UDC [616.12-005.4+618.19-006]:616.12-008.331.3:577.115

Feroz Shah, Sid' E., Malynovska O.
Zaporizhzhya Medical Academy of Postgraduate Education, Zaporizhzhya, Ukraine

Шах Фероз, Сидь Е.В., Малиновская А.Я.
Запорожская медицинская академия последипломного образования, Запорожье, Украина

The Relationship of the Markers of Endothelial Dysfunction with Lipid Profile in Patients with Stable CAD Combined with Breast Cancer

Связь маркеров эндотелиальной дисфункции с показателями липидограммы у пациентов со стабильной ишемической болезнью сердца в сочетании с раком молочной железы

Abstract

Introduction. The main way to reduce the negative effects of coronary artery disease (CAD) is its prevention and timely detection, as well as comprehensive approach to treatment. In recent years, there has been the increase of worldwide morbidity and mortality from breast cancer. It can be assumed that with the increase of the age of women the frequency of combination of these diseases also increases. It should also be noted that the combination of ischemic heart disease with tumors occurs almost 2 times more often than it is diagnosed during the lifetime of patients, which increases the relevance of timely diagnosis of the combination of ischemic heart disease with breast cancer.

Purpose. To determine the relationship of the markers of endothelial dysfunction with lipidogram in patients with stable CAD in combination with breast cancer.

Materials and methods. The results of the study are based on the data obtained in the comprehensive survey of women in 2015–2016 on the base of PI "Zaporizhzhya regional clinical oncology center" ZCC. We examined 101 women with stable CAD; 70 patients were diagnosed with breast cancer (BC) $T_2N_0M_0$, and 31 patients had no oncopathology. On the outpatient base, 31 practically healthy women comparable in age and social status were examined.

Results and discussion. The level of vascular endothelial growth factor (VEGF) was significantly higher in patients with stable CAD in combination with BC – 327.8 [308.2; 340.5] PG/ml than in the group of persons with stable CAD without neoplasm 213.7 [197.7; 227.4] PG/ml. The LDL-C level had a significant direct relationship with VEGF (r=+0.65, p=0.0001), with MMP-9 (R=+0.49, p=0.0001), and inverse relationship with the nitrogen monoxide metabolites (NOx) (r=–0.58, p=0.0001).

Keywords: breast cancer, coronary artery disease, matrix metalloproteinase-9, vascular endothelial growth factor, endothelial dysfunction, lipid profile.

Резюме

Введение. Основным путем к уменьшению негативных последствий ИБС является ее профилактика и своевременное выявление, а также комплексный подход к лечению. За последние годы во всем мире наблюдается рост заболеваемости и смертности от рака молочной железы. Можно предположить, что с увеличением возраста женщины увеличивается и частота

сочетания этих заболеваний. Также необходимо отметить, что сочетание ИБС с новообразованиями встречается почти в 2 раза чаще, чем диагностируется при жизни пациентов, что увеличивает актуальность своевременной диагностики сочетания ИБС с РМЖ.

Цель исследования. Определить связь маркеров эндотелиальной дисфункции с показателями липидограммы у пациентов с ИБС в сочетании с раком молочной железы.

Материалы и методы. Результаты исследования основаны на данных, полученных при комплексном обследовании женщин в 2015–2016 гг. на базе КУ «Запорожский областной клинический онкологический диспансер» (ЗОР). Была обследована 101 женщина с подтвержденной стабильной ИБС, из них 31 пациентка без сопутствующей онкопатологии и у 70 человек был выявлен РМЖ $T_2N_0M_0$. В амбулаторных условиях обследовали 31 практически здоровую женщину, сопоставимую по возрасту и социальному статусу.

Результаты и обсуждение. Уровень сосудистого эндотелиального фактора роста (СЭФР) был достоверно выше у пациентов со стабильной ИБС в сочетании с раком молочной железы – 327,8 [308,2; 340,5] пг/мл, чем в группе лиц со стабильной ИБС без новообразования – 213,7 [197,7; 227,4] пг/мл. Уровень липопротеидов низкой плотности имел значимую прямую связь с СЭФР (r=+0,65, p=0,0001), с ММР-9 (R=+0,49, p=0,0001) и обратную связь с метаболитами оксида азота (r=–0,58, p=0,0001).

