PharmacologyOnLine

Archives • 2021 • vol.3 • 1474-1479

STUDY OF THE RANGE OF THE PHARMACEUTICAL MARKET OF UKRAINE MEDICINES FOR THE TREATMENT OF SEBOREA DERMATITIS OF THE SCALP

Konovalenko I. S.*, Kriukova A. I., Cherkasova A. O., Herasymova I. V., Yurieva H. B.
National University of Pharmacy, 53 Pushkinska str., 61002, Kharkiv, Ukraine
*ilonakonovalenko1601@gmail.com

Abstract

This article represents the results of marketing analysis of the pharmaceutical market of Ukraine medicinal products for the treatment of seborea dermatitis of the scalp.

Materials and methods. Data of the State Register of Medicinal Products of Ukraine, electronic databases, information retrieval program "Morion"; used marketing and graphic methods, methods of monitoring, logical generalization and grouping.

Results. The analysis of registered on the Ukrainian market drugs belonging to group D01A "Antifungal drugs for topical use", namely subgroups D01A C "Imidazole and triazole derivatives" and D01A E "Other antifungal drugs for topical use", showed of the leading drugs of subgroup D01A C "Imidazole and triazole derivatives" (71 %) and subgroups D01A E "Other antifungal agents for topical use" occupy only 29 %. It is noted that the composition of the studied drugs includes 9 active substances of synthetic origin. The most used are derivatives of imidazole, pyrithione, allylamines. It was found that among these drugs, single drugs predominate, the share of which from the total number of trade names is 88 %, while combined - only 12 %. It is noted that the structure of the studied drugs is dominated by mild forms of release: creams – 31 %, ointments – 17 %, gels – 13 %, solutions for external use – 26 %, others (tablets, shampoos, suspensions) - 13 %.

Conclusions. The creation of a new drug for the treatment of seborrheic dermatitis of the scalp in the form of a cream–mask is an urgent task of Ukrainian pharmaceutical production.

Keywords: *marketing researches; medicines for local treatment; seborrheic dermatitis.*

Introduction

Seborrheic dermatitis is a common disease that usually begins during puberty and is most common in people around the age of 40 [1, 2]. Seborrheic dermatitis of the scalp is a very specific chronic disease that worsens the appearance of a person, causing discomfort and moral suffering [3, 4].

According to the analysis of recent studies [5-7], seborrheic dermatitis is registered in 3-5 % of the population, but dandruff, as its mildest form, is more common and is observed in approximately 15-20 % of the population [8, 9]. The prevalence of seborrheic dermatitis does not depend on race [10, 11]. Men get sick more often than women. This disease can also occur in children during the first 10 weeks of life, as well as during puberty and is almost non-existent in the elderly [12-15].

Dermatosis occurs in areas of the body where the largest number of sebaceous glands are centered: on the scalp, nasolabial triangle, the area between the shoulder blades and on the skin of the anterior surface of the chest [16]. The course of seborrheic dermatitis can be supported by a yeast-like fungus of the genus Malassezia. For its part, it is incorrect to call this disease infectious: the causative agent is an opportunistic pathogen that is present in the skin of virtually everyone [17, 18].

Among the reasons that contribute to the development of fungal microflora, the main ones are changes in the quality of sebum and its amount, which significantly violates the barrier function of the skin. Among the causes of these changes are neurogenic factors, immune disorders, hormonal imbalance in the body [19]. Clinically, seborrheic dermatitis is characterized by peeling and inflammation of the skin, and is accompanied by itching. Fine-grained (whitish or dirty-gray scales) or large-layered peeling appears on the scalp [20].

Treatment of seborrheic dermatitis should be comprehensive and purely individual, including oral, which include desensitizing agents, antihistamines, immunomodulators, antifungals, nonsteroidal anti-inflammatory drugs, steroids, and topical treatments and cosmetic skin care. Therefore, the development of new drugs that affect all pathogenetic components is quite relevant [21].

Methods

Data of the State Register of Medicinal Products of Ukraine, electronic databases, information retrieval program "Morion"; used marketing and graphic methods, methods of monitoring, logical generalization and grouping [22].

