

Application of Bioapigyn® Herbal Ointment for the Treatment of Lower Genital Tract Infections

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ABSTRACT

Objective: The purpose of this work was development and testing of new herbal ointment for the treatment of lower genital tract infections in females. **Material and Methods:** 80 female patients with positive swabs to at least one microorganism (*U. urealyticum*, *M. hominis*, *E. coli* and *Candida* sp.) were randomly divided into three treatment groups. First group was treated 12 days (twice a day) with doxycycline antibiotic and 2 g of Bioapigyn® vaginal ointment (once a day), second group with 2 g of ointment only and third group with antibiotic only (12 days; twice a day). **Results:** Following the therapy all the swabs were negative to *M. hominis* regardless of the treatment group. Eradication of *U. urealyticum* was 100%, 87% and 62% and *E. coli* 75%, 67% and 33% in antibiotic + herbal ointment, herbal ointment only and antibiotic only group, respectively. None of the patients in the first and second group developed antibiotic-associated candidiasis compared to 80% positive swabs in the antibiotic only group. **Conclusion:** Bioapigyn® vaginal ointment has significant antimicrobial potential against common vaginal pathogens which is even better compared to standard antibiotic.

Keywords: Bioapigyn® Vaginal ointment, Essential oils, Medicinal plants, Honey, Genital infections.

INTRODUCTION

The lower female genital tract flora is an example of dynamic and complex microbial colonization with very thin line between normal commensal and pathological state. The type of microorganisms and their intrinsic virulence together with the complexity of the genital flora and its numerical dominance in the colonized tissue are identified as the risk factors for the development of the infection. *Candida albicans*, Group B *Streptococcus*, *Gardnerella vaginalis* and *Escherichia coli* are the most commonly isolated microorganisms in the lower female genital tract.¹ *Mycoplasmas* are obligate parasites adhered on the epithelial cells of the genital tract that could be both pathogenic to humans and commensal. Once adhered on the host cell they secrete metabolic products like hydrogen peroxide that destroy both host cells as well as bacteria itself.² *M.*

hominis, *M. fermentans*, *M. genitalium*, *M. ladlawi*, *Ureaplasma urealyticum* and *Ureaplasma parvum* are most commonly isolated from the urogenital tract.³

Among the *Mycoplasmas* *U. urealyticum* was most commonly isolated. The incidence of *U. urealyticum* in the cervix or vagina of sexually active females could be up to 80%. The most common symptoms are infertility, higher incidence of spontaneous abortion, pelvic pain, premenstrual symptoms like spotting, the symptoms of infection of the genital tract as well as itching, burning and vaginal discharge.^{4,5} Since *Mycoplasmas* are lacking cell walls the best treatment option is doxycycline antibiotic.^{5,6} Although, highly efficient in treatment of genital pathogens, frequent development of severe candidiasis represents the major drawback of such therapy.⁵

DOI: 10.5530/ijper.51.3s.7

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Frequent occurrence of the resistance of many pathogens to existing antibiotics stimulated the researchers to turn to the herbal remedies.⁵ There has been increasing interest in the development of new types of effective and nontoxic herbal antimicrobial products.^{5,7} The purpose of this work was to examine the efficacy of new herbal vaginal ointment prepared from the macerates and essential oils of medicinal plants in the combination with honeybees products for the topical treatment of lower genital tract infections in females.

MATERIAL AND METHODS

80 female patients (age range from 19 to 73 years) with positive swabs to at least one microorganism (*U. urealyticum*, *M. hominis*, *E. coli* and *Candida* sp.) were randomly divided into three groups of similar age, life style and health status. Prior to the treatment all the patients signed the informed consent. First group (50 patients) was treated 12 days (twice a day) with doxycycline antibiotic and 2 g of Bioapigyn® vaginal ointment (once a day), second group (15 patients) with 2 g of ointment only and third group (15 patients) with doxycycline antibiotic only. The ointment was composed of the macerates of the following medicinal plants in olive oil: *C. officinalis* (10%), *P. major* (10%), *M. chamomilla* (10%), *H. perforatum* (10%), *A. vulgaris* (10%), *S. officinale* (5%), *L. officinalis* (2.5%), *A. millefolium* (2.5%), *T. serpyllum* (2.5%), *S. officinalis* (2.5%), *M. piperita* (2.5%), *O. europaea* (2.5%) in the combination with *A. sativa* (1.5%), *C. flava* (10%), honey (10%), glycerol (7.5%) and essential oils: *M. alternifolia* (0.3%), *T. vulgaris* ct. thymol (0.3%), *C. camphora* ct. cineol (0.1%), *C. martini* (0.1%), *O. compactum* (0.1%) and *E. caryophyllata* (0.1%). The macerate and ointment preparation were described in details in our previous papers.^{5,7} The difference in the treatment efficiency between the groups was assessed by χ^2 test using STATISTICA 11.0 software and statistical significance was set to $p < 0.05$. The influence of the predictor variable on the outcome of the therapy was assessed by multiple regression and general regression model. The study was approved by ethical comity of the center in November 23, 2013.

