

EXPERIENCE IN USE OF SILVER-CONTAINING HYDROALGINATE DRESSING SILVERCEL[®] FOR VENOUS TROPHIC ULCERS MANAGEMENT

Kirienko A.I., Bogdanetz L.I., Kalinina E.V., Berezina S.S.

Russian National Medical University, City Clinical Hospital No.1 in the name of N.I. Pirogov, Moscow

Venous trophic ulcers affecting 1–2% of capable population in developed countries [2,4,6] occupy leading position (more than 70%) in general structure of lower extremities ulcers having various origin [5] and represent a defect of skin and underlying crus tissues developed consequently chronic venous outflow disturbance and persisted 4–6 weeks [1]. It is obvious taking into account complex mechanism of chronic venous insufficiency (CVI) pathogenesis with development of trophic ulcers and decompensated venous outflow (Class 6 according to no CEAP) that treatment of those complication must be complex in order to influence on main pathogenetic components and must include obligatory elastic compression of lower legs, maintenance of treating conservative regimen, use of long-acting systemic and various topical drugs, and surgical correction of disturbed venous outflow designed for eradication of abnormal veno-venous bypass in order to decrease dynamic phlebohypertension and interrupt cascade of pathological reactions resulting eventually in trophic ulcer development [7]. Yet P.D. Colerige Smith (2003) and H. Partsch (2003) demonstrated that primary radical or palliative surgery is impossible in 70-75% patients having open venous ulcers because for many reasons including non-recanalized form of postthrombotic disease, state of skin covers, concomitant pathology, social conditions, patients' age, and so on [9,11]. Thus, main treatment method for considerable proportion of patient having venous ulcers is topical conservative therapy along with elastic compression and systemic pharmacotherapy.

Modern conservative treatment methods being used in complex provide for closure up to 80% venous ulcers without surgery [7] but don't eliminate their principal cause leading to relapse in most cases.

Topical treatment of trophic venous ulcers plays key role and predetermines subsequent management in many instances. Main objectives of that treatment are inflammatory process arresting, ulcer cleansing from purulent necrotic tissues, stimulation of regeneration process and its ultimate aim is full ulcer healing or sanation.

Infected ulcers with abundant exudation are particularly complicated because of long-term healing and worsening of surround tissues' condition (dermatitis, cellulitis). Use of antibacterial preparations is problematic in such cases because of drug resistant strains development. At the same time an experience was accumulated over centuries concerning use of silver demonstrated its efficacy even against bacterial strains resistant to Methicillin and Vancomycin [10,12].

Distinctive feature of trophic venous ulcers is absence of clear-cut wound process staging, i.e. presence of granulation tissue and even epithelization within the same ulcer along with necrotic and fibrin areas. This fact determines need to use simultaneously several bioactive substances. Therefore, search and development of new generation dressings is relevant which could have effective influence on pathogenic flora and create optimal conditions for healing. Now use of modern hydroactive wound coatings providing healing in moist environment is most efficient topical treatment of trophic venous ulcers. One of such dressings is Silvercel – hydroalginate dressing with silver (Fig. 1).

