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ORIGINAL ARTICLE

Local carboxymethyl-β-glucan and polycarbophil therapy is associated with regression of low-grade cervical cytological abnormalities: a prospective observational study

Melika Dervišefendić Peljto[1*], Mahira Jahić[2]

[1]Primary Health Care Centre Gračanica, Gračanica, Bosnia and Herzegovina; [2]Gynaecological Centre "Dr. Mahira Jahić", Tuzla, Bosnia and Herzegovina

ABSTRACT

Aim To evaluate the association between intravaginal therapy with carboxymethyl-β-glucan (CMBG) and polycarbophil and cytological regression of atypical squamous cells of undetermined significance (ASCUS) and cervical intraepithelial neoplasia grade 1 (CIN 1), compared with standard follow-up.
Methods This prospective observational controlled study included 80 women aged 23–49 years with ASCUS or CIN 1. Forty patients received intravaginal CMBG/polycarbophil spray, and 40 were managed with standard follow-up. Allocation was based on clinical assessment and therapy availability, without randomisation. The primary outcome was cytological normalisation after 12 months, based on Papanicolaou smear results.
Results After 12 months, abnormal cytology was observed in 4 (10.0%) patients in the treatment group and 18 (45.0%) in the control group (RR 0.22; 95% CI 0.08–0.60; $p < 0.001$). Normal cytology was observed in 36 (90.0%) and 22 (55.0%) patients, respectively ($p < 0.001$). Human papillomavirus (HPV) persistence was detected in 2 (5.0%) patients in the treatment group and 5 (12.5%) in the control group ($p = 0.432$).
Conclusion Intravaginal CMBG/polycarbophil therapy was associated with a higher rate of cytological normalisation than standard follow-up in women with ASCUS and CIN 1.

Keywords: cervical intraepithelial neoplasia, human papillomavirus, vaginal therapy

INTRODUCTION

Human papillomavirus (HPV) is the principal aetiological factor in the development of cervical intraepithelial lesions and cervical cancer (1,2). Although most HPV infections are transient and resolve spontaneously within 12–24 months, persistent infection with high-risk HPV types is associated with the development of cytological abnormalities and progression to cervical intraepithelial neoplasia (1,2).

Low-grade cervical abnormalities, including atypical squamous cells of undetermined significance (ASCUS) and cervical intraepithelial neoplasia grade 1 (CIN 1), regress spontaneously in a substantial proportion of cases (3–5). Consequently, the standard clinical approach is based on surveillance without immediate therapeutic intervention. Nevertheless, some abnormalities may persist or progress, which represents a clinical challenge and may lead to considerable patient anxiety.

In recent years, several local therapeutic approaches have been developed with the aim of modulating the vaginal microenvironment and stimulating local immune responses. Carboxymethyl-β-glucan (CMBG) activates receptors involved in innate immune responses, whereas polycarbophil, a bioadhesive polymer, allows prolonged contact of active compounds with the cervical epithelium (6–8).

Previous studies evaluating topical β-glucan-based therapy in women with HPV-related low-grade cervical abnormalities have reported progressive cytological regression during follow-up, including improvement of ASCUS, low-grade squamous intraepithelial lesion (LSIL), and HPV/CIN 1 lesions. These findings suggest that local immunomodulatory therapy may be associated with epithelial repair and regression of low-grade cytological abnormalities, thereby providing both biological and clinical rationale for further evaluation of CMBG/polycarbophil formulations (9,10).

The aim of this study was to evaluate the association between intravaginal administration of CMBG/polycarbophil and cytological regression of ASCUS and CIN 1 compared with standard follow-up.

*Corresponding author:
Melika Dervišefendić Peljto
Primary Health Care Centre Gračanica, Gračanica, Bosnia and Herzegovina
E-mail: dervisefendic@gmail.com
ORCID ID: 0009-0009-6305-3592

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MATERIAL AND METHODS

Patients and study design

This prospective, observational, controlled study was conducted in the outpatient setting of a primary health care centre between February 2025 and January 2026. Consecutive patients with cytological findings of ASCUS and/or histologically confirmed CIN 1 lesions who attended follow-up examinations during the study period were included. A total of 80 patients were enrolled, with 40 assigned to the treatment group and 40 to the control group.

