

Flow Sorption Debridement of Aseptic and Purulent Soft Tissue Wounds

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Abstract

Background: Treatment of isolated and combined open soft tissue wounds remains relevant due to the growth of severe injuries, comorbid pathologies, and immunosuppressive conditions, along with a decrease in antibiotic sensitivity of microorganisms. The aim of this study was to compare the effectiveness of the jet oxygen-sorption treatment (JOST) and flow sorption debridement techniques (FSDT) in the therapy of experimental soft tissue wounds.

Methods and Results: The effectiveness of the JOST and FSDT was compared in 2 series of experiments on 288 laboratory Wistar rats with simulated soft tissue wounds. Series 1 (S1) involved 144 animals divided into 2 control groups (CG) and 2 experimental groups (EG); the effectiveness of the developed techniques for the aseptic wound treatment was studied in these groups of animals. Series 2 (S2) involved 144 animals divided into 2 CGs and 2 EGs; in S2, purulent soft tissue wounds were studied. The effectiveness of the developed techniques in the complex treatment of experimental wounds was assessed immediately, on Days 1, 3, 5, 7 and 10 after simulating the pathological process. The assessment included the animals' condition, the dynamics of the course of reparative processes (local symptoms of inflammation; granulation; epithelialization of wounds; and size and dynamics of the area of the defect), and histological research methods.

The use of the JOST has practically no benefits in aseptic wound treatment, compared to FSDT. The use of the JOST and FSDT contributed to a significant acceleration of healing process in aseptic wounds that was expressed in the decreased local inflammatory reactions, higher activity of metabolic processes based on the dynamics of RNA and SH-groups. The most pronounced positive dynamics in the treatment of purulent wounds was observed when applying FSDT. Compared with the findings obtained in CG1-S2, FSDT contributed to a reduction in necrosis termination by 25.7%, fibrinolysis - by 25.5%, granulation - by 20.0%, epithelization - by 18.9%, wound discharge - by 27.8%.

Conclusion: The developed technique of FSDT in the complex treatment of soft tissue wounds provides the most pronounced positive dynamics, accelerates reparative tissue processes, and reduces the duration of wound cleansing and healing for both aseptic and purulent wounds. (*International Journal of Biomedicine*. 2022;12(1):49-54.)

Key Words: soft tissue wounds • jet oxygen-sorption treatment • flow sorption debridement techniques

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Introduction

Treatment of isolated and combined open soft tissue wounds remains relevant due to the growth of severe

injuries, comorbid pathologies, and immunosuppressive conditions, along with a decrease in antibiotic sensitivity of microorganisms.⁽¹⁻⁴⁾ The development of surgical wound infection significantly aggravates the course of pathology;

its complications account for one-third of deaths in the postoperative period. Suppression of inflammation, prevention or reduction of bacterial contamination and oxidative stress are of great importance in local wound treatment. In this regard, the use of sorbents has proved to be highly effective.

Novel materials, techniques and devices are constantly being introduced into surgical practice to advance clinical outcomes of this group of patients, but their effectiveness is still not adequate. Effects based on the use of oxygen therapy and sorbents that potentiate the repair of tissue defects have proven appropriate in various areas of medicine.⁽⁵⁻⁹⁾

The aim of the study was to compare the effectiveness of the jet oxygen-sorption treatment (JOST) and flow sorption debridement techniques (FSDT) in the therapy of experimental soft tissue wounds.

Materials and Methods

The JOST and FSDT were applied using an original device consisting of a nozzle, mixing chambers in series, containers for powdered drugs, a gas flow switch and a gas pressure regulator, and a system of silicone tubes (Fig.1). Sources of oxygen, carbon dioxide or sterile air can be used to create a sorption-gas suspension.

