

Polish Gynaecology

Ginekologia Polska



Reprint

October 2009

Ginekol Pol. 2008, 79, 494-498
(nr 7/2008)

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Evaluation of Cicatridina efficacy in healing and repairing process of uterine cervix, vagina and vulva – open no-randomized clinical study

Ocena skuteczności stosowania Cicatridiny w procesie gojenia i reparacji szyjki macicy, pochwy i krocza – otwarte nierandomizowane badanie kliniczne

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Abstract

Purpose: The aim of the study was to evaluate the efficacy of Cicatridina application in healing and repairing process after operative procedures concerning uterine cervix, vagina and vulva and after brachytherapy due to cervical and endometrial cancer.

We also analyzed Cicatridina effect on vaginal atrophical signs in post-menopausal women.

Patients and Methods: The examined group consist of 319 women. They were divided into 2 arms.

The active arm concerns 213 women who used Cicatridina, while controlled one consists of 106 women.

The effect of treatment was estimated after 6 weeks and 3 months by the visual inspection of the cervix and vagina. We also analyzed the subjective filling of patients bound to sexual intercourses by using of Visual Analogue Scale (0% – no effect; 100% – disappearance of pathological symptoms).

Results: In active arm according to control one the reparation of cervix was more often: after surgery procedures (respectively after 6 weeks 93% vs 70%; after 3 months 99% vs 89%) and after brachytherapy (respectively after 3 months 86% vs 0%). In brachytherapy group the lack of discomfort during sexual intercourses was also more often in active arm (respectively 55% vs 0%).

In postmenopausal women reduction of symptoms associated with atrophic vaginitis was observed only in active group (respectively after 6 weeks 43% vs 0%; after 3 months 57% vs 0%). In the group of patients after episiotomy due to delivery the relief of discomfort during sexual intercourses was also more often in active arm (respectively 94% vs 25%).

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Otrzymano: 15.06.2008

Zaakceptowano do druku: 05.07.2008

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Conclusion: *Cicatridina causes fast healing of cervix after gynecological procedures. It influences improvement of atrophical, inflammatory and after radiation therapy effects which improve quality of life and comfort of vagina after brachytherapy due to cervical and endometrial cancer.*

Cicatridina causes similar effect in vagina of pos-menopausal women as locally used estrogens. Cicatridina also causes the feeling of relief and comfort in vagina after delivery as well as fast healing after episiotomy.

Key words: **Cicatridina / repair process / uterine / cervix / vagina / vulva /
/ brachytherapy / menopause / episiotomy /**

Streszczenie

Cel pracy: *Celem pracy była ocena skuteczności stosowania Cicatridiny w postaci globulek w procesie gojenia i reoperacji po zabiegach operacyjnych na szyjce macicy, pochwie i sromie oraz brachyterapii z powodu raka szyjki macicy i raka błony śluzowej trzonu macicy a także jej wpływu na objawy atroficzne w pochwie kobiet po menopauzie.*

Materiał i metody: *Materiał obejmował 213 kobiet, u których zastosowano Cicatridinę oraz 106 kobiet z grupy kontrolnej.*

Efekt leczenia oceniono po upływie 6 tygodni i następnie 3 miesiące od rozpoczęcia terapii poprzez wizualną ocenę szyjki macicy i/lub pochwy. Oceniano również subiektywne odczucia pacjentek dotyczące dolegliwości związanych ze współżyciem płciowym poprzez zastosowanie procentowej skali zgłaszanych odczuć (0% brak poprawy – 100% całkowite ustąpienie objawów lub dolegliwości).