Ключевые слова: рак молочной железы, ишемическая болезнь сердца, матриксная металлопротеиназа-9, сосудистый эндотелиальный фактор роста, эндотелиальная дисфункция, липидный профиль.

■ INTRODUCTION

The World Health Organization notes that cardiovascular diseases and their complications are the main cause of premature death and early disability in most economically developed countries. Unfavorable dynamics of mortality from cardiovascular diseases, which remains a serious problem today, is particularly concerned. Coronary artery disease (CAD) is one of the most common chronic diseases that a practitioner has to deal with. This disease is one of the most urgent social and medical problems of our time. Therefore, the main way to reduce the negative effects of coronary artery disease is its prevention and timely detection, as well as comprehensive approach to treatment [1–4].

Breast cancer (BC) is the most common neoplasm among women, which ranges from 19 % to 31% of all malignant tumors. In recent years, there has been an increase in worldwide morbidity and mortality from breast cancer. Every year more than 1 million new cases of breast cancer are registered in the world. According to The national cancer registry in Ukraine, the incidence of breast cancer is about 70.9 cases per 100 thousand of the female population, and the mortality rate reaches 31.5 cases per 100 thousand of the female population [5–7].

The development of stable CAD in women is gender-specific and begins in the postmenopausal period. Over 55 years of age also accounts for the peak incidence of breast cancer. It can be assumed that with the increase in the age of women it also increases the frequency of the combination of these diseases. It should also be noted that the combination of ischemic heart disease and tumors occurs almost in 2 times more often than it is diagnosed during the lifetime of patients, which increases the relevance of timely and

▼ ▲ К содержанию

while alive diagnosis of the combination of CAD with breast cancer. In this clinical situation, it is equally important to identify the presence of tumors in a patient with coronary artery disease, and to recognize coronary artery disease in an oncological patient in time. In this regard, there is a need for research aimed at studying the characteristics of the course of CAD in patients with breast cancer at different stages of development of the neoplastic process [8–10].

Neurohumoral factors and endothelial dysfunction play an important role in the pathogenesis of CAD, which can be the leading factors of its progression. At the same time, the role of coronary angiogenesis in the course of stable coronary artery disease is not unambiguous, since on the one hand collateral circulation helps to preserve the vital activity and functional state of the myocardium, and, on the other hand, there is a threat of neovascularization of atherosclerotic plaque, which can lead to its destabilization, and in breast cancer it can contribute to tumor metastasis. Acting on the vascular wall and myocardium, vascular endothelial growth factor (VEGF) and matrix metalloproteinase-9 (MPP-9) cause a number of adverse metabolic effects, causing endothelial dysfunction. In this regard, the determining of the level of VEGF and MPP-9 in comparison with lipidogram is an urgent task in patients with CAD and breast cancer, which was the reason for this study [11, 12].

■ PURPOSE

To determine the relationship of markers of endothelial dysfunction with lipidogram in patients with stable CAD in combination with breast cancer.

■ MATERIALS AND METHODS

The results of the study are based on the data obtained in a comprehensive survey of women in 2015–2016 on the basis of PI "Zaporizhzhya regional clinical Oncology center" ZCC. We examined 101 women with stable CAD, 70 patients were diagnosed with breast cancer $T_2N_0M_0$, and 31 patients were without oncopathology. On an outpatient basis, 31 practically healthy women comparable in age and social status were examined.

The study was conducted in compliance with all the principles of the Helsinki Declaration on patient rights. According to it, all examined persons before the beginning of research manipulations were fully informed about purpose and objectives of the study, as well as familiarized with all the volume of medical manipulations to which they will be subjected, as all patients personally and voluntarily signed a form of informed consent to participate in the study. In order to verify the diagnosis, identify complications and comorbidities, all patients were subject to general clinical, instrumental and laboratory examination.

Inclusion criteria in the study: female patients aged 50–65 years; postmenopausal period of at least 1 year; the presence of stable CAD a known duration of the disease more than 6 months; detected stage II breast cancer ($T_2N_0M_0$).

Exclusion criteria from the study: atrial fibrillation and atrial flutter; congenital and acquired heart diseases; heart failure higher than II NYHA functional class; diabetes mellitus type 1 or 2; life-threatening ventricular

▼ ▲ К содержанию

arrhythmia; infectious disease in the acute period; other acute diseases of the internal organs in the stage of decompensation; patient's refusal to participate in the study for any reason at any time from the start of the study till its end.

