Development of the method of the bulbar conjunctiva images estimation for investigation of microcirculation state in cardiovascular diseases

Anishchanka U[1], Konstantinova E[2], Lapitskii V[1], Levshinskii L[1], Trukhan V[1]

[1] United Institute of Informatics Problems, Minsk, Belarus
[2] Belarussian Center "Cardiology", Minsk, Belarus

Abstract

Purpose: **The results of some studies specify the important role of microcirculation disturbances in ischemic heart disease (IHD) and essential hypertension (EH) pathogenesis. Among clinical methods of microcirculation research the most perspective is the biomicroscopy of bulbar conjunctiva. However, the outdated methods of application of semiquantitative criteria systems for the estimation of the microcirculation system condition cause subjectivity and incomparability of results received by different researchers. The purpose of this study is the creation of the algorithm and the medical-technological complex (MTC) for the automated quantitative estimation of the microcirculation system state and primary evaluation of its possibilities in clinical investigations.**

Material and methods: **To observe microcirculation on the bulbar conjunctiva we have used an intra-vital videomicroscopic system.**

Results: **We have worked out the computer tools for documentation and estimation of bulbar conjunctiva images. To quantitative evaluation images we have developed the qualitative-quantitative scale of Möriche and Volkov. The quantitative evaluation algorithm of bulbar conjunctiva images includes the calculation of the vascular and intravascular coefficients for arterioles, capillaries, venules and ones for extravascular space. For estimation of the algorithm and the MTC possibilities in clinical investigations we were observed microcirculation in healthy subjects, patients with IHD and EH.**

Conclusions: **Our findings have demonstrated that present algorithm and the MTC will permit to increase the informatively and diagnostic significance of the conjunctival biomicroscopy method and to create a single approach to the estimation of the microcirculation system state.**

Key words: microcirculation, biomicroscopy, bulbar conjunctiva, digital and analog engineering, images estimation.

ADDRESS FOR CORRESPONDENCE:
Uladzimir Anishchanka
United Institute of Informatics Problems
6 Surganova Str., Minsk, 220012, Belarus,
Tel. +375 17 2840985, Fax: +375 17 2840320.
e-mail: anishch@newman.bas-net.by

Introduction

At the present time the results of some researches specify the important role of microcirculation disturbances in ischemic heart disease (IHD) and essential hypertension (EH) pathogenesis. The attention which has considerably increased to microcirculation by cardiologists' part for last years is connected to its special value in operating cardiovascular system which consists of providing an optimum microenvironment of any tissue working structures. Therefore now the characteristic of blood system circulation condition are not be able considered enough full without detailed studying a microcirculation system. Among numerous clinical methods of microcirculation research the most perspective is the biomicroscopy of bulbar conjunctiva. The value of this method in clinical researches is caused its information completeness, availability, non-invasivity, nearness to natural conditions, an opportunity of supervision practically all parts microcirculatory network. So, the conjunctiva biomicroscopy allows to estimate a condition of microvessels (arterioles, capillaries, venules), perivascular spaces, structure of blood flow, kind and a degree of intravascular disorders of microcirculation. The modern level of digital and analog engineering development, computer methods gathering and storage of the videoinformation allows to receive on the personal computer qualitative microcirculatory network images and to carry out their automated processing that opens real opportunities for increase of diagnostic precision and information completeness of this method.

Now investigations of conjunctiva microcirculation with using computer added analytical systems are carried out in several research centers [1,2]. Thus authors are carrying out a quantitative estimation separate characteristics of a microvascular network: diameter of vessels, their form, flow structure or velocity in one kind vessels [3]. Such approach allows receiving the information about separate parts of microcirculatory net, but it does not give an opportunity to estimate a state of this system as a whole. It may be used in research of microcirculatory disorders at the established clinical forms of various diseases and an efficiency estimation of the influences directed to the correction of concrete abnormalities. Semi-quantitative criteria used for studying the microcirculation of system are the reason of significant subjectivity and, frequently, incomparability of the results received by various researchers.