Wyniki: *W grupie stosującej Cicatridinę w porównaniu do grupy kontrolnej w większym odsetku doszło do wygojenia szyjki po zabiegach (odpowiednio w 6 tygodniu po leczeniu 93% vs 70% i w 3 miesiącu 99% vs 89%); do poprawy wizualnej po brachyterapii (odpowiednio 86% vs 0% po 3 miesiącach); braku dyskomfortu przy współżyciu po brachyterapii (odpowiednio 55% vs 0%); ustąpienie dolegliwości wśród pacjentek w okresie fizjologicznego przekwitania (odpowiednio w 6 tygodniu po leczeniu 43% vs 0% i w 3 miesiącu 57% vs 0%); oraz braku dyskomfortu przy współżyciu po nacięciu krocza w (odpowiednio 94% vs 25%).*

Wnioski: *Cicatridina powoduje szybsze gojenie się szyjki macicy po zabiegach ginekologicznych.*

Po brachyterapii z powodu raka szyjki i trzonu macicy Cicatridina wpływa na poprawę objawów atroficzno-zapalnych i popromiennych co poprawia jakość życia oraz zwiększa komfort w pochwie. U kobiet po fizjologicznym przekwitaniu Cicatridina wywiera podobny efekt w pochwie jak stosowane lokalnie estrogeny.

Cicatridina zwiększa komfort w pochwie po przebytych porodach a krem powoduje szybsze gojenie się rany po epizjotomii.

Słowa kluczowe: **Cicatridina / proces gojenie / szyjka macicy / pochwa / srom /
/ brachyterapia / przekwitanie / epizjotomia /**

Introduction

The vaginal ecosystem of a mature healthy woman consists of anaerobic and aerobic flora in a reciprocal equilibrium, in which lactic acid rods, *Lactobacillus*, prevail protecting the site from colonization with undesirable microbes. The system may be disturbed by any local or generalized pathology [1, 2, 3, 4].

Factors which disturb the system include:

- surgical procedures on the uterine cervix and vagina, including procedures linked to delivery;
- hormonal disturbances (menopause, disturbances of the menstrual cycle, pregnancy);
- immune disturbances, e.g. immunosuppression in the course of treatment with cytostatic agents and antibiotics;
- post-irradiation reaction, particularly following brachytherapy used in the treatment of cancers of the uterine cervix and *endometrium*;
- application of vaginal anti-inflammatory and spermicidal drugs;
- other factors (hygienic errors, sexual activity).

In the post-delivery and, in particular, breast-feeding periods, in the course of menopause, irradiation and chemotherapy, vaginal dryness is frequently noted, with an increased pH of vaginal secretion and a disturbed metabolism of collagen, which promotes the development of vaginal infections [4, 5, 6].

Hyaluronic acid (the main component of Cicatridina) traps water while its ability to bind protein molecules and form a proteoglycan network improves both tissue hydration and import of nutrients, securing appropriate tissue tonus, trophism and elasticity. In conditions of atrophy and dystrophy of vaginal mucosa it promotes the regeneration of the epithelium. Due to its presence in the extracellular matrix and its capacity to modulate pro-inflammatory cytokines and cell migration the acid favourably affects healing processes including the formation of a normal epithelium [7, 8].

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Table I. Groups of studied patients.

Patient Groups	Active arm	Control arm
Following procedures on the uterine cervix	71	36
With CIN I - CIN III subjected to electroconization	23	9
With ectopic uterine cervix subjected to electrocoagulation	32	15
With ectopic uterine cervix subjected to cryotherapy	16	12
Following brachytherapy	42	20
Following brachytherapy due to cancer of the uterine cervix	11	10
Following brachytherapy due to endometrial cancer	31	10
In the period of physiological menopause	30	30
Following episiotomy in the course of delivery	70	20
TOTAL	213	106

Table II. Healing of the uterine cervix in the group of patients following procedures on the uterine cervix.

	Active arm					Control arm				
	N	After 6 weeks		After 3 months		N	After 6 weeks		After 3 months	
		N	%	N	%		N	%	N	%
With CIN I - CIN III subjected to electroconization	23	20	86.96	23	100.00	9	5	55.56	8	88.89
With ectopic uterine cervix subjected to electrocoagulation	32	30	93.75	31	96.88	15	11	73.33	12	80.00
With ectopic uterine cervix subjected to cryotherapy	16	16	100.00	16	100.00	12	9	75.00	12	100.00
TOTAL	71	66	92.96	70	98.59	36	25	69.44	32	88.89

Table III. Evaluation of vaginal lesions in patients following brachytherapy.

