Article's History: Received: 02.05.2025; Revised: 22.07.2025; Accepted: 02.09.2025

Bulletin of Medical and Biological Research

Vol. 7, No. 3
2025

DOI: 10.63341/bmbr/3.2025.80

Journal homepage: https://bmbr.com.ua/en

UDC 616-001.4:577.112

Histological and histochemical changes in the treatment of wounds with an injectable implant based on high-molecular hyaluronic acid and sodium succinate: Experimental study

Svitlana Korkunda*

PhD in Medical Sciences, Associate Professor
Kharkiv National Medical University
61022, 4 Nauky Ave., Kharkiv, Ukraine
https://orcid.org/0009-0002-4132-109X

Abstract. The aim of the study was to evaluate the effectiveness of an injectable implant combining hyaluronic acid and sodium succinate for accelerating the reparative processes of donor wounds after autodermoplasty in patients with deep burns. The study was conducted from 1 January to 30 June 2014 in the Department of Combustiology of the Kharkiv Medical Academy of Postgraduate Education at the City Clinical Emergency and Urgent Care Hospital named after Prof. O.I. Meshchaninov, where in 50 patients with donor wounds after autodermoplasty the effectiveness of the hyaluronic acid and sodium succinate injectable implant and standard therapy was compared according to clinical, morphological and biochemical parameters. The results showed that by the 10th day, complete healing was observed in 78% of patients in zone A (39 out of 50), while in zone B this indicator was only 6% (3 out of 50). By the 14th day, epithelisation was completed in 100% of cases in zone A, compared with 42% in zone B (21 out of 50). Morphological analysis showed a higher mitotic index in zone A – 16.1% versus 6.8% in zone B on the 10th day, which reflected more active cell renewal. Biochemical studies confirmed a more pronounced increase in catalase activity in zone A (from 28.2 to 36.6) compared with the control zone (from 25.8 to 27.4). Scars in zone A formed delicate and elastic, while in zone B dense and less organised structures predominated. The injectable implant of hyaluronic acid with sodium succinate accelerated healing and improved scar quality compared with standard therapy. The results obtained may be used by burn specialists, plastic surgeons and clinical pharmacologists in the practice of burn centres and departments of reconstructive surgery for optimising the treatment of donor wounds after autodermoplasty

Keywords: donor site; regeneration; cell proliferation; collagen fibres; scars; antioxidant enzymes; tolerability

INTRODUCTION

According to the World Health Organisation, about 180,000 deaths caused by burn injury are registered worldwide each year [1]. The survival of patients with deep burns directly depended on the timely and adequate closure of wound surfaces, including through autodermoplasty. However, performing this procedure was accompanied by the formation of donor wounds, which became an additional site of injury. The presence prolonged the duration of inpatient treatment, intensified the pain syndrome, increased the risk of secondary infection, and created prerequisites for the development of pathological scars. The use of traditional approaches (gauze dressings, air-drying or local antiseptics) allowed epithelisation to be achieved, but did not ensure rapid restoration of full skin cover or reduce the risk of complications. For this reason, the problem of optimising the treatment of donor wounds in combustiology remained unresolved and required the introduction of modern biocompatible materials and implants capable of accelerating reparative processes and improving the quality of newly formed tissue.

International data confirmed the effectiveness of hyaluronic acid in the treatment of burn wounds and in improving the quality of tissue regeneration. In the study by Y. Dong *et al.* [2], the use of a conformal hydrogel based on hyaluronic acid with adipose tissue stem cells was integrated with cell therapy, which led to accelerated epithelisation

Suggested Citation:
Korkunda S. Histological and histochemical changes in the treatment of wounds with an injectable implant based on high-molecular hyaluronic acid and sodium succinate: Experimental study. Bull Med Biol Res. 2025;7(3):80–91. DOI: 10.63341/bmbr/3.2025.80

*Corresponding author

and enhanced angiogenesis compared with the control group. The study combined the biopolymer and cells into a single therapeutic system, demonstrating the promise of this approach. The analysis conducted by E. Alemzadeh *et al.* [3] showed that the inclusion of stem cells in a hyaluronic acid-based hydrogel modulated the expression of interleukin-1β (IL-1β), transforming growth factor β1 (TGF-β1), and basic fibroblast growth factor (bFGF), resulting in faster wound healing. The authors confirmed that regulation of the cytokine profile was a key mechanism for improving the morphology of the regenerated skin. In the study by Á. Sierra-Sánchez *et al.* [4], the use of dermal substitutes containing hyaluronic acid, led to faster epithelisation and restoration of skin structures. The researchers emphasised that the use of such materials reduced the severity of inflammation and promoted a more ordered process of regeneration. In the study by S.V. Korkunda *et al.* [5], it was noted that the use of hyaluronic acid in the complex treatment of patients with wound defects contributed to faster epithelisation and a reduction in the severity of inflammatory reactions, which highlighted its therapeutic potential in regenerative medicine.

Numerous studies were aimed at creating modified materials based on hyaluronic acid capable of combining biocompatibility with additional functional properties. In the study by Z. Wang *et al.* [6], the development of films based on chitosan and derivatives of hyaluronic acid demonstrated increased strength and biodegradability, which ensured faster healing of skin defects compared with unmodified materials. The authors emphasised that the combination of polymers improved both the mechanical characteristics and the biological activity of the coating. The study conducted by Z. Hussain *et al.* [7] showed that the functionalisation of hyaluronic acid polymeric nanoparticles improved the delivery of active substances to deeper layers of the skin, resulting in significantly higher wound-healing effectiveness. It was proven that such an approach provided increased bioavailability and a pronounced anti-inflammatory effect. In the work by S. Zhang *et al.* [8], the creation of hybrid hydrogels based on arginine derivatives and hyaluronic acid led to the formation of materials with antioxidant properties, which contributed to the reduction of oxidative stress in the area of injury. The authors confirmed that these properties promoted more harmonious skin recovery and a reduction in the intensity of the inflammatory response. In the study by M.V. Balanenko [9], the creation of biomedical dressings based on a chitosan nanocomposite demonstrated the prospects of combining national biotechnologies with innovative approaches of tissue engineering. It was established that the created materials exhibited antibacterial activity and contributed to the course of regenerative processes, which was important for the treatment of donor wounds in clinical practice.

Studies devoted to improving the treatment of donor wounds confirmed the effectiveness of modern biopolymeric dressings and hyaluronic acid-based materials. In the study by N.M. Nor [10], the use of film wound dressings for the treatment of donor sites in patients with deep burns was evaluated clinically, and the results demonstrated a reduction in epithelisation time and a decrease in the frequency of infectious complications. It was emphasised that the choice of dressing materials directly influenced the speed of regeneration and the quality of the formed skin. U.Ye. Sobina [11] investigated the possibilities of creating a medical device based on hyaluronic acid, designed for use in regenerative medicine. The author showed that the combination of natural polymers with bioengineering technologies made it possible to create a product with the potential to optimise wound healing. In the study by G. Papa *et al.* [12], a comparison of hyaluronic acid- and silver-based dressings in patients after autodermoplasty was conducted. The results demonstrated that the use of hyaluronic acid-containing materials improved scar quality and contributed to better functional characteristics of donor sites.

