

THE EFFICACY APPLICATION OF COMBINATION AS AN ACTOPROTECTOR AND ANTIDEPRESSANT IN THE TREATMENT OF LOCOMOTOR DISORDERS IN THE ELDERLY

Ilitski Andrei N.¹
<http://orcid.org/0000-0002-1090-4850>
 E-mail: a-ilitski@yandex.ru

Prashchayeu Kiryl I.²
<http://orcid.org/0000-0002-5436-9431>
 E-mail: prashchayeu@gmail.com

Nemykin Oleg N.³
<http://orcid.org/0000-0001-7663-9976>

Litvinov Andrei E.⁴
<http://orcid.org/0000-0003-0228-5225>

¹ Researching Medical Center "Gerontology" (Moscow, Russia), Vice-director, Chairman of Department of Clinical Gerontology, MD, PhD, DSc, Prof. / Belarusian Association of Gerontology & Geriatrics, Chairman

² Researching Medical Center "Gerontology" (Moscow, Russia), Director, MD, PhD, DSc, Prof. / The open Institute of Human and Nature (Lithuania, Vilnius)

³ National Research University "Belgorod State University" (Belgorod, Russia), Department of Medicine, resident, MD

⁴ Belgorod Regional Hospital for elders (Belgorod, Russia), Chairman of Department of Neurology, MD

ABSTRACT

OBJECTIVE

Here are the results of original research on the effectiveness if added to standard therapy an actoprotector (Actovegin) and antidepressant (Fluvoxamine) in elderly patients with comorbidity (as the pathology of the central nervous system and locomotor disorders).

METHODS

We are examined per 63 patients at a mean age 67 years, which diagnosed comorbidity as the dyscirculatory encephalopathy II stage with ataxic syndrome, mild depressive episode, I-II radiographic stage osteoarthritis of hip and knee joints.

RESULTS

In the basic group after exposure therapy there was a decrease content of interleukin and tumor necrosis factor- α in blood. There improved results in the 6-minute walk test, increased motivation to improve their self-state. At the dynamics of Hamilton Depression Scale results there are decreased intensity on a number of parameters: «depressive mood», «sense of guilt», «insomnia», «psychic anxiety», «somatic anxiety», «hypochondria», «paranoid symptoms», «obsessive symptoms» and increased «activity». Meanwhile, in the control group no significant changes were observed.

CONCLUSION

The application a combination of an antidepressant and actoprotector promotes correction of pro-inflammatory changes. First, this approach can reduces expressiveness of depression. Secondly, it allows decreasing the involuntary age-related changes in muscle tissue the arising from the immune inflammation. Addition to conventional therapy as a combination of an antidepressant and actoprotector has proved significantly greater antidepressive effect compared to standard therapy. Also, it significantly enhances the motivation of older people to improve their self physical condition. This applies primarily to the locomotor function.

KEYWORDS: Actoprotector, Antidepressant, Actovegin, Fluvoxamine, Depression, Locomotor, Disorder, Elderly

accompany locomotor disorders, allows more efficient recover this function in the elderly [5, 6].

INTRODUCTION

In the last years more and more widely using in geriatrics finds a group of drugs called actoprotectors, which enhance physical performance and endurance at their age-related decline [1, 2]. At application in elderly actoprotectors have a number of very valuable properties, which allow inhibiting the natural age-involutive processes. Specifically, the actoprotectors are having anti-hypoxic effect and them capable to improve long-term memory. Also they improve exercise capacity and have an anti-asthenic effect. All these properties can have an importance in arresting geriatric syndrome such as locomotor disorder [3, 4].

According to the data of several authors, often requires the use of antidepressants in the elderly due to the fact that the breach of movement associated with depression, decreased motivation for improvement, dysfunctional psychological background. In this context the elimination of these conditions which

OBJECTIVE

The aim of the study is to examine the effectiveness of complex application actoprotector Actovegin and antidepressant Fluvoxamine in the treatment of elderly patients with combined pathology of the central nervous system and locomotor disorders.

METHODS

General notes. This study was a prospective, open-label study, it used the technique of double-blind control.

During the research has been studied the effectiveness of addition to the standard treatment of the complex as an actoprotector (Actovegin) and antidepressant (Fluvoxamine) in elderly patients with combined pathology of the central nervous system and locomotor system.

