

The Treatment of Menorrhagia with Bioapigyn® Herbal Ointment and Pessaries

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Summary

The purpose of this work was the development and application of a new herbal ointment and pessaries for the topical treatment of menorrhagia using macerates and essential oils of medicinal plants as active ingredients. Fifty subjects with proven menorrhagia ranging from 32 to 54 years were divided into two groups (each had 25 participants) of similar age, health status and lifestyle. The first group used 2 g of ointment every eight hours while the second group used pessaries instead. The results were obtained at baseline and following the third menstrual cycle. In both groups a significant decrease was observed for all the symptoms ($p < 0.05$). Significantly better results were obtained in the case of the ointment compared to the pessaries as expected due to the higher percentage of the active ingredients. The average duration of bleeding was reduced from 7.4 to 4.7 days in the case of the ointment and from 7.3 to 5.1 days in the group who used pessaries. The average number of painkillers is reduced from 22.1 to 10.6 and from 22.9 to 13.1 in the group using the ointment and pessaries, respectively. Decrease in other symptoms ranged from 71.4% up to 88.2% in the group using the ointment and from 57.3% to 73.7% in the case of pessaries usage. The obtained results could be correlated with the use of active ingredients with proven haemostatic, vasoconstrictor, astringent and spasmolytic activity.

Key words

Olive oil macerates; medicinal plants; essential oils; menorrhagia; herbal ointment; pessaries

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Introduction

Menorrhagia is the most common form of abnormal uterine bleeding characterized by prolonged and abundant menstrual bleeding whereby over 80 mL of blood per cycle is lost (Oehler and Rees, 2003; Livdans-Forret et al., 2007; Beebeejaun and Varma, 2013). The signs and the symptoms of menorrhagia may include: changing the sanitary pad or tampon every hour for several hours, using twice as many pads or tampons during the menstrual period, waking during the night to change the pad or the tampon, bleeding for longer than a week, blood clots that appear longer than a day, the inability to perform normal daily activities due to severe bleeding, anemia symptoms, such as fatigue or lack of breath.

According to Beebeejaun and Varma (2013) the most common causes of menorrhagia are: hormonal imbalance, dysfunction of the ovaries, uterine fibroids, polyps of the uterus, intrauterine device for birth control, pregnancy complications due to miscarriage, implantation of a fertilized egg in the fallopian tube instead of the uterus, cancer (uterine, ovarian, cervical), hereditary bleeding disorders (blood clotting disorders), drugs, other medical conditions (pelvic inflammatory diseases, thyroid problems, endometriosis, liver and kidney disease). The standard treatment of menorrhagia may include drug therapy such as: iron supplements in the case of anemia, non-steroidal anti-inflammatory drugs, oral contraceptives and progesterone tablets. In the cases of un-successful drug therapy, there is an option of surgical treatment like dilatation and curettage, embolization of blood vessels of the uterus (in the case of presence of myomas), myomectomy, endometrial ablation, hysterectomy (Beebeejaun and Varma, 2013; Bradley and Gueye, 2016). Herbal preparations with either astringent and/or uterotonic activity have also been used to combat menorrhagia (Livdans-Forret et al., 2007).

The purpose of this work was the formulation and application of the herbal preparations in the form of ointment and pessaries for the treatment of menorrhagia in reproductive age females.

Materials and methods

Patients

Among 112 females reported to the Center due to heavy menstrual bleeding in 50 of them menorrhagia was confirmed. The subjects were randomly divided into two groups (each had 25 participants) of similar age, health status and lifestyle. All the patients signed written consent for the participation in the study.

Preparation of the macerate

The macerate was prepared from dried plant material of 15% of *Capsella bursa-pastoris* (L.) Medik., 15% of *Alchemilla vulgaris* L., 15% of *Achillea millefolium* L., 15% of *Plantago major* L., 10% of *Polygonum aviculare* L., 10% of *Salvia officinalis* L., 5% of *Quercus robur* L., 5% *Olea europaea* L., 5% *Calendula officinalis* L., 5% *Matricaria chamomilla* L. (Suban, Strmec Samoborski, Croatia) and extra virgin olive oil. Solid:liquid ratio was 1:5. Maceration time was 21 days at 50°C. The macerate was separated from the solid part by filtration.

Preparation of the ointment

For the preparation of the ointment 80% of the macerate, 5% of glycerol (Kemig, Zagreb, Croatia), 4.3% of honey (Kemig) and 10% of *Cera alba* (Kemig) was heated to 60°C for ten minutes, mixed and then cooled to the room temperature. The mixture was homogenized and supplemented with 0.2% of *Melaleuca alternifolia* (Maiden & Betche) Cheel oil, 0.1 % *Syzygium aromaticum* (L.) Merr. & L.M.Perry oil, 0.1% of *Cymbopogon martini* (Roxb.) W.Watson oil, 0.1% *Cinnamomum camphora* (L.) J.Presl ct. cineol oil, 0.1% of *Thymus vulgaris* L. ct. timol oil and 0.1% of *Origanum compactum* Benth. oil, homogenized once again and packed into 50 mL tubes (Oreščanin and Findri Guštek., 2016; 2017). All essential oils were of pharmaceutical grade produced by Pranarom International, Ghislenghien, Belgium.

Preparation of the pessaries

For the preparation of the pessaries (Oreščanin et al., 2015) 40% of the macerate, 4.3% of *Cera alba* (Kemig) and 54.6% of Witepsol E75 (Kemig) were heated until 60°C, mixed slowly for 10 minutes and allowed to cool to 30°C. Pharmaceutical grade essential oils (Pranarom International) of *M. alternifolia* (0.2%), *T. vulgaris* (0.2%), *E. caryophyllata* (0.2%), *C. camphora* ct. cineol (0.1%), *C. martini* (0.1%) and *O. compactum* (0.1%) were added into the mixture, mixed thoroughly and packed into high quality plastic strips (Meyer GMBH, Ober-Mörlen, Germany) containing ten single cells each of 3 g.