RESULTS AND DISCUSSION

The number of the positive swabs to the selected microorganisms prior and after the therapy depending on three different therapeutic approaches was presented in Table 1. Before the therapy *Ureaplasma urealyticum* was identified as the major pathogen in all three groups followed by *Candida* sp. The highest percentage (64%) of the positive swabs to *Ureaplasma* was found in the group below 40 years of age which was in agreement with previous

research.^{1,4,5} Higher prevalence was linked with younger age, frequent change of partners, lower socio-economic status and use of oral contraceptives.

Following the treatment with antibiotic and herbal ointment all the swabs were negative to *U. urealyticum*, *M. hominis*, and *Candida* sp. as well as 75% swabs to *E. coli*. The treatment with the ointment only resulted with 100% negative swabs for *M. hominis*, and *Candida* sp. while the treatment efficiency of *U. urealyticum* and *E. coli* was 87% and 67%, respectively. The treatment with the antibiotic only resulted in 100% negative swabs *M. hominis*, 62% to *U. urealyticum*, 33% to *E. coli*. In the first and second group none of the patients developed antibiotic-associated yeast infection while in the antibiotic only group 80% of them were positive to *Candida* sp. There was no significant difference in the treatment efficiency between the first and the second group for neither of the tested microorganism. On the contrary, a significant difference was obtained between the first and the third group for *U. urealyticum*, *E. coli* and *Candida* sp. as well as between second and third group in eradication of *Candida* sp. and *U. urealyticum*. Based on the results of multiple regression analysis and general regression model applied on the whole population the outcome of the therapy for *U. urealyticum* as the major pathogen correlated significantly ($R=0.74$; $p=0.0377$) with the predictor variables (the type of therapy, Age, No. of births, No. of abortions, No. of miscarriages, Contraception, No. of partners, Menopause, Other health problems). Among them, the type of the therapy was the only variable with statistically significant contribution ($p=0.0004$). Similar results were obtained for *Candida* sp. ($R=0.52$; $p=0.0481$). For other two microorganisms there was no statistically significant correlation with the predictor variables which could be explained with low number of valid cases.

Obtained results showed superiority of Bioapigyn® vaginal ointment compared to Doxycycline in eradication of all tested microorganisms. The additive effect between the antibiotic and herbal ointment resulted with even better treatment efficiencies for all microorganisms. Similar results were reported by Orešćanin et al., 2015 following the treatment of female patients with the combination of Doxycycline and herbal pessaries composed of the macerates of the same plants as those used in the present research. The efficacy of the eradication of *U. urealyticum* with doxycycline and herbal pessaries was 91.5% compared to 69.1% in the patients treated with doxycycline and miconazole based pessaries.⁵ Besides, none of the patients developed antibiotic-associated yeast infections in the group treated with

Table 1: Number of positive swabs to selected microorganisms prior and following the therapy with or without antibiotic and Bioapigyn® herbal vaginal ointment

Microorganism	Doxycycline + Bioapigyn® ointment N=50		Bioapigyn® ointment N=15		Doxycycline N=15	
	Prior	After	Prior	After	Prior	After
<i>Ureaplasma urealyticum</i>	41	0	15	2	13	5
<i>Mycoplasma hominis</i>	5	0	3	0	2	0
<i>Escherichia coli</i>	4	1	3	1	3	2
<i>Candida sp.</i>	11	0	7	0	9	9

herbal pessaries compared to app. 27% positive swabs to *Candida sp.* in miconazole group.⁵

