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ANTIINFLAMMATORY ACTIVITY OF LEFLUNOMIDE FOR COMBINED APPLICATION WITH CELECOXIB AND AMLODIPINE IN ADJUVANT ARTHRITIS AGAINST THE BACKGROUND OF ARTERIAL HYPERTENSION

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The purpose of the work was to study the anti-edema activity of leflunomide in combination with celecoxib and amlodipine under the conditions of experimental rheumatoid arthritis associated with arterial hypertension. Experiments were carried out on sexually mature nonlinear white rats of both sexes with a starting weight of 201.56 ± 2.42; (n = 174). Experimental RA was induced by subcutaneous injection of the complete AF into the plantar part of the posterior (left) limb. The drugs under study were: leflunomide (LF), 20 mg tablets; celecoxib (CC), 100 mg capsules, and amlodipine (AM), 10 mg tablets. Under the conditions of experimental RA that developed against the background of AH, there was a significant increase in the foot volume by 136-147 % (from 1.16 RU to 2.74 RU) compared to the values in animals of the intact group. Combined application of CC with LF against the background of the combined pathology led to a significant, compared to data in animals with a combined pathology and in rats treated with LF only, reduction in foot volume by 14.4-45.2 % and by 18-41.4 % respectively at all terms of observation. Particularly significant this effect was in the acute development of AA against the background of hypertension. With combined use of leflunomide, celecoxib and amlodipine only in the acute period of inflammation that develops against the background of arterial hypertension, an anti-edema effect is recorded at the level of 12%, which is significantly reduced in other observation periods.

Key words: leflunomide, anti-edema, rheumatoid arthritis, arterial hypertension, comorbid pathology.

The work is a fragment of the research project "Efficacy of cardioprotective and gastrointestinal immunity of immunosuppressants and calcium antagonists of dihydropyridine series in combination with rheumatoid arthritis against the background of arterial hypertension", state registration No. 0117U006446.

Treatment of comorbid states, which prevalence reaches over 60% in young patients and grows with age, is one of the most urgent tasks of modern medicine. Pharmacological correction of rheumatic diseases associated with cardiac pathology, namely with rheumatoid arthritis (RA), combined with arterial hypertension (AG), involves the use of drugs belonging to various pharmacotherapeutic groups [2, 4, 6]. For treatment of RA itself, the disease-modifying agents (gold preparations, cytostatics, antibiotics, sulfonamides, medicinal immuno-biological preparations - immunosuppressors of synthetic and biological origin) and symptomatic medicinal products (non-steroidal anti-inflammatory drugs (NSAID) and glucocorticoids) are used [2, 14]. For the purpose of pharmacological correction of hypertension, antihypertensive drugs of various pharmacological groups, namely beta blockers, diuretics, angiotensin II receptor antagonists, ACE inhibitors, calcium channel blockers are used. It is known that one of the promising fields of RA therapy is the use of immunobiological drugs [5, 11, 14].

Cytostatic drugs, or so-called immunosuppressants (methotrexate, azathioprine, cyclophosphan, chlorobutin, leukeran, etc.) are used in patients with progressive severe RA [11, 13]. Methotrexate in rheumatoid arthritis has become the gold standard of treatment in many countries, because it quickly stops the effect of hyperactive immunity on the joint elements, inhibits the development of acute rheumatism, helps maintain the limbs function. At the same time, its insufficient efficacy in numerous patients, a number of side effects, in many cases intolerance, as well as complications due to interaction with drugs of other pharmacotherapeutic groups used concomitantly for the treatment of associated pathology, in particular cardiac, justified the expediency of searching new drugs. Thus, specifically for the RA treatment, leflunomide (LF) immunosuppressor was developed and implemented [1, 3, 4, 15].

As a rule, using immunosuppressors of synthetic origin is accompanied by the assignment of NSAID. The combination of analgesic, anti-inflammatory and antipyretic effects in NSAID provides them with one of the first places in the clinical application rate for pain syndromes of different genesis and justifies the feasibility of their assignment in RA. Significant progress in RA pharmacotherapy is due, in particular, to the introduction of selective cyclooxygenase inhibitors (COX-2) in the clinical practice. Special attention shoud be paid to preparations of the coxibs group. Celecoxib (CC) is the most commonly used for treatment of the pain syndrome (including RA) and is quite safe in compliance with the dosage and regimen. Its efficacy has a high degree of evidence obtained in clinical trials. At the same time, data on the pharmacodynamic interaction of synthetic origin immunosuppressors and coxibs against the background of RA, as well as in combined pathology - RA and AH - is not sufficient.