Distribution of patients into groups was carried out after establishing the compliance of patients with the criteria for inclusion/exclusion of the study depending on the presence of breast cancer:

- the first group included 70 patients with stable CAD with BC (mean age 57 [55; 62] years);
- second consisted of 31 patients with stable CAD without tumors (mean age 56 [53; 60] years);
- the third group included 31 healthy women (mean age 56 [54; 57] years).

Clinical examination of patients. All the examined patients underwent general clinical, instrumental and laboratory diagnostics in order to verify the diagnosis and identify concomitant pathology. Clinical examination included the collection of complaints, anamnesis, taking into account the duration of coronary artery disease, objective examination, instrumental and laboratory methods of diagnosis. Verification of the diagnosis was performed: stable CAD – according to the ESC guidelines on the management of stable coronary artery disease (2013), breast cancer was diagnosed according to the recommendations of the working group NICE (2013) and ESMO (2013).

We used stress testing for diagnosing ischaemia. All patients were examined on bicycle exercise testing, used 12-lead ECG monitoring. The main diagnostic ECG abnormality during ECG exercise testing consists of a horizontal or down-sloping ST-segment depression ≥0.1 mV, persisting for at least 0.06–0.08s after the J-point, in one or more ECG leads.

Immunoenzyme analysis. For immunoassay, blood sampling was carried out from the ulnar vein in polyethylene tubes to obtain blood plasma, in tubes previously was added 0.5 M EDTA solution. The plasma was transferred to tubes of the "Eppendorf" type and the samples were stored at –20 °C for no more than three months before the study. The vascular endothelial growth factor and matrix metalloproteinase-9 levels in blood plasma were determined by enzyme immunoassay using standard Human VEGF-a (MMP-9) ELISA kit (RayBiotech, USA) according to the procedure set out in the instructions for test systems. The optical density was estimated using spectrophotometry at a wave length λ=450 nm. The extent was determined using a semi-automatic flatbed analyzer "SUNRISE TS" (Austria). The minimum level of detection of VEGF and MMP-9 was 10 PG/ml.

Nitrate recovery to nitrite was performed using nitralyzer reactors (World Precision Instruments, Inc., USA.) according to the method given in the instructions to the set.

Medical treatment of patients. They prescribed Bisoprolol (Concor, Merck & Co) was administered at an initial dose of 2.5 mg per day with subsequent titration, individually, depending on the heart rate. Acetylsalicylic acid ("Aspirin-cardio", Bayer) was administered at a daily dose of 100 mg in the morning. All patients with stable CAD without tumors was prescribed atorvastatin (Torvacard, Zentiva) 40 mg. All patients with stable CAD and breast cancer with the method of adaptive randomization was prescribed statin, rosuvastatin (Rosucard, Zentiva) at 10 mg/day or atorvastatin

К содержанию

(Torvacard, Zentiva) in a daily dose of 20 mg. We used minimal doses of statins due to elevated alanine aminotransferase and/or aspartate aminotransferase. Patients whose LDL-C value did not reach the target level after 2 months, have normalized alanine aminotransferase and aspartate aminotransferase increased the dose of statin 2 times. The follow-up period was 6 months. The clinical treatment efficacy was evaluated depending on the stability of functional class of angina pectoris in patients seeking medical care or exercise tolerance stability at bicycle exercise investigation after 6 months. The increase in the functional class of effort angina or tolerance reduction to physical activity while bicycle exercise investigation led to the change in the Treatment Protocol that was taken as the end point of the study.

Treatment of breast cancer was carried out according to the clinical practice guidelines "Primary breast cancer" ESMO (2015). Women passed the complex treatment: it was conducted breast – conserving surgery to establish the purity of the barriers of resection when the tumor size is to 3 cm, next was used postoperative radiotherapy for breast cancer. We used chemotherapy according to ESMO (2015) regimens based on Cyclophosphamide/Metotrexate/5-fluorouracil (CMF) 6 cycles. Cyclophospamide (Sandoz) (600 mg/m^2), Metotrexat (Ebewe) (40 mg/m^2), 5Fluouracil (Ebewe) (600 mg/m^2).

