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Investigation potential of laser Doppler flowmetry for patients with secondary lymphedema of lower extremities examination

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Abstract
Nowadays diseases of the lymphatic vessels are widely spread pathologies. So the development of non-invasive diagnostic methods is relevant. It is strictly interesting to investigate potential possibilities of laser Doppler flowmetry (LDF) in the appraisal of pathological changes of lymphodynamics. This method is widely used for investigation of blood vessels diseases, not for lymphatic ones. The aim of our research was to analyze changes of the accessory indexes of the LDF-gramme, registered from patients with secondary lymphedema of lower extremities. The investigation group included 10 patients, 27-65 years old, both sexes, with a clinically-manifested secondary lymphedema of lower extremities. The control group included 30 healthy volunteers, same age. Parameters of microcirculation were assessed through the system Biopac LDF 100C (Biopac instruments, USA). The investigation protocol included a 2-minutes long LDF-gramme recording on each lower extremity. In the course of output LDF signal processing amplitude–frequency spectra were constructed. For describing characteristic spectrum changes we used special indexes: *low frequency flaxmotions investment* and *flaxmotions index*. Patterns of amplitude-frequency spectra, registered from the investigation group differed from the control group. In the investigation group a significant decreasing of low frequency flaxmotions investment ($p<0.05$) were registered. Because of that, it was traced a trend to decreasing of flaxmotions index. According to the general conception of LDF-spectra areas, these changes are evidence of decreasing of the investment of local active mechanisms for modulation of the liquid stream in the microvasculature. We think that lymphatic microcirculation can also take part in forming of the output LDF signal because of the slowdown of the lymph flow and changing of the chemical structure of the lymph. This process changes the optical characteristics of the lymph and makes it recognizable for LDF. This phenomenon can be interpreted as a consequence of vessels dysfunction. Decreasing of the investment of local active mechanisms, probably, is caused by depression of lymphangion motility. These results are adjusted to relevant information about the pathogenesis of secondary lymphedema. So, it is possible to say that LDF has a diagnostic potential for patients with secondary lymphedema of lower extremities at the stage of initial structural and functional changes. A perspective aim for next study is inventing new algorithms of LDF-signal processing for more-detailed registration of non-periodic components of lymphodynamics. These results give a possibility for future development of LDF using in diagnostics of lymph vessels pathologies and monitoring of the effectiveness of the treatment.

Keywords
Laser Doppler Flowmetry, Secondary Lymphedema, Noninvasive Diagnostic Methods, Microvasculature, Lymphodynamics

1. Introduction

Nowadays diseases of the lymphatic vessels of lower extremities are widely spread pathologies. For example, WHO statistic says, that 10 % of humankind suffer from lymphedema of lower extremities. So the development of modern non-invasive diagnostic methods using is really actual. It is especially important to invent such methods those are possible to register initial pathological mechanisms of the disease, before some strong clinical implications can be detected. It is strictly interesting to investigate potential possibilities of laser Doppler flowmetry (LDF) in the appraisal of pathological changes of lymphodynamics.

This method is widely used for investigation of blood vessels diseases, not for lymphatic ones. Why a high potential of this method is supposed, it is because that's application point is microcirculature – the site of arterial, venous and lymphatic systems integration [1], [2]. So pathological process in any system indispensably provokes some changes of microcirculatory blood stream characteristics. This method has high sensitivity, but absence of clear clinical application algorithms and result interpretation criteria are making difficulties in using of this method in clinical practice.

The aim of our research was to analyze changes of accessory indexes of the LDF-gramme (used in the blood vessels investigation) in the examination of patients with secondary lymphedema of the lower extremities, which can be used in the future as the interpretation criteria. In the context of this aim, we have accomplished LDF-gramme registration among 2 groups of patients and control group, constructed amplitude-frequency specters of LDF signal and estimated accessory indexes.

2. Methods

2.1. Participants

Our investigation was based on the Saint-Petersburg State University polyclinic.

The investigation group included 10 patients, between 27 and 65 years old, both sexes. All patients had a clinical-manifested secondary lymphedema of lower extremities.

The control group included 30 healthy volunteers at the same age, without pathology of arterial and lymphatic vessels of the lower extremities.

2.2. Procedure

Complex investigation included a clinical examination, an anthropometry and laser Doppler flowmetry.

Parameters of microcirculature were assessed through an LDF system Biopac MP 100 (Biopac instruments, USA) with original software and special skin transducer TSD 140 8*17 mm. LDF transducer was superimposed on the area above the medial ankle with the help of special adhesive disks. The laser Doppler investigation protocol included a 2-minutes long LDF-gramme recording on each lower extremity in a horizontal body position.

2.3. Measurements

In the course of output LDF signal processing amplitude–frequency spectra were constructed (with the help of the original software). Firstly the visual assessment and comparison of specters was carried out.

Amplitude-frequency spectrum has 3 characteristic areas of flaxmotions:

1. *Low frequency flaxmotions* area (LF) (0.05-0.2 Hz). Low frequency flaxmotions are caused by myogenous, neurogenous vessel tone and endothelial factors effect;
2. *High frequency flaxmotions* area (HF) (0.2-0.4 Hz). High frequency flaxmotions are caused by venous pressure gradient as a result of pulling action of the breast during respiratory movements;
3. *Cardiorythmic area* (CF) (0.8-1.6 Hz). These flaxmotions are caused by the heart working, the left ventricle propulsive action and sphygmic wave expanding. [3-5]

For describing characteristic spectrum changes we used special indexes: *low frequency flaxmotions investment* and *flaxmotions index*.

