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CLINICAL CHARACTERISTICS OF POSTOPERATIVE SKIN SCARS IN PATIENTS WITH DIFFERENT CIRCADIAN RHYTHMS USING THE PLACENTA CRYOEXTRACT

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Wound healing is a complex and dynamic process that depends on the coordinated activity of different types of epithelial cells, connective and vascular tissue. In previous studies in our department, the authors described that the healing of purulent wounds is significantly affected by the human chronotype, so patients with the morning type of chronotype tolerated surgery better than patients with the evening type, who were also operated on in the morning. Thus, the formation of a postoperative scar can be affected not only by the location of the wound, prolonged inflammatory process, as well as the time of surgery and the biological rhythm of the patient. From the data presented in the article we can conclude about our study, namely that the cryoextract of the placenta has a positive effect on wound healing not only in the early postoperative period, but also throughout the treatment period.

Key words: biological rhythm, scar, scar prevention, cryoextract, placenta.

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КЛІНІЧНА ХАРАКТЕРИСТИКА ПІСЛЯОПЕРАЦІЙНИХ РУБЦІВ ШКІРИ У ПАЦІЄНТІВ РІЗНИХ ЦИРКАДНИХ РИТМІВ ПРИ ВИКОРИСТАННІ КРІОЕКСТРАКТУ ПЛАЦЕНТИ

Загоєння ран – складний і динамічний процес, який залежить від узгодженої діяльності різних типів клітин епітелію, сполучної та судинної тканини. У попередніх дослідженнях нашого відділення автори описували, що на загоєння гнійних ран суттєво впливає хронотип людини так пацієнти з ранковим типом хронотипу краще переносили операцію, ніж пацієнти з вечірнім типом, які також були прооперовані вранці. Таким чином, на формування післяопераційного рубця може вплинути не тільки місце розташування рани, тривалий запальний процес, а також час операції та біологічний ритм пацієнта. З наведених у статті даних можна зробити висновок про наше дослідження, а саме про те, що кріоекстракт плаценти позитивно впливає на загоєння ран не тільки в ранньому післяопераційному періоді, а й протягом усього періоду лікування.

Ключові слова: біологічний ритм, рубець, профілактика рубців, кріоекстракт, плацента.

The work is a fragment of the research project "Diagnosis, surgical and medical treatment of patients with injuries, defects and deformations of tissues, inflammatory processes of maxillofacial localization", state registration No. 0119U102862, "Introduction of the components of the molecular age into the periodontal tissue in case of burned diseases for the development of methods of prevention and treatment" state registration No 0120U101151.

Intensive development of aesthetic procedures increases every year, which increases the audience that turns to maxillofacial surgeons, in addition, the number of complications after surgery increases, which leads to an increase in the percentage of pathological scars [8, 9].

Wound healing is a complex and dynamic process that depends on the coordinated activity of different cell types in the epithelium, connective and vascular tissue [3, 5].

This process consists of 3 phases which are closely connected among themselves. The first is the inflammatory (or migratory) phase, which lasts only a few days, during which a number of cytokines and growth factors accumulate inflammatory cells, such as macrophages, neutrophils and fibroblasts, for use in the second phase. The proliferative second phase usually lasts for weeks and is characterized by the formation of granulation tissue. Fibroblasts synthesize the framework of the extracellular matrix, which builds a structure that in turn stimulates vascular ingrowth [6, 10, 11].

The last stage is wound closure and this process usually lasts 6–7 months. During this phase, the scar begins to shrink. The number of inflammatory cells also gradually decreases.

Thus, the formation of a postoperative scar can be influenced not only by the location of the wound, prolonged inflammatory process, as well as the time of surgery and the patient's chronotype [7].

The term "chronotype" is used to define the individual characteristics of the circadian rhythm of man [4]. Oscar Okvist, a Swedish psychologist, identified three types of chronotype in his research:

- morning (“larks”);
- intermediate (“pigeons or asynchronous”);
- evening (“owls”).