Despite the significant volume of experimental and clinical studies, scientific research still lacked sufficient data regarding the evaluation of the effectiveness of injectable implants based on hyaluronic acid in combination with sodium succinate in the treatment of donor wounds in combustiology. The aim of the study was to determine the clinical outcomes of using an injectable implant based on hyaluronic acid in combination with sodium succinate in patients with burn injury.

MATERIALS AND METHODS

Study design, patient characteristics and ethical aspects. The study was conducted as an open comparative single-group design with intra-individual control: the donor site of each patient was conditionally divided into two equal parts, where one half received an injectable implant based on hyaluronic acid and sodium succinate, and the other – standard local treatment. The period of implementation lasted from 1 January to 30 June 2014, which provided sufficient time for recruiting the planned sample of patients, carrying out the 14-day treatment and observation cycle, and performing laboratory and statistical processing of the results. The study was conducted in the Department of Combustiology, Reconstructive and Plastic Surgery of the Kharkiv Medical Academy of Postgraduate Education on the basis of the City Clinical Emergency Hospital named after Prof. O.I. Meshchaninov (Kharkiv, Ukraine).

The study included 50 patients with donor wounds after autodermoplasty for thermal burns of IIIA-IIIB degree with an area of up to 5% of body surface. Among the participants, there were 28 men and 22 women aged 18 to 65 years. The localisation of burns was distributed as follows: hand – 8 patients, forearm – 8, shoulder – 10, torso – 9, thigh – 9, shin – 6. Patients with donor sites corresponding to the indicated parameters were included; in women of reproductive age, a negative pregnancy test was a mandatory condition. Individuals with burn disease, hypersensitivity to the components of the study drug, active inflammatory processes at the site of administration, a tendency to form hypertrophic scars, blood coagulation disorders, diabetes mellitus, as well as those who received thrombolytic or anticoagulant therapy within two weeks prior to inclusion, were not allowed to participate. In addition, patients with severe decompensated diseases or acute conditions that could affect the treatment results, as well as those who required medications not provided for by the protocol or were already participating in other clinical trials, were excluded.

The ethical principles of the study complied with the provisions of the Declaration of Helsinki of the World Medical Association [13], which defined the priority of patient

safety, voluntariness of participation, and mandatory informed consent. In addition, the protocol was developed taking into account the requirements of the international guideline on Good Clinical Practice [14], which guaranteed the reliability of the obtained clinical data and the protection of participants' rights. All participants signed written informed consent, which included confirmation of voluntary participation in the study and acceptance of the conditions regarding the processing of personal data in compliance with the principles of confidentiality and anonymisation of the obtained information.

Treatment interventions and therapy protocol. Before the start of therapy, all patients underwent screening, which included clinical examination and laboratory tests. Treatment was started immediately after autodermoplasty. The donor site was conditionally divided into two equal parts. In one zone an injectable implant (zone A) containing hyaluronic acid and sodium succinate (Hyalual, "Yuria-Pharm", Ukraine) was used. The drug was injected directly under half of the wound in a dose of 1-2 ml, depending on its area, immediately after surgery and again after three days. The other half of the donor surface was treated according to the standard protocol (zone B): a sterile gauze napkin without additional impregnation was applied to the entire area, after which drying was carried out with a specialised medical heat fan WarmTouch WT 6000 (Covidien, USA), certified for use in burn surgery departments. Patients were examined daily, which included an assessment of general condition, visual characterisation of the donor site, and registration of subjective complaints. Dressings in the control zone were carried out once a day, synchronously with daily examinations. Treatment lasted until complete epithelialisation, and the main criterion of effectiveness was the assessment on the 14th day. Advanced clinical and laboratory examinations were performed on the specified control days – on days 1, 3, 7, 10 and 14, which included general clinical examination (body temperature, auscultation of the heart and lungs, palpation and percussion of the abdomen, condition of the skin and mucous membranes), laboratory tests (complete blood count, general urine analysis, biochemical blood parameters), as well as visual assessment of the donor wound. Histological and histochemical studies, including determination of the mitotic index and cellular activity, were performed on the 3rd and 10th days. The activity of antioxidant enzymes – superoxide dismutase (SOD) and catalase – was determined on the 3rd and 14th days. Tolerability of therapy was assessed after the completion of the treatment course, while all adverse reactions were recorded daily. In cases where complete epithelialisation of the donor site occurred earlier than 14 days, the final clinical and laboratory examination was carried out on the day of healing.

Methods of assessing clinical and morphological treatment results and statistical analysis. The assessment of effectiveness was carried out according to primary and secondary criteria. The primary criteria included the duration of treatment (in days) until complete epithelialisation of the donor site and the morphological characteristics of tissues determined by the results of histological and histochemical studies in dynamics. The drug was considered effective if complete epithelialisation of the donor surface was achieved without complications, while partial epithelialisation was qualified as an insufficient therapeutic result. The secondary criteria were the average healing time of the donor site in the observation groups, changes in histological parameters in biopsies during treatment, and the results of histochemical studies reflecting the features of proliferative and reparative processes in the control and experimental zones.

For clinical assessment, a categorical scale from 0 to 3 points was used. The degree of epithelialisation was defined as complete (0 points), more than 50% of the surface (1 point), 25-50% (2 points) or less than 25% (3 points). The character of epithelialisation was assessed as continuous (0 points), marginal and insular (1 point), marginal only (2 points) or absent (3 points). Inflammatory changes in the wound and adjacent tissues were classified from the absence (0 points) to mild (1 point), moderate (2 points) or severe (3 points). Skin itching in the healing area was also assessed gradually: from absence (0 points) to mild (1 point), moderate (2 points) and severe (3 points). Morphological characteristics of tissue quality included relief smoothness, where 0 points corresponded to absence of irregularities, 1 point – mild, 2 points – moderate and 3 points – severe changes. Tissue colour was defined as normal (0 points), with mild hyperaemia (1 point), marked hyperaemia (2 points) or purplish-cyanotic shade (3 points). Tolerability of therapy was assessed comprehensively, taking into account patients' subjective complaints, clinical data and laboratory test results, as well as the frequency and nature of adverse reactions. For the integrated assessment a three-level scale was used: good tolerability was defined by the absence of pathological changes or deviations in clinical and laboratory parameters and patients' complaints; satisfactory corresponded to temporary and minor deviations that did not require therapy modification or additional interventions; unsatisfactory was established in cases of severe pathological changes requiring discontinuation of the drug and the appointment of alternative treatment.

Statistical data processing was carried out using MS Excel (Microsoft Office, USA). For quantitative variables the mean value (M), median (Me), standard deviation (SD), minimum (Min) and maximum (Max) values were calculated. For qualitative indicators, absolute (n) and relative (%) frequencies were determined. Normality of distribution was checked using the Shapiro-Wilk test. In cases of normal distribution a paired Student's t-test was used, and in its absence – the Mann-Whitney test. Categorical data were compared using Pearson's χ^2 test or Fisher's exact test. Differences were considered statistically significant at $p < 0.05$ (for the Shapiro-Wilk test – $p < 0.01$). The limitation of the study was that it did not provide for the assessment of long-term quality of formed scars and long-term functional results, which reduced the possibility of a comprehensive analysis of therapy effectiveness.

