Efficiency of the pharmacological treatment for the grade 1 cervical intraepithelial neoplasia.

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Introduction

The most common cervical precancerous disease is low-risk cervical intraepithelial neoplasia or CIN 1. These lesions spontaneously regresses in 57%, persists in 32%, progresses to carcinoma in situ in 11% and to invasion in 1% of cases[1]. Pharmacological treatment of lesions in CIN 1 with glycyrrhizinic acid could reduce persistent HPV infection, the incidence of CIN 1, and the use of more aggressive therapies.

Aim

The aim of the study is to investigate efficiency of medication treatment for CIN 1 lesions.

Materials and methods

A prospective study was done in Riga East Clinical University Hospital from July 2017 to May 2022. Women with histologically confirmed CIN 1 in cervical biopsies were included in the study. Participants of the study group members used glycyrrhizinic acid spray (*Epigen* spray) topically for 6 months 10 days per month (Epigen 10-days subgroup) or 20 days per month (Epigen 20-days subgroup). Women in the control group had no any treatment. During two follow-up visits 6 months apart cytological, colposcopic, and histological examination is done. If CIN2 or 3 was detected at the first follow-up visit, women underwent large loop excision of the transformation zone (LLETZ) and were no longer invited for a second visit. All patients are screened for human papillomavirus before enrollment and during the 1st follow-up visit. Permission from the RSU Ethics Committee was obtained for the research. Chi-square and Fisher exact test is used for statistical analysis of nonparametric data and two-tailed independent t-test for parametric data.

Results

When comparing the Epigen 20-days subgroup to the control group, there were no statistically significant differences in cytological and colposcopic changes. However, in histological findings, the persistence of CIN 1 was more common in the Epigen group, 87% in Epigen and 62 in the control group, and progression to CIN 2 was more common in the control group 7% in Epigen and 31% in Control group.

LLETZ after 1st follow-up visit was also statistically significantly more frequent in the control group (10% in the Epigen 20-days subgroup vs 30% in the Control group, p=0.032).

No statistically significant difference was found between the Epigen 20-days subgroup and control group in cytological, colposcopic, or histological changes at the 2nd follow-up visit or of both follow-up visits in total, non in intention to treat analysis non in the per-protocol analysis.

No statistically significant difference was found in the incidence of improvement or deterioration in cytological, colposcopic, and histological findings between Epigen 10-days use and the control group at either the first or second control visit.

HPV types 16, 31, 33, 51, and 56 are the most commonly detected among enrolled women. No statistically significant difference is found in the incidence of high-risk HPV types elimination or decreasing of concentration between Epigen 20-days and control group.