	Active arm					Control arm				
	N	Healing after 3 months		Improvement after 3 months		N	Healing after 3 months		Improvement after 3 months	
		N	%	N	%		N	%	N	%
Patients following brachytherapy due to cervical cancer	11	2	18.18	9	81.82	10	0	0.00	0	0.00
Patients following brachytherapy due to endometrial cancer	31	3	9.68	27	87.10	10	0	0.00	0	0.00
TOTAL	42	5	11.90	36	85.71	20	0	0.00	0	0.00

Aim of study

The study aimed to evaluate the efficacy of Cicatridina application in the form of vaginal ovules (sodium hyaluronate 5mg, oil extract of *Centella asiatica*, oil extract of marigold, oil extract of tea-tree) in the processes of healing and repair following surgical procedures on the uterine cervix, vagina and vulva and following brachytherapy due to cancers of the uterine cervix and endometrium. The study also aimed to evaluate efficacy in the management of vaginal atrophy signs/symptoms in post-menopausal women.

The action of the preparation was compared with a group of untreated women following the same procedures.

Material

The material included 213 women in whom the effects of intravaginally applied vaginal ovules of Cicatridina were evaluated as compared to a control group of 106 women. In the group of patients following episiotomy due to delivery the women received also a locally applied cream. (Table I).

Methods

In patients following uterine cervix procedures on Cicatridina was applied in order to accelerate re-epithelization of the uterine cervix and the treatment was started within 24 hours of the procedure.

In women following brachytherapy indications for treatment included the detection of inflammatory-necrotic lesions, cohesion of vaginal walls and symptoms which disturbed sexual intercourse. The patients started the treatment 3 to 6 months after the completion of radiotherapy, when they were regarded as cured and reported for control examination.

In the group of patients in the period of physiological menopause the indications for treatment included vaginal dryness and itching and discomfort in sexual intercourse. They started treatment following the visit during which they reported the complaints.

In the three groups of patients (following procedures on uterine cervix, following brachytherapy and in the period of physiological menopause) Cicatridina vaginal ovules were administered once daily, in the evening for 10 days and, then, for the period of one month every other day and, in cases when improvement was noted, every third day for another month.

Following delivery patients were recommended therapy during the first control examination (6 weeks after delivery) if they complained of vaginal dryness and itching. For 10 days the vaginal ovules were used daily and, then, for 20 days every other day. If the post-episiotomy scar became hard and painful, cream was applied locally 2-3 times daily for 10 days.

The effects of the treatment in women following procedures on uterine cervix, following brachytherapy and in the period of physiological menopause were evaluated after 6 weeks and, then, 3 months after start of therapy by visual appraisal of the uterine cervix and/or vagina. Subjective symptoms of the patients were also noted, including complaints associated with sexual intercourse using a percentage scale of the reported complaints (0% = no improvement, 100% = full disappearance of signs/complaints).

Results

In the group examined following procedures on the uterine cervix 6 weeks after the procedure most of the patients manifested a healed up uterine cervix, with no deformations or endometriotic foci and in none of the cases was the uterine ostium narrowed. (Table II).

In the control examination following 3 months the percentage of patients with a healed cervix was even higher in the group. The control group manifested worse results: in two cases following electroconization 2mm foci of endometriosis and in one patient narrowing of uterine cervix were detected.

Among 42 patients subjected to surgery and, then, to brachytherapy due to cancer of the uterine cervix and endometrium (the women used no sex hormones) in five cases healing was noted after 3 months (no vaginal narrowing, no foci of necrosis or sticking of vaginal walls) and in 36 patients a notable improvement was detected by colposcopic examination.

Table IV. Reduction of complaints reported at the start of the therapy in women in the period of physiological menopause.

Active arm					Control arm						
		After 6 weeks		After 3 months				After 6 weeks		After 3 months	
N	%	N	%	N	%	N	%	N	%	N	%
30	13	43.33	17	56.67	30	0	0.00	0	0.00	0	0.00

Table V. Discomfort in the course of sexual intercourse in the group of women following episiotomy during delivery.

Active arm			Control arm		
		After 3 months			After 3 months
N	%	N	%	N	%
70	4	5.71	20	16	85.00

Table VI. Application of Cicatridina cream in the group of women following episiotomy in the course of delivery.