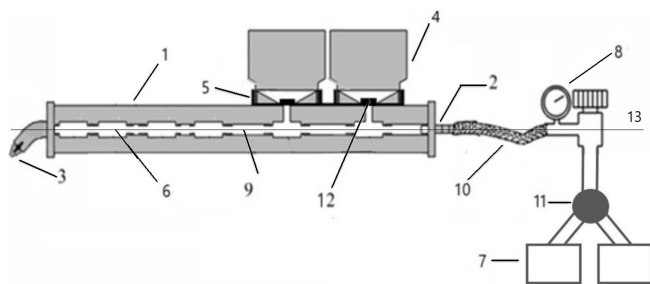


Fig. 1. Scheme of the device for FSDT

1 – Body frame of the device, 2 – Adapter, 3 – Nozzle for directing the outgoing flow, 4 – Containers for powdered drugs, 5 – Connecting collar, 6 – Mixing chambers, 7 – Gas sources, 8 – Gas pressure regulator, 9 – System of silicone tubes, 10 – Hose, 11 – Gas flow switch, 12 – Valves that regulate the supply of drugs, 13 – Imaginary horizontal axis around which the body of the device (1) is rotated by 180°.

The JOST technique included 3 successive stages of wound surface therapy by using:

- (a) a dispersed flow of physiological solution - a special device UGOR-1M;
- (b) an oxygen flow (a pressure of 6 atm) - a special device for the flow sorption debridement technique;
- (c) a suspension of atoxyl in oxygen until a uniform layer covering the wound was formed - a special device for the flow sorption debridement technique.

The FSDT was also performed in 3 successive stages, but instead of oxygen, carbon dioxide was used (a pressure of 6 atm); this was due to the absence of signs of anaerobic infection in purulent wounds (simulation of the wound

process was performed using *St. aureus*), higher safety of the technique applied. The FSDT is crucially different from the JOST technique by the possibility of using a gas sorption mixture depending on the nature of the microflora (anaerobes or aerobes), i.e., the possibility of using oxygen, carbon dioxide, or air.

The effectiveness of the JOST and FSDT was compared in 2 series of experiments on 288 laboratory Wistar rats with simulated soft tissue wounds. Series 1 (S1) involved 144 animals divided into 2 control groups (CG) and 2 experimental groups (EG); the effectiveness of the developed techniques for the aseptic wound treatment was studied in these groups of animals. Series 2 (S2) involved 144 animals divided into 2 CGs and 2 EGs; in S2, purulent soft tissue wounds were studied (Table 1).

Table 1.

Characteristics of the subgroups in Series 1 and 2 of experiments

Subgroup	Number of animals	Brief description of the study groups
Series 1 / aseptic wounds		
CG1-S1	36	No treatment
CG2-S1	36	Applications of atoxyl on the wound surface
EG1-S1	36	JOST using atoxyl
EG2-S1	36	FSDT using atoxyl
Series 2 / purulent wounds		
CG1-S2	36	No treatment
CG2-S2	36	Applications of atoxyl on the wound surface
EG1-S2	36	JOST using atoxyl
EG2-S2	36	FSDT using atoxyl

In animals of CG1-S1 and CG1-S2, no wound treatment was performed, the natural course of the wound process was studied. In the remaining groups, wound dressings were performed daily. In animals of CG2-S1 and CG2-S2, atoxyl was additionally applied on the wound surface. In animals of EG1-S1 and EG1-S2, the JOST using atoxyl was performed. In animals of EG2-S1 and EG2-S2, the FSDT using atoxyl was performed. The described procedures were performed in both series of experiments daily until the wound closed.

The atoxyl preparation applied in the study is a super-finely dispersed enterosorbent of the fourth generation with wound healing, antimicrobial, bacteriostatic, and detoxifying effects, recommended for external use in the complex treatment of purulent wounds, trophic ulcers, and burns. The preparation has no effect of reverse sorption.

All procedures with animals were performed under general anesthesia (Zoletil-100) in compliance with sterility.