The study included 32 patients (control group) at a mean age 67,1+0,8 years, which has a combination of dyscirculatory encephalopathy stage II with a

mild case of ataxic syndrome and osteoarthritis of the hip and knee joints, all of which led to the development locomotor dysfunction and the 31 patients of basic group (mean age 67,2±0,7 years), who received Actovegin and Fluvoxamine in addition to conventional therapy.

Inclusion criteria is a combined pathology:

- the dyscirculatory encephalopathy stage II with ataxic syndrome,
- mild depressive episode,
- I-II radiographic stage osteoarthritis of hip and knee joints with I-II degree-dysfunction of these joints.

Exclusionary criteria are includes the presence of:

- other classes of severity of this pathology,
- other diseases, which cause restriction of mobility (for instance, a chronic cardiac insufficiency as III or higher functional class (NYHA-classification), a chronic respiratory failure-severe),
- stable residual post-stroke changes or consequences of other pathology, accompanied by locomotor dysfunction,
- a rough mental disorders that leads to the unavailable of a productive contact with patient,
- acute somatic diseases.

Diagnostic criteria

Diagnostics of osteoarthritis of the joints was based on such evidence:

- restriction of mobility the affected joints and painfulness in their motion,
- articular crepitus,
- myofibrosis zones in the muscles that surround the joints; in some cases, the presence of synovitis,
- the absence of systemic manifestations,
- at the X-ray examination – the joint space narrowing, the areas of subchondral sclerosis with cystoid radiolucency.

As diagnostic criteria of the dyscirculatory encephalopathy were used:

- typical complaints of the patients (depressed mood, fluctuation of the mood, dizziness, tinnitus, joint pain, and pain along the spine),
- neurological examination data (asymmetry of tendon-periosteal reflexes, ataxic syndrome).
- for the confirmation of diagnosis we used a neurovisualisation methods, particularly magnetic resonance imaging (identified: leukoaraiosis, cerebral atrophy, lacunar infarctions).

At the mild depression diagnostics we used a number of criteria, which match those of criteria under the section F32.0 of International Classification of Diseases, 10-th Edition [7].

Characteristics of the treatment. Patients of the basic group and the control group received conventional therapy, which is used cerebroangioregulators, disaggregants, anti-atherosclerotic drugs for the specified multimorbid complex. Also we used the nonsteroidal anti-inflammatory drugs for pain syndrome, that accompanied of articular pathology.

In our research 2 drugs was added to the standard therapy: an antidepressant and actoprotector. As the antidepressant added to the therapy, patients received the Fluvoxamine (trade name - Fevarin, producer «Abbott Biologicals SAS», France). Fevarin is a selective serotonin reuptake inhibitor. The drug has antidepressive effect with a distinct component of antianxiety. Fluvoxamine was appointed in tablet form at a dosage of 50 mg 1 time a day for three months.

As actoprotector added to the therapy, was prescribed the Actovegin (producer 'Nycomed GmbH', Germany). First this drug was appointed by injection in a dose of 5ml (200 mg) to 200.0 ml of solution as an infusion for 10 days. In the following patients received tableted Actovegin for 2 weeks.

The test of efficiency in therapeutic complex using based on the assessment of:

- the neuroimmunoendocrine proinflammatory reaction status (definition of levels proinflammatory interleukins and tumor necrosis factor- α (TNF- α);
- the physical activity status (6-minutes walk distance test);
- the psychological background (the questionnaire «Recovery locus of control»);
- intensity of depression (Hamilton Depression Rating Scale).

The neuroimmunoendocrine changes determined the content of proinflammatory cytokines (interleukins 1, 2, 6 (IL-1, IL-2, IL-6); TNF- α) by immunoenzyme method using a test-systems based on a photometer «Multiskan Plus» at a wavelength of 450 nm.

The state of physical activity detected by 6-minutes walk distance test, which was to determine the distance that the patient was able to walk for six minutes, including rest periods due to the illness.

Assessment of psychological status was performed by using of the questionnaire «Recovery locus of control». The questionnaire consists of nine items, each of which is in a utterance, the extent to which the consenting of the patient must express in points: «totally agree» (4 points), «agree» (3 points), «do not know» (2 points), «disagree» (1 point) and «totally disagree» (0 points) in the right-questions, and vice versa - in a «mirror» questions.

