especially to the reflection on women's health when dealing with infections such as candidiasis that, depending on the treatment, can contribute to the improvement of the quality of life of this population. The data produced point to the need to seek training strategies for professionals who treat these women in health services, especially nurses.

It also reflects on the need to modify the medications of choice in Brazil for the treatment of VVC. Based on the results, it is understood that, when evaluating the cost-benefit of this replacement, there would be fewer women with recurrent cases of the disease and less expenditure for the public health service if the government invested in an antifungal that has shown effectiveness in clinical trials around the world, such as clotrimazole. Finally, it is suggested that the prescription protocols used should be updated.

CONCLUSION

The results obtained amounted to a sample of 10 articles, mostly published in 2020, with Iran as the most frequent country of origin and clinical trials as the main design, thus corresponding to level II evidence. In addition, regarding the treatment and efficacy of antifungals in VVC, it was found that most antifungals acted effectively. However, the use of clotrimazole was emphasized.

It is important to highlight the relevance of the participation of health professionals, especially nurses, in the implementation of new protocols and treatments for vulvovaginal candidiasis. They play a crucial role in educating patients about preventive and infection control measures, early identification of symptoms and evaluation of treatment efficacy, as well as monitoring side effects.

Therefore, this study plays a key role in contributing to the advancement of knowledge and the improvement of clinical practice of nursing and other health professionals in the treatment of vulvovaginal candidiasis. The identification of the efficacy of clotrimazole reinforces the importance of careful evaluation of antifungal choice and duration of treatment for a more effective approach to this condition.

CONTRIBUTIONS

Conception or design of the study: Carvalho ALM, Silva-Júnior FL, Moreira KFG, Data collection: Moreira KFG, Feitosa CDA, Analysis and interpretation of the data: Moreira KFG, Feitosa CDA, Writing of the article or critical review: Moreira KFG, Silva-Júnior FL, Magalhães CFCB, Nascimento MO, Feitosa CDA, Final approval of the version to be published: Moreira KFG, Silva-Júnior FL, Feitosa CDA.

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