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BASIC PRINCIPLES OF EXPERIMENTAL SIMULATION OF LIPOSUCTION AND ABDOMINOPLASTY

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According to forecasts, by 2035, 50 % of the world's population will suffer from obesity, and we aimed to develop effective experimental models for the correction of its consequences, in the form of aesthetic defects of the anterior abdominal wall. By following a diet high in carbohydrates and saturated fat, obesity was achieved in 100 % of experimental animals. To ensure the possibility of conditional extrapolation of the obtained results to people, interventions and their combination were carried out in compliance with the basic principles of clinical operative technique. The rate of postoperative complications ranged from 7.1 % to 14.3 %, and changes in anthropometric parameters affected by obesity achieved aesthetic improvement and were characterized by statistical significance ($p<0.05$). The result of this work was a step-by-step algorithm with the possibility of dynamic control over functional, physiological, biochemical and pathomorphological changes in the organism of experimental animals. The insignificant number of postoperative complications and the simplicity of the proposed techniques for performing abdominoplasty, liposuction and their combination allow us to recommend the described techniques as effective mechanisms for experimental research into methods of surgical correction of aesthetic defects of the anterior abdominal wall.

Key words: liposuction, abdominoplasty, obesity, experiment, anterior abdominal wall, aesthetic defects

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ОСНОВНІ ПРИНЦИПИ МОДЕЛЮВАННЯ ЛІПОСАКЦІЇ ТА АБДОМІНОПЛАСТИКИ В ЕКСПЕРИМЕНТІ

Згідно прогнозів, до 2035 року 50 % населення світу страждатиме на ожиріння, розробку ефективних експериментальних моделей корекції наслідків якого, у вигляді естетичних дефектів передньої черевної стінки, ми взяли за мету. Шляхом дотримання дієти із високим вмістом вуглеводів та насичених жирів було досягнуто ожиріння у 100 % дослідних тварин. Для забезпечення можливості умовної екстраполяції отриманих результатів на людей, втручання та їх комбінація проводилась із дотриманням основних принципів клінічної оперативної техніки. Рівень післяопераційних ускладнень коливався від 7,1 % до 14,3 %, а зміни антропометричних показників, що зазнали впливу ожиріння, досягнули естетичного покращення й характеризувався статистичною достовірністю ($p<0,05$). Результатом даної роботи став покроковий алгоритм із можливістю динамічного контролю за функціональними, фізіологічними, біохімічними й патоморфологічними змінами в організмі дослідних тварин. Незначна кількість післяопераційних ускладнень та простота запропонованих технік виконання абдомінопластики, ліпосакції та їх комбінації дозволяють рекомендувати описані методики в якості дієвих механізмів експериментального дослідження способів хірургічної корекції естетичних дефектів передньої черевної стінки.

Ключові слова: ліпосакція, абдомінопластика, ожиріння, експеримент, передня черевна стінка, естетичні дефекти

The work is a fragment of the research project "Strategy of accelerated recovery in the postoperative period during minimally invasive operations on organs of the abdominal cavity, anterior abdominal wall and veins of the lower extremities", state registration No. 0121U109258.

The World Federation of Obesity in its latest report for 2023 states that this pathology is observed in 38 % of the global population, and by 2035 its prevalence will be over 50 %. As for Ukraine, the annual projected growth of the prevalence of obesity in the period 2020-2035 is at the level of 1.6 %, and its economic impact in the European region will be 2.6 % of GDP as of 2035 [15].

Obesity is accompanied by the appearance of aesthetic defects of the anterior abdominal wall (AAW), for the correction of which, along with conservative therapy, liposuction, abdominoplasty or a combination of these techniques are used. According to the latest report of the International Association of Aesthetic and Plastic Surgery, in 2022, 2 303 929 liposuctions and 1 180 623 abdominoplasty were performed in the world and they were among the top five most popular plastic surgeries [3]. It is worth noting that the number of these surgical interventions increased by 21.1 % and 19.1 %, respectively, which, among other things, may be caused by an increase in the weight of an average adult and a teenager over 16 years of age by approximately 1.5 kg, as a result of the introduced restrictions caused by the COVID-19 pandemic. A decrease in physical activity, an increase in the consumption of processed food, especially among children, will only worsen the situation with the prevalence of obesity in the future and will force to adjust the modeled prognostic trends in a larger direction [15].