In the S1, wound simulation included skin shaving in the wither area followed by its excision with a superficial fascia 1.5cm in diameter, according to the established pattern. After meticulous hemostasis, the resulting defect was abundantly washed with a sterile solution. The aseptic wound was formed.

In S2, a suspension of *St. aureus* (109 microns/ml) was introduced into the wound after simulation, and the wound was closed. Three days after wound contamination, the sutures were removed, the wound edges were separated. In all animals, there were signs of a pronounced inflammatory reaction and the purulent wound was formed.

The effectiveness of the developed techniques in the complex treatment of experimental wounds was assessed immediately, on Days 1, 3, 5, 7 and 10 after simulating the pathological process. The assessment included the animals' condition, the dynamics of the course of reparative processes (local symptoms of inflammation; granulation; epithelialization of wounds; and size and dynamics of the area of the defect), and histological research methods.

Statistical analysis was performed using the Statistica 6.1 software package (Stat-Soft Inc., USA). The normality of distribution of continuous variables was tested by the Kolmogorov-Smirnov test with the Lilliefors correction and Shapiro-Wilk test. For descriptive analysis, results are presented as mean±standard deviation (SD). For data with normal distribution, inter-group comparisons were performed using Student's t-test. Mann-Whitney U test and Wilcoxon criterion were used to compare means of variables not normally distributed. Spearman's rank correlation coefficient was calculated to measure the strength and direction of the relationship between two variables. A probability value of $P<0.05$ was considered statistically significant.

Work on the animals was done in compliance with the principles of the Helsinki Declaration on the humane treatment of animals, stated in normative documents of the European community(86/609/EU), Manual on Experimental (Preclinical) Study of New Pharmacological Substances, and "Good laboratory practice" (MHRF Order No. 708H dated 23.08.2010).

Results

The peri-wound edema was arrested most rapidly in CG2-S1, compared to CG1-S1, by 13.6% (Table 2). In EG1-S1 and EG2-S1, the elimination of peri-wound edema was found in 2.48±0.41 and 2.48±0.32 days after injury, respectively. In CG1-S2 and CG2-S2, peri-wound edema was eliminated in 3.91±0.20 and 3.50±0.20 days, respectively; in EG1-S2 and EG2-S2 – 3.43±0.20 and 3.41±0.20 days, respectively.

Experimental hyperemia of the paravul area was eliminated faster in CG2-S1 than in CG1-S1 by 5.6%. The use of the JOST in the complex treatment of aseptic wounds resulted in the relief of experiments hyperemia in 2.31±0.55 days after injury in EG1-S1 and in 2.37± 0.30 days after injury in EG2-S1. In CG1-S2, experiments hyperemia was eliminated in 3.88±0.21 days. In CG2-S2, EG1-S2, EG2-S2, hyperemia was reduced most rapidly, more than in CG1-S2 – by 14.5%, 18.9%, and 19.1%, respectively.

Wound exudate decreased in 3.50±0.36 days in CG1-S1. In CG2-S1, EG1-S1, EG2-S1, wound exudate decreased most rapidly in CG1-S1 – by 22.3%, 71.1%, and 70.9%, respectively.

Table 2.

Terms for relief of local signs of inflammation in the study subgroups, days

Sign	Series 1				Series 2			
	CG1	CG2	EG1	EG2	CG1	CG2	EG1	EG2
Edema	3.25±0.27	2.81±0.32	2.48±0.41*	2.48±0.32*	3.91±0.20	3.50±0.20*	3.43±0.20*	3.41±0.20*
Hyperemia	2.87±0.46	2.71±0.30	2.31±0.55	2.37±0.30	3.88±0.21	3.32±0.20*	3.15±0.20*	3.14±0.20*
Wound exudates/discharge ¹	3.50±0.36	2.72±0.34	2.45±0.31*	2.48±0.31*	6.28±0.32	5.46±0.43	4.73±0.39*	4.54±0.38*

¹– Reduction of the amount to scant discharge; * $P<0.05$ - compared with CG1

In the S2, the amount of wound discharge decreased in 6.28±0.32 days in CG1-S2. In CG2-S2, EG1-S2, EG2-S2, wound discharge decreased most rapidly in CG1-S2 – by 13.1%, 24.7%, and 27.8%, respectively.