In his research, he described that patients with the morning type accounted for 15 % of the total number of respondents, with the intermediate – 65 %, and with the evening – 20 %. So people with the morning chronotype are characterized by the fact that they wake up early, active mainly until noon. The intermediate type wakes up 1–2 hours later, but the activity is maintained for the whole day, the evening type – wakes up late, little able to work until noon, but productivity increases until the evening.

Biological rhythms play an important role in adaptation and survival in the environment, it affects not only the mental state, but also reparative functions, and rehabilitation in the postoperative period [15].

In previous studies of our department, the authors described that the healing of purulent wounds is significantly affected by the human chronotype. Thus, patients with the morning type of chronotype tolerated surgery better than patients with the evening type, who were also operated on in the morning [2].

The purpose of the study was to develop the optimal method of prevention of pathological scars in patients after elective surgery in the intraoperative period using placental cryoextract.

Materials and methods. A total of 40 patients took part in the study, who were hospitalized for planned surgical interventions in the head and neck. Patients were interviewed during the hospitalization, as well as questionnaires to determine the chronotype. During our study, we examined and photoregistered patients for 90, 180 and 360 days.

From the obtained survey data, patients were divided into 2 groups, namely:

Group 1 – 20 persons, a group of patients who underwent intradermal injection of the drug “Cryocel – cryoextract of the placenta” (DP “Interdisciplinary Science Center of Cryobiology and Cryomedicine HAH, AMS and Ministry of Health of Ukraine”, Ukraine) during surgery.

The first group consisted of 2 subgroups, which were distributed depending on biological rhythms:

The first subgroup (1.a – with the morning chronotype) consisted of 10 people who underwent surgery in the morning, namely from 08:00 to 12:00. The second subgroup (1.b – with evening chronotype) consisted of 10 patients who underwent surgery after 15:00. Group 2 – control. The control group consisted of 20 patients, who were divided into 2 subgroups, respectively:

The second subgroup (2.a – with the morning chronotype) consisted of 10 people who underwent surgery in the morning, namely from 08:00 to 12:00.

The second subgroup (2.b – with evening chronotype) consisted of 10 patients who underwent surgery after 15:00. All patients in this group were operated according to the classical method without the use of additional preventive measures.

To obtain results and to assess wound healing and the quality of postoperative scar formation, we used the following parameters:

- P-1 – Vascularization (from 0–2 points);
- P-2 – Pigmentation (from 0–2 points);
- P-3 – Height of the scar (from 0–2 points);
- P-4 – Surface (from 0–2 points);
- P-5 – Scar density (from 0–2 points);
- P-6 – Subjective feelings of the patient (itching) (from 0–2 points);
- P-7 – Subjective feelings of the patient (pain) (from 0–2 points).

Results of the study and their discussion. On the 90th day of the clinical study for patients with morning type chronotype were characterized by the following data: in subgroup 1a 2 patients with 6 points, two people with 5 points, 3 points 1 case, 2 patients with 7 points and 4 points 3 persons, using the computer program Microsoft Excel and STATISTICA received an average quality score scale, which was 5.1 ± 0.43 points, in the control group 2a, the points were divided as follows, namely 3 patients with 5 points, 1 person had 6 points, 1 clinical case – 7, 2 patients with 8 points, and 1 person with 10 and 12 points, respectively, the average quality of this subgroup was 7.5 ± 0.74 points.

From the obtained results it is possible to state reliably that the average qualitative indicator of the first group 1a was lower than in group 2a, in this group we used in injection of a cryoextract of a placenta at an intraoperative stage. The difference between the indicators of the first group of the first subgroup (1a) and the second group of the first subgroup (2a) was 32.0 % (fig. 1).

For patients with evening type chronotype 1b subgroup on the 90th day of the clinical study, the following data were observed, in one patient 3 points, in 3 people – 4 points, in 2 patients – 5 points and in 2 clinical cases – 6, in 2 people 7 points, the average quality indicator was 6.8 ± 0.55 . For 2 groups 2 subgroups the result was as follows: one person had a score of 4 points, and one clinical case of 7, 2 patients received 8 points, one patient had a case of 9 points, 2 people – 10, and 1 patient with 11 and 12 points, the average quality of the subgroup was 9.2 ± 0.82 points. From the data obtained after surgery on the scale of evaluation of postoperative scars, we observed that the average quality of group 1b was 26.1 % lower than subgroup 2b.