Results

In the first phase of the study, we used the Anatomical Therapeutic Chemical Classification System (ATC), adopted by the WHO as an international standard methodology for conducting statistical surveys on drug consumption in different countries [23-25]. The analysis of registered on the Ukrainian market drugs belonging to group D01A "Antifungal drugs for topical use" was conducted on the basis of the data of the State Register of Medicinal Products of Ukraine. It is estimated that the total number of registered drugs in this group is 51 trade names.

As a result of studying the received list of medicines it is established that the following subgroups belong to this group: D01A C "Imidazole and triazole derivatives" and D01A E "Other antifungal agents for topical use".

According to the analysis of the obtained data, we determined that the leading positions are occupied by drugs of subgroup D01A C "Imidazole and triazole derivatives" (71 %), and drugs of subgroup D01A E "Other antifungal agents for topical use" - only 29 %.

A further study of the range of registered producers of antifungal drugs for topical use by producer countries showed that 12 countries were registered on the Ukrainian market: India (16 %), Ukraine (3 %), Switzerland (12 %), Germany (11 %), Poland (10 %), Turkey, Spain, Italy and Jordan (5 % each), all other producer countries – 28 % (Fig. 2).

The main ukrainian producers of dermatological drugs are the following pharmaceutical companies: PJSC "Kyivmedpreparat", Borschagovsky Chemical-Pharmaceutical Plant, PJSC "Fitopharm", Chempharmzavod "Red Star", Joint Ukrainian-Spanish Enterprise "Sperko Ukraine", LLC "Pharmaceutical Company" », PJSC« Pharmaceutical firm «Darnitsa», PJSC «Farmak».

We also analyzed the dosage forms of antifungal drugs for topical use, presented on the

market of Ukraine (Fig. 3). It was found that the structure of the studied medicinal forms is dominated by mild forms of release, namely: creams – 31 %, ointments – 17 %, gels – 13 %, solutions for external use – 26 %, others (tablets, shampoos, suspensions) - 13 %.

Discussion

It is known that the optimal composition of any dosage form involves a scientifically selection of active pharmacological ingredients and excipients in the required concentrations. It should be noted that due to the right combination, a high therapeutic effect can be achieved. Therefore, the next stage of the study was the analysis of the composition of active components that are included in the studied list of drugs (Fig. 1).

It is noted that the composition of the studied drugs includes 9 active substances of synthetic origin. The most commonly used are imidazole derivatives (clotrimazole, ketoconazole, bifonazole, econazole nitrate, sertocannazole nitrate) and pyrithione (zinc pyrithionate), allylamines (terbinafine hydrochloride), and uric acid is used as the second active ingredient. Some manufacturers combine synthetic and natural ingredients (such as thick extracts of calendula and yarrow), but such drugs do not exceed 1 %. At the same time, at this stage of the analysis, we drew attention to the fact that among these drugs are dominated by mono-drugs, the share of which from the total number of trade names is 88 %, while combined – 12 %.

We analyzed the most common combinations of substances that are part of the combined drugs. It was found that the following combinations are most often used: clotrimazole and salicylic acid (Clotrisal®, PJSC Kyivmedpreparat, Ukraine); ketoconazole and zinc pyrithionate (Keto Plus, Glenmark Pharmaceuticals Ltd., India; Dermazol® Plus, Kusum Healthkker HTP LTD, India); clotrimazole and gentamicin sulfate (Clotrex, Borschagovsky Chemical-Pharmaceutical Plant, Ukraine). Based on the above, we can talk about the rationality and viability of the development of combined drugs with the use of new and modern antifungal substances, namely the yeast-like fungus of the genus Malassezia (Malassezia).

Production of a new Ukrainian drug in the form of a cream–mask for application to the scalp for the treatment of seborrheic dermatitis is an urgent and promising task of Ukrainian pharmaceutical production.

