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# Use of Fetal Stem Cells for Anti-Aging and Rejuvenation Therapy

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## Abstract

**Background:** The main objective of our study was investigation of fetal stem cells (FSCs) effects on principal processes of human organism aging.

**Material and Methods:** The main group (MG) was composed of 164 female patients and 165 male patients. Cardiovascular type of aging was remarkable for 66 patients, endocrine- 65, neuro-psychic- 70, metabolic- 50 and mixed type- was presented in 78 patients. For statistical analysis we studied the group of patients with mixed type of aging. All patients in the MG underwent treatment using FSCs. Preparations containing FSCs were individually selected for each patient depending on a definite type of aging; suspensions were administered via the parenteral route.

**Results:** Patients experienced a syndrome of early post-infusion improvement which was presented as enhanced physical and emotional activity; better mood, improved sleep and appetite. Anti-aging therapy using FSCs can promote a favorable effect on the lipids and carbohydrates metabolism; laboratory parameters of male health and overall physical state in patients; psycho-functional and emotional health were improved too. We recorded healthier skin in our patients; its dryness and scaliness (roughness) reduced; skin suppleness and elasticity increased and the patients also reported less number of wrinkles. Based on calculations we revealed that over 18 months after FSCs transplantation the aging rate among the patients became lower by 35.33%, whereas over 30 months it was reduced by 56.68%.

**Conclusion:** Treatment using FSCs allows correlating internal factors of pre-term fading which result in lower external signs of aging among the patients; that, in bulk, contributes to overall revitalizing and rejuvenation along with inhibiting the rate of aging by way of promoting better life quality and life expectancy among the patients.

**Keywords**

Aging; Anti-aging therapy; Biological age; Aging rate index; Fetal stem cells

**Abbreviations:** TPR: Total Peripheral Resistance; FSCs: Fetal Stem Cells; RBA: Reference Biological Age; APP: Arterial Pulse Pressure; BM: Body Mass; SHA: Subjective Health Assessment; SMB: Static Mass Balancing; SBP: Systolic Blood Pressure; IBH: Inhale Breath-Holding; ABA: Actual Biological Age; ARI: Aging Rate Index; BA: Biological Age; HbA1c: Glycosylated Hemoglobin; SHBG: Sex Hormone Binding Globulin; FTI: Free Testosterone Index; PSA: Prostate-Specific Antigen; HDL: High-Density Lipoproteins; LDL: low density lipoproteins; ECLIA: Electrochemiluminescence Immunoassay Analysis; TSH: Thyroid Stimulating Hormone; BMI: Body Mass Index

## Introduction

Aging is a naturally determined, generally biological and inevitable process which takes place in conformity with individual genetic program of the organism and overall health state infrequently does not match up to age specific grades in the individual. Different organs and systems are growing old with different rates and within various time intervals. Mode of life and external factors (stress, radiation, environmental pollution etc.) tend to inhibit or accelerate aging of human.

Process of aging could be represented as changes which emphasize an extent of organism adaptation during different age periods. Age-related changes of cardiovascular system much restrict all adaptation properties of organism which is growing old. Being one out of two vitally important organs of human heart mass is decreased with age; cardiomyocytes structure can be compromised; internal membrane of blood vessels is thickened and density of capillaries becomes lower; total peripheral resistance (TPR) is increased; protein-lipids blood profile is impaired etc. Above enumerated changes are connected with the other provoking factors: physical exercising, stress, emotional and psychosocial states which can contribute to disease appearance in respect to incompliance between myocardium demand in oxygen and blood oxygen supplying. Growth of cardiovascular pathology is unprecedentedly high all over the world which made this problem of paramount significance.

During XX century in industrially developed countries demographic situation was regarded as tendency to growing old among population along with increasing absolute and relative number of aged people. In accordance with demographic prognosis, the whole globe was inhabited by over 590 million of elderly people pursuant to the data for 2000. Until 2025 demographers predict a number of elderly people worldwide can increase up to 1 billion and 100 million. In Ukraine a number of people in retirement age will be making up more than 20%. For the recent 60 years women have made up to ⅔ of total population because of tendency to high mortality rates among men in active work capacity age. Majority of countries worldwide reveal extremely high mortality rates among the persons aged from 75 to 79 years.

In future European program of "Healthy Aging" accounts for elevation of average life expectancy in the least up to 75 years along with health improvement in the age of 75 years and older without significant growth of invalidity among the population. The scientists believe a number of people in their age over 80 years will be gradually increasing [1-3].

There are several theories to explain the process of aging: programmed aging ("theory of biological clock"), genetic theory,

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structural theory, theory of free radicals and immunology theory. Certain factor or a bulk of factors can play a leading role in each definite clinical case [4,5].