Statistical processing of the results

The obtained data had a distribution different from the normal, and are presented in the form of the median and interquartile range of Me [Q25; Q75]. The results of the study were processed by methods of parametric or nonparametric statistics, depending on the sample distribution, using specialized computer applications ApacheOpenOffice (version 4.1) and PSPP (version 0.10.2, GNU Project, 1998–2016). When testing statistical hypotheses, the null hypothesis was rejected at the level of statistical significance (p) below 0.05. When comparing more than two independent variables, the analysis of variance (One-way ANOVA) was used, followed by the use of a posteriori tests. Equality of variances was tested using the Levene test. In case of equality of variances in the studied groups, the Scheffe criterion was used, and in the absence of equality of variances, the T2-Tamhein test was used. In the case of data distribution different from normal, the analog of dispersion analysis by the Kruskal – Wallis method with subsequent post-hoc analysis using the data criterion was used. The relationship between quantitative traits with normal distribution was estimated using Pearson correlation coefficient (r). In a distribution different from normal, by calculating the Spearman rank correlation coefficient (R). The reliability of the correlation coefficients was evaluated based on the properties of the correlation coefficients and the number of degrees of freedom.

■ RESULTS AND DISCUSSION

Biochemical parameters of endothelial function in the examined persons are presented in table 1.

Baseline values of vascular endothelial growth factor among patients with CAD were significantly elevated. VEGF level was significantly higher in

Table 1
Biochemical parameters of endothelial function in the examined persons

Variable	In the group of patients		
	CAD in combination with BC (n=70)	CAD without neoplasm (n=31)	Healthy individuals (n=31)
	1	2	3
VEGF, PG/ml	327.8 [308.2; 340.5]	213.7 [197.7; 227.4]	192.3 [162.6; 207.8]
P-value	p_{1-2}<0.0001	p_{2-3}<0.0001	p_{1-3}<0.0001
MPP-9, PG/ml	223.6 [192.5; 261.8]	136.6 [125.6; 140.3]	69.4 [58.8; 82.6]
P-value	p_{1-2}<0.0001	p_{2-3}=0.004	p_{1-3}<0.0001
NOx, μmol/l	16.3 [14.3; 18.2]	23.4 [21.7; 24.7]	26.7 [25.8; 27.3]
P-value	p_{1-2}<0.0001	p_{2-3}=0.01	p_{1-3}<0.0001

patients with stable CAD in combination with BC 327.8 [308.2; 340.5] PG/ml than in the group of persons with stable CAD without neoplasm 213.7 [197.7; 227.4] PG/ml and in the group of healthy individuals was 192.3 [162.6; 207.8] PG/ml (p<0.05). In the group of patients with stable CAD without tumors, this figure was 11.1% higher than in healthy individuals (p<0.05). A significant increase in VEGF levels was observed in the group of patients with stable CAD associated with breast cancer compared to healthy individuals by 1.7 times (p<0.05).

Similar differences were noted for matrix metalloproteinase-9 (MMP-9). The highest level of MPP-9 was in the group of patients with stable CAD in combination with breast cancer, and amounted to 223.6 [192.5; 261.8] ng/ml and significantly exceeded 1.3 times the level of 136.6 [125.6; 140.3] ng/ml of this indicator in the group of patients with stable CAD without tumors (p<0.05). In the group of patients with stable CAD without tumors, where this figure was significantly higher in 2 times compared with healthy individuals (p<0.05). A significant increase in the level of MPP-9 in the group of patients with stable CAD in combination with breast cancer compared with healthy individuals was in 3.2 times, and in 1.3 times compared with the group of patients with stable CAD without tumors (p<0.05).

Significantly, the content of nitrogen monoxide metabolites (NOx) decreased in blood plasma, both in the group of patients with stable CAD in combination with BC to 16.3 [14.3; 18.2] μmol/l, and in the group of patients with stable CAD without neoplasm to 23.4 [21.7; 24.7] μmol/l compared with the value of this indicator in healthy individuals 26.7 [25.8; 27.3] μmol/l (p<0.05). At the same time, this indicator was significantly 30.3% lower against the level of the group of patients with stable CAD without neoplasm (p<0.05), which indicates a significant decrease in endothelial function in patients with stable CAD, which is enhanced when combined with tumor diseases of the breast.