Table 3.

Detection of the signs of the wound process in Series 2 of experiments, days

Sign	CG1-S2	CG2-S2	EG1-S2	EG2-S2
Necrolysis	3.5±0.2	3.3±0.2	2.7±0.2*	2.6±0.2*
Fibrinolysis	5.1±0.3	4.8±0.3	3.9±0.2*	3.8±0.2*
Granulation	3.5±0.3	3.3±0.2	3.0±0.2*	2.8±0.2*
Epithelialization	5.3±0.3	5.0±0.3	4.5±0.3*	4.3±0.3*

*– $P<0.05$ compared with CG1

Necrolysis duration of 3.5±0.2 days was found in CG2-S2 and was shorter by 5.8% in CG2-S2, 22.9% in EG1-S2, and 25.7% in EC2-S2 (Table 3).

Fibrinolysis was observed in 5.1±0.3 days in CG1-S1 and was found earlier by 5.9% in CG2-S2, 23.2% in EG1-S2, and 25.5% in EG2-S2.

Granulations appeared within 3.5±0.3 days in CG1-S2, faster by 5.8% in CG2-S2, 14.3% in EG1-S2, and 20.0% in EG2-S2.

Epithelialization was noted in 5.3±0.3 days in CG1-S2 and was faster by 5.7% in CG2-S2, 15.1% in EG1-S2, and 18.9% in EG2-S2.

Table 4.

Dynamics of RNA and SH-groups in Series 1 of experiments, relative units (U)

Subgroup	Day 1	Day 3	Day 7	Day 10
RNA level				
CG1-S1	0.23±0.01	0.27±0.01*	0.30±0.02*	0.30±0.02*
CG2-S1	0.24±0.01	0.26±0.01*	0.32±0.02**	0.33±0.02**
EG1-S1	0.26±0.01	0.28±0.01	0.32±0.02	0.34±0.02
EG2-S1	0.26±0.01	0.27±0.01	0.33±0.02	0.35±0.02
SH-group level				
CG1-S1	0.26±0.01	0.27±0.01	0.28±0.02	0.27±0.01
CG2-S1	0.27±0.02	0.27±0.02	0.29±0.01	0.28±0.02
EG1-S1	0.28±0.02	0.28±0.02	0.34±0.02	0.30±0.02
EG2-S1	0.26±0.02	0.28±0.02	0.33±0.02	0.29±0.01

* $P < 0.05$ - compared to Day 1; ** $P < 0.05$ - compared to CG1-S1.

In the S1, the highest RNA level (0.23±0.01U) was detected in the growth plate in CG1-S1 on Day 1, demonstrating the severity of metabolic processes in this area (Table 4).

The level of SH-groups on Day 1 prevailed in the more superficial layers and was more pronounced in the intact epithelium. The level of SH-groups in the germ layer was 0.26±0.01U. On Day 3, the RNA level increased in deeper layers of the epidermis in CG1-S1; the perinuclear accumulation of RNA was rarely observed. On Day 5, the distribution of SH-groups in the epidermis was practically equal to findings obtained on Day 3. In CG1-S1, on Days 7 and 10, a further increase in the intensity of metabolic processes was observed in the damage zone in GC1-S1; this was supported by an increase in the levels of RNA and SH-group up to 0.30±0.02U and 0.28±0.02U by Day 7 and 0.30±0.02U and 0.27±0.01U by Day 10, respectively.