The principal task of anti-aging medicine is not only to predict upcoming problems, but also identifying for the patient exact ways of such problems solution. This refers to a regimen of nutrition, fluid maintenance, mode of life, physical exercises, vitamins-mineral complexes with inclusion of various nutritional supplements, hormonal preparations, herbal remedies etc.

Aging is associated with molecular-biological changes, particularities of genetic information encoding and its regulation. Organism senescence begins with aging and death of separate cells. Cells of human body are exposed to permanent division when a bulk of new cells is generated and these cells gradually grow older. Processes of aging are accelerated after the age of 25-30 years, when biological upgrowth is almost completed. A number of old cells in human is being elevated with age. Cells are dying off, yield to lysis, can block capillaries and interfere with inflow of nutritional substances exacerbating eradication of metabolic by-products from the cells. Simultaneously, this reduces adaptive and defense reserves of the organism and creates a favorable base for appearance of diseases. Aging process is accompanied by disruption of homeostasis and decrease of regenerative capacity in all tissues and organs. With age healing of wounds is decelerated, hair appears grey and its shedding starts, volume of skeletal muscles and their strength decrease, ratio between cell components of blood is compromised and neurogenesis is reduced. Stock stem cells are responsible for homeostasis and regenerative activity of such tissues, which under the effect of microenvironment with age could degrade their functional efficiency [6].

There is no classical approach to the problem of anti-aging in contemporary science. Scientists made an endeavor to establish methods of treatment or to try creating proper medical forms to improve quality of patient's life along with elongation of life expectancy [7]. Interest to stem cells in respect to their therapeutic potential for treatment of age-related diseases and states has been recently increased.

Biological processes of human organism along with a plenty of factors affecting likely processes are interrelated between each other. Against the background of analysis on general biological approach to the problem of organism aging, cell therapy is considered to be one of the ways to improve life quality and prolong life span in human which can reinforce the organism with a new building material and will induce a favorable impact on microenvironment of patient's own stem cells.

The objective of this study was investigation of the effects of FSCs on the principal processes of human organism aging. Expedience of FSCs application for anti-aging therapy is based on their capacity and applicability for correction of human physiology condition in a wide range of possible pathologies and causes of their appearance; these cell types also have minimum of contraindications for treatment use. The most reasonable is use of FSCs and their preparations for a purpose of anti-aging effect.

Therapeutic effects of fetal tissues and FSCs are promoted by capacity of such cells bearing specific growth factors, cytokines, "cytomyelins", interleukins and the other signal molecules which activate specialized and progenitor cells. Biologically active compounds stimulate regeneration in the recipient as well as restore cellular and tissues homeostasis which has been broken down. Replacement of affected specialized stem cells in the organs of recipients is a significant component of treatment effectiveness. Immaturity of fetal immune system in early period is also not less important immunology aspect. Transplants of hematopoietic tissue in early embryonic period do not have mature lymphocytes; therefore, they cannot recognize and do not subject tissues in a "foreign" recipient to an attack; graft-versus-host disease is not possible at all. Embryonic FSCs are tolerant to hypoxia because of glycolysis; therefore, ischemic lesions at time of manipulations in vitro do not exert effects on their viability. Proliferative or immature FSCs mostly do not have long processes or strong cell-cell adhesion and, subsequently, are less vulnerable to traumatization at time of preparing suspensions containing isolated cells. Such properties allow preserving higher cells viability compared to adult stem cells after a process of cryopreservation and use of FSCs in suspensions for injection. [8].

## Materials and Methods

The patients with mixed type of aging were included into the main group (MG) for statistical analysis, those who received treatment by use of FSCs, whereas control group (CG) allocated the patients who were not administered FSCs preparations.

The MG consisted of 164 female patients and 165 male patients. Cardiovascular type of aging was found in 66 patients, endocrine- 65, neuro psychic- 70, metabolic- 50 and mixed type- 78 patients (Figure 1). The average age of female patients was 61.66 ± 7.14 years and male- 59.07 ± 8.83 years.

Nowadays, there is an opportunity to use different diagnostic methods for defining an individual profile of aging organism and, consequently, selecting the program for prophylaxis of aging [9]. Before stem cell therapy with inclusion of fetal preparations for each patient "aging prognosis" was established by our doctors in accordance with a specially developed algorithm of actions [10]. Biological age of human was determined by us using the method after V.P. Voytenko [11-14].

The following formulas were used for calculation of biology age in the patients:

Women: $RBA_w$ (reference biological age) = -1.463 + 0.415 × APP (arterial pulse pressure) + 0.248 × BM (body mass) + 0.694 × SHA (subjective health assessment) - 0.14 × SMB (static mass balancing).