The questionnaire includes the following items: «what would happen to me in the future depends on myself, not from what other people have done for me», «a real changes depends on what I doing to help myself», «I am sure, that I will do everything possible to achieve the most complete recovery, regardless of circumstances», «the achieving of improvement - now it is a matter of my own determination, but is not someone else will», «it does not matter how much help I get - eventually, it needs to make own efforts», «it is often, that better to wait and to see what will happen», «my own efforts are not very important, in fact, my restore depends on the people around», «my own contribution to my recovery does not have to be very large», «I nearly do not control (or not in control) of the improving process».

When applying this questionnaire the total point can range from 0 to 36, the higher the score, the higher the level of motivation to overcome the health problems we have in this patient.

Depression severity we determined using the Hamilton Depression Rating Scale, which is one of the most commonly used scales to assess the severity of depression and determine the dynamics of the patient with already established diagnosis in the process of treatment. In the version of the scale, which we applied contains 21 questions; each question is offered from 3 to 5 choices. The questions cover various issues: depressed mood (sadness, hopelessness, helplessness, feelings of inferiority); sense of guilt; suicidal intent; early, middle or late insomnia; working ability and activity; retardation (slowness of thinking and speech, impaired ability to concentrate, decreased motor activity; agitation; psychic anxiety; somatic anxiety (physiological symptoms of anxiety: gastrointestinal - dry mouth, flatulence, indigestion, diarrhea, belching; cardiovascular - palpitations; headaches , breathing - shortness of breath, hyperventilation, frequent urination, increased sweating), gastrointestinal somatic symptoms, general somatic symptoms;

sexual disorders; hypochondria; weight loss; a critical attitude to the disease; diurnal fluctuations of the mood; depersonalization and derealization (feeling of unreality); paranoid symptoms; obsessive and compulsive symptoms.

When interpreting the results, we took into account that the total point can range from 0 (no depression) to 52, which corresponds to an extreme expression degree of depressive symptoms. The total final point from 0 to 6 is regarded as the absence of a depressive episode, 7-15 points - the presence of «mild depressive episode», 16 points or higher - as «severe depressive episode».

Statistics. We used assessment method significance differences between two sets of data by applying the Student t-test. The difference indices are a significant at $t \geq 2$, in this case – $p < 0.05$. In conducting statistical processing, the data were introduced into a spreadsheet «Excel».

Mathematical and statistical processing performed using the program «Statgraphics plus for Windows», version 7.0.

Other notes. This study was reviewed and received admission the Ethics Committee «Researching Medical Center» Gerontology» (No. 2011-11-1, dated 18 November 2011). A part of the study results were published in the Russian-language magazine «Fundamental Research».

RESULTS

The neuroimmunoendocrine changes. We found that the addition of a combination of Actovegin and Fevarin to traditional therapy resulted in significant anti-inflammatory effect. In particular, we have shown the reduction a content of IL-1, IL-2, IL-6 and TNF- α level in blood in a basic

Table 1. Dynamics of pro-inflammatory status in therapy

Index	Control group		Basic group	
	Before	After	Before	After
IL-1 (pg/ml)	345,2 \pm 9,5	347,1 \pm 9,7	346,9 \pm 9,6	305,8 \pm 9,3 ^a
IL-2 (pg/ml)	152,6 \pm 9,3	153,3 \pm 9,4	150,6 \pm 9,5	111,3 \pm 9,1 ^a
IL-6 (pg/ml)	4,2 \pm 0,3	4,2 \pm 0,2	4,1 \pm 0,3	3,1 \pm 0,2 ^a
TNF- α (pg/ml)	138,4 \pm 9,0	139,3 \pm 9,1	137,6 \pm 9,2	107,7 \pm 7,8 ^a

a $p < 0,05$ in the dynamics of therapy in the basic group and between a control and basic groups.
 IL=Interleukin; TNF- α =Tumor necrosis factor- α .

group. It is noticed, no significant changes of content of these signaling-molecules in the control group (I).