The purpose of this study is the creation of the algorithm and the medical-technological complex (MTC) for the automated quantitative estimation of the microcirculation system state and primary evaluation of its possibilities in clinical investigations.

Material and methods

To observe microcirculation directly on the bulbar conjunctiva we have used an intra-vital video-microscopic system. It consists of slit lamp, adapter, videocamera and personal computer. We have worked out the computer tools for documentation and estimation of bulbar conjunctiva images. To quantitative evaluation images we have developed the qualitative-quantitative scale of Möriche [4,5] and Volkov [6]. The status of the conjunctival microcirculation was examined by taking the vascular and intravascular coefficients for arterioles (a), capillaries (c), venules (v) and ones for extravascular space. The quantitative evaluation algorithm of bulbar conjunctiva images includes the determination of mean vascular diameters, corresponding parameters characterizing the microcirculatory phenomena and calculation of the following coefficients: irregular of vessels diameter ($C_{id}^{(a,c,v)}$), vessels wind ($C_{w}^{(a,c,v)}$), capillary density (C_{s}^{c}), arteriole-venular ratio (C_{av}), arteriole-venular anastomosis density (C_{ava}), network area (C_{net}), haemorrhages (C_{hr}), extravascular oedema (C_{evo}) and deposits (C_{evd}) areas, irregular of blood flow ($C_{ibf}^{(a,c,v)}$), intravascular aggregation ($C_{agr}^{(a,c,v)}$), dissemination of aggregates ($C_{dar}^{(a,c,v)}$). Based on these parameters the vascular (VI), intravascular (IVI), extravascular (EVI) and summary microcirculatory (SMI) indices were determined. For primary estimation of a MTC with expert system possibilities in clinical investigations we were observed conjunctival microcirculation in 133 healthy subjects young (29-35) and middle (36-50 years) age, 45 patients with IHD 42-58 years and 16 people with early stage EH 33-41 years. Some specific clinical and laboratory methods of investigation were applied to exclude or diagnose IHD and EH.

Results

Four groups of healthy subjects were studied: young women – subgroup A (n=20; 31.2±0.4 years) and middle – subgroup B (n=20; 41.8±0.72 years) age, young men – subgroup C (n=20; 31.7±0.5 years) and middle – subgroup D (n=20; 41.5±1.8 years) age. It was not found a significant difference between subgroups in means following coefficients: $C_{id}^{a,c,v}$, $C_{w}^{a,v}$, C_{av}, C_{ava}, C_{net}, C_{hr}, C_{evd}, $C_{ibf}^{a,c}$, $C_{agr}^{a,c,v}$, $C_{da}^{a,c,v}$. But in middle age women it was significant lower C_{evo} (0.62±0.05 in compare with 0.91±0.08; 0.89±0.09 and 0.83±0.07 in subgroups A, C, D, respectively). In middle age men it was determined significant lowering of C_{s}^{c} (0.083±0.006 in compare with 0.13±0.007; 0.14±0.009 and 0.12±0.008 in subgroups A, B, C, respectively) and C_{ibf}^{v} (0.81±0.07 in compare with 0.95±0.05; 0.97±0.08 and 0.96±0.06 in subgroups A, B, C, respectively).