Men: $RBA_m$ (reference biological age) = 26.985 + 0.215 × SBP (systolic blood pressure) - 0.149 × IBH (inhale breath-holding) +

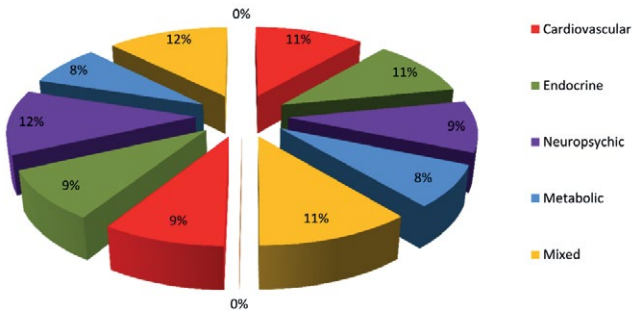


**Figure 1:** Aging types among women and men.

0.723 × SHA (subjective health assessment) - 0.151× SMB (static mass balancing).

Actual biological age (ABA) was calculated according to the formulas:

Women: $ABA_w = 0.581 \times CA$ (chronological age in years) + 17.24

Men: $ABA_m = 0.629 \times CA$ (chronological age in years) + 18.56

Rate of aging = RBA - ABA. If RBA - ABA = 0- this corresponds to statistical normal ranges. When RBA - ABA>0, then a rate of aging is elevated; if RBA - ABA<0, then rates of aging are decreased.

Aging rate index (ARI) was defined by the formula: [15]

For men $ARI_m$ = WC (waist circumference) × BM (body mass) / HW (hip width) × $H^2$ (height in m.) × (17.2 + 0.31 × $AD_m$ (age difference – chronological age (CA) and age of ontogenetic norm for men (21 years) (CA-21)) + 0.0012 × $(AD_m)^2$

For women $ARI_w$ = WC (waist circumference) × BM (body mass) / HW (hip width) × $H^2$ (height in m.) × (14.7 + 0.26 x $AD_w$ (age difference - chronological age (CA) and age of ontogenetic norm for women (18 years) (CA-18)) + 0.001 × $(AD_w)^2$

ARI from 0.95 to 1.05 - normal. ARI <0.95 - slowed down rate of aging. ARI >0.95 - accelerated rate of aging.

Taking into account the aging rate index (ARI),

Biological age in men ($BA_m$) = $ARI_m$ × (CA-21) + 21

Biological age in women ($BA_w$) = $ARI_w$ × (CA -18) + 18

All patients of the MG have undergone one course of treatment using FSCs preparations. Prior to stem cells transplantation all patients were orally acquainted with the plan of treatment and procedures for diagnosis; later the patients reported about their health state and we informed them on the results of laboratory and instrumental investigations. All patients were informed in details on FSCs suspensions and methods for stem cells transplantation. As soon as doctors presented a clarified treatment description, all patients in the MG signed their written informed consent for treatment by use of FSCs.

Stem cells preparation was made of 5-12 weeks gestation embryonic fetuses [16]. Embryos were received in medical institutions as a result of abortion according to social indications from healthy women, who were previously examined for viral and hemic infections. All works with fetal material were conducted in accordance with current Ukrainian legal and ethical standards [17-19]. The study was approved by the local ethics committee established on the base of Kyiv City Clinical Emergency Hospital being located on the address: 3 Bratyslavska str., Kyiv City, Ukraine.

FSCs preparations were individually selected for every patient in the MG depending on aging type which was defined (cardiovascular, endocrine, neuropsychic, metabolic and mixed type) [4] from clinic cryobank, where the suspensions of FSCs were stored in liquid nitrogen at – 196°C. The main parameters for selection of suspensions were as follows: week of gestation (5-12 weeks), nucleated cells count per 1 mL (1 to 50x$10^6$/mL), a number of colony-forming units (CFU > 0.01), count of CD34+ cells – > 0.05x$10^6$, number of CD133+ cells – > 0.05x$10^6$, cells viability prior to cryopreservation was > 30%.

All FSCs suspensions stored in cryobank for clinical use were tested for bacterial and viral infections (HIV-1, HIV-2, HBV, HCV, HGV, HPV, CMV, EBV, HHV6, HSV-1,2, Rubella, Parvovirus B19, Treponema pallidum, Toxoplasma gondii, Chlamidia trachomatis, Mycoplasma hominis, Mycoplasma genitalium, Ureaplasma Parvum, Urealyticum); suspensions had a definite number of nucleated cells and CD34+, colony forming units and cell viability prior to cryopreservation.