RESULTS

Comparative characteristics of clinical outcomes in zones A and B. Clinical results showed significant differences in the speed and quality of healing of donor wounds depending on the treatment approaches used. In patients in whom an injection implant based on hyaluronic acid and sodium succinate was administered in zone A, the recovery processes took place more dynamically and were accompanied

by distinct positive changes from the very first days of treatment. This was manifested both in faster epithelialisation of the wound surface and in a reduction in the severity of inflammatory reactions and in a more orderly formation of tissues. For a detailed reflection of the process dynamics during the observation period on days 1, 3, 7, 10 and 14, the results of the clinical assessment of the condition of donor wounds in zone A were summarised in Table 1.

Table 1. Dynamics of donor wound healing in zone A (n=50)

Indicator	Expression	Day 1	Day 3	Day 7	Day 10	Day 14
Degree of epithelialisation	0 – complete	–	–	12	39	50
	1 – more than 50%	–	–	15	11	–
	2 – 25-50%	–	–	23	–	–
	3 – <25%	50	50	–	–	–
Character of epithelialisation	0 – continuous	–	–	12	36	50
	1 – marginal and insular	–	–	30	14	–
	2 – marginal	–	50	8	–	–
	3 – absent	50	–	–	–	–
Inflammatory changes	0 – none	–	–	12	19	27
	1 – slight	–	10	15	28	22
	2 – moderate	35	36	23	3	1
	3 – severe	15	4	–	–	–
Skin itching	0 – none	–	–	–	–	–
	1 – slight	–	–	–	–	41
	2 – moderate	–	–	–	–	9
	3 – severe	–	–	–	–	–
Relief irregularity	0 – none	50	–	–	–	21
	1 – slight	–	–	–	–	25
	2 – moderate	–	–	–	–	4
	3 – severe	–	–	–	–	–
Colour intensity	0 – normal	–	–	–	–	–
	1 – moderate hyperaemia	–	–	–	–	40
	2 – severe hyperaemia	50	–	–	–	10
	3 – purple-cyanotic	–	–	–	–	–

Source: compiled by the author

The analysis of Table 1 data demonstrated that at the initial stage (1-3 days) all patients had minimal epithelialisation (<25% of the surface), which corresponded to the expected course of the early postoperative period after autodermoplasty. Such a result indicated the adequacy of the research model and the absence of initial deviations between patients. By the 7th day, in 24% of cases (12/50) complete epithelialisation was noted, in another 30% restoration of more than half of the surface was observed, and in 46% – from 25 to 50%. Such dynamics demonstrated the activation of reparative processes under the influence of the injection implant, which allowed a significant number of patients to enter the phase of full recovery much earlier than usually expected with standard therapy. By the 10th day, in 78% of participants (39/50) complete epithelialisation was observed, while the remaining 22% reached this indicator by the 14th day. Thus, the absolute majority of patients completed the healing process within the first ten days, which clinically meant a significant reduction in the duration of inpatient treatment. The character of epithelialisation also confirmed the high quality of recovery: by the 7th day in 24% of cases the newly formed epithelium was already continuous, and by the 14th day this indicator was 100%, which indicated the uniformity and stability of regeneration.

The inflammatory component, typical for postoperative wounds, gradually decreased. At the start of the study, severe inflammation was noted in 15/50 patients, but by the 10th day only isolated moderate manifestations remained, and by the 14th day severe cases completely disappeared. This meant that the implant had a pronounced anti-inflammatory effect, which contributed to a more stable course of the reparative process and reduced the risk of infectious complications. Regarding subjective complaints, itching was recorded only on the 14th day: in 82% of cases it was slight, and in 18% – moderate. Such dynamics indicated that itching appeared as a symptom of tissue remodelling and did not negatively affect the overall clinical result. Morphological markers of skin quality showed gradual improvement: by the 14th day in 42% (21/50) of patients the relief irregularity completely disappeared, while the rest had only slight or moderate manifestations; no severe cases were recorded. This demonstrated a reduced risk of hypertrophic or keloid scars. Hyperaemia, which at the beginning was present in 100% of patients (50/50), gradually decreased: by the 14th day only 10 cases of moderate changes remained. Such a result confirmed the normalisation of microcirculation and the adequacy of vascularisation of the restored tissues, which, together with morphological indicators, pointed to the high quality of regeneration. Unlike zone A, where an injection implant was used, zone B used a standard approach to the treatment of donor wounds, which included gauze dressings and drying with a specialised heat blower. The dynamics of recovery in this group proved to be less intensive: the process of epithelialisation proceeded more slowly, with a larger proportion of cases of pronounced

inflammatory manifestations and uneven structure of the newly formed tissue. Detailed indicators of the clinical evaluation of the condition of donor sites in zone B during the entire observation period were presented in Table 2.

Table 2. Dynamics of donor wound healing in zone B (n=50)

Indicator	Expression	Day 1	Day 3	Day 7	Day 10	Day 14
Degree of epithelialisation	0 – complete	–	–	–	3	21
	1 – more than 50%	–	–	2	29	24
	2 – 25-50%	–	–	22	16	5
	3 – <25%	50	50	26	2	–
Character of epithelialisation	0 – continuous	–	–	–	3	21
	1 – marginal and insular	–	–	6	16	29
	2 – marginal	–	31	44	31	–
	3 – absent	50	19	–	–	–
Inflammatory changes	0 – none	–	–	5	12	19
	1 – slight	–	6	15	21	20
	2 – moderate	35	38	30	17	11
	3 – severe	15	6	–	–	–
Skin itching	0 – none	–	–	–	–	–
	1 – slight	–	–	–	–	24
	2 – moderate	–	–	–	–	22
	3 – severe	–	–	–	–	4
Relief irregularity	0 – none	50	–	–	–	11
	1 – slight	–	–	–	–	23
	2 – moderate	–	–	–	–	16
	3 – severe	–	–	–	–	–
Colour intensity	0 – normal	–	–	–	–	–
	1 – moderate hyperaemia	–	–	–	–	23
	2 – severe hyperaemia	50	–	–	–	23
	3 – purple-cyanotic	–	–	–	–	4

Source: compiled by the author

Analysis of the results in zone B showed a significantly slower course of reparative processes compared to the experimental area. Already on the 7th day, there were no recorded cases of complete epithelisation, while most wounds (52%, 26/50) remained at the level of 25-50% restored surface, and in 26 patients (<25%) only initial signs of healing were observed. Such a delay indicated insufficient stimulation of cellular and vascular repair mechanisms under standard treatment, which caused the prolonged persistence of the defect. Only on the 10th day did 3 patients show complete epithelisation, whereas in zone A, this figure reached 39 cases, which made the difference fundamental. On the 14th day only 42% (21/50) achieved complete healing, while the rest continued to demonstrate incomplete tissue restoration, which in the clinical context meant the risk of infectious complications, the need for continued inpatient treatment and increased cost of therapy. The nature of epithelisation also confirmed the delay in recovery: even on the 14th day, in the majority of patients (29/50) the marginal or island type prevailed, which reflects the fragmentary closure of the wound surface. Complete restoration was recorded in less than half of the cases, which indicated insufficient integration of the cellular matrix and uneven epithelial growth. This created the prerequisites for the formation of scar changes, especially under conditions of repeated injuries or additional infectious load.