References

1. Martínez-Pulgarín DF, Ávila MY, Rodríguez-Morales AJ. Interventions for Demodex blepharitis and their effectiveness: A systematic review and meta-analysis. Cont Lens Anterior Eye. 2021 Dec;44(6):101453. doi: 10.1016/j.clae.2021.101453. Epub 2021 May 7. PMID: 33972176.
2. Borda LJ, Perper M, Keri JE. Treatment of seborrheic dermatitis: a comprehensive review. J Dermatolog Treat. 2019;30:158-169.
3. Naldi L, Diphoorn J. Seborrhoeic dermatitis of the scalp. BMJ Clin Evid. 2015;2015:1713. Published 2015 May 27.
4. Tao R, Li R, Wang R. Skin microbiome alterations in seborrheic dermatitis and dandruff: A systematic review. Exp Dermatol. 2021 Oct;30(10):1546-1553. doi: 10.1111/exd.14450. Epub 2021 Aug 27. PMID: 34415635.
5. Victoire A, Magin P, Coughlan J, van Driel ML. Interventions for infantile seborrhoeic dermatitis (including cradle cap). Cochrane Database Syst Rev. 2019 Mar 4;3(3):CD011380. doi: 10.1002/14651858.CD011380.pub2. PMID: 30828791; PMCID: PMC6397947.
6. Savla K, Le JT, Pucker AD. Tea tree oil for Demodex blepharitis. Cochrane Database Syst Rev. 2020 Jun 20;6(6):CD013333. doi: 10.1002/14651858.CD013333.pub2. PMID: 32589270; PMCID: PMC7388771.
7. Adalsteinsson JA, Kaushik S, Muzumdar S, et al. An update on the microbiology, immunology and genetics of seborrheic dermatitis. Exp Dermatol. 2020;29:481-489.
8. Saxena R, Mittal P, Clavaud C, et al. Comparison of healthy and dandruff scalp microbiome reveals the role of commensals in scalp health. Front Cell Infect Microbiol. 2018;8:346.
9. Magiatis P, Pappas P, Gaitanis G, et al. Malassezia yeasts produce a collection of exceptionally potent activators of the Ah (dioxin) receptor detected in diseased