Suspension defrost was carried out in accordance with standard protocols. The containers were taken out the liquid nitrogen immediately before transplantation, immersed in a water bath at +37˚C and kept till the liquid phase. Further procedures were performed at indoor temperature following strict compliance with aseptic requirements. Additional control of suspension quality, including microscopic studies and calculation of viable cells were conducted before transplantation; trypan blue staining method was applied for visualization under the microscope by means of counting chamber or automated cell analyzer 1450001 TC10™ Automated Cell Counter.

Several different types of FSCs suspensions were used to treat one patient that allowed getting a more pronounced positive effect. The preparation was administered intravenously via blood transfusion system on the top of 200 mL 0.9% saline solution after previous intravenous jet pre-medication with dimedroli 10 mg. and prednisolone 30 mg. The rate of administration was 20-40 drops per minute. The amount of administered suspension was not less than 2.0 mL per one course of treatment; the number of nucleated FSCs - from 1 to 50x$10^6$/mL, the percentage of living cells - not less than 30%. Every additional suspension was administered subcutaneously during several days in the amount of not less than 2.5 mL, creating a depot in subcutaneous fat.

The patients with mixed type of aging were included in the group for statistical analysis. The parameters of peripheral blood such as lipid profile, glycosylated hemoglobin (HbA1c), insulin, testosterone, sex hormone binding globulin (SHBG), free testosterone index (FTI), and prostate-specific antigen (PSA) were taken into account. The obtained results were processed using a variation statistical inference by nonparametric Wilcoxon test. Calculations were conducted by means of computer software program *Statistica*.

## Results and Discussion

All patients revealed a syndrome of early post-infusion effects which were represented by higher physical and mental capacity among the patients; improvement of mood, better sleep and appetite were also reported by such patients.

No phenomenon of adverse reaction, allergy manifestation or complications after administration of suspensions with FSCs was observed in the patients under study. All our patients followed their routine mode of living and dietary regimen; they received treatment in accordance with previously established schemes of conventional therapy developed by their doctors.

It is generally admitted that with age sizes of adipose tissues become larger and lipoidosis of internal organs develops; in this respect - concentration and ratio of lipid fractions changes throughout blood and tissues of human body. Cholesterol is an initial material for synthesis of biliary acids and steroid hormones. It is an essential component of cellular membranes, however, unfortunately with growing older biochemical properties of membranes in men change; they are becoming robust in particular. Cholesterol is a constituent part of atherosclerotic damage of vascular walls and it participates in formation of biliary calculi.

We have analyzed the levels of lipids in peripheral blood of the MG patients with a problem of mixed type aging prior to treatment,

over 6, 9 and 12 months after FSCs transplantation. Enzymes colorimetric method was used for definition of such concentration in blood among the patients under study. In patients of the study group we have established increased levels of cholesterol at baseline if compared to commonly-accepted normal rates over 21.8% in men and 22.4% for women which constituted 6.09 ± 0.89 mmol/L and 6.12 ± 0.76 mmol/L respectively.

Among the patients of the CG the baseline levels of cholesterol in men composed 5.99 ± 0.67 mmol/L and 6.05 ± 0.72 mmol/L in women, that was by 19.8% higher than the reference ranges for men and higher by 21% in women.

Over 6 months after treatment with FSCs cholesterol level decreased in men to 5.77 ± 0.59 mmol/L whereas in women the value was lower up to 5.76 ± 0.60 mmol/L. In the patients of the CG the same indexes were lower and made up 5.86 ± 0.64 mmol/L for men and 5.92 ± 0.66 mmol/L for women. Tendency to cholesterol reduction was preserved during the whole period under observation and over 12 months after administration of FSCs this value exceeded the normal ranges in men by 10.9% and over 10.8% in women, which made up 5.44 ± 0.36 mmol/L and 5.41 ± 0.33 mmol/L respectively. Among patients of the CG cholesterol ranges were by 14.4% higher than the reference range for men and by 15.8% – a normal range for women which constituted 5.72 ± 0.48 mmol/L and 5.79 ± 0.71 mmol/L respectively. All values obtained were significant in comparison with the results we acquired before therapy using FSCs. Dynamics of lipids profile in men and women is presented in the (Tables 1 and 2).

The parameter of triglycerides was within acceptable ranges in the patients both before FSCs transplantation and during the whole period under observation. Within a period of the study one can emphasize a tendency of triglycerides levels to downgrading both in men and women. The results we received became apparently insignificant in men, $p>0.05$, ranges of triglycerides were reduced over 14.7% compared to the baseline; however, such results were significant in the group of women, $p<0.05$, their values of triglycerides were reduced by 26.5%. In CG, which allocated both men and women, the level of triglycerides remained within normal limits at the baseline, whereas until the endpoint of observation their ranges varied; however, such values were within the laboratory permissible levels.

