Clinical application of laser Doppler flowmetry in neurology

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Summary  Laser Doppler flowmetry is a contemporary method for microcirculatory investigation used in different medical fields including neurology.

Aim: To present principles and clinical application of laser-Doppler method in neurology and related pathologies.

Methods: The diagnostic value was studied by evaluating systematic literature and personal experience. It is based on Doppler principle and uses a laser-generated monochromatic light beam, a fiber-optic probe and sensitive photodetectors. The tissue perfusion of a sample volume is calculated by multiplying the number of moving blood cells and their velocity and is presented in perfusion units.

Results: A high diagnostic value was established in studying microcirculation and its autoregulation using a battery of functional tests for evaluation of vasomotor response mediated by sympathetic neural, axon-reflex, receptor or endothelial mechanisms. It has clinical significance in assessment of Raynaud's phenomenon, distal autonomic neuropathy of the small C fibers due to diabetes mellitus, peripheral arterial occlusive disease, systemic autoimmune diseases, chronic venous insufficiency, peripheral neuropathies, for medical expertise of occupational diseases as hand-arm vibration syndrome, toxic neuropathies, etc. By iontophoretic transducer different drugs or substances might be applied locally to test an effect, physiological or pathophysiological mechanisms. Unlike the contemporary ultrasound investigations it studies the blinded sphere for neurosonology — microcirculation and its autoregulation.

Conclusions: Laser Doppler flowmetry is a valuable and reliable method for diagnostics of microcirculation and perfusion, for assessment of autoregulation and effect of treatment, for experimental studies and research. In combination with ultrasound sonography it gives a thorough information for both macro- and microcirculation.

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Introduction

Laser Doppler flowmetry (LDF) is a contemporary noninvasive method for microvascular investigation used in different medical fields including neurology.

The Doppler shift of the laser beam is the carrier of the information about microcirculatory blood flow.


The aim of the study was to present the principles and clinical application of laser-Doppler method in neurology and related pathologies.

Methods

The diagnostic value of LDF was studied by evaluating the systematic literature and our personal experience submitting some data for illustration.

Results

The working of LDF is based on Doppler principle using a laser-generated monochromatic light beam, a transducer with optic fibers and sensitive photodetectors. The light beam is reflected and scattered by the moving blood cells undergoing a change of the wave length (Doppler shift), dependent on the number and velocities of the cells in the investigated sample volume but not on the direction of their movement [6]. The scattered laser beam is perceived by detectors with the help of optic fibers. The signals are analyzed giving values to the number of the cells and their velocities and perfusion is their product.

The depth of penetration of laser beam depends on the tissue characteristics and its vascularisation, on the length of the light wave, the distance between the optic fibers. So the penetration of light source with wave length 633 nm is less than that with 780 nm. By investigation of the skin the depth is from 0.5 to 1.5 mm, and the sample volume is about 1 mm². Only the movement in microvessels but not in the bigger blood vessels contributes to the perfusion value because the vessel wall is enough to exclude the greatest part of the laser beam.

Calibration of different apparatuses makes their values equal.

LDF of the skin is easiest to access noninvasively and thus global skin blood flow including both nutritious (capillaries) and thermoregulatory (arterioles, venules and their shunts) microvessels is investigated. The information about thermoregulatory blood flow prevails because the blood flow from the richly sympathetically innervated arterio-venular anastomoses and subpapillary plexus contribute predominantly to the laser-doppler signal, especially of the volar site of the hand and plantar site of the feet. About 90—98% of the

\[ \text{finger pulmonary perfusion passes through arteriovenular anastomoses} \]

Registration of initial skin perfusion in controlled standard laboratory conditions is measured at first with the natural superficial skin temperature of the patient and then the perfusion is recommended to be measured at 32–33 Celsius superficial skin temperature in order to make skin perfusion at a definite site between different persons comparable.

The accuracy and sensitivity of LDF is improved by applying standardized functional tests [8]. Monitoring of microvascular responses to autonomic vasomotor stimuli is a recognized method for functional diagnosis and assessment of peripheral dysautonomy and function of small unmyelinated autonomic fibers [9].

Thus in orthostatic test constriction of skin precapillary and arteriolar sphincters and microvessels due to the increased sympathetic mediation induces a decrease of skin blood flow. Posture changes of the limbs below heart level activate sympathetic vеноarteriolar axon-reflex mechanisms and cause increased skin microvascular resistance like in orthostatism with decrease of skin perfusion. Testing of vеноarteriolar reflex at the finger pulp by LDF is an indicator of unmyelinated autonomic C fiber function [8] and pure postganglionic sympathetic nervous activity [10]. It is more sensitive method for assessment of autonomic dysfunction than the sympathetic skin response [11].

Vasoconstrictor response is changed in the limbs of patients with peripheral arterial occlusive disease [12], diabetic [13] or venous hypertensive microangiopathy [14]. In diabetics type 2 and patients with chronic venous insufficiency a primary defect of vеноarteriolar axon-reflex is speculated [7]. Dysregulation of feedback mechanisms between venules, identifying the transmural pressure and arterioles, controlling precapillary resistance is found in secondary Raynaud’s phenomenon, too [15,16] (Fig. 1).

