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ABSTRACT

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XENODERMAL GRAFTS SATURATED WITH SILVER NANOPARTICLES IN PREPARATION FOR PLASTIC CLOSURE OF POSTOPERATIVE WOUNDS IN PATIENTS WITH NECROTIZING FASCIITIS

Introduction. Necrotizing fasciitis (NF) is a severe infection associated with substantial tissue loss and a high risk of wound surface contamination. Standard xenodermal implants used for temporary coverage of postoperative defects frequently experience recurrent bacterial colonization.

Objective was to evaluate the effectiveness of lyophilized xenodermal implants saturated with silver nanoparticles in improving the preparation of postoperative wounds for autografting in patients with NF.

Materials and Methods. The study involved 20 patients with wounds following NF debridement. Patients were divided into two groups: the experimental group received lyophilized xenodermal implants saturated with silver nanoparticles, while the control group received standard xenodermal implants. Evaluations included granulation tissue formation speed suitable for autografting, incidence of secondary infections, and xenodermal implant adhesion duration.

Results. The mean time for granulation tissue formation suitable for grafting in the experimental group was 9.2 ± 0.7 days compared to 14.5 ± 1.1 days in the control group ($p<0.05$). No secondary infections occurred in the experimental group, whereas the control group had 3 cases. The adhesion duration of xenodermal implants was significantly longer in the experimental group (4.5±0.4 days versus 2.8±0.25 days, $p<0.05$).

Conclusions. Using xenodermal implants saturated with silver nanoparticles facilitates faster granulation tissue formation, reduces bacterial complication risk, and enhances preparation outcomes for postoperative wound closure.

Keywords: fasciitis, necrotizing; heterografts; silver; nanoparticles; granulation tissue; wounds and injuries; preoperative period; skin transplantation.

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КСЕНОДЕРМОІМПЛАНТАТИ, НАСИЧЕНІ НАНОЧАСТИНКАМИ СРІБЛА У ПІДГОТОВЦІ ДО ПЛАСТИКИ ПІСЛЯОПЕРАЦІЙНИХ РАН У ПАЦІЄНТІВ ІЗ НЕКРОТИЗУЮЧИМ ФАСЦІЇТОМ

Вступ. Некротизуючий фасциїт (НФ) – важка інфекція, яка супроводжується значними втратами тканин та високим ризиком інфікування ранових поверхонь. Стандартні ксенодермоімплантати, що використовуються для тимчасового закриття післяопераційних дефектів, часто ускладнюються повторною бактеріальною колонізацією.

Мета роботи – оцінити ефективність застосування ліофілізованих ксенодермоімплантатів, насичених наночастинками срібла, для покращення підготовки післяопераційних ран до аутодермопластики у пацієнтів із НФ.

Матеріали та методи. В дослідженні взяли участь 20 пацієнтів з ранами після санації НФ. Пацієнтів розподілили на дві групи: основна група отримувала ліофілізовані ксенодермоімплантати з наночастинками срібла, контрольна – стандартні ксенодермоімплантати. Оцінювали швидкість формування грануляцій, придатних для аутодермопластики, частоту вторинних інфекцій і тривалість адгезії імплантата до рани.

Результати. Середній час формування грануляційної тканини, придатної для пластики, у дослідній групі становив 9,2 ± 0,7 доби, тоді як у контрольній – 14,5 ± 1,1 доби ($p<0,05$). Вторинних інфекцій у дослідній групі не спостерігали, в контрольній групі – 3 випадки. Тривалість адгезії ксенодермоімплантатів була значно вищою у дослідній групі (4,5±0,4 доби проти 2,8±0,25 доби, $p<0,05$).

Висновки. Використання ксенодермоімплантатів, насичених наночастинками срібла, сприяє швидшому формуванню грануляційної тканини, знижує ризик бактеріальних ускладнень та покращує результати підготовки післяопераційних ран до пластичного закриття.

Ключові слова: фасциїт некротизуючий, гетеротрансплантати, срібло, наночастинки, грануляції, рани і ушкодження, передопераційний період, пересадка шкіри.