The study of methods of correction of aesthetic defects of the AAW in patients with obesity remains an urgent problem not only due to the impossibility of eliminating the latter by lifestyle changes, but also due to the high risk of postoperative complications, the level of which, according to a number of studies, can be up to 46.5 % [10].

Randomized, comparative, prospective trials of surgical intervention data in humans are very rare, expensive, and have many ethical problems. In this situation, experimental models can become a solution, because their stability and reproducibility allow us to achieve a significant understanding of changes and methods of influence of various operative interventions [4]. When choosing an object of research, a strong argument in favor of rats is the conditional extrapolation of results to humans due to morphological similarity. The possibility of dynamic control not only of functional, physiological and biochemical processes in the body of an experimental animal, but also of pathomorphological changes after surgical interventions, significantly expands the possibility of creating and testing new or a combination of already existing methods of surgical correction of aesthetic defects of the AAW with the use of experimental animals [5, 14]. At the same time, when analyzing literary sources, it was not possible to find specific answers regarding the optimal methods of their modeling.

The purpose of the study was to develop effective models of liposuction, abdominoplasty and the method of their combination in an experiment.

Materials and methods. A two-stage experimental study was planned to realize the set goal. First, obesity was modeled, and then, surgical interventions were performed and their effectiveness was investigated. 98 sexually mature female white inbred rats aged 120 days were selected, from which 2 groups were formed by a blind method: control (n=7) and experimental (n=91).

During the research, the basic principles of the Council of Europe Convention on the Protection of Vertebrate Animals Used in Experiments and Other Scientific Purposes were observed [6].

Modeling of obesity in experimental groups was carried out in two stages. For 8 weeks, drinking water was replaced with a 60 % fructose solution, which was combined with a balanced diet. After the completion of the first stage, during the next 8 weeks, saturated fats in the form of pork lard in the volume of 45 % of solid feed were additionally introduced into the diet of experimental animals. To control the dynamics, the anthropometric parameters of the experimental animals were measured every 4 weeks (abdominal circumference (AC), chest circumference (TC), body length (BL) and the body mass index (BMI), Lee index and the coefficient of body weight gain (CBWG) [1].

To carry out the second stage of modeling, 6 groups (n=14 in each) were formed from the experimental group using a blind method, which were distributed as follows: No. 1 – liposuction; No. 2 – abdominoplasty; No. 3 – one-time liposuction with abdominoplasty; No. 4 – liposuction and delayed abdominoplasty after 3 days; No. 5 – liposuction and delayed abdominoplasty after 6 days; No. 6 – liposuction and delayed abdominoplasty after 12 days; control group No. 7 (n=7) – no interventions.

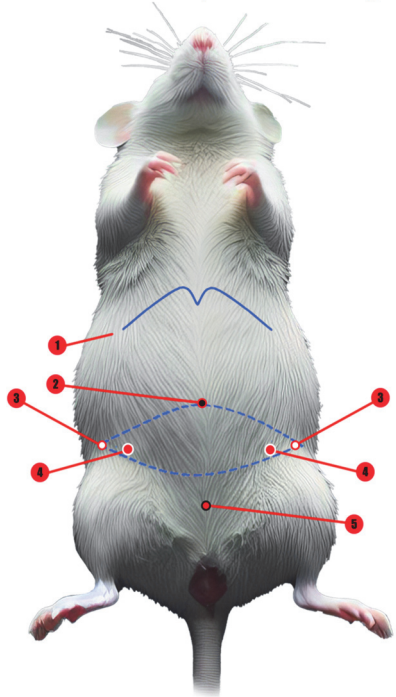

Fig. 1. Landmarks during operative interventions 1 – costal arches and the edge of the xiphoid process; 2 – the middle of the distance between the distal edge of the xiphoid process and the outlet of the urethra; 3 – extreme lateral points of tibial folds; 4 – holes for liposuction; 5 – opening of the urethra.