Identify the relationships between the indicators of endothelial function and lipidogram was performed using correlation analysis. The obtained data are shown in table 2.

Our correlation analysis showed the presence of a significant direct correlation between TC and VEGF (R=+0.29, p=0.01), as well as between

▼ ▲ К содержанию

Table 2
Correlations between endothelial function and lipid profile

Variable	VEGF, PG/ml	MPP-9, PG/ml	NOx, μmol/l
TC, mmol/l P-value	R=+0.29 p=0.01	R=+0.30 p=0.01	R=–0.24 p=0.04
LDL-C, mmol/l P-value	r=+0.65 p=0.0001	R=+0.49 p=0.0001	r=–0.58 p=0.0001
HDL-C, mmol/l P-value	r=–0.49 p=0.0002	R=–0.36 p=0.002	r=+0.40 p=0.001
TG, mmol/l P-value	R=+0.21 p=0.08	R=+0.18 p=0.13	R=–0.19 p=0.12
AI P-value	r=+0.42 p=0.0004	R=+0.37 p=0.002	r=–0.34 p=0.003

TC and MMP-9 (R=+0.30, p=0.01). LDL-C level had a significant direct relationship with VEGF (r=+0.65, p=0.0001), with MMP-9 (R=+0.49, p=0.0001) and inverse relationship with NOx (r=–0.58, p=0.0001).

Between the level of HDL-C, and VEGF and MMP-9 using the correlation analysis it was revealed a significant inverse relationship (r=–0.49, p=0.0002) and R=–0.36, p=0.002, respectively), and between HDL-C and NOx relationship was a direct opposite of the weak force (R=+0.40, p=0.001). There were no significant relationships between the level of TG and the indicators of endothelial function (p>0.05). There was a direct correlation between the level of VEGF and the concentration of MPP-9 (R=+0.83, p<0.05), and the inverse relationship between VEGF and NO (r=–0.84, p<0.05).

The effect of VEGF and MMP-9 on the vascular wall and myocardium causes a number of adverse metabolic effects, causing endothelial dysfunction. Literary sources indicate that endothelial dysfunction plays an important role in the pathogenesis of stable CAD, which may be the leading cause of its progression in patients with breast cancer [15].

Our data are comparable with the results of the study of V.I. Volkov et al. which found a correlation level of MMP-9 with the contents of TC and LDL. The found correlation between MMP-9 and the lipid spectrum in these groups suggests that an increase in the concentration of lipids in the blood contributes to an increase in the level of MMP-9 [16].

Our results are consistent with the study of J.W. Gaubatz et al., in which the inverse relationship of MMP-9 with HDL-C was revealed. The authors conclude that the levels of metalloproteinases associate with the remodeling of the walls of the carotid arteries [17].

At the same time, VEGF and MMP-9 are one of the most significant factors that can influence the formation of a new abnormal vascular bed in the tumor. In this regard, the study of VEGF and MMP-9 levels in comparison with patients with stable CAD and breast cancer makes it possible to understand their role in the clinical course of coronary artery disease. However, data on the role of MMP-9 in the forecast for the BC are not very numerous and there is still no consensus on this issue, which requires further scientific research.

■ CONCLUSIONS

1. The course of stable CAD confirmed breast cancer are accompanied by an increase in VEGF and MMP-9, which is accompanied by a decrease in the level of nitrogen monoxide metabolites.
2. The strongest positive correlations were found between VEGF and MMP-9 and low-density lipoproteins, which may be a mechanism for increasing VEGF and MMP-9 with increasing levels of low-density lipoproteins among patients with stable CAD.

