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Diurnal and long-term variations of lymph capillary pressure in health

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Abstract The variability of pressure in the cutaneous lymph capillaries on the forefoot was determined in 2 groups of healthy volunteers. In group A, including 12 subjects (8 men, 4 women; mean age 28 years, range 22 to 37 years) measurements were performed in the morning and late afternoon of the same day. In group B (12 subjects, 5 women, 7 men; mean age 53 years, range 23 to 72 years) measurements of lymph capillary pressure were repeated within an interval of 7 weeks. The superficial microlymphatics were visualized by intravital fluorescence microlymphography, cannulated with glass micropipettes, and the lymph capillary pressure was measured using a servo-nulling pressure system. The lymph capillary pressure measured in the morning (mean 7.5±4.4 mm Hg; range −4 to 16 mm Hg) did not differ ($p>0.05$) from the pressure in the late afternoon (mean value 5.6±3.4 mm Hg; range −1 to 13 mm Hg). In group B initial lymph capillary pressure (mean 3.9±2.9 mm Hg, range −1.1 to 9.7 mm Hg) was not different ($p>0.05$) compared to the pressure after 7 weeks (2.9±2.7 mm Hg; range −1.0 to 6.8 mm Hg). In conclusion, lymph capillary pressure in healthy subjects does not exhibit significant changes during the daytime and the long-term reproducibility is good.

Key words Microcirculation · Microlymphatics · Capillary pressure

Introduction

Recently, a method has been developed to measure lymph capillary pressure (LCP) in the human skin [1]. LPC has been measured in healthy controls [1—4] as well as in patients with primary and secondary lymphedema [2, 5]. In primary and secondary lymphedema the existence of a *microlymphatic hypertension* could be demonstrated [2, 5]. The objective of the present study was to analyse the variability of LCP during the daytime and to examine the long-term reproducibility in health.

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Materials and methods

Microlymphatic pressure (LCP) measurements were performed in group A to investigate the diurnal variability. Twelve healthy volunteers (8 males, 4 females, mean age 28 years, range 22 to 37 years) without any clinical signs and history of lymphatic, arterial or venous disease were enrolled in the study. The subjects did not take any medication and the women were not on oral contraceptives. LCP was measured in the morning between 8 and 10 a.m. and in the afternoon after 4 p.m. on the same day in each individual.

In group B including 12 healthy subjects (5 women, 7 men) with a mean age of 53 years (range 23 to 72 years) LCP measurements were repeated after an interval of 7 weeks. LCP was measured in the afternoon.

Oral informed consent was obtained from each individual. The study was approved by the Ethical Committee of the Department of Medicine, University Hospital, Zürich.

Site of the measurement in both groups was the right forefoot at the bases on the dorsum between the first and second toe. The volunteers were examined after at least 20 min rest in the supine position. The foot was placed at heart level and fixed with a vacuum pillow to avoid movement artifacts. Before the lymphatic capillaries can be punctured, they have to be visualized. A relatively atraumatic fluorescence microlymphography (FML) technique [6, 7], which we have developed in our clinical microcirculation laboratory was used. The lymphatic capillaries were visualized with FITC-dextran (fluorescein-isothiocyanate-labeled dextran 150000; Sigma Chemical, St. Louis, USA). 0.01 ml of FITC-dextran (25% w/v in sterile saline) was injected into the subepidermal layer of the skin using a steel microneedle (0.2 mm outer diameter; A. Bott, Zürich, Switzerland) connected to a microsyringe (Hamilton, Bonaduz, Switzerland). The microlymphatics were made visible by the FITC-dextran, which acted as a contrast medium, as it passed from the initial depot site along the lymphatic capillaries. Video recordings were obtained using fluorescence video microscopy. The method for obtaining LCP measurements has been previously reported in detail (1). LCP was measured using the servo-nulling pressure system (Model 5A; IPM, San Diego, CA, USA) a counterpressure pump (Type 203; Lung Dynamics Systems, Royston, UK), a pressure transducer (Statham, Spectra Med P 23 XL, USA) and a pressure amplifier (Gould Biophysical Universal Amplifier 13-4615-58, Gould, Cleveland, OH, USA). A glass micropipette, with a tip diameter of 7–9 μm was inserted into a well-delineated lymphatic capillary by means

of a micromanipulator (Leica, Glattbrugg, Switzerland). Intralymphatic pressure was measured after connection of the servo-nulling system [8]. The capillaries selected for micropuncture were at least 2.5 mm away from the initial FITC-dextran depot. Mean LCP was calculated from measurements in at least 2 capillaries per subject. The correct intralymphatic position of the micropipette was checked by the servo-nulling system itself: the feedback gain of the servo-controlled counter pressure system could be varied without changing the recorded pressure [1, 9].

Statistics

Statistical analysis of the pressure values was performed on a personal computer (Apple Macintosh II CX) using a statistic programme (StatView II^{TM}, Abacus Concepts). Diurnal and long-term reproducibility were assessed using single factor ANOVA for repeated measurements.

Results

Diurnal variability

In 12 volunteers 33 different capillaries were cannulated both in the morning and in the afternoon and LCP measurements were performed. Mean pressure in the morning was 7.5±4.4 mm Hg (range −4 to 16 mm Hg) and in the late afternoon 5.6±3.4 mm Hg (range −1 to 13 mm Hg). The difference between the two sets of pressure data was not significant ($p>0.05$; ANOVA). Mean registration time of LCP in the morning was 96 s, and in the afternoon 104 s.

Long-term reproducibility

In group B initial mean LCP was 3.9±2.9 mmHg, ranging from −1.1 to 9.7 mm Hg. Three capillaries per subject were cannulated on both occasions. After 7 weeks the mean LCP of 2.9±2.7 mm Hg with a range from −1,0 to 6.8 mm Hg was not different $p>0.05$) compared to the initial pressure. The registration times were 110 s and 115 s, respectively.

Discussion

The results of the present study demonstrate a low variability and sufficient reproducibility of lymph capillary pressure measurements in the human skin at the forefoot. This concerns both the diurnal measurements in the morning and afternoon of the same day, and the long-term comparison after 7 weeks.

In contrast to our expectations the microlymphatic pressure showed a tendency towards lower values in the evening than in the morning. We initially expected higher pressure values in the evening resulting from a potentially minor edema formation during the day. However, the slightly higher pressure values ($p>0.05$) measured in the morning might be caused by a less activated muscle pump of the lower limb. During the day healthy subjects, who are not predominantly working in a standing position, apparently keep their lymph capillary pressure relatively constant by activating their muscle pump which may serve to expand and compress the initial lymphatics and lymph collectors when walking around [10].

Therefore the increase in transcapillary filtration rate during the day is compensated probably by an increase in lymph flow with constant lymph capillary pressure. Because in healthy subjects no obstruction in the lymphatic system is present no significant change in microlymphatic pressure occurs. In addition the investigators and the volunteers themselves did not observe any edema formation at the ankle or foot at the time of the second lymph capillary pressure measurement.

The long-term reproducibility of lymph capillary pressure measurements has been confirmed. The mean difference of 0.9 mm Hg in an interval of seven weeks is acceptable and parallels pressure fluctuations during a single measurement [3]. The mean microlymphatic pressure in group B showed a trend towards lower values than in group A, which could possibly result from the higher mean age in group B. Further studies including a greater number of subjects are required to verify, if a correlation exists between microlymphatic pressure and age.

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