Allocation to the treatment or control group was based on clinical assessment and therapy availability in routine outpatient practice, without formal randomisation. Therefore, the study was not designed to establish a causal treatment effect, and the results were interpreted as associations between CMBG/polycarbophil therapy and clinical outcomes. Because the allocation was not randomised, selection bias cannot be excluded; patients receiving therapy may have differed from controls in unmeasured factors such as adherence to follow-up, health-related behaviour, sexual behaviour, vaginal microbiome status, motivation, or socioeconomic background.

Women aged 23–49 years with ASCUS or CIN 1 findings and available HPV testing were eligible for inclusion. Exclusion criteria included higher-grade lesions (CIN 2 or higher), previous excisional cervical procedures, pregnancy, systemic immune disorders, or concurrent use of other intravaginal therapies.

Methods

Patients in the treatment group applied an intravaginal spray containing CMBG/polycarbophil once daily for 20 consecutive days, followed by a 10-day treatment-free interval. This cyclic regimen was selected because similar topical beta-glucan-based protocols have previously been used in women with ASCUS, LSIL, and HPV/CIN 1 lesions, with reported progressive cytological regression during follow-up. Treatment lasted for at least 3 months and was extended up to 6 months in cases of persistent cytological abnormalities. Patients in the control group underwent standard cytological and colposcopic surveillance according to routine clinical practice.

Formal adherence monitoring and systematic adverse-event collection were not performed. Therefore, treatment adherence and tolerability could not be formally quantified and were considered additional limitations of the study.

At baseline, all patients underwent Papanicolaou (Pap) testing, HPV testing, and colposcopic examination. Follow-up visits were performed after 6 and 12 months.

The primary outcome was normalisation of cytological findings after 12 months, based on Pap smear results. Histological confirmation of regression was not systematically required unless clinically indicated. Secondary outcomes included cytological regression after 6 months, HPV negativisation, persistence of HPV infection, and lesion progression. Progression to CIN 2 was analysed separately as a clinically relevant safety outcome.

Statistical analysis

Categorical variables were presented as numbers and percentages, and continuous variables as mean ± standard deviation (SD). Between-group differences were analysed using the χ^2 test or Fisher's exact test for categorical variables, as appropriate, and Student's t-test for continuous variables. Fisher's exact test was preferred for small cell counts. Relative risk (RR) with 95% confidence intervals (CI) was calculated for the primary and selected secondary outcomes. Because the study was non-randomised and the sample size was relatively small, baseline comparability was interpreted cautiously, considering both p-values and absolute differences. Adjusted regression analysis was considered; however, because of the small sample size and low number of events in some subgroups, a formal multivariable model was not considered reliable. Instead, sensitivity analyses stratified by baseline cytology and baseline HPV status were performed. Statistical significance was defined as $p < 0.05$.

RESULTS

A total of 80 women were included in the study, with 40 participants in the treatment group and 40 in the control group. Mean age was 35.8 ± 7.6 years in the treatment group and 35.7 ± 7.4 years in the control group (p = 0.953). Smoking was reported by 24 (60.0%) women in each group, while baseline HPV positivity was present in 9 (22.5%) and 7 (17.5%) women, respectively (p = 0.576). ASCUS was the predominant baseline cytological finding, observed in 29 (72.5%) women in the treatment group and 28 (70.0%) in the control group, whereas CIN 1 was present in 11 (27.5%) and 12 (30.0%) women, respectively (Table 1).