On the 180th day of the clinical study for patients with the morning type of chronotype were characterized by the following data: in 1a subgroup 1 patient with a score of 2, six people with three points, 4 people with 4 points, the average quality score on the scale was 3.1 ± 0.17 points, in the control group 2a points were distributed as follows, namely three patients scored 4 points, three people had 5 points, 1 clinical case, case 6 and 2 patients with 7 points, the average quality of this subgroup was 5.3 ± 0.36 points. Analyzing the results, we can note the following that the best result was in group 1a, it was in this group in the intraoperative phase used cryoextract of the placenta, which helped to obtain such data. Compared with other subgroups, the results were such that the average quality in group 1a compared with 2a was 41.5 % lower, and the clinical rate of patients with the morning type of chronotype decreased relative to the previous study period by 39.2 %. (fig. 2).

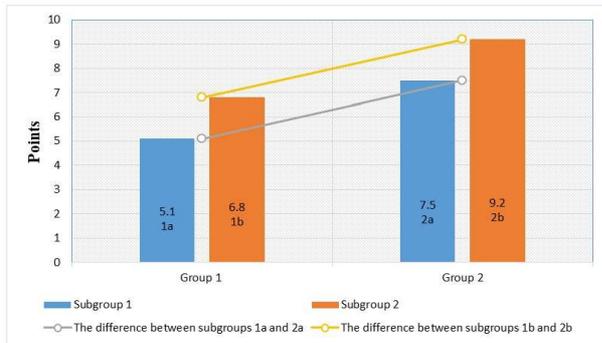


Fig. 1. Mean quality rate for 90 days

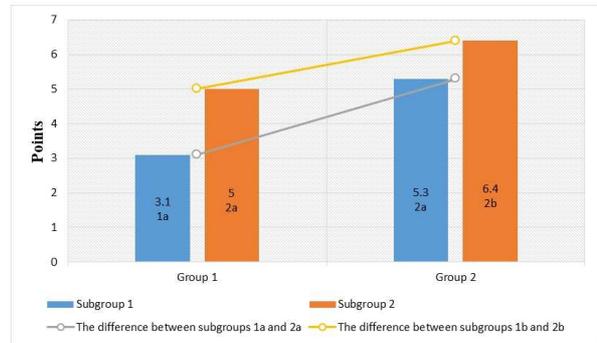


Fig. 2. Mean quality rate for 180 days

For patients with evening type chronotype 1b subgroup on 180 days of the clinical study, the following data were observed, one patient with 3 points, 3 persons with 4 points, 4 patients received 5 and 6 points, 1 person 6, and 1 patient 7 points, mean the qualitative indicator was 5.0 ± 0.47 . For subgroup 2b the result was as follows: two persons with 4 points, 2 clinical cases of 5 points, 2 patients received 6 points, 2 cases with 8 points, 2 persons with 9, the average quality of the subgroup was 6.4 ± 0.61 points. From the data obtained after surgery on the scale of evaluation of postoperative scars, we observed that the average quality of group 1b is correspondingly less than 2b by 21.9 %, and the clinical indicator relative to the 90th day of the clinical trial decreased by 26.5 %.

On the 360th day of the clinical study for patients with morning type chronotype were characterized by the following data: in the first group of the first subgroup 1 person with a score equal to 0, almost all patients, namely 8 cases of 1 point, and 1 person with 2 points, the average quality indicator on the evaluation scale was 1.0 ± 0.14 points, in the control group 2a, received the following data on the distribution of points, namely 2 patients with 1 point, noted 3 people with 2 points, 2 clinical cases with 3 points, 1 patient with 4 points and 1 person with 5 points on the evaluation scale, the average quality of this subgroup was 2.8 ± 0.46 points. From the obtained results it was observed that the best indicator was in 1 group 1