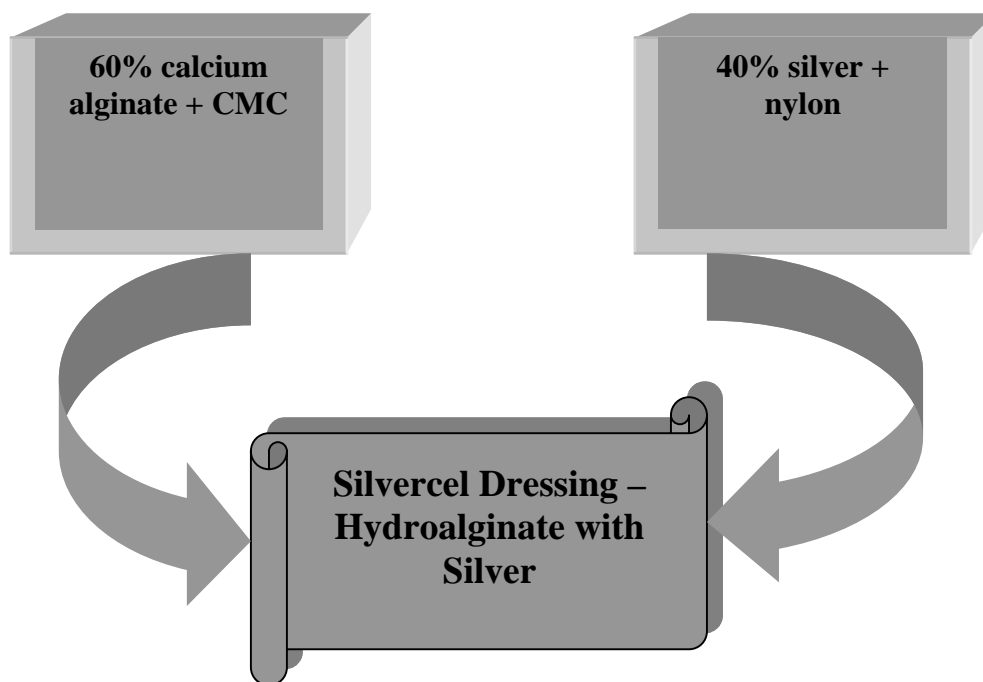


Fig. 1. Composition of Silvercel dressing

A research study was performed in faculty surgery clinic (Russian National Medical University) located in phlebologic center (City Clinical Hospital No.1 in the name of N.I. Pirogov) examined efficiency of Silvercel hydroalginate dressing (Johnson & Johnson Company) in treatment trophic venous ulcers being at I–II stage of wound process according to moist healing principle.

OBJECTIVE: Examining efficiency, safety, and tolerance of Silvercel dressing (hydroalginate with silver) in treatment in treatment trophic venous ulcers being at I–II stage of wound process with optimization of its use order.

MATERIALS AND METHODS:

Twenty patients were involved in study having trophic venous ulcers with underlying varicose (70%) or postthrombophlebitic (30%) lower legs diseases. All patients were observed in consultative-diagnostic center (city clinical Hospital No.1) during one month from March till April 2006. Sample studied included 13 males (65%) and 7 females (35%) aged 36–75 years. Mean age of patients was 52.5 ± 1.6 years. All patients had single trophic ulcer persisted 1.5 month – 7 years (1 year in two, approximately 7 years in one, 8 months in two, and 1.5–4 months in 15 cases). Twelve

patients (60%) had ulcer opened for the first time, and 8 patients (40%) had relapsing ulcer. Mean area covered with ulcerous defect was $10.2 \pm 2.1 \text{cm}^2$ ranging from 8.0 to 12.0cm^2 .

Most patients (70%) had concomitant diseases in their medical history (essential hypertension, stenocardia) demanding symptomatic hypertensive therapy all the time during treatment course (Monopril, Capoten). Three patients had obesity of III–IV degree. Previous treatment included use of gauze tampons with antiseptics, ointment dressings (Levosin, Levomecol), purifying dressings (*TenderWet-Activ*). Fifteen patients underwent elastic compression of lower legs (bandaging or compressive hosiery), while 5 others didn't use it.

Elastic compression using middle stretching bandages and systemic pharmacotherapy (micronized Diosmin) were provided to all patients without fail over period of clinical trial.

All study participants met INCLUSION CRITERIA according to protocol:

- Males and Females aged 18–75 years receiving outpatient treatment for venous ulcers;
- Trophic ulcers located in one or both shins and having area from 5 to 20cm^2 ;
- Ulcer history at least 2 months or ulcer relapses.
- Patients were included who gave verbal informed consent and adhered to physician prescriptions concerning therapy assigned.

EXCLUSION CRITERIA:

- Patient severe general condition resulted from somatic pathology and hindered him (her) from adherence to regimen prescribed by study protocol;
- Absence of willingness to cooperate in patient

CRITERIA FOR ASSESSMENT OF TREATMENT EFFICIENCY:

- Visually assessed regeneration process in trophic ulcer region;
- Pain syndrome dynamics;
- Cytological examination of smears-imprints obtained from ulcer defects;
- Bacteriological examination of ulcer;
- Computerized planimetry of ulcer;

- Absence of side effects.