Inflammatory reactions persisted much longer than in zone A. While at the beginning 15 patients had pronounced changes, even on the 14th day 11 individuals retained moderate manifestations, and complete absence of inflammation was recorded in only 19/50. Such dynamics indicated insufficient control over the exudative phase of the wound process and the likelihood of chronic inflammation, which is often associated with the formation of coarse pathological scars. Subjective symptoms were also more pronounced. On the 14th day, almost all patients reported itching: in 44% it was moderate, and in 8% severe. Such intensity of itching is an indirect marker of active remodelling with increased proliferative activity of fibroblasts, which is associated with the risk of hypertrophic scar formation and impaired tissue elasticity. Morphological parameters of the quality of the restored skin were also less favourable. In 32% of cases, significant surface unevenness was recorded, whereas in zone A no such manifestations were observed. This meant that standard treatment did not ensure sufficient restoration of the dermal structure and left a risk of cosmetic and functional defects. Hyperaemia proved to be more persistent and pronounced. On the 14th day, 23 patients still had pronounced hyperaemia, and in 4 more cases signs of purplish-cyanotic colouring were observed, indicating stagnant phenomena in the microcirculatory bed and incomplete normalisation of tissue vascularisation. This indicator reflected the insufficient maturity of the newly formed vessels and the risk of secondary complications, in particular hypoxia of the regenerated areas.

The overall analysis of the results in zones A and B revealed significant differences in the speed and quality of reparative processes. In zone A, where the Hyalual injectable implant was used, epithelisation occurred much more

dynamically: already on the 7th day, 24% of donor surfaces were fully restored, whereas in zone B none of the wounds reached this level. On the 10th day, 78% of patients in zone A had complete healing, which strongly contrasted with 6% in zone B. By the end of the 14-day observation, 100% of cases in zone A were completely epithelised, while in zone B this result was recorded in only 42% of patients. An important factor was also the reduction of the inflammatory component: in zone A, by the 14th day there remained only one case of moderate inflammation, while in zone B these manifestations persisted in 11 patients. Subjective symptoms also differed: in zone A, itching was mild in 82% and moderate in 18% of patients, whereas in zone B almost half (44%) reported moderate and another 8% severe itching, indicating a risk of scarring. Morphological signs confirmed the advantages of the implant: in zone A, most patients had a smooth surface, only 29% had minor or moderate changes, while in zone B more than 78% retained deformations. Skin colour normalised more quickly in zone A, where hyperaemia persisted in 20%, whereas in zone B pronounced redness was recorded in 46% of patients, and another 8% had a bluish tint. This indicates a higher quality of recovery in zone A. The obtained results indicate that the use of an injectable implant based on hyaluronic acid and sodium succinate in the treatment of donor wounds after autodermoplasty ensured faster and higher- quality epithelisation compared with the standard approach. The drug contributed to a more ordered course of regeneration, reduced inflammation intensity, limited itching and improved morphological characteristics of the restored skin. This makes it possible to consider it a promising means for optimising the recovery of postoperative wounds in clinical combustiology.

Morphological and biochemical bases of therapy effectiveness. To assess the biochemical mechanisms underlying the regenerative effect of the injectable implant, the activity of key antioxidant enzymes – SOD and catalase – was analysed. These enzymes play a leading role in neutralising reactive oxygen species, reducing oxidative stress in tissues and creating favourable conditions for cell proliferation. The results of the study in zone A, where the preparation based on hyaluronic acid and sodium succinate was used, are presented in Table 3.

Table 3. Dynamics of antioxidant enzyme activity in zone A (n=50)

Indicator	Evaluation point	M	Me	SD	Min	Max
SOD	Day 3	9.11	9.1	0.79	7.8	10.5
	Day 14	10.03	9.8	0.66	9.2	11.3
Catalase	Day 3	28.2	28.2	1.36	26.2	30.8
	Day 14	36.6	36.9	1.64	33.2	38.8

Source: compiled by the author

The analysis of the data in Table 3 showed that in zone A the activity of antioxidant enzymes increased during the course of treatment, reflecting the biochemical prerequisites for accelerated wound healing. The SOD level rose from 9.11 ± 0.79 on the 3rd day to 10.03 ± 0.66 on the 14th day. This meant that tissues more actively utilised the superoxide radical, reducing oxidative stress and preventing damage to cellular structures. At the same time, a marked increase in catalase activity was observed – from 28.2 ± 1.36 to 36.6 ± 1.64, which indicated the strengthening of detoxification mechanisms for hydrogen peroxide, one of the main by-products of metabolism. Such dynamics were typical for tissues with a high level of proliferative processes, since the effective functioning of the antioxidant system created conditions for preserving cell viability, active collagen synthesis and the ordered formation of new connective tissue. The obtained results explain why in zone A regeneration occurred faster: the reduction of oxidative stress and the increase of antioxidant protection contributed to a more harmonious course of reparative processes. In zone B, where standard treatment was applied, the dynamics of these enzyme changes reflected less intense reparative processes. Detailed indicators are presented in Table 4.

Table 4. Dynamics of antioxidant enzyme activity in zone B (n=50)

Indicator	Evaluation point	M	Me	SD	Min	Max
SOD	Day 3	7.24	7.1	0.75	6.1	8.8
	Day 14	8.68	8.8	0.6	7.2	9.8
Catalase	Day 3	25.8	25.8	1.33	23.2	27.8
	Day 14	27.4	27.4	1.12	25.2	29.4

Source: compiled by the author

The analysis of the data in Table 4 showed that in zone B the activity of antioxidant enzymes also increased, but it was less pronounced compared with zone A. The SOD level increased from 7.24 ± 0.75 on the 3rd day to 8.68 ± 0.6 on the 14th day, which indicated some activation of superoxide radical neutralisation mechanisms. At the same time, the values remained lower than in zone A, which reflected less intensive metabolic processes and weaker protection against oxidative stress. Catalase rose from 25.8 ± 1.33 to 27.4 ± 1.12, but such an increase was minimal and did not ensure a sufficient level of hydrogen peroxide detoxification. This meant that in the control zone, tissue regeneration was accompanied by less effective antioxidant protection, which could lead to more prolonged inflammation and slower formation of mature granulation tissue. In general, the dynamics in zone B confirmed the lag in the quality of biochemical recovery mechanisms compared to the experimental zone. To com-

prehensively characterise reparative processes, indicators of the mitotic index and mitotic activity in donor wound biopsies were analysed. These parameters reflect the intensity of cell division and proliferation, which are key for restoring damaged tissues. The obtained results are presented in Table 5.