human skin. J Invest Dermatol. 2013;133:2023-2030.
10. Golińska J, Sar-Pomian M, Rudnicka L. Diagnostic Accuracy of Trichoscopy in Inflammatory Scalp Diseases: A Systematic Review. Dermatology. 2021 Jul 15:1-10. doi: 10.1159/000517516. Epub ahead of print. PMID: 34265772.
11. Vázquez-Herrera NE, Sharma D, Aleid NM, Tosti A. Scalp Itch: A Systematic Review. Skin Appendage Disord. 2018 Aug;4(3):187-199. doi: 10.1159/000484354. Epub 2017 Nov 29. PMID: 30197900; PMCID: PMC6120392.
12. Naldi L, Diphoorn J. Seborrhoeic dermatitis of the scalp. BMJ Clin Evid. 2015 May 27;2015:1713. PMID: 26016669; PMCID: PMC4445675.
13. Chronic pruritus associated with dermatologic disease in infancy and childhood: update from an interdisciplinary group of dermatologists and pediatricians / M. Metz, U. Wahn, U. Gieler et al. // Pediatric Allergy and Immunology. – 2013. – Vol. 24, Issue 6. – P. 527–539.
14. Wikramanayake TC, Borda LJ, Miteva M, Paus R. Seborrheic dermatitis — Looking beyond Malassezia. Exp Dermatol. 2019;28(9):991-1001. https://doi.org/10.1111/exd.14006.
15. Park T, Kim HJ, Myeong NR, et al. Collapse of human scalp microbiome network in dandruff and seborrhoeic dermatitis. Exp Dermatol. 2017;26(9): 835-838. https://doi.org/10.1111/exd.13293.
16. Rudramurthy SM, Honnavar P, Dogra S, Yegneswaran PP, Handa S, Chakrabarti A. Association of Malassezia species with dandruff. Indian J Med Res. 2014;139(3):431-437.
17. Kistowska M, Fenini G, Jankovic D, et al. Malassezia yeasts activate the NL-RP3 inflammasome in antigen-presenting cells via Syk-kinase signalling. Exp Dermatol. 2014;23(12):884889.https://doi.org/10.1111/exd.12552.
18. Gupta AK, Versteeg SG. Topical Treatment of Facial Seborrheic Dermatitis: A Systematic Review. Am J Clin Dermatol. 2017;18(2):193-213. https://doi.org/10.1007/s40257-016-0232-2.
19. Borda LJ, Perper M, Keri JE. Treatment of seborrheic dermatitis: a comprehensive review. J Dermatolog Treat. 2019;30(2):158-169. https://doi.org/10.1080/09546634.2018.1473554.
20. Paulino LC. New perspectives on dandruff and seborrheic dermatitis: lessons we learned from bacterial and fungal skin microbiota. Eur J Dermatol. 2017;27(S1):4-7. https://doi.org/10.1684/ejd.2017.3038.
21. Morand SC, Bertignac M, Iltis A, et al. Complete Genome Sequence of Malassezia restricta CBS 7877, an Opportunist Pathogen Involved in Dandruff and Seborrheic Dermatitis. Microbiol Resour Announc. 2019;8(6): e01543-18. Published 2019 Feb 7. https://doi.org/10.1128/MRA.01543-18.
22. *Derzhavnyi reestr likars'kykh zasobiv. On-line versiia*. Available at: http://www.moz.gov.ua/ua/ portal/mtph_register_medicines/.
23. Okokon EO, Verbeek JH, Ruotsalainen JH, Ojo OA, Bakhoya VN. Topical antifungals for seborrhoeic dermatitis. Cochrane Database Syst Rev. 2015 May 2;(5):CD008138. doi: 10.1002/14651858.CD008138.pub3. PMID: 25933684; PMCID: PMC4448221.
24. Belousova, T. A., Horiachkina, M. A., Shranova, D. H. (2013). *Bulletin of Dermatology and Venereology,6,* 132–138.
25. Kamamoto CSL, Nishikaku AS, Gompertz OF, Melo AS, Hassun KM, Bagatin E. Cutaneous fungal microbiome: Malassezia yeasts in seborrheic dermatitis scalp in a randomized, comparative and therapeutic trial. Dermatoendocrinol. 2017;9(1):e1361573. Published 2017 Oct 23. https://doi.org/10.1080/19381980.2017.1361573.

Figure 1. The analysis of the composition of active components of medicinals for seborea dermatitis of the scalp

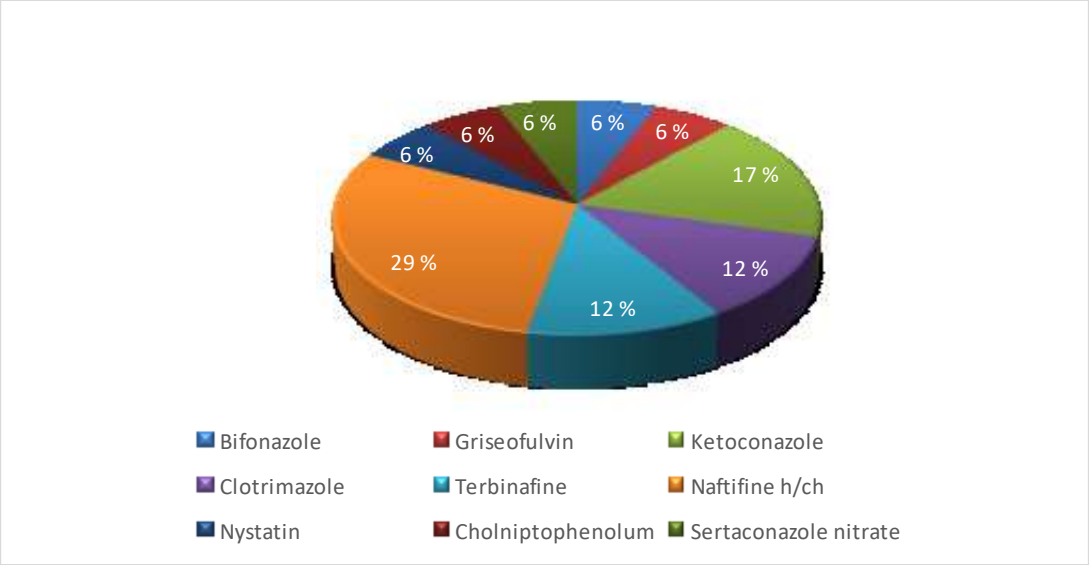

Figure 2. The analysis of the range of registered producers of antifungal drugs for topical use by producer countries