Visual assessment of regeneration process in trophic ulcer region (granulations degree, epithelization, amount of wound effluent, pain in wound area, condition of surrounding tissues) was performed using scoring system (Table 1) at the start of study, at control visits every 3–4 days, and at the end of study.

Cytological and bacteriological examinations were performed before the start and at the end of study.

Table 1. Scores demonstrating condition of ulcer and surrounding tissues

Features	Their Expression (Score)
Degree of granulations	2 – partial 4 – full 6 – excessive
Degree of epithelization	0 – absent 2 – minor 4 – evident marginal 6 – full
Degree of wound discharge	0 – absent 2 – moderate 4 – intense
Wound pain	0 – absent 2 – minor 4 – moderate 6 – severe
Dermatitis	0 – absent 1 – present

Cytological examination of smears-imprints obtained from ulcer defects was performed using following technique: Ethanol fixed preparations were stained with azure-eosine by Romanovsky. Imprints were analyzed under light microscope 'Opton' (Germany) using 630-fold optical magnification. Cytogram type was defined depending on amount of different type cells, their functionality, and presence of both free and phagocytized microorganisms [3]. – (Kuzin)

Bacteriological examination was performed using following technique: Sterile discs of filter paper 5–6mm in diameter having sorption capacity 20 μ l were used for microorganisms' quantification in wound discharge. Discs with material were placed in tube containing 1ml of sterile salt solution and shaken up thoroughly. Then serial 10-fold dilutions were prepared with consequent inoculation 0.1 ml out of each dilution on Petri dishes containing 5% blood agar and Levin's nutrient medium. Dishes were incubated at 37°C during 22–24 hours with counting of colonies harvested and calculation of microorganisms' number in original sample (CFU/ml). Sensitivity to antibiotics was determined using technique of disc diffusion on Muller-Hinton medium.

Computerized planimetry of ulcer was performed at each control visit using transparent plastic templates: Ulcer outline was rounded with image scanning and calculation of ulcer area using AutoCad software.

DRESSING DESCRIPTION

Silvercel dressing according to manufacturer recommendations is intended for treatment of nonhealing infected wounds including trophic venous ulcers occupying some layers of skin or its total thickness and having moderate or abundant exudation. This dressing consists of sterile non-woven pad containing calcium G-alginate with high content of hyaluronic acid, CMC, and metal silver coating nylon fibers. Combined treatment effect of that dressing is resulting from capacity of alginate and CMC for regulation of wound moisture, and wide spectrum of silver ions antibacterial action [8].

TREATMENT TECHNIQUE

Ulcer was cleansed with salt solution before application of Silvercel hydroalginate dressing. Dressing was cut off according to ulcer size, loosely applied to ulcerous defect, covered on top with gauze pad having several layers. Then monolayer compression bandage was applied using elastic bands of middle tensility.

Silvercel dressing was changed depending on exudation and drench of its upper layers every day or every 2–3 days. Treatment efficiency was assessed at control visits every 3 days. Actisorb[®] dressings were applied later (after full wound cleansing from fibrin and devitalized tissues).

TREATMENT RESULTS

Moderate or abundant exudation was noted in all patients at the start of study. Two patients had some areas of purulent necrotic tissues on ulcer surface but in other cases fibrinous deposits predominated. Treatment provided demonstrated high efficiency of Silvercel dressing in patients having venous ulcers of I–II stage that implied full cleansing of ulcer surface in all cases within one month and in most cases (60%) on days 10–14. Regeneration process in patients was expressed variously. Ulcer surface cleansing became clinically apparent through elimination of necrotic tissues, fibrin incrustations, and decrease of inflammatory processes being confirmed by cytological (Table 2) and bacteriological (Table 3) examination.