The dynamics of clinical efficiency. In the study has been proven a higher clinical effect of the combination of additional actoprotector and antidepressant than an application of only conventional therapy. Thus, in the control group,

the distance that an elderly patient was able to go for six minutes, before the start of therapy corresponded to 456,6±32,6 meters (m) and after the treatment - 564,5±31,7 m. The distance, which patients in the basic group was able to go before the therapy, was equal to 454,7±30,7 m; after the treatment it was significantly higher value of the index in the dynamics and compared to a control group (497,7±30,8 m); p<0,05 (Figure 1).

Figure 1. Dynamics of test results 6-minutes walk distance under influence of simple traditional therapy or adding to it a combination of an antidepressant and actoprotector.

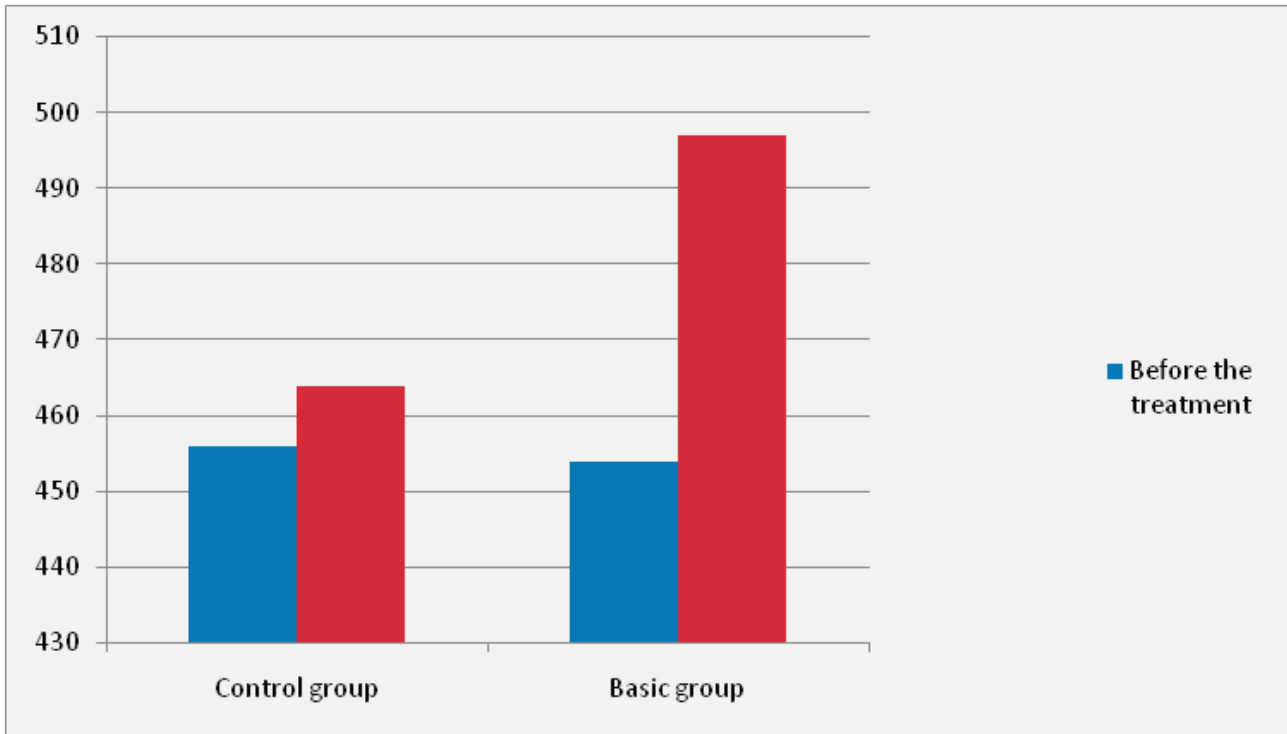


Table 2. The dynamics of motivation to improve of the locomotor function under influence the complex treatment.