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In the world, the most extensive combined use of NSAID with antihypertensive drugs is observed. This is due to various reasons: NSAID is characterized by pro-hypertensive effect [2] and more than half of patients with RA who use NSAID are registered with AH; arterial pressure destabilization is often recorded against the background of RA; actually pain syndrome on the background of RA can lead to hypertension; RA often occurs against the background of AH [11, 12].

Amlodipine (AM) has the widest use in cardiology as a hypotensive drug. It leads to a smooth decrease in blood pressure without changing the heart rate, it is metabolically neutral and reduces endothelial dysfunction due its effect on the NO system [3, 7].

Studies devoted to determination of the efficacy and safety of immunosuppressors used in combination with calcium antagonists of the dihydropyridine series and selective cyclooxygenase 2 inhibitors at different phases of the inflammatory process development under the conditions of combined pathology (RA with AH) were not carried out.

The purpose of the work was to study the anti-edema activity of leflunomide in combination with celecoxib and amlodipine against the background of experimental rheumatoid arthritis associated with arterial hypertension.

Materials and methods. The experiments were carried out on sexually mature non-linear white rats of both sexes with the starting weight of 201.56 ± 2.42 g (n = 174), which were kept on a standard balanced diet in vivarium under the conditions of free access to food and water at the temperature 20-22^{o} C and the relative humidity of 40-60 %. The studies were carried out in compliance with the requirements of the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg, 1986).

Animals were divided into 8 groups: group 1 (n = 10) - intact animals kept in the laboratory in cages during the same period as animals of other groups. The rest of the animals (n = 164) were modeled AH, or experimental RA - adjuvant arthritis (AA), or comorbid pathology - AG + AA. Thus, group 2 (n = 15) were rats, which reproduced the RA model by a single administration of the Freund's complete adjuvant (AF, control for AA), and animals of this group were not subject to saline loading at all.

In animals (n = 134) AH was induced by salt loading in the conditions of drinking water replacement with 1% solution of sodium chloride with free access to it during 21 days [30, 33, 36, 43]. After 21 days the registration of the blood pressure was performed by means of the sphygmomanometric method using Ugo Basile sphygmomanometer (Italy), blood pressure was determined in animals subjected to saline loading (n = 134). For the next study, only those rats (n = 90) who demonstrated hypertension (elevated blood pressure above 10-12% of the baseline value) were selected.

Following randomization of rats with AH, appropriate groups of animals were formed, each including 8 female and 7 male rats. Group 3 included 15 rats with AH, which were continued salt loading and were not apply any treatment to (control for AH). Group 4 consisted of 15 specimens who, against the background of AH (21 days after the beginning of AH model formation), were given a single dose of complete AF, thus forming a comorbid state - AH + AA under prolonged salt loading (control of the comorbid pathology). Therapeutic measures for animals of group 4 were not taken.

The fifth, sixth, seventh and eighth groups included animals (15 rats in each group), which, against the background of the comorbid state development and salt loading prolongation, were administered LF, LF and AM (LF + AM), LF and CC (LF + CC) and LF, CC and AM (LF + CC + AM) respectively. The ninth group included 15 rats, which were injected LF against the background of AA (animals without AH).

Experimental RA was induced by subcutaneous administration of complete AF into the plantar part of the posterior limb (left), which is one of the most adequate agents capable of reproducing the above mentioned pathological condition, reflecting the immune mechanisms of RA pathogenesis [6, 15]. The mechanism of development of AA induced by administration of complete AF, clinical symptoms, and effects of drugs are most similar to those observed in humans in RA [11, 15].

The studied drugs were: leflunomide (LF), 20 mg tablets; celecoxib (CC), 100 mg capsules and amlodipine (AM), 10 mg tablets.

CC and AM medicinal products were used daily in therapeutic doses, in terms of animals: for CC - 15 mg / kg, for AM - 1.5 mg / kg of the animal body weight. The use of LF was as follows: the first three days - at the dose of 15 mg / kg (shock dose), and then - daily at the dose of 1.5 mg / kg (therapeutic dose). All drugs were injected through a special metal probe into the stomach in 1% starch mucilage 1 time per day (from 10 to 13 o'clock).

