

UDC 615.281.8:615.454.2:618.1

YU. V. LEVACHKOVA, T. G. YARNYKH, O. M. LITVINOVA

National University of Pharmacy

ANTIVIRALS: TODAY AND THE PROSPECTS OF DEVELOPMENT IN UKRAINE

It was made a diligent examination of drugs for therapy of genital herpes (GH). It has been proved, that there is an insufficient quantity of domestic medicinal forms on pharmaceutical market of Ukraine. It is necessary to develop combined drugs with wide therapeutic spectrum for treatment of GH. The range of drugs, based on combination of synthetic and bioactive substances of plant origin should be extended.

Key words: antivirals; genital herpes; acyclovir; suppositories; infection; treatment

INTRODUCTION

Today, the therapy of virus infection is the most actual problem of medicine, because of occurrence this disease and severity of pharmacotherapy. Herpetic infection is the most widespread among all virus infections. Genital herpes (GH) is one of the most socially important problem in clinical practice of dermatovenereologist, obstetrician-gynecologists and urologists. The number of ill people with GH during last 10 years increased to 30 % [1]. More than 90 % of people in the world currently are infected by HSV (herpes simplex virus) and 20 % of them have various clinical implication of infection. Only 5 % of ill people have typical symptoms, but in 80 % of cases, infection hasn't clinical implication.

The main role in etiology of GH belongs to HSV 2, but pathogene could be either HSV 1 or combination of both types of HSV, which have from 50 to 100 % people [6]. More than 100 types of herpes virus are described now, from which only 8 types are clinically important. Currently, it is known about 450 pathogenic viruses for people.

Main groups of viruses include: 170 respiratory viruses; 90 enteric viruses, about 100 arboviruses, pathogens of hepatitis, A, B, C, D, E, F, G; HIV-1, HIV-2, more than 100 viruses of papilloma, parvovirus, hantavirus, adenovirus. The infections, which connected with HSV 1 and HSV 2 are dominated. GH is characterized by polymorphism of clinical implications, recurrent chronicity, different complications, including inflammatory process of pelvic organs, abnormality of fertility, intrauterine infection of fetus and neonate [7, 10].

The highest prevalence of GH is registered among people of 20-29 years old, second peak is in age 35-40 years. The zymosis depends on degree of infection and immune system.

© Levachkova Yu. V., Yarnykh T. G., Litvinova O. M., 2014

According to clinical finding, GH is divided into 4 types: first clinical episode of primary GH; first clinical episode in the presence GH; herpes recidivicus; atypical GH; asymptomatic GH [3, 5].

The therapy of GH is not easy process because there are not any drugs, which could eliminate virus from the body completely. That's why the main aim of the therapy is acceleration of epithelialization's processes reduction in number of relapses and increase of the disease-free survival.

Currently, for therapy we can use antiviral therapy, immunotherapy and combination of these methods according to stage and severity of disease [9].

The aim of this study is analysis of drug's assortment, which used in antiviral therapy, to evaluate next optimization of drug's providing.