All operative interventions were performed in compliance with the principles of asepsis under ether anesthesia, marking was performed after determining anatomical landmarks (Fig. 1). Abdominoplasty was started with a horizontal incision on the front abdominal wall between the extreme lateral points of the tibial folds on both sides 1 cm above the location of the opening of the urethra to avoid its injury. The skin flap was mobilized to the costal arches and xiphoid process with the help of scissors and tweezers, after which a transverse abdominoplasty was performed with excision of the skin flap, the upper point of which was pre-marked midway between the distal edge of the xiphoid process and the urethral outlet. The surgical intervention was completed by applying layer-by-layer sutures. To perform liposuction of the anterior abdominal wall with the help of a sterile syringe, it was infiltrated with Klein's solution in a volume of 10 % of the weight of the experimental animal, followed by two horizontal incisions 5 mm long and 1 cm medial from the extreme lateral points of the tibial folds on both sides and dissection with the aim of reduction of traumatization of surrounding tissues. A pre-designed and custom-made blunt-ended smooth cannula with a diameter of 4 mm and a portable medical aspirator were used for aspiration of adipose tissue. After the aspiration process was completed, the wounds were sutured in layers. Postoperative results were evaluated on the 3rd, 6th, and 12th day, which is due to the principles of conditional extrapolation of the time scale of experimental animals to humans.

Statistical processing of the data obtained during the experiment was carried out using Microsoft Excel 365 software and an additional package of XrealstatsX add-ons. To determine the normality of the distribution, d'Agostino-Pearson and Shapiro-Wilk tests were performed for α=0.05 in six groups for three periods (3rd, 6th and 12th postoperative day). Since, according to the analysis, the distribution in most samples was different from the normal one, the Mann-Whitney U-test for two independent samples was used to assess the reliability of the data difference.

Results of the study and their discussion. To analyze the results of the experiment, the development of obesity was evaluated at the first stage, and at the second stage, the volume of fat aspirated during liposuction, the size of the skin flap removed as a result of abdominoplasty, changes in anthropometric data of the experimental animal (weight and AC), as well as the characteristics of the scar and the presence of postoperative complications.

After the obesity simulation was completed, the following changes in anthropometric indices were obtained (Table 1).

Table 1

Comparison of anthropometric characteristics of experimental animals from the control and experimental groups before and after modeling obesity

	Control group		Experimental group	
	Before	After	Before	After
Weight, g	132.86±2.48	157.57±1.99	132.52±2.58	225.08±23.56
BL, cm	18.67±0.78	18.67±0.78	18.55±0,74	18.55±0.74
TC, cm	9.99±0.23	9.99±0.23	9.98±0.2	12.09±0.98
AC, cm	10.47±0.28	10.54±0.28	10.56±0.23	13.89±0.98
BMI, g/cm^2	0.38±0.03	0.45±0.04	0.38±0.03	0.65±0.05
Lee index, g/cm	273.7±11.83	289.73±12.86	274.34±12.44	327.66±9.96
CBWG, g/kg	0	20.85±1.31	0	78.3±20.21

In the experimental group, the weight of the animals increased by 69.91±18.04 %. BL remained unchanged, however, AC increased by 31.53±9.84 % and TC increased by 21.2±9.56 %, which can be explained by the increase in fat “pillows” present at the measurement points. BMI increased by 70.56±18.51 % and Lee's index increased by 19.26±4.16 %.

In the control group, the average weight of rats increased by 18.62±1.17 %; BL and TC remained unchanged during the entire period, which can be explained by the selection of only adult sexually mature rats that have already reached their maximum indicators of these anthropometric data; AC increased by 1.64±0.68 %; BMI increased by 18.62±1.17 %; the Lee index increased by 5.85±0.35 %. Despite the absence of any kind of intervention or therapy, some of the indicators of the control group also increased dynamically, which was caused by providing better housing conditions and a balanced diet after the start of the experiment.

The result of modeling at the first stage of the study was the presence of obesity in 100 % of the animals of the experimental group, which is confirmed by the value of the Lee index above 310 g/cm. In addition, CBWG in this group was 3.76 times higher than the similar indicator in the control group as a result of the simulation. After conducting a comparative analysis of the obtained data after the completion of the first stage in the experimental group, a statistically significant difference ($p<0.001$) of all the studied indicators was obtained, which confirms the effectiveness of this method of modeling obesity.