Table 5. Indicators of mitotic index and mitotic activity

Indicator	Evaluation point	Zone A (n = 50)	Zone B (n = 50)
Mitotic index, %	Day 3	10.6±1.92	8.81±1.77
	Day 10	16.1±4.71	6.8±1.68
Mitotic activity, %	Day 3	5.95±1.91	4.1±0.78
	Day 10	7.28±2.54	5.1±1.63

Source: compiled by the author

The analysis of the data demonstrated that the dynamics of the mitotic index and mitotic activity directly reflected the differences in the morphological mechanisms of tissue restoration between zone A and zone B. In zone A, an increase of the mitotic index to 16.1% on the 10th day meant active proliferation of epithelial cells and fibroblasts, which contributed to faster formation of granulation tissue and subsequent organisation of mature connective tissue. The increase of mitotic activity to 7.28% indicated stable involvement of cells in division processes, providing a sufficient pool of cells for collagen synthesis and dermal structure restoration. This explains the more orderly organisation of collagen fibres and the reduced risk of pathological scarring in this group. In zone B, where indicators tended to decrease (mitotic index – 6.8%, mitotic activity – 5.1% on the 10th day), the cell cycle was less active. This meant that recovery processes proceeded more slowly, with less intensive formation of new cells and collagen synthesis. Morphologically, such dynamics could lead to less mature and less organised connective tissue, with a higher likelihood of coarse fibrous structures, which are a prerequisite for pathological scar formation. Thus, the data confirmed that the implant ensured a favourable microenvironment for cell proliferation and morphogenesis of new tissues, whereas standard therapy did not create sufficient conditions for such activity. At the stage of fibrous connective tissue formation, morphological differences between zones A and B were identified. In biopsies from zone A, already on the 3rd-5th day, intensive formation of thin collagen fibres was recorded in combination with numerous fibroblasts and a branched network of capillaries. This indicated active remodelling of granulation tissue and the creation of conditions for a rapid transition to the stage of mature recovery. In the control zone B, the number of vessels was lower by 15-20%, and the appearance of signs of fibrous tissue formation occurred later (after the 6th day), which potentially increased the risk of delayed reparative processes and pathological scar formation. Morphological characteristics of this stage are shown in Figure 1.

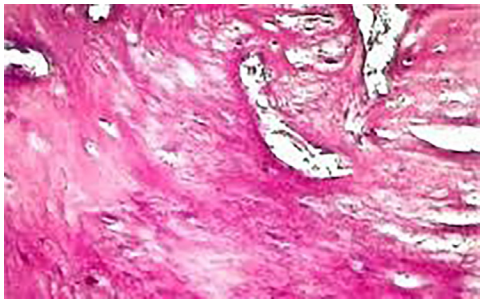

Figure 1. Formation of fibrous connective tissue in zone A (3rd-5th day of treatment)
Source: obtained by the author

On the 10th-14th day in zone A, the final stage of the reparative process was observed, characterised by the ordered formation of scar tissue. Collagen fibres had a more mature morphological structure, were tightly oriented in parallel bundles, which provided tissue with mechanical stability. The vascular network was represented by individual capillaries with signs of stabilisation of the walls, and the cellular infiltrate was minimised, which indicated the completion of the inflammatory stage and the transition to tissue remodelling. The obtained changes reflected favourable conditions for the formation of a thin and elastic scar without a tendency to hypertrophy. In zone B, the tissue structure remained less organised compared with zone A. Collagen fibres were arranged chaotically, were predominantly thin and immature, which indicated an unfinished process of the remodelling. The vascular component was poorly developed: isolated vessels with signs of lumen reduction were recorded, which reduced the quality of tissue nutrition. In the intercellular substance, a significant number of mesenchymal cells remained, and compaction of the interfibrillar matrix was noted, which created prerequisites for the formation of a denser and more rigid scar. Such a combination of morphological characteristics indicated a slower nature of regeneration and less favourable conditions for tissue recovery. In contrast, in zone A the process ended with the formation of a delicate and elastic scar, which corresponded to higher-quality repair (Fig. 2).

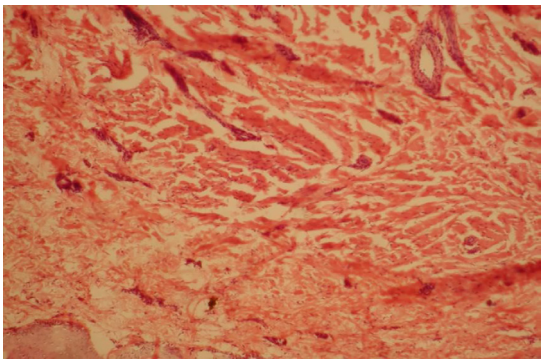

Figure 2. Formation of scar connective tissue in zone B (10th-14th day of treatment)
Source: obtained by the author

In addition, the tolerability of therapy was satisfactory in both zones: throughout the entire treatment period, no unforeseen side effects, acute complications or exacerbations of chronic diseases were detected. In zone A, the injectable implant was evaluated as well tolerated: no clinically significant deviations in laboratory parameters or pathological changes during objective examination were recorded, and subjective complaints were limited to mild itching, which was transient and did not require correction of therapy. In zone B, tolerability also remained satisfactory, but on the 14th day 22 patients reported moderate itching, and in 4 cases it was severe, indicating a less favourable course of the reparative process. The obtained data indicated that the use of an injectable implant based on hyaluronic acid and sodium succinate contributed to the activation of antioxidant enzymes, stimulation of cell proliferation and more orderly formation of connective tissue. In zone B, similar processes were significantly slower and accompanied by a less pronounced antioxidant response. This confirmed the important role of the preparation in accelerating regeneration and improving the quality of donor wound healing.

DISCUSSION

The obtained results confirmed that the use of an injectable implant based on hyaluronic acid and sodium succinate ensured faster and higher-quality healing of donor wounds compared to the standard approach. The use of the preparation was accompanied by more organised epithelialisation, a reduction in the severity of inflammation, and the formation of more elastic scar tissue. Morphological and biochemical studies indicated the activation of reparative processes and the normalisation of tissue homeostasis. The tolerability of therapy remained good, without the development of clinically significant complications or adverse reactions.

In zone A, complete epithelialisation was achieved in 78% (39/50) of patients as early as on the 10th day and in 100% (50/50) by the 14th day, whereas in zone B the corresponding figures were 6% (3/50) and 42% (21/50). Inflammatory manifestations disappeared more quickly in zone A, where on the 14th day these manifestations persisted only in isolated cases, while in zone B moderate changes were recorded in 22% of patients. This correlated with the data of S.F. Forghani *et al*. [15], who demonstrated that hyaluronic acid-based gels accelerated the healing of burn wounds in animal models. The results in zone A confirmed these data and indicated the universality of reparative mechanisms under the influence of hyaluronic acid. Similarly, G. Huerta-Ángeles & E. Mixcoha [16] noted that hyaluronic acid acted as a modulator of inflammation and stimulated reparative mechanisms, which explained the faster normalisation of tissue homeostasis in the present study. The analysis of biopsy samples showed an increase in the mitotic index in the experimental zone, indicating the activation of proliferative activity of cells. This was consistent with the concept of stimulating cell migration by biopolymer matrices [17]. In the review by G. Kaur *et al.* [18], this very mechanism, crucial for rapid recovery of damaged tissues, was highlighted. The quality of the scar formed was characterised by a more uniform structure and less pronounced relief defects. A similar effect was demonstrated in the studies of A.M. Jorgensen *et al.* [19], where the inclusion of hyaluronic acid in composite biomaterials accelerated wound closure and improved the quality of regenerated tissue.