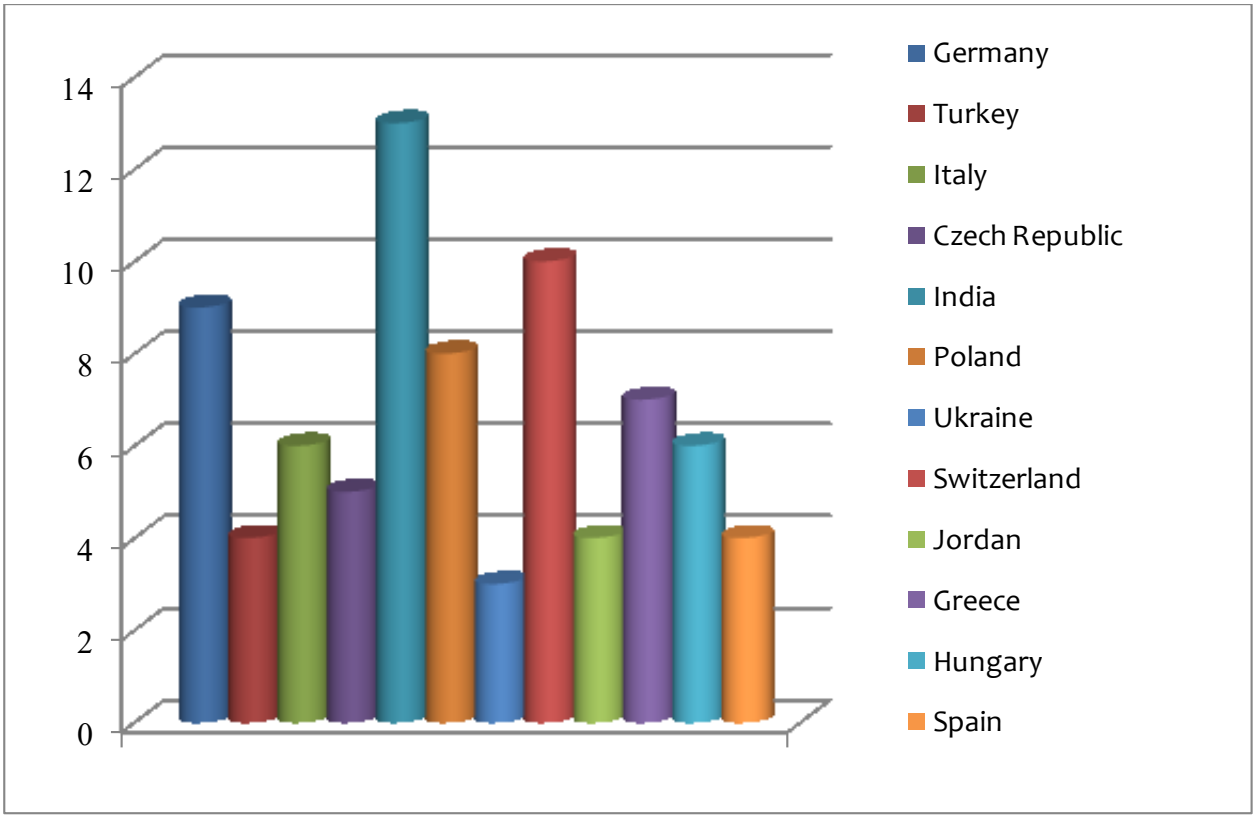

Figure 3. The analysis of the dosage forms of antifungal drugs for topical use, presented on the market of Ukraine