RESULTS AND DISCUSSION

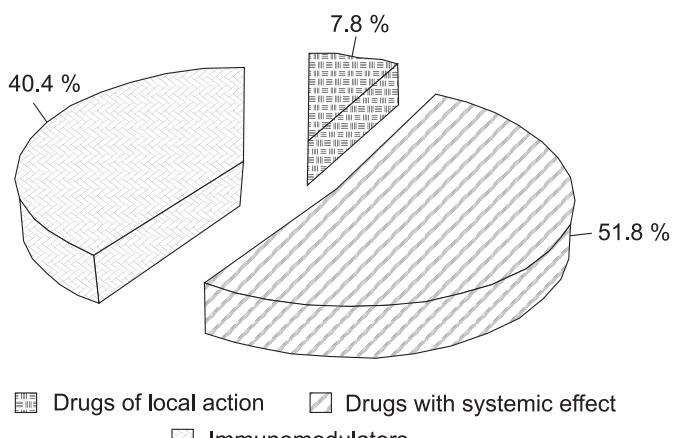
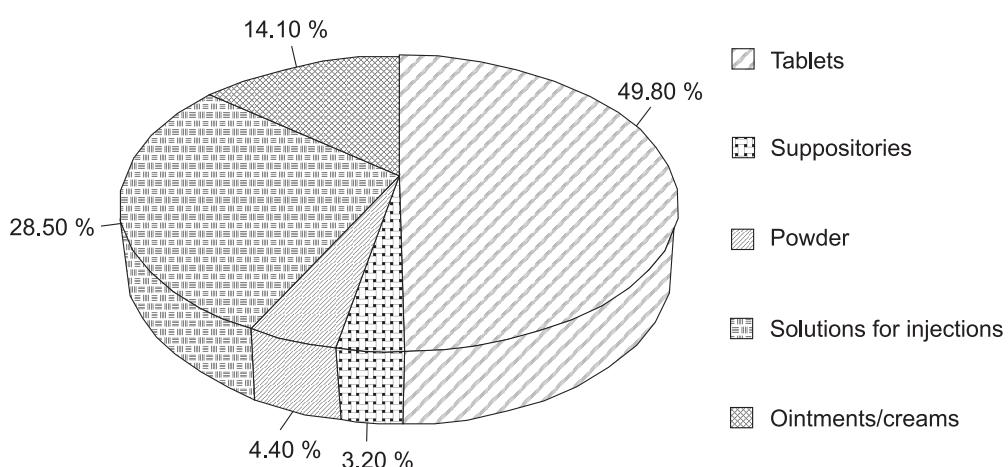
General assortment of antivirals on Ukrainian pharmaceutical market is represented by 411 names. Annual volume of this group in Ukraine is about 300 mln hrn [2, 8].

The list of antivirals of different dosage forms includes: 51,8 % of drugs with systemic effect (using for ARVI and herpes infection therapy); 40,4 % of immunomodulators; 7,8 % of drugs with local action (Fig. 1).

Different dosage forms can be used for therapy of infection: tablets (49,8 %), powder (4,4 %), solutions for injections (28,5 %), ointments and creams (14,1 %), suppositories (3,2 %) (Fig. 2).

There is multivariable range of antivirals, which have efficiency clinically proven on the world's markets. On the basis of features of application, the drugs can be divided in some groups:

- drugs for therapy DNA – containing viruses;
- drugs for therapy RNA – containing viruses;
- antivirals with action similar to antibiotics;
- interferon inducers;

**Fig. 1. Relation between antivirals, based on action.****Fig. 2. Relation between antivirals of different dosage forms.**

Table

ANTIVIRALS OF SYSTEMIC EFFECT AND LOCAL ACTION FOR GH THERAPY ON PHARMACEUTICAL MARKET OF UKRAINE

Product name	Drug substance	Dosage form	Manufacturer, country
1	2	3	4
MEDOVIR	Acyclovir	Powder for preparation of solution of injection	Medochemie LTD, Cyprus
ACYCLOVIR - DARNITSA	Acyclovir	Tablets	Darnitsa, Ukraine
ACYCLOVIR - PFARMEX	Acyclovir	Tablets	"Pharmex Group", Ukraine
ACYCLOVIR - FARMAK	Acyclovir	Tablets	"Farmak", Ukraine
GERPEVIR®	Acyclovir	Powder for preparation of solution of injection	"Kyivmedpreparat", Ukraine
VIROLEX	Acyclovir	Tablets	KRKA, Slovenia
VIROLEX	Acyclovir	Powder for preparation of solution of injection	KRKA, Slovenia
ACYCLOVIR STADA®	Acyclovir	Tablets	Stada Arzneimittel AG, Germany
ACIVIR	Acyclovir	Tablets	Unimax Laboratories, India Mepro Pharmaceuticals Pvt. Ltd., India
BIOCYCLOVIR-BIOPHARMA	Acyclovir	Powder for preparation of solution of injection	"Biopharma", Ukraine
ACYCLOVIR	Acyclovir	Tablets	JSC "Lekhim-Kharkiv", Ukraine
GEVIRAN	Acyclovir	Tablets	"Polpharma", Poland
ACYCLOVIR - ASTRAPHARM	Acyclovir	Tablets	"Astrapharm", Ukraine
ZOVIRAX™	Acyclovir	Tablets	GlaxoSmithKline, Great Britain