Items	Control group		Basic group	
	Before	After	Before	After
1. "What would happen to me in the future depends on myself, not from what other people have done for me"	2,8±0,2	2,8±0,1	2,8±0,1	3,2±0,1 ^a
2. "A real changes depends on what I doing to help myself"	2,8±0,1	2,9±0,02	2,8±0,2	3,4±0,1 ^a
3. "I am sure, that I will do everything possible to achieve the most complete recovery, regardless of circumstances"	2,9±0,1	2,8±0,2	3,0±0,2	3,7±0,1 ^a
4. "The achieving of improvement - now it is a matter of my own determination, but is not someone else will"	2,7±0,1	2,8±0,2	2,7±0,2	3,7±0,2 ^a
5. "It does not matter how much help I get - eventually, it needs to make own efforts"	2,7±0,2	2,6±0,3	2,6±0,2	3,4±0,2 ^a
6. "It is often, that better to wait and to see what will happen"	2,9±0,2	2,9±0,3	2,9±0,1	3,4±0,2 ^a
7. "My own efforts are not very important, in fact, my restore depends on the people around"	2,7±0,2	2,7±0,1	2,8±0,1	3,6±0,2 ^a

8. "My own contribution to my recovery does not have to be very large"	2,8 \pm 0,1	2,7 \pm 0,2	2,8 \pm 0,2	3,5 \pm 0,1 ^a
9. "I nearly do not control (or not in control) of the improving process"	2,8 \pm 0,3	2,9 \pm 0,3	2,9 \pm 0,2	3,7 \pm 0,1 ^a
10. Summary point	25,2\pm0,2	25,3\pm0,3	25,4\pm0,2	30,5\pm0,2^a
a p<0,05 in the dynamics of therapy in the basic group and between a control and basic groups.				

The dynamics of motivation to improve self-state. The dynamics of motivation on improve the state was assessed on the basis of inventory «Recovery locus of control». In this case, we have found a significant increase in points for all positions in the basic group after the combination treatment (p<0,05). In the control group were found no significant points change, including the summary point (II).

The dynamics of depression. In assessing the level of depression in the dynamics of therapy on the Hamilton scale, we obtained the following results (III).

Before the start of experiment in the control group and basic group are scores were the similar at all scales. In the control group after the treatment no significant changes of these parameters has not been registered. In the basic group there was a significant decrease of points in the number of scales, such as «depressed mood», «sense of guilt», «insomnia», «psychic anxiety», «somatic anxiety», «hypochondria», «paranoid symptoms» and «obsessive symptoms». Been registered a significant increase in points at the parameter «activity». No changes in scales – «suicidal intent», «retardation» and «agitation».

In general, it should be noted that before the start of therapy total score in both groups had no significant differences and it was described as «mild depressive episode». After the end of the observation in the basic group there was a significant smoothing of depressive symptoms, while in the control group, these patterns have been received.

DISCUSSION AND CONCLUSION

According to different authors motor function is an integral and depends not only on the state of the locomotor apparatus, but also the emotional and mental status of elderly [8, 9]. A considerable role here belongs to depression.

Systemic impact of depression on the body quite versatile. In the initial stages of the disorder is a key the behavioral aspect when the constantly depressed mood, pessimism, focus on their painful experiences lead to hypochondriacal self-observation with a tendency to decrease the self-loading [10]. The changing a life position leads to rejection of the professional activity, the narrowing a circle of friends. Result is that there is an infringement of

Table 3. The dynamics of depression under influence of combination therapy (in points).

Scales	Control group		Basic group	
	Before	After	Before	After
Depressed mood	1,3 \pm 0,01	1,3 \pm 0,02	1,3 \pm 0,02	0,6 \pm 0,02 ^a
Sense of guilt	1,2 \pm 0,02	1,1 \pm 0,03	1,2 \pm 0,01	0,6 \pm 0,01 ^a
Suicidal intent	0,4 \pm 0,02	0,4 \pm 0,01	0,5 \pm 0,02	0,5 \pm 0,01
Insomnia	1,1 \pm 0,01	1,1 \pm 0,02	1,1 \pm 0,02	0,6 \pm 0,01 ^a
Activity	1,4 \pm 0,01	1,5 \pm 0,02	1,5 \pm 0,02	1,8 \pm 0,01 ^a
Retardation	1,1 \pm 0,01	1,1 \pm 0,02	1,1 \pm 0,02	1,0 \pm 0,01
Agitation	1,0 \pm 0,01	1,1 \pm 0,02	1,1 \pm 0,01	1,1 \pm 0,01
Psychic anxiety	1,9 \pm 0,01	1,9 \pm 0,02	1,9 \pm 0,01	0,9 \pm 0,02 ^a
Somatic anxiety	1,8 \pm 0,02	1,9 \pm 0,02	1,8 \pm 0,01	0,9 \pm 0,02 ^a
Hypochondria	1,4 \pm 0,01	1,3 \pm 0,02	1,4 \pm 0,02	0,7 \pm 0,01 ^a
Paranoid symptoms	1,4 \pm 0,01	1,3 \pm 0,03	1,4 \pm 0,02	0,7 \pm 0,01 ^a
Obsessive symptoms	1,3 \pm 0,01	1,2 \pm 0,03	1,3 \pm 0,02	0,6 \pm 0,02 ^a
Summary point	9,5\pm0,3	9,4\pm0,4	9,4\pm0,2	6,0\pm0,3^a
a p<0,05 in the dynamics of therapy in the basic group and between a control and basic groups.				