■ REFERENCES

1. Townsend, N., Wilson, L., Bhatnagar, P., Wickramasinghe, K., Rayner, M., & Nichols, M. (2016) Cardiovascular disease in Europe: epidemiological update 2016. *European heart journal*, vol. 37, no 42, pp. 3232–3245.
2. World Health Organization (2015) *World malaria report 2014 – World Health Organization,* Geneva, Ice Press. 228 p.
3. Gandzyuk V. (2014) Analiz zahvoryuvanosti na ishemichnu hvorobu sertsya v Ukraïni [Analysis of ischemic heart disease morbidity in Ukraine]. *Ukrainian Journal of Cardiology*, no 3, pp. 45–52.
4. Task Force Members, Montalescot G., Sechtem U., Achenbach S., Andreotti F., Arden C., ... & Di Mario C. (2013) 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. *European heart journal*, vol. 34, no 38, pp. 2949–3003.
5. Korzhenkova G. (2013) Skrining raka molochnoi zhelezi [Breast cancer screening]. *Journal of radiology and nuclear medicine*, no 1, pp. 46–49.
6. Siegel R.L., Miller K.D., Jemal A. (2015) Cancer statistics, 2015. *CA: a cancer journal for clinicians*, vol. 65, no 1, pp. 5–29.
7. Fedorov V., Cheburkaeva M. (2015) Rasprostranennost' i faktori riska raka molochnoi zhelezi [Prevalence and risk factors of breast cancer]. *Fundamental research*, no 1, pp. 414–419.
8. Seruga B., Zadnik V., Kuhar C.G., Marinko T., Cufer T., Zakotnik B., Amir E. (2014) Association of aromatase inhibitors with coronary heart disease in women with early breast cancer. *Cancer investigation*, vol. 32, no 4, pp. 99–104.
9. Bradshaw P.T., Stevens J., Khankari N., Teitelbaum S.L., Neugut A.I., Gammon M.D. (2016) Cardiovascular disease mortality among breast cancer survivors. *Epidemiology (Cambridge, Mass.)*, vol. 27, no 1, pp. 6–13.
10. Rutter C.E., Chagpar A.B., Evans S.B. (2014) Breast cancer laterality does not influence survival in a large modern cohort: implications for radiation-related cardiac mortality. *International Journal of Radiation Oncology, Biology, Physics*, vol. 90, no 2, pp. 329–334.
11. Elski V., Vatutin N., Kalinkina N., Salakhova A. (2008) Rol' disfunktsii endoteliya v geneze serdechno-sosudistih zabolevanii [Role of endothelial dysfunction in the genesis of cardiovascular diseases]. *Journal of AMS Ukrainy*, vol. 14, no 1, pp. 51–62.
12. Okrut I., Kontorschikova K., Shakerova D. (2012) Kliniko-laboratornaya otsenka endotelial'noi disfunktsii i aktivnosti svobodnoradikal'nogo okisleniya pri rake molochnoi zhelezi [Clinical and laboratory evaluation of endothelial dysfunction and activity of free radical oxidation in breast cancer]. *Medical Almanac*, no 2, pp. 68–70.
13. National Collaborating Centre for Cancer (UK). (2013) *Familial breast cancer: classification and care of people at risk of familial breast cancer and management of breast cancer and related risks in people with a family history of breast cancer* [Electronic resource]. Available at: http://www.nice.

▼ ▲ К содержанию

14. Senkus E., Kyriakides S., Ohno S., Penault-Llorca F., Poortmans P., Rutgers E., Cardoso F. (2015) Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Annals of oncology*, vol. 26 (suppl. 5), pp. v8–v30.
15. Lupach N., Khludeeva E., Potapov V., Lukianov P. (2010) Matriksnie metalloproteinazi, oksidantnii status i disfunktsiya endoteliya u lits s giperholesterinemiei i u patsientov s razlichnimi formami ishemicheskoi bolezni serdtsa [Matrix metalloproteinases, oxidative status and endothelial dysfunction in persons with hypercholesterolemia and in patients with various forms of ischemic heart disease]. *Pacific Medical Journal*, no 4, pp. 71–74.
16. Volkov V., Kalashnik D., Serik S. (2006) Izmenenie urovnya matriksnoi metalloproteinazi-9 u bol'nih so stabil'noi i nestabil'noi stenokardiei [Change of the level of matrix metalloproteinase-9 in patients with stable and unstable angina]. *Ukrainian therapeutical journal*, no 1, pp. 4–7.
17. Gaubatz J.W., Ballantyne C.M., Wasserman B.A., He M., Chambless L.E., Boerwinkle E., Hoogeveen R.C. (2010) Association of circulating matrix metalloproteinase with carotid artery characteristics: the Atherosclerosis Risk in Communities Carotid MRI Study. *Arteriosclerosis, thrombosis, and vascular biology*, vol. 30, no 5, pp. 1034–1042.

Received/Поступила: 22.09.2018
Contacts/Контакты: sidev@mail.ru