Treatment of animals began 7 days after the introduction of AF (acute period of AA). Under the conditions of combination therapy using drugs of various pharmacotherapeutic groups (LF with AM, or LF with CC, or LF with CC and AM), drugs were also administered daily, once a day, but one by one, at

the intervals of 30 min. The LF use duration is due to the fact that the first clinical effect of this drug should be expected in 2-4 weeks, and the pronounced effect - in 6-8 weeks.

Registration of the foot volume was performed with Ugo Basile plethysmometer (Italy) in intact rats (animals of all groups, basal data), 21 days after the beginning of salt loading (in rats with pre-formed AH), and also after 1, 2, 4, 6 , 8, 9 weeks after AF administration and the use of drugs.

Anti-exudative (anti-edema) activity (AEA) of LF, CC, AM for independent and combined use was calculated as the ratio of the difference between foot volume in untreated and treated animals with comorbid pathology to the foot volume in untreated rats and was expressed as a percentage.

Data Processing. Normality of distribution was assessed by the Shapiro-Wilk (W) criterion. The data is presented as a mean arithmetic and standard error of the mean value representativeness. The reliability between the mean values in two samples was determined by the Student's t-test in normal distribution. Statistically significant differences were considered at a significance level of at least 0.05.

Results of the study and their discussion. In the process of AH formation by salt loading (during 21 days), the volume of foot in rats was gradually growing by 11-14.9 % (table 1) compared to the initial data. In the intact animals, the similar degree changes of the studied index were registered. In fact, the same increase in the foot volume of intact animals and in rats in the AH formation can testify to the rats growth. Under the conditions of AA development, a significant increase in the volume of the injured (left) foot of rats was registered, starting from the 1st day after the AF administration. 7 days after the inflammatory process induction, the foot volume in rats increased by 91% as to this index, which was inherent in intact animals (table 1), and was twice as large during the entire observation period (table 2).

Table 1

Volume of foot (RU, M ± m) in white rats in arterial hypertension formation (within 21 days) and in experimental rheumatoid arthritis development

Group, number of animals (n)	Term of observation, day			
	initial data	7	14	21
Intact	1.03±0.04	1.12±0.09	1.13±0.10	1.15±0.04
AH	1.01±0.03	1.12±0.06	1.14±0.05*	1.16±0.05*
AA	1.03±0.07	2.14±0.12*	2.25±0.15*	2.30±0.15*

Note. * - p <0.05 compared to the given index in intact animals for the corresponding period of observation.

In the animals of group 3 (AH control) during the following 60 days, under the conditions of the saline load continued, the foot volume was gradually growing and exceeded the values recorded in the intact group animals by 14% after 80 days from the beginning of the salt loading and by 25.9 % of the value registered on the 21st day of AH (table 2). Consequently, hypertension leads to edema of limbs in rats, which increases with the duration of saline loading.

Under the conditions of experimental RA that developed against the AH background, there was a significant increase in foot volume by 136-147 % (from 1.16 RU to 2.74 RU) compared to values in the intact group animals, and these changes were observed in all periods of the actual inflammatory process development, even in the period of its extinction, which indicates an increase of the limbs edema in the comorbid state (table 2). It is likely that AH contributed to a more significant increase of the limb edema just in the acute period (up to 14 days) since AA induction, indicating an increase of this index by 20.7% compared to that registered in animals with AA only within the same period.

The CC drug did not completely eliminate the limbs edema in rats, but significantly reduced it - by 16-21 % (from 2.74 to 0.93 RU) compared to the data recorded in the control animals with the combined pathology and those with AA only. The anti-inflammatory effect of CC was characterized by stability throughout the observation period.

In general, the results of our study are consistent with the data of other researchers.

LF immunosuppressor against the background of a comorbid state showed significant anti-edema activity compared to this index in animals with AA and lost it in the combined pathology, as evidenced by the foot volume increase within the period from 28 to 60 days. [1, 4, 13].