During the second stage of the experiment, operative interventions were carried out according to the selected groups. The average duration of liposuction was 28.4±1.7 min, abdominoplasty – 24.8±2.3 min, and their simultaneous performance – 52.7±3.1 min.

The amount of aspirate obtained during liposuction was 4.95±0.5 ml, which is equivalent to 1771.12±43 ml in a person weighing 80 kg. After the sedimentation process was completed, it was established that the volume fraction of fat in the aspirate was 40.5±1.98 % and equal to 2±0.18 ml.

The skin-fat flap, which was removed during abdominoplasty, was 4.73±0.38 cm long and 1.84±0.07 cm wide.

When measuring dynamic changes in anthropometric indicators on the 3rd, 6th, and 12th postoperative day, the following data were obtained (Table 2).

Indices of weight and AC of experimental animals have a steady tendency to decrease during the second stage of the experiment in all experimental groups, except for the control group. There is also a direct strong correlation between the duration of the postponement of abdominoplasty in combination with liposuction and the mass index of body weight loss (r=0.62) and reduction in abdominal girth (r=0.63). A simple linear regression was used to check the dependence of the decrease in anthropometric indicators on

the time since the operation. The obtained results confirmed a statistically significant relationship between the studied indicators (R^2=0.38, F(df)=6.16, p=0.032). The regression coefficient for anthropometric data was 2.35 with a standard error of 1.44.

Table 2

Dynamic changes in the anthropometric parameters of experimental animals in the postoperative period

Group	Weight reduction in % Me (LQ;UQ)			AC reduction in % Me (LQ;UQ)		
	3rd day	6th day	12th day	3rd day	6th day	12th day
1	2.3 (1.9; 2.4)	4.8 (4.6; 4.9)	8.1 (7.8; 8.4)	2.2 (1.8; 2.5)	5 (5; 5.4)	8.6 (7.9; 9.5)
2	2.4 (1.8; 2.6)	4.5 (4.3; 5.1)	6.9 (6.5; 7.3)	2 (1.8; 2.5)	4.3 (3.7; 5)	8.6 (8.5; 8.6)
3	3.5 (3.4; 3.6)	6 (5.8; 6.4)	8.9 (8.7; 9.1)	2.8 (2.6; 3.2)	6.4 (6.1; 6.8)	9.3 (9.1; 9.3)
4	4.5 (4.2; 4.9)	6.8 (6.5; 7.3)	9.4 (9.3; 9.5)	4.2 (3.6; 4.3)	6.4 (5.7; 6.4)	10 (9.8; 10)
5	7.2 (6.6; 7.8)	8.8 (8; 9.2)	10.5 (10.4; 10.6)	6.4 (6.1; 6.9)	8.2 (8.2; 9.2)	10.4 (10; 10.7)
6	10.3 (9.9; 10.5)	11.6 (11.1; 11.7)	13.1 (12.8; 13.3)	10.4 (9.9; 10.4)	12.1 (11.8; 12.1)	12.9 (12.5; 12.9)

Statistical analysis demonstrated the absence of a significant decrease in weight ($p>0.05$) of experimental animals compared to the control group based on the results of the second stage of the experiment in groups 1-4 and a statistically significant decrease ($p<0.05$) in groups 5-6. However, the decrease in AC was confirmed by the presence of a statistically significant difference in all studied groups, except for group 4 (p=0.06).

Analysis of the structure of postoperative complications showed that suppuration of postoperative wounds was observed in 7.1 % of experimental animals in groups 1, 2, 5 and 6, as well as in 14.3 % of group 3, and was the most frequent complication, the correction of which was carried out with the help of sanitation and treatment with betadine solution. Seroma was diagnosed in 14.3 % of animals of group 3 and in 10 % of groups 2 and 4, and for its elimination a puncture was performed followed by aspiration of the contents. However, these complications were insignificant, and as a result, all experimental animals continued to participate in the experiment.

Despite the fact that rodents are most often used in experimental models, there are controversial materials in the literature regarding the extrapolation of experimental data for clinical application, and some researchers even lead a discussion about the “crisis of reproducibility” in biomedical research [12].