Table 1. Baseline clinical and diagnostic characteristics of participants

Parameter	Treatment group (n = 40)	Control group (n = 40)	p
Age (years), mean ± SD	35.8 ± 7.6	35.7 ± 7.4	0.953
Smoking status, n (%)	24 (60.0%)	24 (60.0%)	1.000
Parity, mean	1.73	1.63	0.540
ASCUS at baseline	29 (72.5%)	28 (70.0%)	0.805
CIN 1 at baseline	11 (27.5%)	12 (30.0%)	0.805
HPV positive	9 (22.5%)	7 (17.5%)	0.576
Minor colposcopic changes	13 (32.5%)	10 (25.0%)	0.459

ASCUS, atypical squamous cells of undetermined significance; CIN, cervical intraepithelial neoplasia; HPV, human papillomavirus.

After 6 months, abnormal cytological findings were observed in 14 (35.0%) women receiving CMBG/polycarbophil therapy compared with 28 (70.0%) women in the control group (RR 0.50; 95% CI 0.31–0.80; p = 0.003) (Table 2). Conversely, normal cytology was recorded in 26 (65.0%) women in the treatment group and 12 (30.0%) women in the control group (RR 2.17; 95% CI 1.28–3.66; p = 0.003). ASCUS was present in 11 (27.5%) women in the treatment group and 19 (47.5%) in the control group, while CIN 1 was detected in 3 (7.5%) and 7 (17.5%) women, respectively. No cases of CIN 2 were observed in the treatment group, whereas two cases (5.0%) occurred in the control group.

Table 2. Secondary clinical outcomes after six months

Outcome	Treatment group	Control group	p
	N (%)		
Abnormal cytology*	14 (35.0%)	28 (70.0%)	0.003
Normal cytology	26 (65.0%)	12 (30.0%)	0.003
ASCUS	11 (27.5%)	19 (47.5%)	0.105
CIN 1	3 (7.5%)	7 (17.5%)	0.311
CIN 2	0 (0.0%)	2 (5.0%)	0.490

* Abnormal cytology includes ASCUS, CIN 1, and CIN 2; ASCUS, atypical squamous cells of undetermined significance; CIN, cervical intraepithelial neoplasia.

Table 3. Primary cytological outcome after 12 months

Outcome	Treatment	Control	p
	N (%)		
Abnormal cytology*	4 (10.0%)	18 (45.0%)	< 0.001
Normal cytology	36 (90.0%)	22 (55.0%)	< 0.001
ASCUS	3 (7.5%)	11 (27.5%)	0.037
CIN 1	1 (2.5%)	5 (12.5%)	0.201
CIN 2	0 (0.0%)	2 (5.0%)	0.494

* Abnormal cytology includes ASCUS, CIN 1, and CIN 2; ASCUS, atypical squamous cells of undetermined significance; CIN, cervical intraepithelial neoplasia.

Table 4. Human papillomavirus (HPV) status at baseline and after 12 months

Time point	HPV status	Treatment group (n = 40)	Control group (n = 40)	p
		N (%)		
Baseline	Positive	9 (22.5%)	7 (17.5%)	0.576
	Negative	31 (77.5%)	33 (82.5%)	
12 months	Positive	2 (5.0%)	5 (12.5%)	0.432
	Negative	38 (95.0%)	35 (87.5%)	

HPV, human papillomavirus.

At 12 months, abnormal cytology was present in 4 (10.0%) women in the treatment group and 18 (45.0%) women in the control group (RR 0.22; 95% CI 0.08–0.60; p < 0.001). Normal cytological findings were observed in 36 (90.0%) women receiving therapy compared with 22 (55.0%) women undergoing standard follow-up (RR 1.64; 95% CI 1.21–2.21; p < 0.001). ASCUS persisted in 3 (7.5%) women in the treatment group and 11 (27.5%) women in the control group, while CIN 1 was observed in 1 (2.5%) and 5 (12.5%) women, respectively. No cases of CIN 2 were detected in the treatment group, whereas two cases (5.0%) remained present in the control group (Table 3).