Table continued

1	2	3	4
ZOVIRAX™	Acyclovir	Lyophilizate for preparation of solution of injection	GlaxoSmithKline, Manufacturing, Italy
ACIC®	Acyclovir	Tablets	Salutaz Pharma GmbH, Germany, Sandoz Pharmaceuticals d.d
MEDOVIR	Acyclovir	Tablets	Medochemie LTD, Cyprus
CYMEVENE	Ganciclovir	Lyophilizate for preparation of solution of injection	F. Hoffmann-La Roche Ltd. Switzerland
FAMVIR®	Famcyclovir	Tablets	Novartis Pharma, Spain
VALACICLOVIR-KR	Valacyclovir	Tablets	Chervona zirkva, Ukraine
VALCIK	Valacyclovir	Tablets	Pharmascience Inc., Canada
VALTROVIR	Valacyclovir	Tablets	"Kyivmedpreparat", Ukraine
VALAVIR®	Valacyclovir	Tablets	"Farmak", Ukraine
VALTREX™	Valacyclovir	Tablets	"GlaxoSmithKline Pharmaceuticals S.A.", Spain
GERPEVAL	Valaciclovir	Tablets	"Phytopharm", Ukraine
ARPEFLU®	Umifenovir	Tablets	"Lekpharm", Belorus
EREBRA® HIPORHAMIN EXTRACT	Hiporhamin extract	Tablets	"Pharmcentre Vilar", Russia
KAGOCEL®	Kagocel	Tablets	"Niarmedic Plus", Russia
AMIZONUM®	Amizonum® (enisiamium iodide)	Tablets	"Farmak", Ukraine
IMUSTAT	Umifenovir	Tablets	"Darnitsa", Ukraine
NOVIRIN	Inosine pranobex	Tablets	"Kyiv vitamin plant", Ukraine
ISOPRINOSINE	Inosine pranobex	Tablets	Liaomedicamenta Technical Pharmaceutical Sociedad, Portugal, Pharmaceutical plant TEVA, Hungary
ACYCLOVIR-PHARMEX	Acyclovir	Cream	"Pharmex Group", Ukraine
GERPEVIR®	Acyclovir	Ointment	"Kyivmedpreparat", Ukraine
ZOVIRAX®	Acyclovir	Cream	Glaxo Operations UK Limited, Great Britain
ACICLOVIR-FARMAK	Acyclovir	Cream	"Farmak", Ukraine
ACICLOVIR-VISHFA	Acyclovir	Ointment	Pharmaceutical fabric, Jitomir, Ukraine
VIROLEX	Acyclovir	Ointment	KRKA, Slovenia
AGERP	Acyclovir	Ointment	Joint Ukrainian-spanish enterprise "Sperco Ukraine", Ukraine
ACIC®	Acyclovir	Ointment	Salutaz Pharma GmbH, Germany, Sandoz Pharmaceuticals d.d
ACIVIR	Acyclovir	Ointment	Temiz Medicare Limited, India Mepro Pharmaceuticals Pvt. Ltd., India
ACYCLOSTAD®	Acyclovir	Ointment	Stada Arzneimittel AG, Germany
PANAVIR®	Panavir®	Suppositories	"Lanapharm", Russia

- homeopathic drugs;
- immune adjuvants.

By the chemical composition, antivirals are classified as: interferon and its products, nucleosides, lipids and its derivatives, adamontane and its derivative drugs of plant origin.

Studying the range of drugs, which are registered on the 1st March 2014 it was set, that needs in antivirals for patients are satisfied (Table).

It should be mentioned, that the range of existing antiherpes drugs during last years increased significantly, but the most effective are acyclovir, valacyclovir, pencyclovir, gancyclovir, famcyclovir [4, 11].

According to this data, the number of dosage form with local action is insignificant. That's why, the development of new combined antiviral in suppositories, used for gynecology is the most prospective direction.

CONCLUSIONS

1. Analysis of data of antiviral medicines, which are registered in Ukraine, shows that medicines of systemic action consist 51,5 % of all.
2. Analysis of market proves, that foreign medicines dominated between all registered drugs on Ukrainian pharmaceutical market.
3. Development and introduction of new domestic antiviral remedies in forms of suppositories is perspective direction of pharmaceutical sector.