Combined application of the CC with LF against the background of a combined pathology led to a significant, compared to data in animals with a combined pathology and in rats treated with LF only, reduction in the foot volume by 14.4-45.2 % and by 18-41.4 % respectively at all terms of observation. This effect was particularly significant in the acute development of AA against the background of AH. Thus, in the conditions of pharmacodynamic interaction of NSAID and immunosuppressors against the background of AH associated with AA, a growth of the anti-edema activity is recorded. Obviously, LF potentiates the anti-edema activity of CC. Probably, in the combined of LF and CC the anti-edema activity of LF is “recovered”, which did not manifest itself against the background of a comorbid state. [2, 3]. Under the conditions of comorbidity, AM

did not exhibit anti-edema activity, but, on the contrary, substantially increased the edema of the limbs in rats compared to unlabeled animals with a comorbid state and with AA (table 2). An unexpected result was obtained by the interaction of LF with AM in the context of associated pathology. In spite of the fact that LF lost its anti-edema activity and, like AM, increased the limb edema in animals due to associated pathology, the combined use of these agents resulted in an anti-edema effect characterized by a decrease in foot volume by 9-18 % compared to values in animals treated with LF only [5]. Combined use of the three studied drugs did not normalize the foot volume in animals with associated pathology - AH with AA, although it reduced the foot volume by 9-14 % compared to the rate recorded in animals treated with LF only. Strengthening the anti-edema effect due to the use of three drugs was not observed. On the contrary, it was significantly lower than that recorded in animals treated with CC only in the period from the 28th to the 60th day. Probably, the use of LF and AM decreased the anti-edema effect of CC, and CC contributed to the manifestation of anti-edema effect of LF and AM. Mechanisms of LF interaction with CC and LF with AM on the background of AA associated with AH are currently unknown and require special further studies [2, 7].

Table 2

Foot volume in rats (RU, M ± m) under the conditions of mono- and combination therapy with Leflunomide, Celecoxib and Amlodipine and anti-edema activity (%) of drugs against te background of rheumatoid arthritis associated with arterial hypertension

Group, index	Term of observation, days&				
	Data on the 21st day ‴	14 (21+14)	28 (21+28)	42 (21+42)	60 (21+60)
1	2	3	4	5	6
Intact	1.15±0.04	1.16±0.07	1.18±0.05*	1.20±0.03*	1.28±0.10*
AH, % (до інт.)	1.16±0.10	1.19±0.04* +2.6	1.23±0.05* +3.5	1.32±0.08* +14	1.46±0.1* +26
AA, % (до інт.)	2.30±0.15*	2.27±0.07* +98.3	2.50±0.09* +111.9	2.44±0.14* +103.3	2.40±0.11* +87.5
AH+AA, % (to int.) % (to AA)	1.16±0.10	2.74±0.11* +136 +20.7	2.52±0.15* +147 +0.8	2.44±0.2* +141.6 0	2.43±0.09*♯ +140.6 +1.25
AH+AA+CC AEA	1.16±0.10	2.30±0.1*λ 16	2.10±0.1*♯λ 17	1.93±0.04*♯λ 21	2.0±0.07*♯λ 17
AA+LF AEA (to AA)	1.16±0.10	2.11±0.10* 7.0	2.08±0.12*♯ 16.8	1.99±0.11*♯ 18.4	2.08±0.09*♯ 13.3
AH+AA+LF AEA	1.16±0.10	2.56±0.09* 6.6	2.63±0.11* +4.4	2.84±0.12* +16.4	2.54±0.10* +4.5
AH+AA+LF +CC AEA	1.16± 0.10	1.5± 0.02*♯λ Q 45.2	1.99± 0.07*λQ 21	1.93± 0.07*λQ 20.9	2.08± 0.05*λ Q 14.4
AH+AA+AM AEA	1.16±0.10	3.51±0.1*♯λ +28.1	2.9±0.2* +15.1	2.9±0.12* +18.9	5.1±0.3*♯λ +109.9
AH+AA+LF+ +AM AEA	1.16± 0.10	2.33± 0.02*λ Q 15	2.38± 0.07* 5.6	2.44± 0.08*Q 0	2.08± 0.05*♯λQ 14.4
AH+AA+LF+ +CC+AM AEA	1.16± 0.10	2.41± 0.15*∂ 12.0	2.37± 0.12*ά 6.0	2.44± 0.08*άQ 0	2.3± 0.15*∂ά 5.4

Notes: 1) - values registered at 21 days from the beginning of the salt loading (i.e., animals with pre-formed AH) and registered at the same time in animals with AA only; 2) & - in brackets - the general term of observing animals (from the beginning of the AH formation) is indicated; outside brackets - numbers indicate the time period after the AF administration; 3) * - p≤0.05 compared to the initial index value; 4) ♯ - p≤0.05 compared to the values in animals with AA only within the corresponding observation period; 5) º - p≤0.05 compared to the values in animals with a combined pathology; 6) Q - p≤0.05 compared to the values under the conditions of using LF only against the background of a combined pathology; 7) ∂ - p≤0.05 compared to the values in animals with a combined pathology, treated with AM; 8. ά - p≤0.05 compared to the values in animals with a combined pathology treated by CC only.