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ABBREVIATIONS

NF – necrotizing fasciitis
AgNPs – silver nanoparticles
$AgNO_3$ – silver nitrate

INTRODUCTION

Necrotizing fasciitis (NF) is an aggressive and rapidly progressing skin infection characterized by necrosis of the fascia and subcutaneous tissue [1, 2]. At first glance, the incidence of NF appears low, estimated to be between 0.86 and 32.64 cases per 100,000 population [3]. However, we believe it is significantly higher because NF is often misdiagnosed, delayed in diagnosis, and not always correctly coded [4]. Due to its insidious onset and rapid progression, NF is easily misdiagnosed at early stages, leading to extremely high rates of disability and mortality if left untreated [5].

The surgical treatment of NF is challenging and requires a multi-stage approach. The initial stage involves thorough necrosectomy with excision of non-viable tissues to prevent further infection spread. Such surgical interventions, especially after repeated sanitations, create substantial wound defects requiring subsequent reconstructive surgery. Immediate plastic reconstruction post-necrosectomy is often impossible due to several factors, including severe patient condition from sepsis or intoxication, extensive surgical intervention, wound colonization by pathogenic bacteria, and the unpreparedness of the wound surface for accepting an autograft.

Open wound surfaces create significant challenges for further patient treatment, characterized by considerable wound fluid loss, high risks of nosocomial antibiotic-resistant infection, and frequent dressing changes, further complicating the healing process. Thus, postoperative wound management must aim at temporarily closing defects using methods that mimic skin's protective function, minimize fluid loss through the wound surface, and prepare the wound for subsequent plastic closure.

For successful autografting, the wound surface must be cleared of necrotic tissues, supported by vascularized granulations, and free from bacterial pathogens or reduced to minimal levels. Morphologically, wounds after necrosectomy due to necrotizing fasciitis resemble post-burn wounds, often treated with skin substitutes such as xenodermal implants.

Lyophilized pig skin transplants produced by the Institute of Biomedical Technologies (Ternopil, Ukraine) are available in Ukraine and successfully used for treating post-burn wounds. However, their application for postoperative wounds after necrotizing fasciitis is often complicated by recurrent bacterial colonization and purulent exudate formation, limiting their effectiveness.

One promising direction to combat wound infection complications involves using materials enriched with silver ions or silver nanoparticles (AgNPs), such as Aquacell Ag. Silver has pronounced antimicrobial properties, crucial in the context of antibiotic-resistant strains [6–9]. However, due to high costs, these materials have not yet found widespread use in Ukraine.

Considering the above, we propose a method combining the benefits of xenodermal implants with the antimicrobial properties of silver. This method involves saturating lyophilized pig skin implants with silver nanoparticles immediately before application to the wound. Such an approach potentially offers not only temporary closure of wound surfaces but also preparation for subsequent reconstructive surgery.

Objective: To assess the antimicrobial effectiveness, stimulation of granulation tissue development, and creation of optimal conditions for autografting using lyophilized pig skin xenodermal implants saturated with silver nanoparticles, preparing postoperative wounds for plastic closure after necrosectomy due to necrotizing fasciitis.

MATERIALS AND METHODS

This study is based on observations of 20 patients with wounds following necrotizing fasciitis debridement. Patients undergoing extensive necrosectomies, thorough surgical wound cleaning, and general condition stabilization were included. The area of wound defects post-necrosectomy ranged from 100 to 300 cm^2.

Two patients had soft tissue defects on the cranial vault, eight had upper limb defects, eight had lower limb defects, and two had soft tissue defects in the perineal region.

The effectiveness of temporary wound closure using lyophilized pig skin xenografts produced by the Institute of Biomedical Technologies (Ternopil) was evaluated.

The procedure was performed under general anaesthesia in an operating room. Thorough necrosectomy and excision of visually non-viable tissues were carried out. To minimize wound contamination and bacterial colony formation, the wound surface was irrigated with a large volume (3–6 liters) of saline. A control bacteriological swab was collected, and freshly prepared xenodermal implants were placed on the wound. To improve wound drainage, xenodermal implants were perforated with a scalpel blade. Subsequently, thick-layer aseptic gauze dressings were applied.