The results of morphological analysis showed that in zone A on the 10th day the mitotic index reached 16.1 ± 4.71%, whereas in zone B it was only 6.8 ± 1.68%. Mitotic activity was also higher in zone A (7.28 ± 2.54%) compared to the control (5.1 ± 1.63%), which indicated a pronounced stimulation of cell proliferation. These data correlate with the results of the clinical study by H. Kim *et al*. [20], which showed that topical formulations with active amino acid- and hyaluronic acid-based components contributed to reduced scarring and the normalisation of cellular activity in patients with burns. Similar effects were also observed in the present clinical observations, where in zone A the formation of higher-quality granulation tissue and a reduced risk of hypertrophic changes were recorded. The study by M. Miastkowska *et al*. [21] demonstrated that the gel form based on hyaluronic acid in combination with nanostructured carriers provided controlled release of active substances, enhancing cell regeneration. In the cohort of patients studied, an increase in proliferative activity of cells was also noted, which was confirmed by morphological indicators and was consistent with the mechanism of controlled release. In the clinical work of R. Yildirim *et al.* [22], it was shown that the use of hyaluronic acid-based dressings for the treatment of superficial facial burns reduced healing time and improved the quality of newly formed tissue, which was consistent with the higher indicators of mitotic activity in zone A. This gave

grounds to consider that the effectiveness of the implant in the treatment of donor wounds had common pathogenetic bases with the successful results of using dressings in clinical practice. Similarly, A.F. Kamdem *et al.* [23] noted the effectiveness of care protocols using hyaluronic acid in children with second-degree burns, where faster recovery and better tissue organisation were observed. In the context of the obtained results, this indicated that Hyalual contributed not only to rapid epithelialisation but also to high-quality tissue remodelling, which was confirmed by histological indicators.

The results of histochemical analysis demonstrated increased activity of antioxidant enzymes in zone A, where the average indicators of SOD increased from 9.11 to 10.03, and catalase – from 28.2 to 36.6 conventional units between the 3rd and 14th day. In zone B, these changes were less pronounced: SOD increased from 7.24 to 8.68, and catalase – from 25.8 to 27.4, which confirmed enhanced antioxidant protection in the implant introduction zone. The increase in antioxidant enzyme activity recorded in zone A reflected more favourable conditions for tissue regeneration. This effect was consistent with the data of S. Zhang *et al.* [24], who emphasised that hyaluronic acid stabilised the cellular microenvironment and helped reduce oxidative stress, creating optimal conditions for cell proliferation. The comparison of these results with clinical observations confirmed that the antioxidant potential of hyaluronic acid was a key factor in forming a favourable course of reparative processes. Similar results were obtained by J.L. Soriano-Ruiz *et al*. [25], who, when creating a thermosensitive gel based on hyaluronic acid, found a significant decrease in the level of reactive oxygen species, which explained faster recovery of tissue structure. In the clinical work of M. Maruccia *et al*. [26], the use of a dermal substitute based on hyaluronic acid in patients with intermediate-deep hand burns provided not only faster epithelialisation but also a lower complication rate, which corresponded to the results obtained in zone A. A similar dynamic indicated the universality of the effect of hyaluronic acid, which was not limited only to donor areas but was also manifested in more complex clinical cases. The study of D. Yoon *et al.* [27] showed that the inclusion of hyaluronic acid in collagen matrices in patients with deep burns reduced inflammatory manifestations and contributed to the orderly formation of collagen fibres. The recorded increase in SOD and catalase activity in zone A was directly related to the well-known antioxidant properties of hyaluronic acid, which determined higher-quality healing results.

The results showed that in zone A by days 10-14 a delicate and elastic scar was formed, with a predominance of mature collagen fibres and minimal cellular infiltration. In contrast, in zone B a less organised structure with thin, chaotically arranged fibres, isolated vessels, and a tendency to rougher scarring was observed. The obtained morphological data were consistent with the conclusions of H. Yang *et al*. [28], who proved that hyaluronic acid contributed to a more ordered organisation of collagen fibres and reduced the likelihood of pathological scar formation in the wound healing process. These results confirmed the observations of M.F. Graça *et al*. [29], who noted that the use of hyaluronic acid-based dressings ensured tissue microrelief alignment, reduced hyperaemia and the risk of hypertrophic changes, which corresponded to even scarring in zone A. Similar results were demonstrated by R. Yang *et al*. [30], who reported that injectable hyaluronic acid hydrogels stimulated angiogenesis, activated fibroblast proliferation, and contributed to the formation of more mature and elastic tissue. In addition, Y. Kawano *et al*. [31] showed that medium-molecular-weight fractions of hyaluronic acid exhibited the greatest effectiveness in regulating the expression of genes associated with collagen synthesis and extracellular matrix remodelling, which ensured high-quality remodelling and reduced the risk of fibrosis. The obtained data confirmed that therapy with the addition of hyaluronic acid and sodium succinate contributed to the formation of a delicate and functionally complete scar, which had better morphological characteristics than in the control zone.

In the study, the tolerability of therapy was assessed as good: in the zone with the use of the injectable implant, no clinically significant deviations in laboratory indicators, pathological changes during objective examination, or severe complications were recorded. Subjective complaints of patients were limited to mild transient itching, which did not require changes in the treatment regimen. In zone B, the tolerability of therapy was assessed as satisfactory, but in a significant proportion of patients on the 14th day itching persisted: moderate in 22 cases and severe in 4, whereas in the experimental zone most participants reported only mild transient sensations. This difference may indicate a longer course of inflammatory processes and less favourable regeneration conditions in the control group. The obtained results are consistent with the data of W. Baranska-Rybak *et al*. [32], who in the work emphasised the need for careful monitoring of delayed reactions after the use of hyaluronic acid preparations. In clinical practice, this was of great importance, since even in the absence of serious complications, monitoring of patients was required for the timely detection of undesirable effects. The authors A. Janovskiene *et al.* [33] in a systematic review also noted that in most cases therapy with the use of fillers was safe, and serious complications were rare. These observations confirmed the general conclusion about a favourable safety profile, which coincided with the data obtained in the experimental sample. The analysis of T. Tamura *et al.* [34] on a large sample (more than 290 thousand cases) confirmed that the frequency of severe complications was low, although attention was required in the case of non-compliance with the administration technique. At the same time, in the work of F. De Francesco *et al*. [35], it was shown that hyaluronic acid when applied topically not only promoted faster healing but also demonstrated a high safety profile without significant side effects.

The obtained results of the clinical study confirmed that the use of an injectable implant based on hyaluronic acid and sodium succinate ensured significantly faster epithelialisation of donor wounds, contributed to the formation of mature connective tissue, and reduced the intensity of inflammatory manifestations. Compared to the control zone, better organisation of collagen fibres, higher levels of antioxidant enzymes, and more pronounced proliferative processes were observed. The tolerability of therapy remained good in both groups, but in the control zone complaints of itching were recorded more often, which reflected less favourable recovery conditions. Taken together, these

data indicate the high clinical and biological effectiveness of the proposed therapeutic strategy in combustiology.