The obtained results may be an experimental justification for initiating a clinical study on the feasibility of the combined use of drugs belonging to various pharmacotherapeutic groups in order to optimize the pharmacotherapy of RA associated with AH [7].

Conclusions

1. Under the conditions of experimental rheumatoid arthritis, leflunomide exhibits anti-edema activity at the level of 13-18 %, which is lost in the conditions of arterial hypertension associated with the rheumatoid process.

2. Celecoxib exhibits pronounced anti-edema activity within 16-21 % in different periods of the comorbid state, which is significantly enhanced in combination with leflunomide, especially in acute inflammation against the background of associated pathology.

3. Pharmacodynamic interaction of leflunomide with amlodipine manifests an anti-edema activity of the immunosuppressor, while the independent application of amlodipine results in the edema growth under the conditions of arterial hypertension associated with adjuvant arthritis.

4. Combined administration of leflunomide, celecoxib and amlodipine only in the acute period of inflammation developing on the background of arterial hypertension, an anti-edema effect is recorded at the level of 12%, which is significantly reduced in other observation periods.

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Реферати

ПРОТИЗАПАЛЬНА АКТИВНІСТЬ ЛЕФЛУНОМІДУ ЗА КОМБІНОВАНОГО ЗАСТОСУВАННЯ З ЦЕЛЕКОКСИБОМ І АМЛОДИПІНОМ НА ФОНІ АД'ЮВАНТНОГО АРТРИТУ, ПОЄДНАНОГО З АРТЕРІАЛЬНОЮ ГІПЕРТЕНЗІЄЮ

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Метою роботи було дослідити протинабрякову активність лефлуноміду за комбінованого застосування з целекоксибом та амлодипіном на тлі експериментального ревматоїдного артриту, асоційованого з артеріальною гіпертензією. Досліди проведено на статевозрілих нелінійних білих щурах обох статей з вихідною масою (201,56±2,42; n=174) г. Експериментальний РА викликали за підшкірного уведення в підошовну частину задньої кінцівки (лівої) повного АФ. Досліджувані лікарські засоби: лефлуномід (ЛФ), таблетки по 20 мг; целекоксиб (ЦК), капсули по 100 мг та амлодипін (АМ), таблетки по 10 мг. За умов експериментального РА, що розвивався на тлі АГ, спостерігалося суттєве зростання об'єму стопи на (136-147) % (з 1,16 у.о. до 2,74 у.о.) порівняно до значень у тварин інтактної групи. Комбіноване застосування ЦК з ЛФ на тлі поєднаної патології призводило до суттєвого, відносно даних у тварин з поєднаною патологією та у щурів, лікованих лише ЛФ, зниження об'єму стопи на (14,4-45,2) % і на (18-41,4) % відповідно у всі терміни спостереження. Особливо значущим цей ефект був у

ПРОТИВОВОСПАЛИТЕЛЬНАЯ АКТИВНОСТЬ ЛЕФЛУНОМИДА ПРИ КОМБИНИРОВАННОМ ПРИМЕНЕНИИ С ЦЕЛЕКОКСИБОМ И АМЛОДИПИНОМ НА ФОНЕ АДЪЮВАНТНОГО АРТРИТА, В СОЧЕТАНИИ С АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ

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Целью работы было исследование противоотечного действия лефлуномида за комбинированного применения с целекоксибом и амлодипином на фоне экспериментального ревматоидного артрита, ассоциированного с артериальной гипертензией. Опыты проведены на половозрелых нелинейных белых крысах обоего пола с исходной массой (201,56 ± 2,42; n = 174) г. Экспериментальный РА вызвали по подкожного введения в подошвенную часть задней конечности (левой) полного АФ. Лекарственные средства: лефлуномид (ЛФ), таблетки по 20 мг целекоксиб (ГК), капсулы по 100 мг и амлодипин (АМ), таблетки по 10 мг. В условиях экспериментального РА, развивался на фоне АГ, наблюдалось значительное увеличение объема стопы на (136-147)% (с 1,16 у.е. до 2,74 у.е.) по сравнению со значениями у животных интактной группы. Комбинированное применение ЦК по ЛФК на фоне сочетанной патологии приводило к существенному, относительно данных у животных с сочетанной патологией и у крыс, леченных только ЛФК, снижение объема стопы на (14,4-45,2)% и на (18-41 4)% соответственно во все сроки наблюдения. Особенно

гострий період розвитку АА на тлі АГ. За комбінованого застосування лефлуноміду, целекоксибу та амлодипіну лише у гострий період запалення, що розвивається на тлі артеріальної гіпертензії, реєструється протинабряковий ефект на рівні 12 %, що суттєво знижується в інші періоди спостереження.