communicative capabilities of patients and reduced compliance to treatment. Together, this results in the restriction of motor activity [11].

In addition, the presence of depression, reduced motivation to recovery, age-related and degenerative diseases of the musculoskeletal system have many similarities at the level of the signal intermolecular interactions. In elderly people circulating signaling molecules with distant effect and neurotransmitters (neuropeptides) with a local action are involved in the regulation of the immune response, in particular the presentation of antigen, antibody production, regulation of the activity of lymphocytes, the proliferation, cytokine production, include the regulation of types of immune response (Th1 or Th2). In the development of inflammation is the activation of the stress-systems and induction the immune response by T2-type. Its helps protect the body from overload proinflammatory cytokines. In some instances under the influence of stress hormones activates the hypothalamic-pituitary axis, triggers inflammation, increased production of IL-1, IL-6, IL-8, IL-18, C-reactive protein and TNF- α . This is accompanied by an increased «local» inflammatory background, which may have a pathogenetic role in the development of allergic diseases, autoimmune diseases, obesity, sarcopenia, vascular lesions, atherosclerosis and depression [12, 13, 14].

It is important, that sarcopenia has a special significance at the locomotor function deterioration. In reducing the of muscle mass attaches great importance to reduce the level of somatotrophic hormone, somatomedin C, estrogens and testosterone, which is associated with increased activity of proinflammatory cytokines. It is proved that the processes of muscular age-atrophy associated with the development of age-proinflammatory status (particularly by IL-1 and IL-6), and increased production of C-reactive protein. Proinflammatory activation, age-hypoxia of the muscle tissue is leads to a reduction of muscle function as a protein depot [15].

Muscle tissue is the largest protein depot in organism, and it has certain specificity, as only there was found systems of proteolysis such as ubiquinone-proteasomal system and caspase-3, which splits actin and myosin into smaller fragments. With increasing age, mainly due to hormonal influences, there is an imbalance between anabolic and catabolic processes. In particular, the decline in anabolic hormones (somatomedin C, testosterone) inhibits anabolism with simultaneous activation of catabolic homeostasis ways. It is interesting to note that skeletal muscles is the organ, which produce somatomedin C, and

it's volume in the system depends on the level of physical activity. Than higher the level of physical activity, the higher the volume of somatomedin C. Is also discussed the role of physical activity in the production of growth factor 1 (IGF-1) that is required for activation of stem cells of muscle tissue (satellite cells), providing it's volume. In complex this leads to decrease of the locomotor function [16, 17].

Recent data indicate that, under the influence of proinflammatory activation and reduce the volume of the locomotor function is disturbed vasomotor reactivity of the cerebral vessels, that is an important mechanism for maintaining the stability of cerebral perfusion. In depression vasomotor reactivity of cerebral vessels significantly reduced. Thus, the study of cerebral perfusion using single-photon emission computed tomography showed an obvious change (reduction) of blood flow in the left frontal lobe in elderly patients with major depressive disorder. This change was reversible and returned to normal after the disappearance of symptoms of depression [18, 19]. The listed data by other authors agreed with the results of our studies that indicate that the addition to conventional therapy antidepressant and actoprotector improves locomotor function as a result of reduced neuroimmunoendocrine proinflammatory activity, and the related positive clinical dynamics.

The application a combination of an antidepressant and actoprotector promotes correction of proinflammatory changes. First, this approach can reduce expressiveness of depression. Secondly, it allows decreasing the involuntary age-related changes in muscle tissue the arising from the immune inflammation.