In CG2-S1, on Day 1, moderate basophilia with a pronounced reaction was revealed in the growth plate. The levels of RNA and SH-groups were 0.24±0.01U and 0.27±0.02U, respectively. On Day 3, we found an increase in the RNA level up to 0.26±0.01U and stabilization of SH-group parameters (0.27±0.02U). On Day 7, the RNA level increased up to 0.32±0.02U in CG2-S1. SH-groups were determined mainly in the surface layers of the defect (0.29±0.01U), which could be evidence of epithelium keratinization. On Day 10, the levels of RNA and SH-groups were 0.33±0.02U and 0.28±0.02U, respectively.

In EG1-S1, on Day 1, the levels of RNA and SH-groups were 0.26±0.01U and 0.28±0.02U, respectively. On Day 3, the RNA level increased to 0.28±0.01U, and the level of SH-groups was stabilized. On Days 7 and 10, we found

a further increase in the RNA level up to 0.32±0.02U and 0.34±0.02U, SH-groups up to 0.29±0.01U and 0.28±0.02U, respectively.

In EG2-S1, on Day 1, the levels of RNA and SH-groups were 0.26±0.01U and 0.26±0.02U, respectively. The growth of SH-groups demonstrated progression in the processes of epithelial cell regeneration. On Day 3, the levels of RNA and SH-groups increased up to 0.27±0.01U and 0.28±0.02U, respectively, being accompanied by regeneration of the skin surface. On Days 7 and 10, at the end of the defect epithelialization, the RNA levels reached 0.33±0.02U and 0.35±0.02U, respectively, SH-groups – 0.33±0.02U and 0.29±0.02U, respectively.

In the S2, we analyzed values of alkaline phosphatase (ALP) as a marker of the duration of wound process and the maturation of granulation tissue (Table 5). In CG1-S2, on Day 1 of the experiment, the ALP level was 27.3±2.3U and increased up to 42.5±2.5U by Day 7. Similar dynamics was noted in CG2-S2; however, on Days 1, 3, 5, and 7, the ALP was higher than in CG1-S2 by 34.5%, 25.1%, 26.4%, and 21.5%, respectively. The most pronounced dynamics in the ALP level was observed in animals of EG1-S2 and EG2-S2 (Day 1 - 50.3±2.6U and 52.5±2.6U, respectively; Day 3 - 57.7±2.7U and 58.1±3.1U, respectively; Day 5 - 65.0±2.7U and 66.9±2.9U, respectively; Day 7 - 75.6±3.1U and 77.6±3.2Us, respectively). On Day 7 after the experiment, the lowest ALP value (46.5±2.5U) was found in CG1-S2, most likely associated with the minimum activity of metabolic processes in the injured tissues.

Table 5.

Dynamics of ALP in purulent wounds of the soft tissues, relative units (U)

Day	CG1-S2	CG2-S2	EG1-S2	EG2-S2
1	27.3±2.3	41.7±2.5 [^]	50.3±2.6 [^]	52.5±2.6
3	37.7±2.3*	50.3±2.6**	57.7±2.7**	58.1±3.1*
5	42.5±2.5*	57.7±2.8**	65.0±2.7**	66.9±2.9*
7	46.5±2.5*	59.2±2.9**	75.6±3.1**	77.6±3.2**

* $P < 0.05$ - compared to Day 1; ** $P < 0.05$ - compared to CG1-S2.

In EG1-S2 and EG2-S2, the microbial contamination of the purulent wound discharge (microbial bodies per ml) was significantly lower than in CG1-S2 at all stages of observation (Table 6).

There were no significant differences between groups in the wound area after simulation (Table 7). In CG1-S1, the wound area steadily decreased during the entire observation period, compared to the initial size, by 34.8%, 61.5%, 82.5, and 99.9% on Days 1, 3, 7, and 10 after wound simulation, respectively.

In EG1-S1 and EG2-S1, the wound area decreased by 39.1% and 38.6% on Day 1, 74.3% and 73.5% on Day 3,

91.8% and 91.0% on Day 7, 99.99% and 99.98% on Day 10, respectively, compared with the initial findings.