At baseline, HPV positivity was detected in 9 (22.5%) women in the treatment group and 7 (17.5%) women in the control group. After 12 months, HPV positivity was observed in 2 (5.0%) and 5 (12.5%) women, respectively (RR 0.40; 95% CI 0.08–1.91; p = 0.432) (Table 4). HPV negativity at 12 months was recorded in 38 (95.0%) women in the treatment group and 35 (87.5%) women in the control group (Table 4).

DISCUSSION

This study showed that intravaginal carboxymethyl-β-glucan/polycarbophil therapy was associated with a higher rate of cytological normalisation than standard follow-up in women with ASCUS and CIN 1.

Low-grade cervical lesions frequently regress spontaneously, and surveillance remains the standard approach for ASCUS and CIN 1 in most clinical settings. However, lesion persistence is clinically relevant because persistent HPV infection is a key factor in the progression of cervical intraepithelial neoplasia (3–5). The present findings suggest that local supportive therapy may have a role in women with low-grade abnormalities.

Lavitola et al. reported improvement in vaginal microbiota restoration and cervical epithelialisation among HPV-positive women treated with carboxymethyl-beta-glucan (9), while Laccetta et al. described favourable cytological outcomes in women with ASCUS and low-grade squamous intraepithelial lesions treated with beta-glucan (10). The direction of the present findings is therefore consistent with earlier reports.

A plausible biological explanation for the observed association is the immunomodulatory activity of beta-glucans. CMBG may activate receptors involved in innate immune responses and stimulate macrophages, dendritic cells, and other immune mediators that participate in antiviral defence and epithelial repair (6–8).

The vaginal microbiome and local immune environment are increasingly recognised as important factors in HPV persistence and clearance (11–14). HPV persistence, HPV-based testing strategies, and cervicovaginal microbiome alterations are also relevant to risk assessment and follow-up in women with cervical abnormalities (15–19). In the present study, HPV positivity was numerically lower after 12 months in the treatment group than in the control group; however, the difference was not statistically significant.

Progression to CIN 2 was not observed in the treatment group, whereas two cases occurred in the control group. This finding is clinically relevant but should not be overinterpreted because of the low number of events. It may reflect the natural course of low-grade cervical lesions, differences between groups, or a possible supportive effect of local therapy. Larger studies with histological confirmation and longer follow-up are required to clarify whether this intervention has any effect on lesion progression.

Several limitations should be acknowledged. The study was conducted in a single centre and included a relatively small number of participants, which limits statistical power and generalisability. Allocation to treatment was not randomised, so selection bias and residual confounding cannot be excluded. Women receiving treatment may have differed from controls in adherence, health-related behaviour, sexual behaviour, vaginal microbiome status, motivation, or socioeconomic factors. No formal multivariable adjustment was performed because of the small sample size and low number of events. HPV-related analyses were underpowered because few participants were HPV-positive at baseline. Cytological normalisation was used as the primary endpoint, while systematic histological confirmation was not performed unless clinically indicated. Adherence and adverse events were not systematically recorded, limiting the assessment of treatment exposure and safety.

CONCLUSION

Intravaginal CMBG/polycarbophil therapy was associated with a higher rate of cytological normalisation compared with standard follow-up in women with ASCUS and CIN 1. Further adequately powered randomised controlled trials with systematic HPV testing, histological confirmation when clinically indicated, adherence monitoring, and safety assessment are required to confirm the clinical value of this therapeutic approach.

FUNDING

No specific funding was received for this study.

CONFLICTS OF INTEREST

None to declare.

ETHICS STATEMENT

The study was approved by the institutional Ethics Committee (approval No. 03-1/2024; April 17, 2025) and conducted in

accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available from the corresponding author upon reasonable request and with permission of the institution.

AUTHOR CONTRIBUTIONS (CRediT)

Conceptualization: M.D.P.; **Data curation:** M.D.P.; **Formal analysis:** M.D.P.; **Investigation:** M.D.P., M.J.; **Methodology:** M.D.P., M.J.; **Supervision:** M.J.; **Writing – original draft:** M.D.P.; **Writing – review & editing:** M.D.P., M.J. All authors have read and agreed to the published version of the manuscript.

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