In the treatment of the elderly is important to correct of their psychological state, relief of depressive events, increasing decline in motivation to improve their eigenstate. Addition to conventional therapy as a combination of an antidepressant and actoprotector has proved significantly greater antidepressive effect compared to standard therapy. Also, it significantly enhances the motivation of older people to improve their self physical condition. This applies primarily to the locomotor function.

REFERENCES

1. Kiecolt-Glaser JK, Belury MA, Porter K, et al. Depressive symptoms, omega-6: omega-3 fatty acids, and inflammation in older adults. *Psychosom Med.* 2007 Apr; 69-33: 217-224.
2. Yang K, Xie G, Zhang Z, et al. Levels of serum interleukin (IL-6), IL-1beta, tumour necrosis factor-alpha and leptin and their correlation in depression. *Aust N Z J Psychiatry.* 2007 Mar; 41-3:

266-273.

3. Boggatz T, Dassen T. Ageing, care dependency, and care for older people in Egypt: a review of the literature. *J Clin Nurs*. 2005 Sep; 14-8B: 56-63.
4. Jonsson AL, Moller A, Grimby G. Managing occupations in everyday life to achieve adaptation. *Am J Occup Ther*. 2009 Jul-Aug; 53-4: 353-62.
5. Macko RF, Benvenuti F, Stanhope S, et al. Adaptive physical activity improves mobility function and quality of life in chronic hemiparesis. *J Rehabil Res Dev*. 2008; 45-2: 323-8.
6. Elenkov IJ. Neurohormonal-cytokine interactions: Implications for inflammation, common human diseases and well-being. *Neurochem Int*. 2008 Jan; 52-1-2: 40-51.
7. World Health Organization. The ICD 10 Classification of Mental and Behavioural Disorders: Diagnostic criteria for research. Geneva: WHO, 1993. Available from: <http://www.who.int/classifications/icd/en/GRNBOOK.pdf> [Accessed on Feb 20 2013].
8. Elon RD. Perspectives on the future of geriatric medicine. *J Am Med Dir Assoc*. 2006 Mar; 7-3: 197-200.
9. van den Biggelaar AH, Gussekloo J, de Craen AJ, et al. Inflammation and interleukin-1 signaling network contribute to depressive symptoms but not cognitive decline in old age. *Exp Gerontol*. 2007 Jul; 42-7: 693-701.
10. Williams BC, Remington TL, Foulk MA, et al. Teaching interdisciplinary geriatrics ambulatory care: a case study. *Gerontol Geriatr Educ*. 2006; 26-3: 29-45.
11. Biein B. An older person as a subject of comprehensive geriatric approach. *Rocz Akad Med Bialymst*. 2005; 50-Suppl. 1: 189-192.
12. Cesari M, Onder G, Russo A, et al. Comorbidity and physical function: results from the aging and longevity study in the Sirente geographic area. *Gerontology*. 2006; 52-1: 24-32.
13. Duursma SA, Overstall PW. Geriatric medicine in the European Union: future scenarios. *Z Gerontol Geriatr*. 2003 Jun; 36-3: 204-215.
14. Fry CL. Globalization and the experiences of aging. *Gerontol Geriatr Educ*. 2005; 26-1: 9-22.
15. Lovell M. Caring for the elderly: changing perceptions and attitudes. *J Vasc Nurs*. 2006 Mar; 24-1: 22-26.
16. Luttje D. Geriatric medicine in the academic world. *Z Gerontol Geriatr*. 2005; 38-Suppl. 1: 152-155.
17. Maki BE, McIlroy WE. Control of rapid limb movements for balance recovery: age-related changes and implications for fall prevention. *Age Ageing*. 2006 Sep; 35 Suppl. 2: 12-18.
18. Johnson AK, Grippo AJ. Sadness and broken hearts: neurohumoral mechanisms and co-morbidity of ischemic heart disease and psychological depression. *J Physiol Pharmacol*. 2006 Nov; 57-Suppl. 11: 5-29.
19. Rejeski WJ, Brawley LR. Functional health: innovations in research on physical activity with older adults. *Med Sci Sports Exerc*. 2006 Jan; 38-1: 93-99.