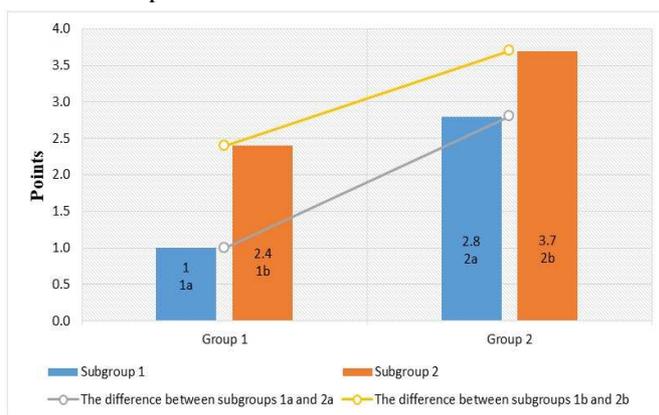


Fig. 3. Mean quality rate for 360 days

subgroup. Comparing the data between the groups obtained the following results, that the indicator in the first group 1 subgroup in comparison with the control group 1 subgroup the indicator was 64.3 % lower (fig. 3). In subgroup 1a, under conditions of treatment with placental cryoextract, there was a significant decrease in the studied index by 67.7 % compared to the previous study period and by 80.3 % compared to the 90th day of the clinical study. In the control group of the first subgroup, this indicator decreased by 62.7 % compared to the 90th day and by 47.2 % for the 180th.

For patients with evening type of biological clock 1b subgroup on 360 days of clinical study observed the following data, two patients 1 point, 3 people 2 points, 2 patients received 3 points, 1 person – 4, and 2 patients 5 points, the average the qualitative indicator was 2.4 ± 0.30 . The clinical rate of patients with evening type chronotype 1b group relative to the previous period of the study, namely 360 days compared with 90 days decreased by 64.7 %, for 180th – 52 %. For subgroup 2b, the result was as follows: one person with 2 points, 4 clinical cases of 3 points, 3 patients received 4 points, 1 case occurred – 5 points and 1 person with 6 points was observed, the average quality of the subgroup was 3.7 ± 0.36 . From the data

obtained after surgery on the scale of assessment of postoperative scars, we observed the following result, that the quality of the first group of the second subgroup is less than the control group 2 subgroup by 35.1 %. For the control group of the second subgroup, the clinical indicator relative to the previous study period decreased by 42.2 %, and compared with the 90th day decreased by 59.8 % (table 1).

Table 1

Characteristics of the clinical state of scars in patients depending on the circadian rhythm

Groups	Day of clinical research		
	90 days	180 days	360 days
1a (n=10)	5.1±0.43	3.1±0.17 * ** *	1.0±0.14 * ** *
1b (n=10)	6.8±0.55	5.0±0.47 *	2.4±0.30 * **
2a (n=10)	7.5±0.74	5.3±0.36	2.8±0.46 * **
2b (n=10)	9.2±0.82	6.4±0.61	3.7±0.36 * **

Notes: * p<0.05 relative to the 90th day of observation; * * p<0.05 relative to the 180th day of observation; * * * p<0.05 relative to the same observation period;

Circadian rhythm plays a fundamental role in the regulation of biological and reparative functions [11]. Roveda and the authors in their research describe the fact that there is a link between the biological clock and diseases [12], such as diabetes, obesity [13]. Chronotype plays an important role in the life of every person [3]. Avetikov and the authors found that wound healing differed depending on the time and method of surgery [1]. Summarizing the data of the clinical study, the best result was obtained by a group of patients with morning chronotype in which placental cryoextract was used. Compared with the control group, which underwent surgical interventions according to the standard method, the difference on the 90th day was 32 %, on the 180th (41.5 %) and on the 360th – 64.3 %. So in patients with morning biorhythm rates were better than in patients, which were operated in the evening, and in patients with evening type of chronotype which were injected with placental cryoextract, we observed the following difference in indicators compared to the control group for the whole period of the study on the 90th day of the clinical study decreased by 26.1 %, on 180th – 21.9 %, on 360th day – 35.1 %. Thus, it can be said that the result of treatment is affected not only by the action of the drug, but also by the time of the operation itself.