The mechanism of calculation of these indexes is described below. Firstly, we calculated average amplitudes in all areas (A_{LF}, A_{HF}, A_{CF}). The sum of squared amplitudes *(M)* is a full potency of the spectrum (Eq. 1):

$$M = A^2 + B^2 + C^2 \quad (1)$$

The investment of each flaxmotion component is estimated using the next formula (for example, for low frequency flaxmotions (A_{LF})) (Eq. 2):

$$A_{LF} = A^2 / M \times 100\% \quad (2)$$

The mirror of integral characteristics of active and passive mechanisms of flaxmotion is a special *flaxmotions index (FI),* estimated the way below (Eq. 3):

$$FI = A_{LF} / (A_{HF} + A_{CF}) \quad (3)$$

2.4. Statistical Analysis

For statistical procession we have used paired non-parametric Mann-Whitney criteria, group differences are thought to be significant with 95% probability ($p<0.05$).

3. Results

Our investigations show that patterns of amplitude-frequency spectra of LDF signal, registered from the investigation group are differ from the control group. These changes were regular.

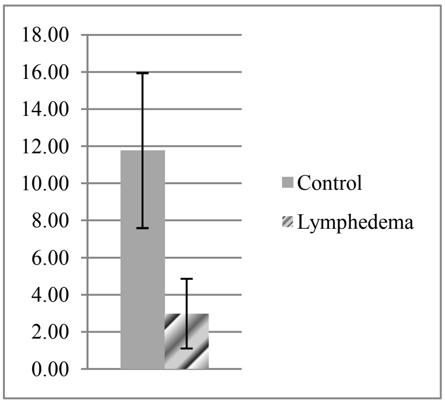

Fig. 1. *Low frequency flaxmotions investment*

First of all, at the visual appraisal, in the spectra of secondary lymphedema patients the low frequency flaxmotions were expressed fewer. After calculating special indexes we were registered a significant ($p<0.05$) decreasing of low frequency flaxmotions investment in this group (Fig. 1):

Because of that, it was traced a trend to decreasing of flaxmotions index (Fig. 2):

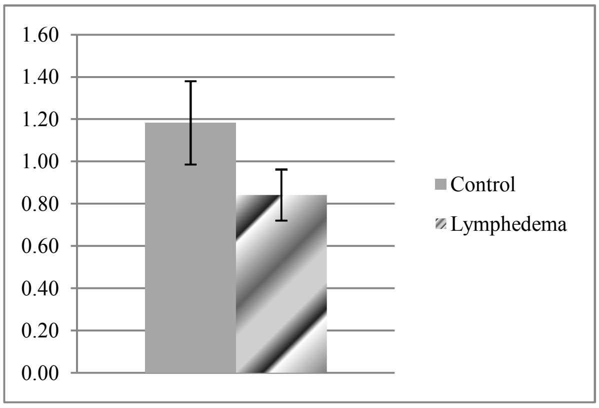

Fig. 2. *Flaxmotions index*

4. Discussion

According to the general conception of such LDF-spectra areas meaning, changes we have got are evidence of decreasing of local active mechanisms investment for modulation of the liquid stream in the microvasculature. This phenomenon can be interpreted as a consequence of vessels dysfunction.

In spite of situation that laser Doppler flowmetry are positioned as only a blood microcirculation investigating method [4] - [6], we think that lymphatic microcirculation also can take part in forming an output LDF signal because of the slowdown of lymph flow and changing of the chemical structure of the lymph (increasing of albumins and globulins content). These proteins form large colloid particles. The linear dimensions of these particles are closer to 40-50 nm [7], This process changes the optical characteristics of the lymph and makes it recognizable for laser Doppler flowmetry.

5. Conclusion

Based on our results we put forward a hypothesis that full output LDF signal is not only formed by microcirculatory bloodstream, but microcirculatory lymph flow also takes part in output LDF signal formation. The decreased rate of flaxmotions index is evidence of disbalance of regulatory mechanisms (active and passive) of microvasculatory blood- and lymphstream. Decreasing of the investment of local active mechanisms during secondary lymphedema, probably, is caused by depression of lymphangion motility.

These results are adjusted to relevant information about the pathogenesis of secondary lymphedema of lower extremities, because the essential part at the stage of initial structural and functional changes is depression of lymphangion motility, followed by increasing of endolymphatic pressure [10].

So, it is possible to say that LDF has a diagnostic potential for patients with secondary lymphedema of lower extremities at the stage of initial structural and functional changes. Compliance between registered LDF-picture and information about secondary lymphedema pathogenesis confirmed the hypothesis that there is a special component of summary LDF-signal, caused by the reflection of laser radiation from elements of the lymph.

The important defect of present algorithms of LDF signal processing is that LDF-spectra, constructed using fast Fourier-transforming or wavelet analysis, are not clearly correct for registering non-periodic flaxmotions. But if the microcirculatory blood and lymph vessels function is the main object of LDF-investigation, it is especially important to get a highly sensitive method for assessing such kind of flaxmotions. So, a perspective aim for next study is inventing new algorithms of LDF-signal processing for more-detailed registration of non-periodic components of lymphodynamics.

These results give a possibility for future development of LDF using in diagnostics of lymph vessels pathologies and monitoring of the effectiveness of the treatment.

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