Excellent results obtained in the current study could be linked with the multi-herbal composition of the ointment containing the ingredients with well proven antimicrobial effect toward various strains of both gram positive and gram negative bacteria and fungi.⁵ Moreover, the plants like marigold, chamomile, plantain, lavender, St. John's wort, oat and comfrey also decrease inflammatory changes and accelerate healing process of the vaginal mucosa, thus preventing adherence of the bacteria onto cell walls. Besides, honey with its well known antimicrobial, prebiotic and probiotic activity⁸ provides healthy balance of the vaginal flora by preventing the transition of the vaginal flora from commensal to pathogenic form. It encourages the development of normal vaginal flora and establishes normal acidic pH of the vagina.

CONCLUSION

Bioapigyn® vaginal ointment showed a significant antimicrobial potential which is even better compared to standard antibiotic alone due to the additive and synergistic effects of bioactive compounds from the oil extracts and essential oils of the selected medicinal plants and honeybees products. It is highly effective in the prevention of antibiotic-associated yeast infection which was linked to well known prebiotic and probiotic activity of honey and low pH value of the ointment (4.43). Furthermore, it showed additive effect with antibiotic which resulted in significantly better treatment efficiency for 3 of 4 tested microorganisms.

ACKNOWLEDGEMENT

The authors are grateful to Findri-Gušteć Centre for healthcare for technical support.

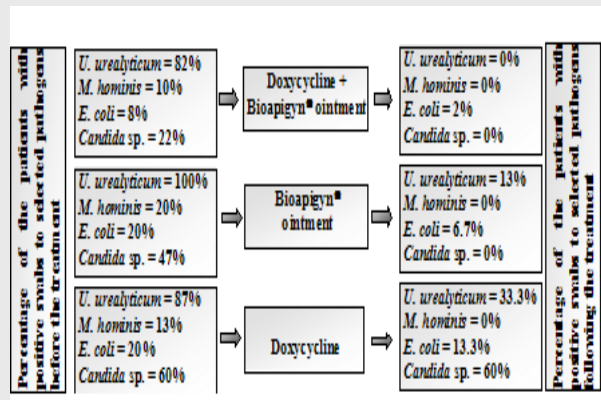
CONFLICT OF INTEREST

None

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PICTORIAL ABSTRACT



SUMMARY

- *Ureaplasma urealyticum* was the most common pathogen isolated in all three groups.
- Bioapigyn® vaginal ointment was composed of the macerates of twelve medicinal plants, six essential oils, colloidal oat and honey as active components while beeswax and glycerol represented excipients.
- Bioapigyn® ointment was superior to Doxycycline in eradication of all tested genital pathogens.
- The best treatment efficiency was achieved by combining antibiotic and Bioapigyn® ointment due to their additive effect.
- None of the patients developed antibiotic-associated yeast infection in the group co-treated with Bioapigyn® vaginal ointment.
- Multi-herbal composition of the ointment containing the ingredients with well proven antimicrobial effect toward various strains of both gram positive and gram negative bacteria and fungi was responsible for excellent treatment efficiency.

ABOUT AUTHORS



Višnja Oreščanin is scientific advisor and full professor in the field of toxicology. During 21 years of her professional experience professor Oreščanin published over 170 scientific papers in the top ranked international scientific journals and conference proceedings, five patents and over 100 technical reports. She is a reviewer for 37 international scientific journals. She is owner and director general of ORESCANIN Ltd., the company established with the aim of developing innovative herbal medicinal products.



Primarius Štefica Findri Guštek, MD, Ph.D., is the founder of the Findri Guštek Center for Health Care, which includes gynecology, occupational health, child and the family medicine. She is coauthor of over 30 papers published in the top ranked international scientific journals and conference proceedings, 1 patent and numerous technical reports. The research interests include: gynecology and obstetrics, development and testing of new products (including herbal medicine) for the treatment of various infections of uro-genital tract and menopausal symptoms, clinical trials.

Cite this article: Višnja O, Štefica FG. Application of Bioapigyn® Herbal Ointment for the Treatment of Lower Genital Tract Infections. Indian J of Pharmaceutical Education and Research. 2017;51(3)Suppl:S176-79.