Data of ulcer cytological examination. Degenerative-inflammatory type of cytogram predominated before treatment in 8 patients (40%), inflammatory-regenerative cytogram at the end of treatment predominated in 11 patients (55%) and regenerative cytogram in 5 patients (25%) (Table 2).

Table 2. Results of ulcer cytological examination before and after treatment using **SILVERCEL** dressing.

Type of Cytogram	Before treatment (n=20)	After treatment (n=20)
Degenerative-inflammatory	8 (40%)	-
Inflammatory	6 (30%)	4 (20%)
Inflammatory-regenerative	6 (30%)	11(55%)
Regenerative	-	5 (25%)

Quantitative and qualitative composition of microflora together with its sensitivity to antibiotics were determined in all patients. Mixed infections were identified usually with predominance of *St.aureus*+*Ac.baumannii* found in 12 patients (60%) while in remaining 8 patients microbial flora was presented with other species (*Pr.mirabilis*, *E.Cloacae*, *Ps.Aerugenosa*) (Table 3).

Table 3. Microbial pattern of ulcer surface before treatment using **SILVERCEL** dressing

Species	Number of observations (n=20) %
<i>St.aureus</i> + <i>Ac.baumannii</i>	12 (60%)
<i>Pr.mirabilis</i>	4 (20%)
<i>E.Cloacae</i>	2 (10%)
<i>Ps.Aerugenosa</i>	2 (10%)

Two patients (10%) having expressed symptoms of local and general inflammation (cellulitis, abundant exudation, pain in ulcer area, subfebrile fever during 5 days, necrotic tissues on ulcer surface, putrefactive odor) received during 10 days along with Silvercel dressing additional systemic antibacterial medication (oral) according to bacteriogram. Treatment provided resulted in decrease of microbial burden on ulcer surface below critical level (from 10^{-8-9} to 10^{-4-5}) within 10-12 days. Those positive changes were clinically expressed through improvement in ulcer condition (decreased exudation, cleansing of ulcer surface, body temperature normalization, elimination of pain syndrome). In 12

patients (60%) without local inflammatory reaction but with initially high critical level of microbial burden (10^{-7-8}) treatment provided with only Silvercel dressing resulted in decrease of microbial burden below critical level (up to 10^{-4-5}). Positive regenerative dynamics in those patients was confirmed by cytological examination. In both groups degenerative-inflammatory and inflammatory cytogram type predominated before treatment but during treatment it changed on regenerative-inflammatory one.

Finally in four cases (20%) without symptoms of local inflammation and with bacterial burden below critical level use of Silvercel dressing resulted in full bacterial elimination.

At first control visit shortly after start of treatment intense exudation was found in 12 patients (60%) while in 8 patients (40%) wound discharge was moderate. Treatment with Silvercel dressing resulted in exudation minimization in 13 patients (65%) within 10 days and after 3 weeks in 18 patients (90%), moreover ulcer surface remained moist and surrounding tissues were dry.

In two patients receiving Silvercel dressings daily during 7–10 days ulcers were cleansed rapidly, necrotic tissues became more loose allowing their easy removal, intense granulations appeared representing positive dynamics in ulcer healing confirmed by bacteriological and cytological examinations. Granulations partially filled ulcerous defect within 10 days in 45% cases while creation of granulation tissue in entire ulcer surface was observed in 35% patients (and at the end of study in 95% patients) (Table 4).

Table 4. Dynamics of granulations development during treatment using **SILVERCEL** dressing

Rate of granulations development in ulcer	VISIT No. (% patients)							
	1	2	3	4	5	6	7	8
Absent	11 (55%)	10 (50%)	7 (35%)	4 (20%)	-	-	-	-
Partial	7 (35%)	8 (40%)	8 (40%)	9 (45%)	9 (45%)	1 (5%)	-	-
Full	2	2	5	7	11	19	19	19

	(10%)	(10%)	(25%)	(35%)	(55%)	(95%)	(95%)	(95%)
--	-------	-------	-------	-------	-------	-------	-------	-------

Pain syndrome expression is an important criterion of treatment efficiency. Severe pains at the start of treatment were noted in 10% patients, moderate ones in 50% patients, minor ones in 30% patients while pain syndrome was absent in 10% patients. In the course of treatment with Silvercel patients noted significant decrease of pain syndrome because dressings didn't adhere to wound surface and their change didn't result in wound trauma. In 10% cases patients noted moderate after treatment course requiring no additional analgetics, in 60% cases transient minor pains, and in 30% cases pains were practically absent (Fig. 2).