REFERENCES

1. Бардова Е. А. Герпетическая инфекция: патогенез, клиника, лечение / Е. А. Бардова // Medix Antiaging. – 2011. – № 2. – С. 44-52.
2. Державний реєстр лікарських засобів (<http://www.drlz.kiev.ua>).

3. Львов Н. Д. Герпесвирусы человека – системная, лимфопролиферативная иммуноонкология / Н. Д. Львов // Рус. мед. журн. – 2012. – № 22. – С. 1133-1137.
4. Мавров И. И. Герпес-вирусная инфекция: глобальная проблема здравоохранения / И. И. Мавров // Дерматол. і венерол. – 2007. – № 1. – С. 3-8.
5. Нагорний О. Є. Епідеміологія генітального герпесу, хламідіозу і трихомонозу в Україні і регіонах за період 2005-2010 рр. / О. Є. Нагорний // Дерматол. і венерол. – 2011. – № 2. – С. 5-14.
6. Овчинникова Л. К. Герпетическая инфекция / Л. К. Овчинникова, Е. А. Овчинникова // Рос. аптеки. – 2008. – № 20. – С. 34-38.
7. Степаненко В. І. Урогенітальні інфекції: трихомоноз, кандидоз, генітальний герпес / В. І. Степаненко, Т. С. Коновалова. – К., 2008. – 286 с.
8. Шаблакова А. С. Маркетинговая оценка позиционирования противовирусных средств / А. С. Шаблакова, А. Ю. Петров // Fundamental Res. – 2012. – № 8. – С. 204-206.
9. Ягудина Р. И. Заболевания, передающиеся половым путем / Р. И. Ягудина, Е. А. Овчинникова // Рос. аптеки. – 2008. – № 16. – С. 24-29.
10. Ashley Morrow R. Time course of sero-conversion by HerpeSelect ELISA after acquisition of genital Herpes simplex virus type 1 (HSV-1) or HSV-2 / R. Ashley Morrow, E. Krantz, A. Wald // Sex. Transm. Dis. – 2003. – Vol. 30. – P. 310-314.
11. Wald A. Comparative efficacy of famciclovir and valacyclovir for suppression of recurrent genital herpes and viral shedding / A. Wald, S. Selke // Sex. Transm. Dis. – 2006. – Vol. 33, № 9. – P. 529-533.

УДК 615.281.8:615.454.2:618.1**Ю. В. Левачкова, Т. Г. Ярних, А. Н. Литвинова****ПРОТИВОВИРУСНЫЕ ПРЕПАРАТЫ: СОСТОЯНИЕ И ПЕРСПЕКТИВЫ СОЗДАНИЯ В УКРАИНЕ**

Проведено изучение ассортимента лекарственных препаратов для лечения генитального герпеса (ГГ). Доказано, что на фармацевтическом рынке Украины недостаточно отечественных лекарственных форм. Для лечения ГГ необходимо разрабатывать комбинированные лекарственные препараты с широким спектром терапевтического действия. Следует расширять номенклатуру лекарственных средств на основе комбинации синтетического сырья и биологически активных веществ растительного происхождения.

Ключевые слова: противовирусные препараты; генитальный герпес; ацикловир; суппозитории; инфекция; лечение

УДК 615.281.8:615.454.2:618.1**Ю. В. Левачкова, Т. Г. Ярних, О. М. Літвінова****ПРОТИВІРУСНІ ПРЕПАРАТИ: СТАН ТА ПЕРСПЕКТИВИ СТВОРЕННЯ В УКРАЇНІ**

Проведено вивчення асортименту лікарських препаратів для лікування генітального герпесу (ГГ). Доведено, що на фармацевтичному ринку України недостатньо вітчизняних лікарських форм. Для лікування ГГ необхідно розробляти комбіновані лікарські препарати із широким спектром терапевтичної дії. Слід розширяти номенклатуру лікарських засобів на основі комбінації синтетичної сировини та біологічно активних речовин рослинного походження.

Ключові слова: противірусні препарати; генітальний герпес; ацикловір; супозиторії; інфекція; лікування

Адреса для листування:

61146, м. Харків, вул. Блюхера, 4.

Тел. (050) 135-42-86.

E-mail: lejuva@mail.ru.

Національний фармацевтичний університет

Надійшла до редакції

13.06.2014 р.