Ключові слова: лефлуномід, протинабрякова дія, ревматоїдний артрит, артеріальна гіпертензія, коморбідна патологія.

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значимым этот эффект был в острый период развития АА на фоне АГ. При комбинированном применении лефлуномида, целекоксиба и амлодипина только в острый период воспаления, развивается на фоне артериальной гипертензии, регистрируется противоотечный эффект на уровне 12%, что существенно снижается в другие периоды наблюдения.

Ключевые слова: лефлуномид, противоотечное действие, ревматоидный артрит, артериальная гипертензия, коморбидной патологии.

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CORRECTION OF BREAST ASYMMETRY: STRUCTURAL CHANGES OF ADIPOSE TISSUE IN AUTOLOGOUS FAT GRAFTING

The purpose of the work was to determine the structural features of adipose tissue during auto transplantation of a fat transplant. It was found that changes in aspirated adipose tissue indicate partial trauma and violation of the integrity of individual adipocytes in preparation for transplantation. However, an analysis of the structural organization of adapted adipose tissue found that the decrease in adipocyte volume was 19,4 % - 23,1%. Thickening of the layers of connective tissue in adapted adipose tissue is due to compensatory-reparative processes and the maturation of the fibrous component and the amorphous substance of the connective tissue during transplant engraftment. These phenomena are accompanied by an increase in the number of migrant cells in perivascular tissue. On the part of the blood vessels of the hemomicrocirculatory bed, changes were found to have a stereotypic nature on the action of exogenous factors.

Key words: adipose tissue, fat transplant, breast volum asymmetry.

Autologous fat grafting (AFG) technique, used for augmentation of the breast or correction of breast asymmetry is becoming more popular for several reasons. First, fat is autologous and, in most cases, abundant. Second, it is malleable material with the ability to naturally integrate into tissue at the site of injection and is widely used in correction of breast asymmetry. Another advantage of AFG is the possibility of removing excess fat from the areas of the inner surface of the knees, the inner surface of the thigh, the anterior abdominal wall, thus, reducing fat in these areas. Owing to these positive properties autologous fat grafting is increasingly being used as an alternative to commercial fillers, if necessary, for soft tissue expansion and correction of aesthetic defects [4]. According to the report of International Society of Aesthetic Plastic Surgery (ISAPS), in 2009, the frequency of use of autologous fat grafting technique accounted for 5.9% in the structure of aesthetic procedures [6]. The effectiveness of the autologous fat transplantation has improved significantly after the development and standardization of lipoaspiration techniques. The refined techniques have led to reduction of injury to adipose tissue during liposuction and preservation of the graft survival [7]. The basic standards for increasing the autologous fat graft survival are the safe lopoaspiration and non-traumatic processing of the fat graft. Lipofilling should be made by tunnel method, without the formation of bulk cavities [9]. I.V. Kraiinik reports that the use of autoplasma proteins with centrifugation, and the formation of a single protein-fat conglomerate and injection of the material through cannulas with a diameter of 2 mm provides high survival rate, and the rate of graft resorption is not more than 15% [2]. According to the publications, autologous graft retention varies from 40 to 90% [5]. Such variability of results suggests that there is no objective method for evaluation the viability of a fat autograft. Moreover, estimation of lipofilling results is subjective, often made “by eye” or by photos before and after surgery, which is not objective. There is no method that determines how much volume is added to donor sites. That is, the volume in the donor site was augmented due to the quantitative increase in adipocytes due to transplantation or due to the qualitative increase in the volume of old adipocytes through weight, gained by a patient. Therefore, determination of the major changes that occur in lipoaspirate and integrated fat, compared to the intact one, is crucial in the state-of-the-art reconstructive surgery.

The purpose of the study was aimed at determination of the structural features of the adipose tissue during autologous fat grafting.

Methods and Material. Flaps of the adipose tissue were used in the primary correction of breast asymmetry (intact group), lipoaspirate (fat from the anterior abdominal wall) and fragments of oleomas were taken during re-correction. Flaps of adipose tissue and lipoaspirate were placed in 10% buffered

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