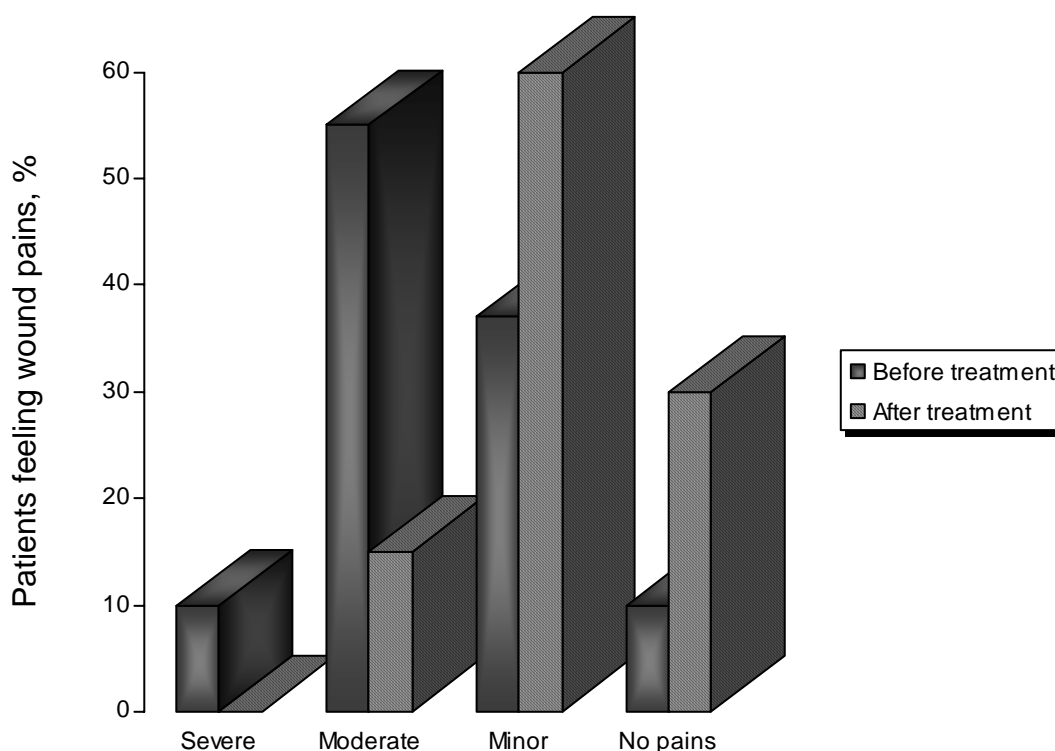


Fig. 2. Dynamic regression of pain syndrome

Clinical example 1. Patient S., aged 42 years received outpatient treatment in phlebologic center (city clinical hospital No.1 in the name of N.I. Pirogov with diagnosis: Postthrombotic disease of right leg at the stage of trophic disturbances. Ulcer of the right shin (Class 6 according to CEAP). Disease history. Patient was affected with acute right-sided iliofemoral phlebothrombosis. Skin hyperpigmentation, induration, and itch appeared 1.5

years thereafter in anterior surface of right shin. Trophic ulcer sized 1.5×1.5cm with scanty purulent discharge was opened there in 2005 November.

The patient received domiciliary outpatient treatment with ointment dressings without improvement. The ulcer sizes increased rapidly, pronounced pain syndrome appeared along with abundant exudation, hyperemia, and edema of soft tissues. The patient addressed in phlebologic center of city clinical hospital No. 1 in the name of N.I. Pirogov.