High-density lipoproteins (HDL) at the baseline in men under observation made up 1.11 ± 0.34 mmol/L and 1.07 ± 0.31 mmol/L in women. The above concentration is an evidence of moderately marked risk of atherosclerosis development both in men and women.

Over 9 months after treatment administered the levels of HDL were stabilized. After 12 months the same ranges in men made up 1.99 ± 0.33 mmol/L and 2.04 ± 0.32 mmol/L in women. The acquired results were significant compared to the data identified prior to treatment by use of FSCs. During the whole period of observation among the patients of the CG the range of HDL was within normal limits. Baseline level of HDL made up 1.2 ± 0.54 mmol/L for men and 1.12 ± 0.35 mmol/L in women. Over 9 months the values of HDL in men constituted 1.3 ± 0.26 mmol/L and over 12 months of observation the same ranges were 1.42 ± 0.35 mmol/L. In women at the same observational periods the levels of HDL were 1.32 ± 0.36 mmol/L and 1.39 ± 0.41 mmol/L respectively.

Content of atherogenic lipids of low density lipoproteins (LDL) before treatment was higher by 14% in men and by 14.9% in women if compared with normal levels. Over 6 months after FSCs transplantation ranges of LDL were reduced to the extent of moderate risk. Already after 9 months the ranges of LDL the ranges of LDL were within normal limits and constituted 3.26 ± 0.40 mmol/L in men and 3.24 ± 0.39 mmol/L in women under study. At the moment of observation over 12 months the above value was within normal ranges both in men and women making up 2.92 ± 0.36 mmol/L and 2.88 ± 0.40 mmol/L respectively. In patients of the CG the baseline level of LDL was 4.23 ± 0.27 mmol/L in women whereas the same values for men made up 4.1 ± 0.35 mmol/L. Within the period of observation the values of LDL did not reach optimal counts and over 12 months both male and female patients remained in the group of moderate risk when their levels of LDL were in ranges from 3.3 to 4.14 mmol/L.

**Table 1:** Dynamic lipids in peripheral blood of men with mixed type aging after FSCs treatment.

| Value (M) | Reference Rate (RR) | BeforeTreatment | After Treatment | | | P* |
|---|---|---|---|---|---|---|
| | | | Over 6 Months | Over 9 Months | Over 12 Months | |
| N | | 37 | 31 | 35 | 24 | |
| Cholesterol, mmol/L | <5.0 | 6.09 ± 0.89 | 5.77 ± 0.59 | 5.76 ± 0.61 | 5.44 ± 0.36 | P<0.05 |
| Triglycerides, mmol/L | <2.3 | 2.18 ± 0.52 | 2.04 ± 0.43 | 2.03 ± 0.31 | 1.86 ± 0.25 | P<0.05 |
| HDPL Cholesterol, mmol/L | RR: >1.6<br>High risk: <0.9 | 1.11 ± 0.34 | 1.40 ± 0.30 | 1.67 ± 0.36 | 1.99 ± 0.33 | P<0.05 |
| LDPL Cholesterol, mmol/L | RR: <3.3<br>High risk: >4.14 | 4.72 ± 0.53 | 3.84 ± 0.49 | 3.26 ± 0.40 | 2.92 ± 0.36 | P<0.05 |

Note: *p – compare to the result before treatment by use of FSCs

**Table 2:** Dynamic lipids in peripheral blood of women with mixed type aging after FSCs treatment.

| Value (M) | Reference Rate (RR) | Before Treatment | After Treatment | | | P* |
|---|---|---|---|---|---|---|
| | | | Over 6 Month | Over 9 Months | Over 12 Months | |
| n | | 41 | 34 | 30 | 24 | |
| Cholesterol, mmol/L | <5.0 | 6.12 ± 0.76 | 5.76 ± 0.60 | 5.71 ± 0.64 | 5.41 ± 0.33 | P<0.05 |
| Triglycerides, mmol/L | <2.3 | 2.23 ± 0.50 | 1.98 ± 0.47 | 1.89 ± 0.35 | 1.64 ± 0.39 | P<0.05 |
| HDPL Cholesterol, mmol/L | RR: >1.6<br>High risk: <0.9 | 1.07 ± 0.31 | 1.49 ± 0.41 | 1.69 ± 0.32 | 2.04 ± 0.32 | P<0.05 |
| LDPL Cholesterol, mmol/L | RR: <3.3<br>High risk: >4.14 | 4.76 ± 0.55 | 3.82 ± 0.49 | 3.24 ± 0.39 | 2.88 ± 0.40 | P<0.05 |

Note: *p – compare to the result before treatment by use of FSCs

Eradication and correction of dyslipoproteinemia under effects of FSCs contribute to improvement of functions of vascular wall endothelium; in particular, this stabilizes its barrier functions as well as induces some favorable influence on vessels tone and permeability of vascular wall; promotes remodeling of the vessels.