Active arm					Control arm						
		After 6 weeks		After 3 months				After 6 weeks		After 3 months	
N	%	N	%	N	%	N	%	N	%	N	%
22	20	90.91	22	100.00	6	4	66.67	6	100.00	6	100.00

During the observation period the women in the control group manifested neither healing nor improvement. (Table III).

In the entire group 23 women recorded no discomfort as a result of sexual intercourse.

In the control group, on the other hand, all the patients reported discomfort or did not have sexual intercourse due to the complaints.

Among 30 patients in the period of physiological menopause who did not decide to start hormonal replacement therapy in the systemic or intravaginal form, local application of Cicatridina proved to be very effective. After 6 weeks 13 patients reported no complaints at all and after 3 months the number of such patients increased to 17. (Table IV).

Among 70 women following spontaneous delivery in the active arm of the study, most of patients reported sensation of relief and vaginal comfort and their sexual intercourses were accompanied by no pain. (Table V).

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In the women following spontaneous delivery with episiotomy in 22 cases examination following 6 weeks demonstrated a thickened, reddened scar. In such patients Cicatridina cream was additionally applied to the vulva. In the control arm such a condition was detected in 6 out of 20 patients. Within 6 weeks following application of the cream differences were detected in the appearance of the scar. (Table VI).

Discussion

Treatment of glandular ectopy and pre-cancerous lesions of the uterine cervix (CIN) is linked to injury of uterine cervical structures, leading to spotting, excessive vaginal secretion, congestion, fibrosis, narrowing of cervical canal and, sometimes endometriosis. The process results in physical discomfort (when using sanitary pads, pain, itching) and psychological tension linked to the anxiety that sexual intercourse or the normal routine of daily life delays the healing process.

A significant effect on the healing process is exerted by hyaluronic acid, acting along multiple pathways: it influences the migration of regenerating cells, cells inducing re-epithelialization, induction of pro-inflammatory cytokines release and secretion of pro-angiogenic factors, which stimulate the healing process at every stage [9, 10, 11, 12].

The results of our studies on women following procedures on the uterine cervix indicate that following application of Cicatridina the healing process can be noted in a higher proportion of the patients. Similar results of hyaluronic acid application have been noted by other authors [13].

Among women using Cicatridina vaginal ovules following delivery a significant majority experienced comfort during sexual relationships and appropriate humidity in vagina while the post-episiotomy scar healed in a higher proportion of the patients. The phenomenon is linked to growth of epithelial cells, supplying them with nutrients and growth of blood vessels [7, 8, 11].

Deficiency of oestrogens due to the physiological loss of ovarian function or surgical castration induces atrophic and atrophic-inflammatory lesions in vagina resulting in the sensation of dryness and itching and even in epithelial injury and sticking of vaginal walls.

If the hypo-oestrogenism is accompanied by post-irradiation injury of vaginal walls following brachytherapy, used in treatment of cervical and endometrial cancer, this poses a significant problem of a deteriorated quality of life [2, 3, 4, 5].

Application of Cicatridina in a significant proportion of studied patients has resulted in healing of the post-radiotherapy wound and has very significantly reduced the complaints. This is consistent with other observations indicating excellent effects of hyaluronic acid in prevention against development of post-operative adhesions [14].

In the presented group of 30 patients in the period of physiological menopause, in 17 cases a marked improvement has been noted by colposcopy and complete absence of complaints such as vaginal dryness and itching or discomfort in sexual relationships, which has contrasted with the pattern observed in the control arm.

The defect of the presented study involves the fact that it was open and not randomized. Application of randomization and a double-blind testing would improve methodological aspect of the study, perhaps allowing to draw even more radical conclusions.

Conclusions

1. Cicatridina results in an improved healing of uterine cervix following gynaecological procedures.
2. Cicatridina increases vaginal comfort following deliveries while the respective cream accelerates healing of post-episiotomy wound.
3. In women following brachytherapy due to cancer of uterine cervix and endometrium Cicatridina reduces atrophic-inflammatory and post-irradiation signs in this way improving quality of life in the patients.
4. In women following physiological menopause Cicatridina induces in the vagina a similar effect to that of locally applied oestrogens.

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