In CG2-S1, we found a reduction in size of the defect by 36.7%, 67.2%, 86.5%, and 99.95% on Days 1, 3, 7, and 10, respectively, compared with the sizes obtained immediately after wound simulation.

In CG1-S2, the wound area steadily decreased during the entire observation period, compared to the initial size, by 27.9%, 55.1%, 72.2%, and 85.4% on Days 1, 3, 7, and 10 after wound simulation, respectively.

In CG2-S2, we found a reduction in size of the defect by 32.7%, 60.9%, 80.1%, and 93.1% on Days 1, 3, 7, and 10, respectively, compared with the sizes obtained immediately after wound simulation.

Table 6.

Dynamics of microbial contamination of the purulent wound discharge (microbial bodies per ml)

Day	CG1-S2	CG2-S2	EG1-S2	EG2-S2
1	10^9-10^{10}	10^8-10^9	10^7-10^9	10^7-10^9
3	10^5-10^8	10^3-10^5	10^2-10^3	10^2-10^3
5	10^3-10^5	10^2-10^3	10^2-10^3	10^2-10^4
7	10^3-10^6	10^1-10^2	10^1-10^2	10^1-10^3

Table 7.

Dynamics of the wound area in animals, mm²

Subgroup	Day after wound simulation				
	Immediately	Day 1	Day 3	Day 7	Day 10
Series 1 / aseptic wounds					
CC1-S1	131.9±13.5	86.1±8.6*	50.8±5.5*	23.1±2.7*	11.5±1.3**
CG2-S1	131.8±13.1	83.8±8.6	43.7±5.3*	17.8±2.7*	6.1±1.3**
EG1-S1	133.8±10.8	81.0±6.1*	35.2±3.1**	11.9±0.9**	1.1±0.1**
EG2-S1	132.9±14.0	81.1±8.3**	35.7±3.9**	12.0±2.0**	1.4±0.6**
Series 2 / purulent wounds					
CG1-S2	116.3±10.7	83.9±7.6*	52.3±5.6*	32.4±3.6*	17.0±1.5**
CG2-S2	118.4±10.5	79.7±7.8*	46.4±5.0*	23.6±2.9**	8.3±1.4**
EG1-S2	118.9±10.1	78.6±6.1*	35.1±3.7**	12.3±1.7**	1.4±0.7**
EG2-S2	117.3±13.3	79.8±8.0*	32.9±4.0**	10.7±2.2**	1.0±0.6**

* $P < 0.05$ - compared to the initial wound size in the group, ** $P < 0.05$ - compared to CG1

In EG1-S2 and EG2-S2, the wound area decreased by 33.9% and 32.0% on Day 1, 70.1% and 71.9% on Day 3, 89.7% and 90.9% on Day 7, 99.99% and 99.99% on Day 10, respectively, with the sizes obtained immediately after wound simulation.

Conclusion

The use of the the jet oxygen-sorption treatment has practically no benefits in aseptic wound treatment, compared to the flow sorption debridement techniques. The use of the the jet oxygen-sorption treatment and flow sorption debridement techniques contributed to a significant acceleration of healing process in aseptic wounds that was expressed in the decreased local inflammatory reactions, higher activity of metabolic processes based on the dynamics of RNA and SH-groups. The most pronounced positive dynamics in the treatment of purulent wounds was observed when applying flow sorption debridement techniques. Compared with the findings obtained in CG1-S2, flow sorption debridement techniques contributed to a reduction in necrosis termination by 25.7%, fibrinolysis - by 25.5%, granulation - by 20.0%, epithelialization - by 18.9%, wound discharge - by 27.8%. The developed of flow sorption debridement techniques in the complex treatment of soft tissue wounds provides the most pronounced positive dynamics, accelerates reparative tissue processes, and reduces the duration of wound cleansing and healing for both aseptic and purulent wounds.

Competing Interests

The authors declare that they have no competing interests.

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