In next part of primary clinical investigation using the created MTC with expert system for the non-invasive automated quantitative estimation of microcirculation state it was observed two groups of people: the 1st – 45 patients with IHD (51.3±6.1 years) and the 2nd – 39 healthy subjects (48.4±5.2 years). Results of conjunctival microcirculation parameters calculation in each group are: in group 1 – C_{id}^{a}=0.81+0.08; C_{w}^{a}=0.91+0.1; C_{s}^{c}=0.04±0.003; C_{id}^{c}=0.78±0.08; C_{w}^{c}=0.81+0.079; C_{id}^{v}=0.82+0.085; C_{w}^{v}=0.7+0.072; C_{av}=0.34±0.04; C_{ava}=0.91+0.1; C_{net}=0.92+0.09; C_{hr}=0.97+0.09; C_{evo}=0.51+0.1; C_{evd}=0.94±0.09; C_{ibf}^{a}=0.78+0.08; C_{agr}^{a}=0.81+0.09; C_{da}^{a}=0.94+0.1; C_{ibf}^{c}=0.83+0.08; C_{agr}^{c}=0.80+0.09; C_{da}^{c}=0.97+0.09; C_{ibf}^{v}=0.76+0.08; C_{agr}^{v}=0.6+0.07; C_{da}^{c}=0.94+0.09; VI=7.54±0.59; IVI=7.43±0.62; EVI=2.42±0.27; SMI=17.3+1.52 and in group 2 – C_{id}^{a}=0.99+0.08; C_{w}^{a}=0.97+0.09; C_{s}^{c}=0.14±0.01; C_{id}^{c}=0.99±0.1; C_{w}^{c}=0.96+0.1; C_{id}^{v}=0.97+0.12; C_{w}^{v}=0.97+0.11; C_{av}=0.57±0.06; C_{ava}=0.97+0.09; C_{net}=1.0+0.006; C_{hr}=1.0+0.0; C_{evo}=0.91+ 0.1; C_{evd}=1.0±0.0; C_{ibf}^{a}=0.99+0.09; C_{agr}^{a}=0.99+0.1; C_{da}^{a}=0.99+0.1; C_{ibf}^{c}=0.98+0.1; C_{agr}^{c}=0.99+0.1; C_{da}^{c}=0.99+0.12; C_{ibf}^{v}=0.96+0.11; C_{agr}^{v}=0.98+0.1; C_{da}^{c}=0.99+0.11; VI=8.53±0.69; IVI=9.85±0.82; EVI=2.91±0.03; SMI=21.5±1.98.

For evaluation of creating MTC possibility to detect early EH microcirculatory sings 30 people (43.2±3.7 years) were observed without clinical EH manifestations. Blood pressure in conditions without physical and other loading in all observed subjects were normal. Results of retina examination were normal also. But after evaluation of bulbar conjunctiva microcirculation state observed subjects were separated in two group. In the first of them (n=14) it was obtained following data: C_{id}^{a}=0.98+0.08; C_{w}^{a}=0.92+0.09; C_{s}^{c}=0.13±0.01; C_{id}^{c}=0.97±0.1; C_{w}^{c}=0.93+0.09; C_{id}^{v}=0.97+0.1; C_{w}^{v}=0.95+0.08; C_{av}=0.57±0.06; C_{ava}=0.91+0.08; C_{net}=1.0+0.006; C_{hr}=1.0+0.0; C_{evo}=0.87+ 0.1; C_{evd}=1.0±0.0; C_{ibf}^{a}=0.99+0.09; C_{agr}^{a}=0.99+0.1; C_{da}^{a}=0.99+0.11; C_{ibf}^{c}=0.98+0.1; C_{agr}^{c}=0.99+0.1; C_{da}^{c}=0.99+0.12; C_{ibf}^{v}=0.96+0.11; C_{agr}^{v}=0.98+0.1; C_{da}^{c}=0.99+0.11. In the second group (n =16) means of microcirculatory coefficients were: C_{id}^{a}=0.96+0.09; C_{w}^{a}=0.91+0.1; C_{s}^{c}=0.08±0.01; C_{id}^{c}=0.9±0.08; C_{w}^{c}=0.87+0.08; C_{id}^{v}=0.89+0.09; C_{w}^{v}=0.86+0.07; C_{av}=0.34±0.04; C_{ava}=0.99+0.1; C_{net}=1.0+0.004; C_{hr}=1.0+0.0; C_{evo}=0.74±0.1; C_{evd}=1.0±0.0; C_{ibf}^{a}=0.93+0.09; C_{agr}^{a}=0.91+0.1; C_{da}^{a}=0.97+0.1; C_{ibf}^{c}=0.94+0.1; C_{agr}^{c}=0.89+0.09; C_{da}^{c}=0.93+0.09; C_{ibf}^{v}=0.86+0.08; C_{agr}^{v}=0.84+0.09; C_{da}^{c}=0.87+0.08.