Conclusions

1. Patients who underwent placenta cryoextract injection during surgery felt better in the postoperative period. According to the data obtained in relation to the first and control groups, patients with morning chronotype type had better results on 90th days of clinical trial on (32.0 %), 180th (41.5 %) and 360th day – (64.3 %).
2. The healing of the wound and the formation of the scar is influenced not only by the action of the drug, but also by the biological clock, analyzing the data obtained when comparing 2a and 2b subgroups, the following results were observed: on 90th days the difference was 18.5 %, on 180th–17.2 % and on 360th day – 24.3 %.
3. The use of placental cryoextract in the postoperative period in subgroups 1a and 1b significantly reduces the number of relapses in the postoperative period.

References

1. Avetikov DS, Lychman VO, Lokes KP, Steblovsky DV, Bondarenko VV, Shlykova OA, Kaidashev IP. Likuvannya odontohennykh flehmon u khvorykh z urakhuvannyam biorytmu zhyttya. Wiad Lek. 2021;74(6):1346–1348. PMID: 34159917. [in Ukrainian]
2. Barone N, Safran T, Vorstenbosch J, Davison PG, Cugno S, Murphy AM. Current Advances in Hypertrophic Scar and Keloid Management. Semin Plast Surg. 2021;35(3):145–152. doi:10.1055/s-0041-1731461.
3. Belfry KD, Deibel SH, Kolla NJ. Time of Day Matters: An Exploratory Assessment of Chronotype in a Forensic Psychiatric Hospital. Front Psychiatry. 2020;11:550597. Published 2020 Dec 18. doi:10.3389/fpsy.2020.550597.
3. Cardinali DP, Brown GM, Pandi-Perumal SR. Chronotherapy. Handb Clin Neurol. 2021;179:357–370. doi:10.1016/B978-0-12-819975-6.00023-6.
4. Gauglitz GG. Management of keloids and hypertrophic scars: current and emerging options. Clin Cosmet Investig Dermatol. 2013;6:103–114.
5. Mo YW, Jung GY. Surgical Results and Patient Satisfaction After A New Surgical Technique for Asian Medial Epicanthoplasty: A Modified Skin Redraping Method Using a Horizontal Point Incision and Staged 'Y-Shaped' Dog Ear Correction. Ann Plast Surg. 2021;87(4):389–395. doi:10.1097/SAP.0000000000002982.
6. Montaruli A, Castelli L, Mulè A, et al. Biological Rhythm and Chronotype: New Perspectives in Health. Biomolecules. 2021;11(4):487. Published 2021 Mar 24. doi:10.3390/biom11040487.
7. Rodrigues M, Kosaric N, Bonham CA, Gurtner GC. Wound Healing: A Cellular Perspective. Physiol Rev. 2019;99(1):665–706. doi:10.1152/physrev.00067.2017.

8. Roy T, Chavez J, R Reid R. Skin Deep: Perception of Scars After Cranial Vault Reconstruction. *Cleft Palate Craniofac J.* 2021;58(11):1376–1381. doi:10.1177/1055665620984349.
9. Roveda E, Bruno E, Galasso L, Mulè A, Castelli L, Villarini A, Caumo A, Esposito F, Montaruli A, Pasanisi P. Rest–activity Circadian Rhythm in Breast Cancer Survivors at 5 Years after the Primary Diagnosis. *Chronobiol. Int.* 2019;36:1156–1165. doi: 10.1080/07420528.2019.1621330.
10. Roveda E, Montaruli A, Galasso L, Pesenti C, Bruno E, Pasanisi P, Cortellini M, Rampichini S, Erzegovesi S, Caumo A, et al. Rest–activity Circadian Rhythm and Sleep Quality in Patients with Binge Eating Disorder. *Chronobiol. Int.* 2018;35:198–207. doi: 10.1080/07420528.2017.1392549.
11. Schlessinger J, Gilbert E, Cohen JL, Kaufman J. New Uses of AbobotulinumtoxinA in Aesthetics. *Aesthet Surg J.* 2017;37(suppl_1):S45–S58. doi:10.1093/asj/sjx005.
12. Toropov O, Avetnikov D, Lokes K, Steblovsky D, Prikhidko R, Shlykova O, Izmailova O, & Kaidashev I. The influence of different types of chronotype on scar formation during the use of placental cryoextract at the intraoperative stage. *The Medical and Ecological Problems.* 2021. 25(1-2), 22–25. doi.org/10.31718/mep.2021.25.1–2.06.
13. Tu L, Lin Z, Huang Q, Liu D. USP15 Enhances the Proliferation, Migration, and Collagen Deposition of Hypertrophic Scar-Derived Fibroblasts by Deubiquitinating TGF- β R1 In Vitro. *Plast Reconstr Surg.* 2021;148(5):1040–1051. doi:10.1097/PRS.00000000000008488.
14. Yang S, Luo YJ, Luo C. Network Meta-Analysis of Different Clinical Commonly Used Drugs for the Treatment of Hypertrophic Scar and Keloid. *Front Med (Lausanne).* 2021;8:691628. Published 2021 Sep 9. doi:10.3389/fmed.2021.691628.