Objective data – local state: Right leg is increased in volume compared to the left one (hip +1.5cm, shin +2cm). Skin covers in lower and middle shin third are hyperpigmented and edematous. There is irregular shaped trophic ulcer in anterior surface of lower shin third sized 8.0×5.0×2.5cm having uneven margins and bottom with single necrotic sites of black color sized 0.3–0.5cm and covered with yellow-greenish fibrin incrustation, faded granulations without epithelization. Pronounced soreness in lower shin third and medial ankle was found under palpation. There were abundant exudation and unpleasant saprogenic odor (Fig. 3a). Mixed infection was determined using bacteriological examination of wound discharge with predominance of *S.Aureus* 10^5 + *Ac.baumannii* 10^4 . Cytological examination of smears-imprints showed predominance of degenerative-inflammatory cytogram type.

Local treatment was performed with Silvercel dressings (Fig.3 a-b) using regimen recommended from manufacturer against a background of systemic pharmacotherapy (micronized Diosmin 1000mg daily) and lower leg compression with elastic bandages having moderate stretchability.\

Improvement of ulcer condition was found after 2 week treatment. It was characterized with decreased exudation and wound cleansing. Necrotic tissues became more loose and easily removable under surgery, intense granulations and marginal epithelization appeared. Unpleasant odor disappeared. Wound size decreased by 10%. The patient tolerated dressing procedures quite well and dressing itself was removable easily and painless. Next 10 days area of ulcerous defect decreased by 30% from initial one, granulations filled entire wound bottom, moreover insular and intense marginal epithelization appeared. Edema and hyperemia of surrounding tissues together along with exudation decreased significantly. Positive dynamics in regenerative process was confirmed with cytological examination (predominance of regenerative-inflammatory cytogram type). Bacteriological examination demonstrated full bacterial elimination (Fig. 3c). Further local treatment was performed with Actisorb[®] dressings.



Fig. 3 a**Fig. 3 b****Fig. 3 c**

In one case we used that dressing for patient affected with obliterating atherosclerosis of lower leg vessels, and purulence of postoperative wound after amputation.

Clinical example 2. Patient Z., aged 65 years is affected with obliterating atherosclerosis of lower extremities during 15 years, led to several reconstructive surgeries (iliofemoral prosthetics, right-sided femoropopliteal bypass). In 2005 December however decompensation of arterial circulation developed in right foot, trophic ulcers appeared onto great toe and lateral foot surface required admittance in surgical department of city clinical hospital No. 57. Primary amputation of right leg was performed at January 20, 2006 at the level of upper shin third. Postoperative period was complicated with stump wound abscess, and full separation of postoperative sutures. Treatment was performed using ointment dressings (Levomecol, Levosin) against a background of antibacterial therapy (i.v. Vancomycin) according to bacteriogram. Wound condition was not improved despite treatment, *S.Aureus* was yet seed in high concentration, intoxication persisted being demonstrated in febrility up to 37.8°C, weakness, and sweating. Therefore reamputation was presumed at the level of hip upper third.

Physical examination at March 26, 2006 performed in phlebologic center of our hospital revealed full postoperative wound dehiscence, edematous soft tissues in wound area, skin hyperemia with single sites of maceration, and sharp pain under palpation. Wound dimensions were 25.0×8.0×4.0cm. Wound bottom was covered with blackish-green necrotic incrustation, abundant exudation was observed along with ichorous odor (Fig. 4a). Bacteriological examination demonstrated *S.Aureus* presence, and cytological examination revealed necrotic-degenerative type of cytogram.

Treatment was performed using disaggregants (Clopidogrel 75mg daily), antibacterial medication according to bacteriogram (i.v. Vancomycin during 2 weeks, Amoxiclav, Fuzidin per os), and local Silvercel dressings changed daily (Fig. 4b).