We also consider noteworthy that in 85.3% of patients from the group with mixed type of aging at time of ultrasound investigations prior to FSCs treatment beginning fatty liver pathology was diagnosed, which over 9 months after treatment was only remarkable for the one third of patients under study.

In particular, demand in carbohydrates and actual employment of them within human organism is reduced with age. In men with advancing age contra-insular effects are increased whereas susceptibility of the receptors to insulin is decreased. We conducted study on the levels of insulin in peripheral blood by use of electrochemiluminescence immunoassay analysis (ECLIA), in this case reference values made up 2.6-24.9 IU/L. After assessment of insulin concentration in peripheral blood for majority of patients under study this value was close to the upper limit at baseline; moreover, these ranges even exceeded the normal limits in some individuals under observation. Mean value of insulin level made up 25.83 ± 6.68 IU/L. At the same time as early as over 6 months under study the patients reported decrease of peripheral blood insulin levels by 20.79 ± 5.51 IU/L. The patients under observation over 12 months revealed the level of insulin at study endpoint which composed 19.6 ± 4.27 IU/L. The baseline ranges of insulin among patients of the CG made up 25.24 ± 8.75 IU/L, whereas over 6 months the same values were 24.3 ± 6.39 IU/L and over 12 months – 24.6 ± 7.03 IU/L respectively.

For evaluation of carbohydrates metabolism, in addition to insulin, we had used a definition of glycosylated hemoglobin (HbA1c) - compound of hemoglobin with glucose which was achieved by use of immunoturbidimetric analysis. Reference values composed the ranges from 4.8 to 6.1 %. Levels of HbA1c are dependent on the mean blood glucose rates during a period of lifespan of red blood cells. At baseline of our observation - HbA1c constituency in peripheral blood made up 5.93 ± 0.48%. During the whole period of the study this score was within a laboratory normal range of 5.67 ± 0.37% over 6 months, 5.62 ± 0.36% in 9 months and endpoint measurement was referred to a period over 12 months after FSCs transplantation where the level of HbA1c was equal to 5.68 ± 0.27%.

After application of FSCs we observed enhanced conative component in 72% of cases which contributed to regulation of nutrition regimens, labor and rest among the patients under study - this fact also had an important positive impact both on overall well-being of individuals and on the ranges of lipids and carbohydrates metabolism in human organism. In patients of the CG the baseline levels of HbA1c constituted 5.9 ± 0.93%, over 6 months of observation – 5.7 ± 0.87% and over 12 months the same values were 5.65 ± 0.71%.

We have determined prostate-specific antigen (PSA) for all men under study. Such a definition was made using the method of immunoassay. At baseline this score was somewhat higher than generally accepted norm from 0 to 4.0 ng/mL and it composed around 4.72 ± 2.24 ng/mL. Over 6 months after treatment conducted this value was reduced up to 4.08 ± 1.65 ng/mL; over 9 months it was 3.85 ± 1.57 ng/mL and the same parameter at its endpoint was equal to 4.08 ± 1.51 ng/mL. All scores were significant, $p<0.05$ compared to the data baseline. The main aim of determining PSA in the group under study is a screening examination to find out sub-clinical forms of prostate cancer in males. Also all men were conducted urology and ultrasound investigations on the prostate gland.

It has been generally recognized that after the age of 40 the levels of sex hormones in men are gradually decreased and their reproductive system undertakes changes. Bioavailable testosterone levels are also reduced on a large scale. Free testosterone index (FTI) was used for evaluation of true androgen status among the men. FTI is a specified rate of correlation between total testosterone and sex hormone binding globuline (Testosterone total/SHBG) and it correlates with the level of bioavailable testosterone. FTI at baseline of observation made up 26.26 ± 4.32% and was preserved near the lower margin of reference rate (RR = 24.3-72.1%). Over 6 months this index was elevated up to 34.6 ± 6.65%. Increase of this parameter was also observed during the whole period of observation. Over 9 months this index was equal to 39.63 ± 8.76% whereas at the endpoint of observation it reached 64.03 ± 9.49%. Acquired results were significant $p<0.05$, if compared to the baseline results. In men who were allocated in the study group the level of thyroid-stimulating hormone (TSH) and prolactin was within the reference rate.