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PREDICTIVE VALUE OF GENERAL BLOOD ANALYSIS INDICATORS TO PREDICT MORTALITY IN ELDERLY PATIENTS

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Management of acute abdominal diseases at senile and elderly patients, prognosis of the outcomes is very important issue of surgery. The purpose of the study was to identify of mortality predictors among the parameters of periphery blood analyses and evaluate the prognostic value in elderly patients. We have analyzed the outcomes of the 216 elderly patients with acute abdomen, who underwent urgent surgical procedure. Results of our study, acquired by binary logistic regression, Pearson correlation and Area Under the Receiver Operating Characteristics analysis revealed that the hemoglobin and white blood count as good predictors. Survival depending of the cut off values for hemoglobin (11.04 g/dl) and white blood count ($14.05 \times 10^3/l$) was statistically different. Thus, anemia positively, leukocytosis negatively correlates with outcomes. Hemoglobin values and leukocyte counts have a high predictive value for predicting mortality after emergency surgery in elderly and senile patients.

Key words: abdominal cavity, hemoglobin, leukocytes, surgical treatment

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ПРОГНОСТИЧНА ЦІННІСТЬ ПОКАЗНИКІВ ЗАГАЛЬНОГО АНАЛІЗУ КРОВІ ДЛЯ ПРОГНОЗУВАННЯ ЛЕТАЛЬНОСТІ У ХВОРИХ ПОХИЛОГО ВІКУ

Ведення гострих захворювань черевної порожнини у пацієнтів похилого віку, а також прогноз результатів оперативних втручань – одна з найважливіших проблем хірургії. Мета дослідження полягала у виявленні предикторів смертності серед параметрів аналізу периферичної крові та оцінці їхньої прогностичної цінності для пацієнтів похилого віку. Ми проаналізували результати 216 пацієнтів з гострим животом, яким у терміновому порядку було проведено хірургічне втручання. Результати нашого дослідження, отримані шляхом побудови бінарної логістичної регресії та обчислення кореляції Пірсона, показали, що такі параметри, як показники гемоглобіну та лейкоцитів, є хорошими предикторами виживання при оперативних втручаннях у осіб похилого віку. Виживання залежно від порогових значень гемоглобіну (11,04 г/дл) та кількості лейкоцитів ($14,05 \times 10^3/l$) мало статистично достовірні відмінності. Таким чином, анемія позитивно, лейкоцитоз негативно корелює з постоперативними наслідками. Значення гемоглобіну та кількість лейкоцитів мають високу цінність для прогнозування смертності після екстрених операцій у пацієнтів похилого та старечого віку.

Ключові слова: черевна порожнина, гемоглобін, лейкоцити, хірургічне лікування.

The study is carried out within the framework of the dissertation on the subject “Surgical tactics for acute abdominal diseases in elderly and senile people”.

According to the World Health Organization, the number of people in older age groups is increasing worldwide. Statistics show that 125 million people aged 80 and over live in different countries [1]. In connection with the increase in the number of elderly and senile people, the incidence of acute pathologies of the abdominal organs, requiring urgent surgical care, also increases [10, 12, 14].