A group of authors led by Nagendrababu V note that one of the most frequent reasons for the presence of errors that cause internal inconsistency is a lack of stable reporting and measurements of anthropometric indicators, in particular, the weight and age of experimental animals [11]. At the same time, the research team of Agoston D claims that in order to optimize the conditional extrapolation of the results and their use in clinical practice, the difference between the time scales of rodent and human life should be taken into account [2].

In the process of finding solutions that could help minimize the mentioned risks, we highlighted the following key points:

– in order to ensure a controlled approach to the research methodology, to obtain an objective assessment of the effect of the interventions and to promote the increase in the reliability and reproducibility of the experimental results, the points of the guideline based on the recommendations of the International Council for Experimental Science and developed by Percie du Sert N with co-authors [13];

– to take into account the difference between the time scales of rodents and humans, during the selection preference was given to sexually mature rats, whose age, after simulating obesity, fell into the range of 150-300 days, which, according to the data of the research team led by Ghasemi A, corresponds to the age of a human 25–40 years [8];

– for stable reporting every 4 weeks, the studied anthropometric parameters of the experimental animals were measured and the BMI, Lee index, and CBMG were calculated based on them, and the postoperative results were evaluated on the 3rd, 6th, and 12th day with the collection of biological samples for morphological and biochemical analysis.

In contrast to the literature data on the extrapolation of research results in clinical practice, Casal D and co-authors point to the similarity of the vascular system of the AAW of rats and humans [5], and a group of researchers led by Villegas-Alzate F in their publication note that anatomically the physiological features of the muscular system of the AAW in the rat are similar to those of humans and this, as a result, allows the use of an operative technique similar to that in humans, which was carried out [14].

As a result of liposuction, 4.95±0.5 ml of aspirate was obtained, the volume fraction of fat in which was 40.5±1.98 % and equal to 2±0.18 ml. Taking into account the average weight of the rat, this amount of aspirate is equivalent to 1771.19±43.08 ml of an adult patient weighing 80 kg. Such data are quite comparable to the results of an experimental study by a team of authors led by Lim KR [9].

When reviewing scientific publications, no specific information was found regarding the size of the skin-fatty flap, which is removed during abdominoplasty in rats, because they completely depend on the anthropometric data of the experimental animal and the distance between generally accepted anatomical landmarks.

During the analysis of changes in anthropometric data, their dynamic decrease was observed in each of the experimental groups, and the longer the period of abdominoplasty postponement was in the groups with a combination of techniques, the greater was the difference with the initial preoperative indicators when they were measured on the 12th day after the last surgical intervention. This trend can be explained by the effectiveness of such a combination, which, together with the influence of catabolic processes in the body of experimental animals, makes it possible to obtain a better effect from these surgical interventions. Similar data were obtained with the results of a group of researchers led by Villegas-Alzate F, who, as a result of the simultaneous combination of liposuction and abdominoplasty, obtained a 9.2 % reduction in the weight of the experimental animals as of the 21st postoperative day, which is comparable to our results in a similar group – 8.9±0.4 % on the 12th postoperative day [14].

Analyzing postoperative complications, we came across a publication by the team of authors led by Villegas-Alzate F, which provide data on the most frequent complications after modeling the correction of aesthetic defects of the anterior abdominal wall: tissue necrosis, non-healing of postoperative wounds, gray matter, and disposition of the scar [14]. We obtained comparable results, as non-healing of postoperative wounds and seroma were the only complications present in experimental animals.

Conclusions

1. Sufficient safety profile (level of postoperative complications up to 14.1 %) and simplicity of the proposed techniques for performing abdominoplasty and liposuction in the experiment, as well as the possibility of dynamic control over functional, physiological, biochemical and pathomorphological changes in the body of experimental animals and the validity of conditional extrapolation of the obtained results for people, allow to recommend the described methods as effective mechanisms of experimental research of methods of surgical correction of aesthetic defects of the anterior abdominal wall.

2. The use of the proposed experimental models will facilitate the development of an optimal algorithm for the combination of operative interventions in clinical practice and the minimization of postoperative complications while preserving the indicators of aesthetic improvement.

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