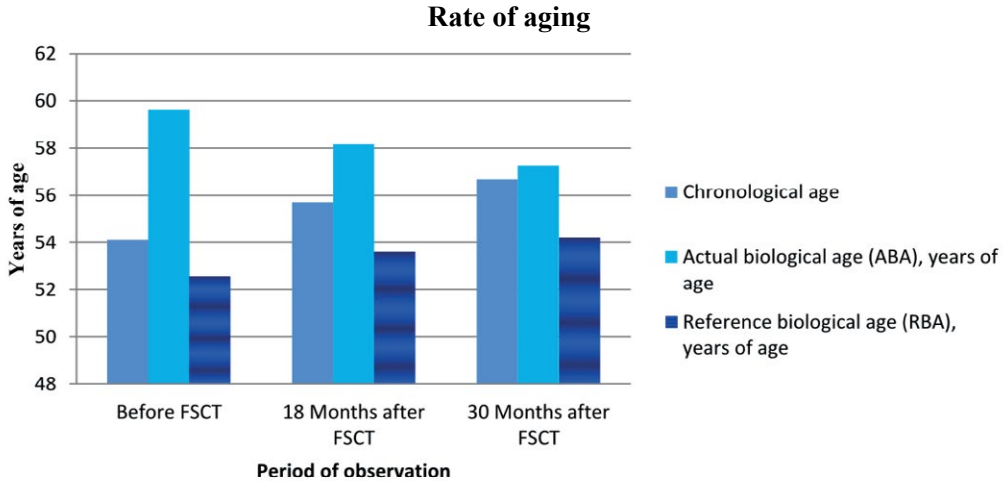


**Figure 2:** Rate of aging.

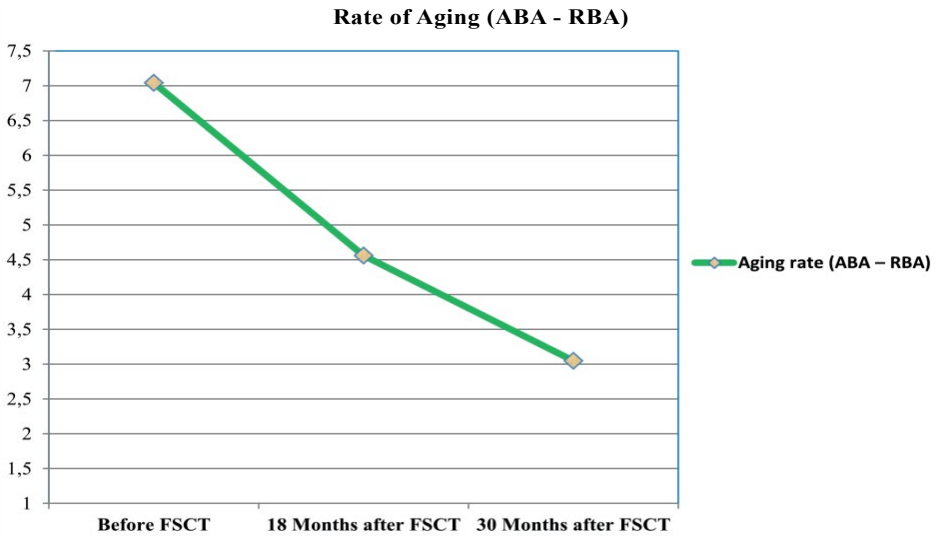


**Figure 3:** Rate of Aging (ABA - RBA).

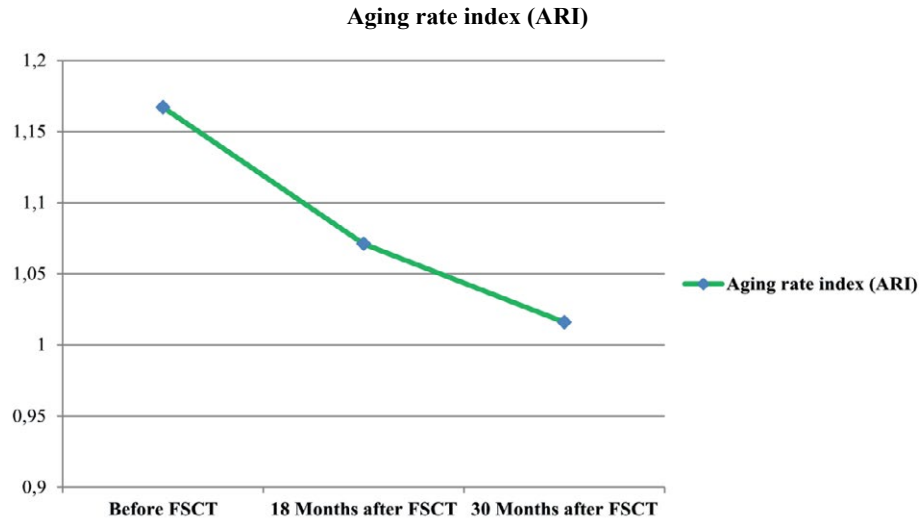


**Figure 4:** Rate of aging (ARI).

All men undergoing treatment by use of FSCs reported decrease of irritability and general fatigability; their memory and concentration improved; less attacks of BP as well as obesity signs were unremarkable; in particular, BMI was reduced by 27.82%; patient's libido increased and they enjoyed their overall general appearance.