Patients consenting to the study were randomized by a blind envelope method into two groups. The experimental group (10 patients) received lyophilized pig skin transplants saturated with silver nanoparticles ex tempore according to our previously developed method (Patent of Ukraine for invention UA 111557) [10]. Results were compared with a control group (10 patients) who received standard xenodermal implants without silver nanoparticle saturation.

An improved and standardized process for silver saturation of xenografts is described below (Fig.1):

1. ***Preparation of antibacterial medium:*** Xenodermal implants were immersed in 100 ml of 0.1% silver nitrate solution ($AgNO_3$) for 20 minutes to allow silver ions to adsorb onto the transplant surface.
2. ***Residual solution wash:*** After incubation, transplants were rinsed in 100 ml distilled water for 1 minute to remove excess ions not bound to the matrix.
3. ***Ammonia solution treatment:*** Transplants were immersed in 100 ml of 0.2% ammonia solution (NH_3) for 2 minutes to facilitate complex formation and stabilization of silver ions in the transplant matrix.
4. ***Second rinse:*** Transplants were again rinsed in 100 ml distilled water for 30 seconds to remove ammonia residues.
5. ***Silver reduction:*** Xenografts were placed in 100 ml of 0.1% ascorbic acid solution for 5 minutes, chemically reducing silver ions to nanoparticles evenly distributed on the transplant surface.
6. ***Final rinse:*** Transplants were rinsed in 100 ml distilled water for 4–5 minutes to remove reagent residues and ensure transplant purity.
7. ***Application to wound surface:*** Prepared xenografts were applied to the cleaned wound surface and fixed with sterile dressing materials.

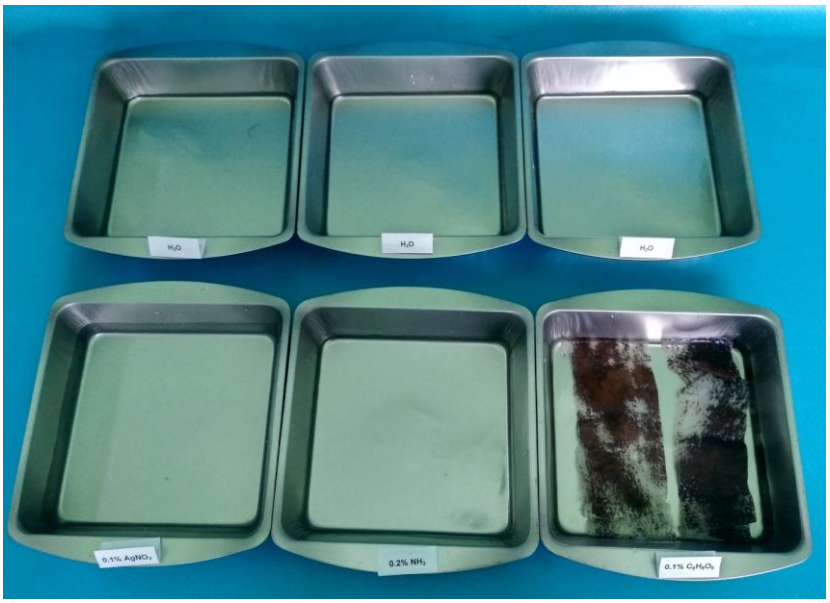

Fig. 1. Saturation of xenodermo-implants with silver nanoparticles before use by alternate immersion in containers with chemicals (see text for explanation)

In the postoperative period, the degree of dressing soakage was monitored, and the outer gauze layers were changed as necessary. If turbid exudate was detected or if the xenodermal implant detached, it was replaced.

The effectiveness was assessed based on the duration of xenograft adhesion to the wound bed, degree of dressing soakage, presence of "slippage," xenograft detachment, and the necessity for its replacement.

The quality of granulation tissue was visually evaluated during the 2nd to 16th days of the study.