CONCLUSIONS

In the course of the analysis of clinical results, it was established that the use of an injectable implant based on hyaluronic acid and sodium succinate contributed to significantly faster epithelialisation of donor wounds compared to traditional treatment. By the 7th day in zone A, complete epithelialisation was recorded in 12 (24%) patients, while in zone B no case of complete healing was observed. By the 10th day, in the experimental group 39 (78%) wounds had completely healed, and by the 14th day this figure reached 100%, whereas in the control zone complete epithelial recovery occurred in only 21 (42%) patients. The morphological characteristics of wounds in zone A reflected a more favourable course of the process due to faster organisation of collagen fibres and a reduction of the inflammatory component: pronounced manifestations, which at the start were detected in 15 patients, completely disappeared by the end of treatment, while in zone B moderate inflammation persisted in 11 cases. The presence of itching in zone A was mainly mild (41 cases slight and 9 – moderate), whereas in zone B itching was slight in 24 patients, moderate in 22, and severe in 4, which indicated a less qualitative course of reparative processes.

The evaluation of morphological and biochemical indicators confirmed the differences between the groups. In zone A, an increase in the activity of antioxidant enzymes was noted: the level of SOD increased from 9.11 to 10.03 units, and catalase – from 28.2 to 36.6 units during the observation period, while in zone B the increase was less pronounced (SOD increased from 7.24 to 8.68 units, catalase – from 25.8 to 27.4 units). A similar tendency was observed also for the mitotic index: in zone A it increased from 10.6% to 16.1%, whereas in zone B it decreased from 8.8% to 6.8%. Mitotic activity in zone A increased from 5.95% to 7.28%, while in zone B only from 4.1% to 5.1%. Histological studies showed that in the experimental group the formation of mature connective tissue occurred faster: by days 10-14 collagen fibres had an ordered structure, the vascular network was sufficiently developed, and the number of mesenchymal-origin cells had significantly decreased. In group B, immature tissue predominated with chaotically arranged collagen fibres, reduced capillaries, and pronounced cellular infiltration. The tolerability of therapy in both zones was assessed as good, but in the control zone subjective complaints of itching were recorded more frequently, while in zone A no adverse reactions, acute complications, or exacerbations of chronic diseases were observed. Overall, the results confirmed the higher clinical and biological effectiveness of the use of the implant, which ensured complete and high-quality tissue recovery in the shortest possible time. Further studies should be aimed at prospective investigation of the long-term effects of therapy and its comparison with other modern methods of treating donor wounds.

ACKNOWLEDGEMENTS

None.

FUNDING

None.

CONFLICT OF INTEREST

None.

REFERENCES

[1] World Health Organisation. Burns [Internet]. 2023 October 13 [cited 2025 January 30]. Available from: https://www.who.int/news-room/fact-sheets/detail/burns
[2] Dong Y, Cui M, Qu J, Wang X, Kwon SH, Barrera J, *et al*. Conformable hyaluronic acid hydrogel delivers adipose-derived stem cells and promotes regeneration of burn injury. Acta Biomater. 2020;108:56–66. DOI: 10.1016/j.actbio.2020.03.040
[3] Alemzadeh E, Oryan A, Mohammadi AA. Hyaluronic acid hydrogel loaded by adipose stem cells enhances wound healing by modulating IL-1β, TGF-β1, and bFGF in burn wound model in rat. J Biomed Mater Res B Appl Biomater. 2019;108(2):555–67. DOI: 10.1002/jbm.b.34411
[4] Sierra-Sánchez Á, Fernández-González A, Lizana-Moreno A, Espinosa-Ibáñez O, Martinez- Lopez A, Guerrero-Calvo J, et al. Hyaluronic acid biomaterial for human tissue-engineered skin substitutes: Preclinical comparative *in vivo* study of wound healing. J Eur Acad Dermatol Venereol. 2020;34(10):2414–27. DOI: 10.1111/jdv.16342
[5] Korkunda SV, Grigorieva TG, Oleinik GA. Clinical results of the use of injectable hyaluronic acid and sodium succinate implants in burn treatment. Emerg Med. 2014;63(8):64–73.
[6] Wang Z, Li K, Xu Q, Fu G, Li H, Yang W. Preparation and evaluation of chitosan- and hyaluronic acid-grafted pullulan succinate films for skin wound healing. Int J Biol Macromol. 2022;223(A):1432–42. DOI: 10.1016/j.ijbiomac.2022.11.100
[7] Hussain Z, Pandey M, Thu HE, Kaur T, Jia GW, Ying PC, *et al*. Hyaluronic acid functionalization improves dermal targeting of polymeric nanoparticles for management of burn wounds: *In vitro*, *ex vivo* and *in vivo* evaluations. Biomed Pharmacother. 2022;150:112992. DOI: 10.1016/j.biopha.2022.112992
[8] Zhang S, Hou J, Yuan Q, Xin P, Cheng H, Gu Z, *et al*. Arginine derivatives assist dopamine- hyaluronic acid hybrid hydrogels to have enhanced antioxidant activity for wound healing. Chem Eng J. 2020;392:123775. DOI: 10.1016/j.cej.2019.123775
[9] Balanenko MV. Biotechnology of creation and application of biomedical dressings based on a chitosan nanocomposite [Master's thesis]. Kyiv: National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute"; 2024.
[10] Nor NM. Treatment of donor wounds in patients with deep burns using film wound dressings. Sci Collect InterConf. 2021;54:429–34.
[11] Sobina UYe. Bioengineering project for the production of a medical device (reagent) based on hyaluronic acid [Bachelor's thesis]. Kyiv: National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute"; 2023.