The treatment

Both groups were treated during three consecutive menstrual cycles. The first group applied 2 g of the ointment deep into vagina every eight hours while the second group used pessaries (one pessary every eight hours). The results were obtained at baseline and following the third menstrual cycle. The improvement was monitored by the reduction in the number of spent sanitary pads or tampons, waking during the night in order to change the pads or tampons, the duration of bleeding, appearance of the blood clots and the number of painkillers consumed.

Statistical analysis

The difference between the values before and following the treatment as well as between two herbal preparations was assessed by t-test using STATISTICA 12.0 software package. The significance level was set to $p < 0.05$.

Results and discussion

The age of the ointment treated women ranged from 32 to 54 years (47.2 ± 4.9) and in the pessaries treated group women were from 33 to 52 years old (47.9 ± 4.3). The average number of spent sanitary pads or tampons before the treatment was 38 ± 7.7 (29-47) in the ointment and 37 ± 7.4 (30-44) in the pessaries treatment group. The average changing during the night was 7 ± 2.2 (5-9) and 6 ± 2.1 (5-8) times in the ointment and pessaries treatment group, respectively. The average duration of bleeding lasted 7.4 ± 2.3 (6-9) and 7.3 ± 2.1 (6-9) day, respectively. The blood clots appeared during the first three days of the period. The average number of consumed painkillers was 22.1 ± 4.4 and 22.9 ± 3.9 in the

ointment and the pessaries treatment group, respectively. Besides, unpleasant odor was present in all participants regardless of the group. Furthermore, 20 participants from the ointment group and 18 participants from the pessaries group suffered from the symptoms like burning, redness, irritation that occurred during or in the end of the cycle. All the parameters showed statistically significant decrease in both groups following the treatment during three consecutive cycles. The average number of spent sanitary pads or tampons decreased to 10.9 ± 2.7 in the ointment and to 14.9 ± 3.9 in the pessaries treatment group and changing during the night to 0.8 ± 0.2 and 1.6 ± 0.3 in the ointment and pessaries treatment group, respectively. The average duration of bleeding was reduced to 4.7 ± 0.7 days in the case of the ointment and to 5.1 ± 0.9 days in the group who used pessaries, while the number of the painkillers was reduced to 10.6 ± 2.2 and 13.1 ± 3.4 , respectively. The blood clots were reduced for 79.6% and 57.3% in the ointment

The deodorant effect of essential oils prevented the development of unpleasant odor.

Conclusion

Conducted preliminary research has shown that both herbal products have a significant positive effect on alleviating the symptoms of menorrhagia since all the observed parameters in both groups of the patients were significantly lower after the treatment. Such results are attributable to the combination of the herbal ingredients with proven haemostatic, astringent, vasoconstrictor, spasmolytic and anti-microbial properties. Significantly better results were obtained in the group using the ointment compared to the group using the pessaries, which was expected since the ointment contains two times more active ingredients compared to the pessaries.

Table 1. Mean values and standard deviations expressed as the percentages of the reduction of menorrhagic symptoms following the treatment with herbal ointment or pessaries and t-test scores between two groups of the subjects.

Parameter	Ointment	Pessaries	P
Reduction in the number of spent sanitary pads or tampons	71.4±5.9	59.7±4.8	<0.0001*
Reduction of waking during the night	88.2±7.3	73.7±6.2	<0.0001*
Reduction of the duration of bleeding	37.1±4.4	29.5±3.6	<0.0001*
Reduction of the blood clots	79.6±6.1	57.3±5.7	<0.0001*
Reduction in the number of painkillers consumed	51.7±4.5	42.6±3.9	<0.0001*

*significant at $P < 0.05$

and pessaries treatment group, respectively. When comparing the percentages of the reduction of each parameter between two groups significantly higher reduction of all parameters was obtained in the case of the ointment use (Table 1). This was expected since the ointment contains 80% of the macerate of the plants with strong haemostatic, astringent, vasoconstrictor and spasmolytic activity, while the content of those plant macerates in the pessaries was only 40%. Moreover, unpleasant odor during the period was also reduced or disappeared completely in both groups. The symptoms like burning, redness, irritation that occurred in the most of the patients after menstruation disappeared completely upon the treatment with ointment and pessaries.

Obtained results could be correlated with the presence of herbal ingredients with proven haemostatic activity such as *C. bursa-pastoris* (EMA, 2010), *A. millefolium* (Rauchensteiner et al., 2004), *P. major* (Samuelsen, 2000), *A. vulgaris* (Shrivastava et al., 2007) and *P. aviculare*. *C. bursa-pastoris*, *A. millefolium* and *A. vulgaris* also acting as vasoconstrictor and *Q. robur*, *S. officinalis*, *A. vulgaris* and *O. europaea* as an astringent (Oreščanin and Findri Guštek, 2016) all of which resulted in reduced bleeding. Furthermore, *C. officinalis*, *Salvia officinalis* L., *Achillea millefolium* L. and *Alchemilla vulgaris* L. have also spasmolytic effect and contributed to the reduction of spasticity and pain (Oreščanin and Findri Guštek., 2016). All these herbal ingredients including all essential oils used due to their powerful antimicrobial effect (Oreščanin et al., 2015) prevented the development of infection with anaerobic bacteria in particular, which is very common during and after the period.

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