The obtained results were analyzed using Student's t-test for statistical significance. Data are presented as mean values ± standard error. A p-value of more than 0.05 was considered statistically significant.

RESULTS

The experimental group demonstrated a reduced volume of wound exudate and dressing soakage compared to the control group. It is noteworthy that a significantly longer fixation duration of the xenodermal implant was observed in the experimental group, averaging 4.5 ± 0.40 days, whereas in the control group, this indicator was only 2.8 ± 0.25 days, on average 1.7 days shorter ($t = 3.597$, $df = 18$, $P < 0.05$).

Consequently, patients in the control group more frequently required repeated surgical interventions and xenograft replacements.

In the experimental group using xenodermal implants saturated with silver nanoparticles, the development of granulation tissue was faster compared to the control group. The average time to formation of granulations suitable for autodermoplasty in the experimental group was 9.2 ± 0.7 days, which was statistically significant compared to the control group (14.5 ± 1.1 days, $p < 0.05$).

No cases of secondary wound infection were observed in the experimental group, while three such

cases occurred in the control group. None of the patients in the experimental group exhibited signs of silver toxicity or other adverse effects. An example of clinical use of xenodermal implants saturated with silver nanoparticles is illustrated in Figures 2–7.

Thus, the study established that using lyophilized xenodermal implants saturated with silver nanoparticles significantly improves the preparation of postoperative wounds for plastic closure compared to the control group using standard xenodermal implants.