[12] Papa G, Mosella F, Meshini G, Sidoti GB, Zaffiro A, Rega U, et al. Improvement of scar quality in split-thickness skin graft donor sites: A single blind randomized clinical trial comparing Rigenase® and polyhexanide versus hyaluronic acid and silver sulphadiazine based dressings. Plast Reconstr Regen Surg. 2023;2(1–2):40–8. DOI: 10.57604/PRRS-188
[13] The World Medical Association. Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects [Internet]. [cited 2025 January 30]. Available from: https://www.wma.net/what-we-do/medical-ethics/declaration-of-helsinki/
[14] International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use ICH Harmonised Guideline: Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2) [Internet]. 2016 [cited 2025 January 30]. Available from: https://www.ema.europa.eu/en/ich-e6-good-clinical-practice-scientific-guideline
[15] Forghani SF, Bagheri T, Naderi Gharahgheshlagh S, Hoveidamanesh S, Ghadimi T, Ghorbanian Kelachayeh S, et al. The effect of hyaluronic acid and iodine complex gel compared to Vaseline on deep second-degree burn wound in rats. Int Wound J. 2024;21(2):e14738. DOI: 10.1111/iwj.14738
[16] Huerta-Ángeles G, Mixcoha E. Recent advances, research trends, and clinical relevance of hyaluronic acid applied to wound healing and regeneration. Appl Sci. 2025;15(2):536. DOI: 10.3390/app15020536
[17] Chornyi O, Fedorenko V, Yaremenko V, Ishchenko O, Gureyeva S. Development of a chitosan polymer based composite haemostatic agent and a method for evaluation of performance. Technol Eng. 2025;26(1):67–78. DOI: 10.30857/2786-5371.2025.1.6
[18] Kaur G, Narayanan G, Garg D, Sachdev A, Matai I. Biomaterials-based regenerative strategies for skin tissue wound healing. ACS Appl Bio Mater. 2022;5(5):2069–106. DOI: 10.1021/acsabm.2c00035
[19] Jorgensen AM, Mahajan N, Atala A, Murphy SV. Advances in skin tissue engineering and regenerative medicine. J Burn Care Res. 2022;44(1):33–41. DOI: 10.1093/jbcr/irac126
[20] Kim H, Kwak I, Kim M, Um J, Lee S, Chung B, et al. Evaluation of a cosmetic formulation containing arginine glutamate in patients with burn scars: A pilot study. Pharmaceutics. 2024;16(10):1283. DOI: 10.3390/pharmaceutics16101283
[21] Miastkowska M, Kulawik-Pióro A, Szczurek M. Nanoemulsion gel formulation optimization for burn wounds: Analysis of rheological and sensory properties. Processes. 2020;8(11):1416. DOI: 10.3390/pr8111416
[22] Yildirim R, Guner A, Cekic AB, Usta MA, Ulusahin M, Turkyilmaz S. Outcomes of the use of hyaluronic acid-based wound dressings for the treatment of partial-thickness facial burns. J Burn Care Res. 2023;44(3):551–4. DOI: 10.1093/jbcr/irz004
[23] Kamdem AF, Parmentier AL, Mauny F, Soriano E. Assessment of care protocol using hyaluronic acid dressing in second-degree skin burns in children. Burns Open. 2021;5(3):118-24. DOI: 10.1016/j.burnso.2021.05.001
[24] Zhang S, Dong J, Pan R, Xu Z, Li M, Zang R. Structures, properties, and bioengineering applications of alginates and hyaluronic acid. Polymers. 2023;15(9):2149. DOI: 10.3390/polym15092149
[25] Soriano-Ruiz JL, Calpena-Campmany AC, Silva-Abreu M, Halbout-Bellowa L, Bozal-de Febrer N, Rodriguez-Lagunas MJ, et al. Design and evaluation of a multifunctional thermosensitive poloxamer-chitosan-hyaluronic acid gel for the treatment of skin burns. Int J Biol Macromol. 2020;142:412–22. DOI: 10.1016/j.ijbiomac.2019.09.113
[26] Maruccia M, Magistri S, Elia R, Maggio G, Giudice G. Hyaluronic acid-based dermal substitute with stromal vascular fraction vs partial thickness skin grafts for the treatment of intermediate- deep burns of the hand: A retrospective case-control study. Ann Burns Fire Disasters. 2024;37(4):305–11.
[27] Yoon D, Cho YS, Joo SY, Seo CH, Cho YS. A clinical trial with a novel collagen dermal substitute for wound healing in burn patients. Biomater Sci. 2020;8(3):823-9. DOI: 10.1039/C9BM01209E
[28] Yang H, Song L, Zou Y, Sun D, Wang L, Yu Z, et al. Role of hyaluronic acids and potential as regenerative biomaterials in wound healing. ACS Appl Bio Mater. 2021;4(1):311–24. DOI: 10.1021/acsabm.0c01364
[29] Graça MF, Miguel SP, Cabral CS, Correia IJ. Hyaluronic acid-based wound dressings: A review. Carbohydr Polym. 2020;241:116364. DOI: 10.1016/j.carbpol.2020.116364
[30] Yang R, Liu X, Ren Y, Xue W, Liu S, Wang P, et al. Injectable adaptive self-healing hyaluronic acid/poly(γ-glutamic acid) hydrogel for cutaneous wound healing. Acta Biomater. 2021;127:102–15. DOI: 10.1016/j.actbio.2021.03.057
[31] Kawano Y, Patrulea V, Sublet E, Borchard G, Iyoda T, Kageyama R, et al. Wound healing promotion by hyaluronic acid: Effect of molecular weight on gene expression and *in vivo* wound closure. Pharmaceuticals. 2021;14(4):301. DOI: 10.3390/ph14040301
[32] Baranska-Rybak W, Lajo-Plaza JV, Walker L, Alizadeh N. Late-onset reactions after hyaluronic acid dermal fillers: A consensus recommendation on etiology, prevention and management. Dermatol Ther. 2024;14(7):1767–85. DOI: 10.1007/s13555-024-01202-3
[33] Janovskiene A, Chomicius D, Afanasjevas D, Petronis Z, Razukevicius D, Jagelaviciene E. Safety and potential complications of facial wrinkle correction with dermal fillers: A systematic literature review. Medicina. 2025;61(1):25. DOI: 10.3390/medicina61010025
[34] Tamura T, Okumura K, Funakoshi Y, Teranishi H. Serious complications of hyaluronic acid fillers – a retrospective study of 290,307 cases. Ann Plast Surg. 2025;94(6):630–3. DOI: 10.1097/SAP.0000000000004327
[35] De Francesco F, Saparov A, Riccio M. Hyaluronic acid accelerates re-epithelialization and healing of acute cutaneous wounds. Eur Rev Med Pharmacol Sci. 2023;27(3):37–45. DOI: 10.26355/eurrev_202304_31320

Гістологічні та гістохімічні зміни при лікуванні ран ін'єкційним імплантом на основі високомолекулярної гіалуронової кислоти та сукцінату натрію: експериментальне дослідження

Світлана Коркунда
Кандидат медичних наук, доцент
Харківський національний медичний університет
61022, просп. Науки, 4, м. Харків, Україна
https://orcid.org/0009-0002-4132-109X

Анотація. Метою роботи була оцінка результативності ін'єкційного імплантату, що поєднує гіалуронову кислоту і сукцинат натрію, для прискорення репаративних процесів донорських ран після аутодермопластики у пацієнтів з глибокими опіками. Дослідження проведено з 1 січня по 30 червня 2014 року у відділенні комбустіології Харківської медичної академії післядипломної освіти на базі Міської клінічної лікарні швидкої та невідкладної допомоги ім. проф. О. І. Мещанінова, де у 50 пацієнтів з донорськими ранами після аутодермопластики порівнювали ефективність ін'єкційного імплантату гіалуронової кислоти з сукцинатом натрію та стандартної терапії за клінічними, морфологічними й біохімічними показниками. Результати показали, що вже на 10-ту добу повне відновлення спостерігалося у 78 % пацієнтів у зоні А (39 із 50), тоді як у зоні В цей показник становив лише 6 % (3 із 50). До 14-ї доби епітелізація завершувалася у 100 % випадків у зоні А, проти 42 % у зоні В (21 із 50). Морфологічний аналіз показав вищий мітотичний індекс у зоні А – 16,1 % проти 6,8 % у зоні В на 10-ту добу, що відображало активніше клітинне оновлення. Біохімічні дослідження підтвердили більш виражене зростання активності каталази у зоні А (з 28,2 до 36,6) порівняно з контрольною зоною (з 25,8 до 27,4). Рубці у зоні А формувалися ніжними та еластичними, тоді як у зоні В переважали щільні й менш організовані структури. Ін'єкційний імплантат гіалуронової кислоти з сукцинатом натрію прискорив загоєння та покращив якість рубців порівняно зі стандартною терапією. Отримані результати можуть бути використані лікарями комбустіологами, пластичними хірургами та клінічними фармакологами у практиці опікових центрів і відділень реконструктивної хірургії для оптимізації лікування донорських ран після аутодермопластики

Ключові слова: донорська ділянка; регенерація; проліферація клітин; колагенові волокна; рубці; антиоксидантні ферменти; переносимість