Inspiratory tests of Valsalva, deep breathing, deep inspiration with abdominal arrest induce sympathetic vasoconstriction activity with significant decrease of skin perfusion. Peripheral microvascular resistance is significantly decreased in diabetes mellitus.

By cold test a somatic afferent part consisted of pain and temperature nerve fibers in the skin and a sympathetic

Figure 1 Finger pulp perfusion during venoarteriolar test in Raynaud’s phenomenon patients [16]. PU — perfusion units at a finger pulp; PUi — initial perfusion; PUB — basal perfusion at 32 °C; PUh — perfusion at heart level; PUd — perfusion in the dependent hand; Controls — group of healthy controls, Primary RP — primary RP group; SSc RP — secondary RP group due to sclerodermy; Vibration RP — secondary vibration-induced RP group; *p < 0.05; **p < 0.0001 in relation to previous perfusion value according to Wilcoxon matched pairs signed rank test.
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The efferent vasoconstrictor part of the reflex arch is evaluated. The effectiveness of the response after cold stress test with temperature below 15°C Celsius might be an index of a sympathetic vasoconstrictor activity [17,18].

Tests of isometric muscular constriction and emotional stress also induce sympathetic skin vasoconstriction [19,20].

By heating test an axon-reflex mediated thermoregulatory microvascular vasodilation is studied as a result of activation of heat-induced nociceptors even at a lack of conscious perception of heat-induced pain [21]. The release of vasoactive peptides from primary nociceptor afferents cause an initial local heat-induced vasodilation at temperatures above 40°C Celsius followed by a sustained plateau phase induced by nitric oxide. Thermoregulatory vasomotor responses are abnormal in Raynaud's phenomena (Fig. 2) and diabetic foot (Fig. 3).

Reactive hyperemia test is mediated by local endothelial dependent vasodilator factors with significant decrease of skin vascular resistance and sudden increase of skin perfusion in healthy persons (Fig. 4). Microcirculatory vasodilator reactivity in response to ischemia reflects functional integrity of terminal vessels and assesses microvascular endothelial dependent dilator capacity in physiological and pathological conditions.

Vascular responses to drugs or chemical substances as physiological or pathophysiological mechanisms in different diseases can be studied experimentally by using an iontophoresis system for delivering minute volumes of a substance non-invasively in a controlled fashion together with LDF.

Along with other spheres of application LDF is a valuable method in neurology to diagnose small fiber neuropathy...
and distal acral vasomotor dysautonomia as an idiopathic or secondary manifestation of polyneuropathies, radiculopathies, mononeuropathies, reflex sympathetic dystrophy, neurovascular syndromes caused by diabetes mellitus, thyroid dysfunction, rheumatic diseases, amyloidosis, lepra, AIDS, venous limb insufficiency, neuropathic pain or occupationally induced by overstrain, vibration, microrotrauma, toxic exposure, etc.

The method is valuable to follow up the effect of applied therapy. It is reliable and with very good reproducibility.

A laser Doppler blood perfusion imager is created scanning tissue with a low-power laser beam and colour-coded images of the blood perfusion in the microvasculature.

Conclusions

Unlike the contemporary ultrasound investigations laser Doppler flowmetry studies the blinded sphere for neurosonology, i.e. microcirculation and its autoregulation. Laser Doppler flowmetry is a valuable, easy to use, non-expensive microcirculatory method of investigation which in combination with ultrasound sonography gives thorough information for both macro- and microcirculation.

- Laser-generated monochromatic light beam is directed towards the surface of the investigated tissue by a probe with optic fibers. The tissue perfusion of the investigated sample volume monitored by the flowmeter is calculated automatically by multiplying the number of the moving blood cells and their velocity and is presented in perfusion units (PU).
- Laser beam penetrates tissues, so monitoring of perfusion is noninvasive, for assessment of the integrity of constrictor microcirculatory mechanisms. Afterwards with increased skin flux, decreased venoarteriolar response and increased skin filtration inducing edema
- Using functional reflex vasomotor tests contribute for differentiation of primary from secondary Raynaud’s phenomenon, diabetic distal sympathetic neuropathy and microangiopathy; small fiber neuropathy; polyneuropathies or radiculopathies with autonomic dysfunction., distal sympathetic neuropathy, neurovascular syndromes, toxic neuropathies and microvascular reflex vasomotor reactivity and evaluation of microcirculatory vasomotor response mediated by sympathetic neural, axon-reflex, receptor or endothelial mechanisms;
- It is reliable to follow up the effect of applied therapy.
- Measurements are less dynamic than with the probe-based single-point laser Doppler monitor but the microcirculation can be studied over a larger area.
- Laser Doppler flowmetry not only measures and monitors microvascular blood flow but also evaluates microcirculation and its autoregulation.

References

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