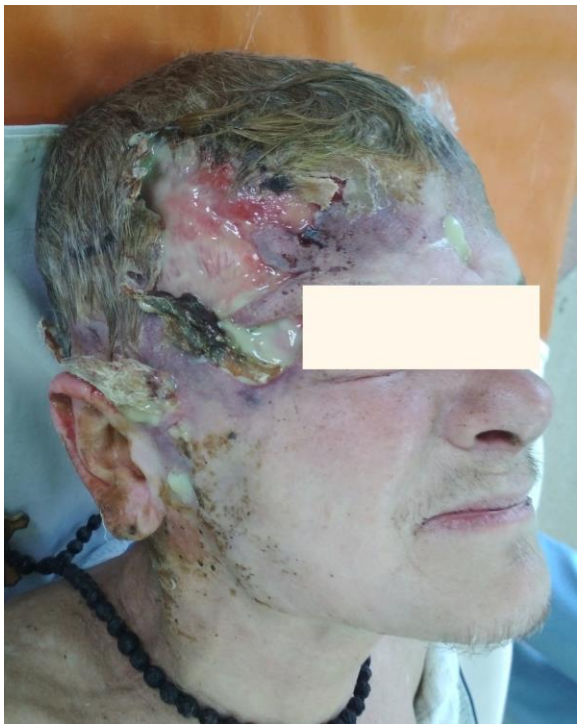

Fig. 2. Wound appearance due to necrotising fasciitis before debridement

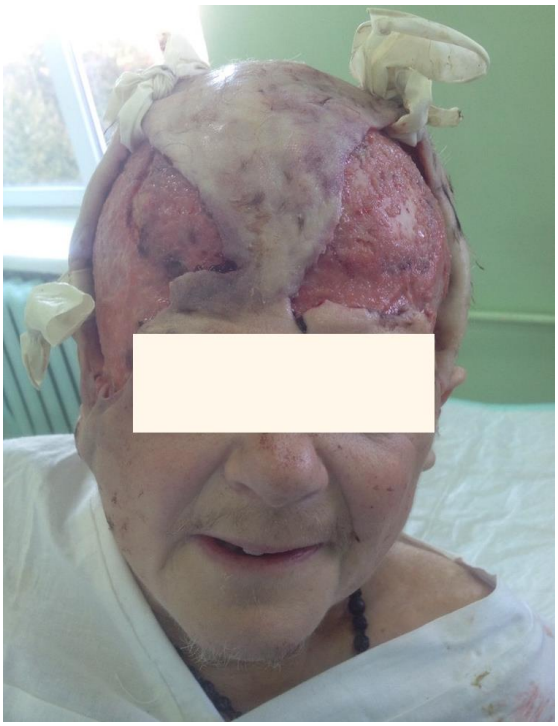

Fig. 3. After debridement

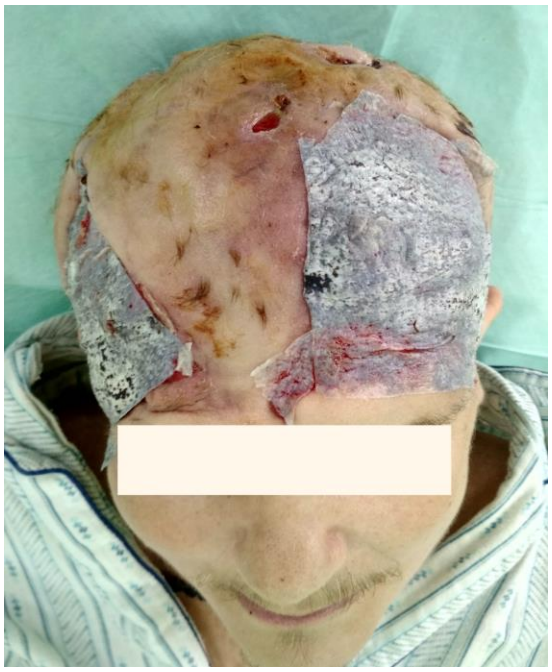

Fig. 4. The wound is covered with a silver-saturated xenoderm implant. The implant is dry, fixed to the wound, and has a characteristic silver lustre

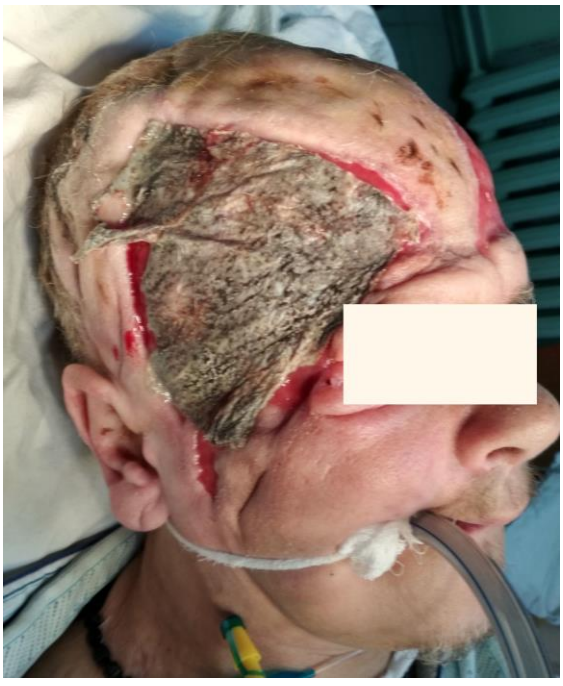

Fig. 5. The xenoimplant, which has partially fulfilled its function, is displaced in some places and is sloughed off. Some areas remain fixed

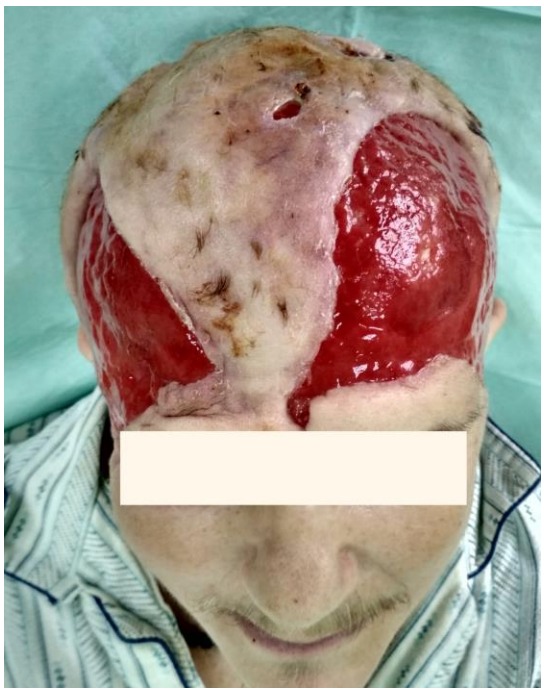

Fig. 6. Bright granulations on the 7th day after removal of the silver-saturated xenoimplant