Improvement was noted at treatment day 10 characterized with arrest of systemic inflammatory reaction (normal body temperature, no weakness and

chill), decreased wound exudation, ulcer cleansing from necrotic tissues, appearance of intense granulations and epithelization areas. Unpleasant odor disappeared. Wound dimensions remained unchanged while soft tissues in stump became less edematous, hyperemia decreased, and skin maceration disappeared. Dressing procedures were well tolerated, painless, and dressing itself was easily removable. Later during treatment granulations filled recesses, exudation became moderate and serous. Minor signs of wound and surrounding tissues inflammation yet observed, but those disappeared at treatment day 30. Granulations covered entire ulcer surface after one month of treatment, and there was intense marginal epithelization (Fig. 4c).



Fig. 5 a

Fig. 5 b



Fig. 5 c

Thus, our study demonstrated high efficiency of hydroalginate Silvercel dressing containing silver not only for trophic venous ulcers of I–II stages but for inflamed purulent wounds. Its use allows to arrest inflammation and cleanse wound surface without additional antiseptics and antibiotics due to:

- ❖ Elimination excessive exudation, creation and maintenance of balanced moist environment essential for healing;

- ❖ Powerful antimicrobial action;
- ❖ Skin defense from maceration;
- ❖ Easy debris removal from wound bottom without injuries of new regenerative tissue thanks to its solidity;
- ❖ Absence of unwanted side effects;
- ❖ Simple and convenient use;
- ❖ Shortened time required for subsequent treatment (surgery or another wound coatings according to regeneration stage).

References

1. Богачев В.Ю., Богданец Л.И., Кириенко А.И., Брюшков А.Ю., Журавлева О.В. Местное лечение венозных трофических язв. //CONCILIUM MEDICUM, 2001 г., №2, с. 45-50.
(Bogachev V.Y., Bogdanetz L.I., Kirienko A.I., Bryuchkov A.Y., Ziravleva O.V. Topical Treatment of trophic venous ulcers. //CONCILIUM MEDICUM, 2001, No.2, p. 45-50.)
2. Вин Ф. Трофические язвы нижних конечностей //Флеболимфология, 1998, 7: 10 – 2.\ (Vin F. Trophic ulcers of lower extremities. //Phlebolympology, 1998, 7: 10 – 2.)
3. Кузин М.И., Костюченко Б.М. Раны и раневая инфекция. – Москва, «Медицина», 1990, с. 153-156.
(Kuzin M.I., Kostyuchenok B.M. Wounds and wound infection. Moscow, 'Medicine', 1990, p. 153-156.)
4. Савельев В.С. Современные направления в хирургическом лечении хронической венозной недостаточности //Флеболимфология, 1996; 1:5 – 7.
(Savelyev V.S. Modern trends in surgery of chronic venous insufficiency. // Phlebolympology, 1996; 1:5 – 7.)
5. Савельев В.С. Флебология. Руководство для врачей, М, Медицина, 2001, стр. 519.
(Savelyev V.S. Phlebology. Manual for physicians., М, Medicine, 2001, p. 519.)
6. Савельев В.С., Кириенко А.И., Богачев В.Ю. Венозные трофические язвы. Мифы и реальность //Флеболимфология, 1996; 1:5 – 7.
(Savelyev V.S., Kirienko A.I., Bogachev V.Y. Venous trophic ulcers. Myths and reality. //Phlebolympology, 1996; 1:5 – 7.)
7. Conciliative document: Task Force on Chronic Venous Disorders of the Leg», 1999.
8. Addison D, Rennison T, Norris S, Del Bono M, Kemp L. Silvercel Alginate A New Silver Dressing. Poster presentation //WUWHS, Paris, 2004.\
9. Colerige-Smith P. From Skin Disorders to Venous Leg Ulcers: Pathophysiology and Efficacy of Daflon 500 mg in ulcer Healing. //Angiology.- 2003.- №54.-p.45-50.
10. Lansdown ABG, Williams A (2004) How safe is silver in wound care? //J Wound Care 13(4): 131-6.

11. Partsch H, Menzinger G, Borst-Krafek B., et al. Does thigh compression improve venous haemodynamics in chronic venous insufficiency? //J Vasc. Surg.- 2003.- № 36.-p.948-52.
12. Percival, Bowler (2005) Bacterial resistance to silver in wound care //J Hospital Infect 60: 1-7.