Biological age of man can both approximately match with chronologic age-then a process of aging will be considered physiological; and also can significantly differ from it - the process of aging will be regarded as pathological in this case [12].

Using the formulas for biological age detection we have analyzed how FSCs can affect the rates of aging in man (Figure 2). In this diagram we indicated a chronologic age of men and its growth during the total period of the study; calculations for actual and reference biological age were conducted at the baseline of observation, over 18 and over 30 months after FSCs administration. Obtained results on biological age have been compared with reference biological age in men which characterized standard rates of aging in population. As a result of performed calculation, it was established that over 18 months after FSCs transplantation the rates of aging were reduced by 35.33%, whereas over 30 months the same values were lower by 56.68% in comparison with rate of aging at the baseline. Aging rate index (ARI) was defined before study and that was an evidence of accelerated tempo of aging. Over 30 months under the study patients had this index reduction and its ranges were within normal limits. Changes of ARI and rates of aging can be described in the chart (Figures 3 and 4).

We can see that use of FSCs slows down a process of aging in men of the study group; their biologic age is approaching to their real age.

In calculation of biological age in the group of women under study difference between ABA and RBA before treatment constituted 0.887 ± 0.131, namely, actual biological age was almost the same as reference biological age. During 3 years under observation in this group of

patients we recorded significant improvement of subjective health evaluation which was analyzed according to some special questions of the questionnaire Subjective Health Evaluation (SHE). In particular, we observed lower effect of weather changes on the patient's general state of health; periods of excitement which negatively influenced night sleep in such patients were rare; their aberration decreased and improvement of memory and concentration was remarkable; signs of pain sensation in the joints and lumbar region reduced; tolerance to physical exercises elevated as well as patient's self-appraisal of state of health. In general, a number of negative patient's answers to 29 questions in the enquirer was decreased by 73%.

Changes of physical health in women we also analyzed in accordance with the results of functional tests. Specifically, at the endpoint of observation for such patients the lowest capacity to hold one's breath on inhalation made up 44 ± 12 sec. whereas on exhale it was 40 ± 15 sec. Static mass balancing – made up 15.40 ± 4.52 sec. which is a parameter of locomotor apparatus functioning, coordination of motions in the patients and their attitude to achieve the best results made up 15.40 ± 4.52 sec. In accordance with data obtained at the endpoint of the study, a state of health could be assessed in the patients as good.

All women in the study group also presented improvement of their skin condition: less skin dryness and scaliness in 85%, its increased flexibility and elasticity in 77%, lower extent of wrinkles in 81%, healthy skin color in 87% of cases. Reduction of brittleness of hair and its shedding as well as restoration of its natural shimmer was presented by 88% of women. Absolutely all women reported some positive changes in psycho functional and emotional spheres.

## Conclusion

Observation in patients who underwent FSCs therapy in our clinic has been conducted for a protracted period of time and one can explicitly and unequivocally prove stem cells effectiveness in anti-aging and rejuvenation therapy. This article is devoted to only separate aspects of human organism aging and we evaluated effects of FSCs on the processes of aging among the treated patients. Based on the data presented we can clearly establish a difference between the processes of aging in men and women organism. Analyzing the results of rejuvenation which we received after administration of FSCs, positive effects of stem cells were established in respect to lipids and carbohydrates metabolism which were evaluated based on dynamics of cholesterol, triglycerides, HDL and LDL concentration, levels of insulin and glycated hemoglobin. Our treatment also had a positive effect on male health. Increasing of free androgen index (FTI) is descriptive due to reduction in androgens deficit being age-related and remained characteristic in the patients before FSCs transplantation.

Among the patients of the study group we revealed increased subjective health estimation as well as improvement of physical and psychoemotional state. In patients who underwent treatment by use of FSCs, biological age tends to be reduced along with a decrease of ARI in such individuals.

Treatment using FSCs allows us correlating internal causes of pre-term human organism aging and helps to decrease external signs of senescence which in whole contribute to possibility of broad-based health promotion and human body rejuvenation, delayed rate of organism aging as well as increased overall life expectancy among the patients.

Further study of all effects promoted by FSCs onto processes of human organism aging opens contemporary opportunity to increase capacity of human body to be adjusted to new social conditions and factors of the environment in order to prevent appearance of multiple age-related diseases and to induce an expedient influence on higher lifespan and longer rates of productive life among people.

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