According to bulbar conjunctiva examination results main differences between these group present as: more high degree of venules and capillary wind, significant decrease of capillary density and AV-ratio, increase of irregular blood flow and intravascular aggregation in venules in the second group in compare with the first. During following clinical examination in all subjects of the second group it was found the hypertensive reaction on physical exercise in condition bicycle test and with correspondence to clinical and laboratory examination it was diagnosed the early stage of EH. The found data in the part of microcirculatory alteration character in more late stages of EH are similar to the literature [7].

Discussion

Our results show that conjunctival microcirculatory changes in men middle age are presented as lowering of capillary density and increase of intravenous abnormalities degree. In this subgroup were observed increase plasma cholesterol level and blood viscosity at the low shear rate. Microcirculatory changes in healthy men middle age my reflect early vascular damage from IHD risk factors influence [8].

Obtained data show that in IHD there are increase of an irregular of microvessels diameter, extravascular oedema and degree of intravascular disturbances in arterioles, capillaries and venules, decrease of capillary density and arteriole-venular ratio. These microcirculation abnormalities were marked by other authors [9], but present system permits to obtain a quantitative evaluation of the visible alterations. Investigation of bulbar conjunctiva with using creating system may be more sensitive to microcirculatory sings of EH early stage than results of retinal microvascular abnormalities evaluation [10].

Conclusions

Thus, a developing system of the criteria based on quantitative definition of parameters of the main phenomena, which are registered at biomicroscopic observation of microcirculatory network, will allow to receive the objective information on a state of microcirculatory system as a whole and to create classification of normal and pathological conditions of conjunctival microcirculation, which are typical for early stages IHD and EH.

References

1. Cheung ATW, Harmatz P, Wun T, Chen PCY, Larkin EC, Adams RJ, Vichinsky EP. Correlation of abnormal intracranial vessel velocity, measured by transcranial Doppler ultrasonography, with abnormal conjunctival vessel velocity, measured by computer-assisted intravital microscopy, in sickle cell disease. Blood, 2001; 1(97), 11: 3401-4.

2. Homma S, Tsushima N, Minamiyama M, Hayashi T, Matsuo H. Microvascular blood is distributed more to venules than to arterioles in patients with Buerger's disease. Observation of bulbar conjunctiva by intravital microscope system. Int Angiol, 2000; 19 (2): 135-41.

3. Komatsu R, Tsushima N, Matsuyama T. Effect of glucagons administration on microcirculation and blood rheology. Clin Hemorheol Microcirc, 1997; 17(4): 271-7.

4. Möriche R. Der Konjunktivalindex bei Hypertoniken und Infarktpatienten mit und ohne Hypertonie. Mitt Ges Inn Med, 1972; 8: 219-21.

5. Möriche R. Die Beurteilung degenerativer Gefassprozesse an der terminalen Strombahn der Conjunctiva Bulbi mit einem Konjunktivalindex. Mitt Ges Inn Med, 1973; 28: 32-6.

6. Volkov VS, Vysotskij NN, Trotsyuk VV, Mishkin VI. Assessment of the state of microcirculation by the method of conjunctival biomicroscopy. Klin Med, 1986; 5: 115-19.

7. Davidova NG, Katsnelson LA, Gurtovaia EE. Changes of bulbar conjunctiva in arterial hypertension. Vestn Ophthalmol, 1990; 106 (5): 37-9.

8. Piatin MM, Chekhova SP, Nikolaeva AA, Lineijtseva LI. Biomicroscopy of the bulbar conjunctival vessels in various types of hyperlipoproteinemia. Ter Arkh, 1982; 54 (1): 49-51.

9. Tepliakov AT, Garganeeva AA, Fedorov AI, Krylov AL, Varvarenko VI. Relation between microcirculatory disorders and coronary circulation in patients with a history of myocardial infarction (clinico-angiographic study). Kardiologia, 1990; 30 (4): 18-22.

10. Wong TY, Klein R, Klein BEK, Tielsch JM, Hubbard L, Nieto FJ. Retinal microvascular abnormalities and their relationship with hypertension, cardiovascular disease and mortality. Surv Ophthalmol, 2001; 46: 59-80.