Conclusions

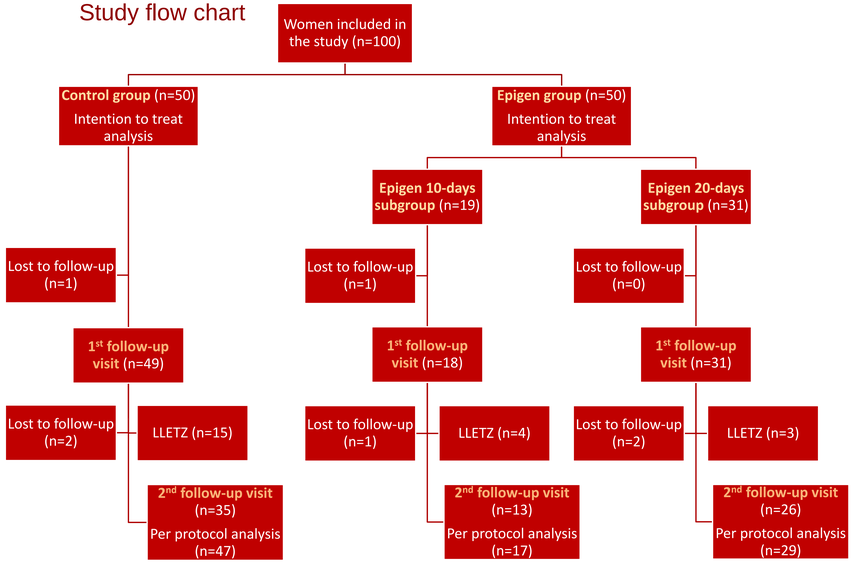
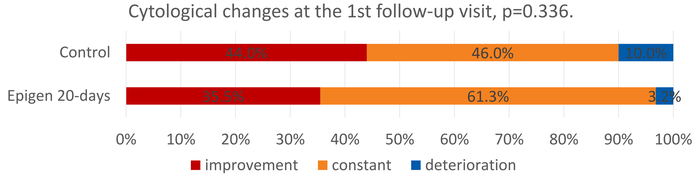
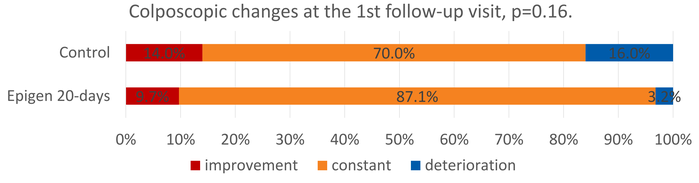
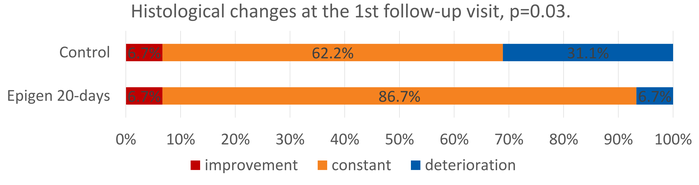
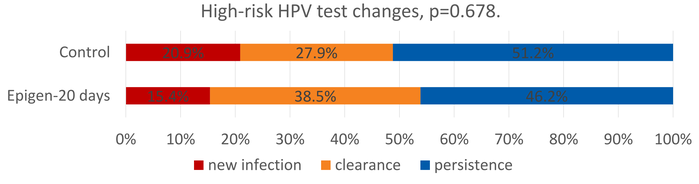
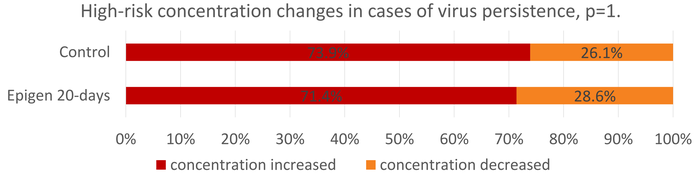
The vaginal spray of the glycyrrhizinic acid used 20 days a month for six months appears to decrease the risk of the deterioration of CIN 1 lesions, but a similar effect is not observed after stopping the usage.

The glycyrrhizinic acid use locally does not affect HPV clearance or decrease in concentration and does not prevent new infection.

Multicenter double-blind randomized controlled trials are needed to confirm this study's findings.

[1] Hoffman BL, Schorge JO, Bradshaw JO, Halvorson LM, Schaffer JI, Corton MM. Williams gynecology. 3 ed. McGraw-Hill Education, 2016.

Study flow chart



		Epigen, n=50	Control, n=50	*P-value*
Age, years		32.5±7.5	32.3±7.8	0.886
Education	basic	4%	8%	0.036
	secondary	32%	54%	
	higher	64%	38%	
Age at the first intercourse		17.8±2.4	17.7±1.8	0.704
Number of partners		5±3.4	5±3.1	0.951
Number of partners 6 and more		34%	26%	0.383
Current partner, months		66.4±71.0	61.6±76.4	0.749
Smoking		30%	30%	1
HPV at inclusion (high-risk HPV)		78% (78%)	82% (78%)	0.617
Contraception	none	22%	32%	0.192
	coitus interruptus	40%	22%	
	calendar method	0	2%	
	condoms	14%	26%	
	oral contraceptive	14%	8%	
	vaginal ring, contraceptive patch	4%	4%	
	intrauterine system	0	2%	
	intrauterine device	4%	0	
	other	2%	4%