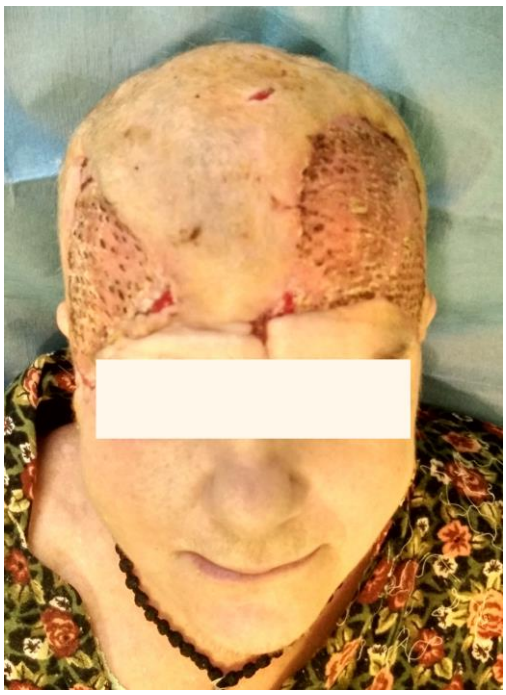

Fig. 7. After autodermoplasty

DISCUSSION

The obtained results demonstrate a high potential for using xenodermal implants saturated with silver nanoparticles in surgical practice for treating postoperative wounds, particularly after necrotizing fasciitis. As other studies indicate, the antimicrobial activity of silver is associated with the nanoparticles' ability to penetrate bacterial walls, causing disruption of cell membranes and intracellular structures, as well as reducing the expression of bacterial resistance factors [6, 8, 11].

Our study identified, in addition to the bacteriostatic action, a pronounced influence of silver nanoparticles on accelerating the development of granulation tissue. This might be attributed to the ability of AgNPs to stimulate neoangiogenesis, activate macrophages, and decrease levels of proinflammatory cytokines, thereby creating optimal conditions for tissue regeneration [9, 12].

Comparisons with other studies also indicate that using silver nanoparticles in 3D-printed constructs or xenodermal implants significantly enhances wound healing efficiency due to prolonged antimicrobial action and reduced risk of chronic inflammation [13–15]. This aligns with literature data regarding the mechanisms of silver nanoparticles in clinical and experimental conditions [7, 16, 17].

CONCLUSIONS

The obtained results demonstrate that the use of xenodermal implants saturated with silver nanoparticles is an effective method for preparing postoperative wounds for plastic closure. This method promotes faster development of granulation tissue, reduces bacterial contamination, and minimizes wound losses, thereby improving the overall treatment outcomes.

PROSPECTS FOR FUTURE RESEARCH

Considering the obtained results, xenodermal implants saturated with silver nanoparticles represent a promising approach to prepare postoperative wounds for subsequent skin grafting after necrotizing fasciitis, particularly under conditions of high bacterial contamination risk and complex wound defects. Further research should focus on optimizing silver nanoparticle concentration and formulation to enhance clinical outcomes and minimize adverse effects, and validating efficacy in larger cohorts of patients with necrotizing fasciitis.

AUTHOR CONTRIBUTIONS

Ihor Stoianovskyi: research concept and design, data collection and interpretation, statistical analysis and manuscript writing, final approval of the article

Sergii Khimich: manuscript proofreading and revision

Natalya Tuzyuk: literature review, data collection and interpretation.

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None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ARTIFICIAL INTELLIGENCE DISCLOSURE

The authors declare that the manuscript was prepared without the assistance of artificial intelligence (AI) tools. All content is the result of thorough research, critical analysis, and original writing by the authors.

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