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Microdialysis—A versatile technology to perform metabolic monitoring in diabetes and critically ill patients

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ABSTRACT

Continuous subcutaneous glucose monitoring has been tested in type 1 diabetes (T1D). Since in critically ill patients vascular access is granted vascular microdialysis may be preferential. To test this hypothesis comparative accuracy data for microdialysis applied for peripheral venous and subcutaneous glucose monitoring was obtained in experiments in T1D patients.

Twelve T1D patients were investigated for up to 30 h. Extracorporeal vascular (MDv) and subcutaneous microdialysis (MDs) was performed. Microdialysis samples were collected in 15–60 min intervals, analyzed for glucose and calibrated to reference. MDv and MDs glucose levels were compared against reference.

Median absolute relative difference was 14.0 (5.0; 28.0)% (MDv) and 9.2 (4.4; 18.4)% (MDs). Clarke Error Grid analysis showed that 100% (MDv) and 98.8% (MDv) were within zones A and B.

Extracorporeal vascular and standard subcutaneous microdialysis indicated similar performance in T1D. We suggest microdialysis as a versatile technology for metabolite monitoring in subcutaneous tissue and whole blood.

1. Introduction

Over the last years, a number of systems for continuous subcutaneous glucose monitoring (CGM) have been marketed and are routinely used in patients with diabetes to obtain more detailed information about 24-h glucose profiles [1–5]. CGM has proven to be useful in order to improve glycaemic control and reduce the risk of hypoglycaemia in type 1 diabetic patients [3,6]. In pregnant women, CGM has been proven effective in lowering HbA1c without higher rates of hypoglycaemia. Data obtained from continuous glucose monitoring were already used to steer insulin titration algorithms under research conditions [7]. In the future, CGM will be an essential part of an artificial pancreas system for automated closed loop glucose control.

In the hospital, numerous factors influencing glycaemic control and possibly leading to glucose excursions out of the desired range exist, e.g. interventions for which the patient has to remain fasting or medications such as corticosteroids or vasopressors. A reliable CGM could help to observe levels of glycaemia not only at defined time-points but continuously, making it possible for physicians and nursing staff to react before the patient is exposed to severe hypo- or hyperglycaemia [8]. The feasibility of CGM in hospitalized patients has been proven; however there were some substantial deviations

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from the subcutaneous to the reference signal [8–10]. The delay between blood and CGM value results from the physiologic lag time between blood and the interstitial space (maximum 10–15 min) but is controversially discussed [11]. Additionally the individual instrumental lag times have to be considered, which are reported to range from 2 to 10 min depending on the investigated CGM system [12]. In the hospital setting, vascular access is granted in the majority of patients and could be used as an alternative site for continuous glucose monitoring.

Therefore, the aim of the present study was to demonstrate, that using the microdialysis technique venous blood glucose concentration can be monitored both using vascular as well as subcutaneous access.

2. Materials and methods

The current publication analyzes two experiments which were performed in type 1 diabetic patients (MDv: 3 female/1 male, age 31.5 ± 7.7 years, BMI 25.8 ± 6.3 kg/m^2, diabetes duration 11.4 ± 9 years; MDs: 8 male, age 31.5 ± 8.0 years, 24.9 ± 1.7 kg/m^2, diabetes duration 13.6 ± 6.6 years). In four patients vascular extracorporeal microdialysis (MDv group) was performed [13], while in eight standard subcutaneous microdialysis (MDs group) was applied. The subjects were investigated over a period of up to 30 h. To simulate glucose excursions meal protocols with different insulin dosing procedures were applied: in the MDv group the insulin dose was administered intravenously using a glucose control algorithm aiming at a target range of 4.4–6.1 mmol/l, in the MDs group insulin was administered subcutaneously using multiple daily injections (MDI) at the patients' discretion aiming to maintain glycaemia at the patients' individual target range. Both studies were approved by the local ethics committee of Medical University of Graz, Austria, and written informed consent was obtained from all patients before any trial related activities.

2.1. *Study period*

For both experiments patients arrived at the research facility at 12 am after a fasting period of at least three hours. For reference measurements arterialized venous blood samples were drawn from a venous line inserted into a vein of the forearm which was placed in a thermo-regulated box (50 °C). Reference plasma glucose concentrations were measured twice using a glucose oxidase based method (Beckman Glucose Analyzer 2, Beckman Instruments Inc., Fullerton, CA). Arterialized venous blood glucose readings were used to prospectively calibrate both microdialysis techniques.

In both experiments, patients received four standardized meals: dinner at 6 pm (37 g of carbohydrates (CHO)), a snack at 10 pm (29 g CHO), breakfast at 8 am (36 g CHO) and lunch at 12 am (31 g CHO).

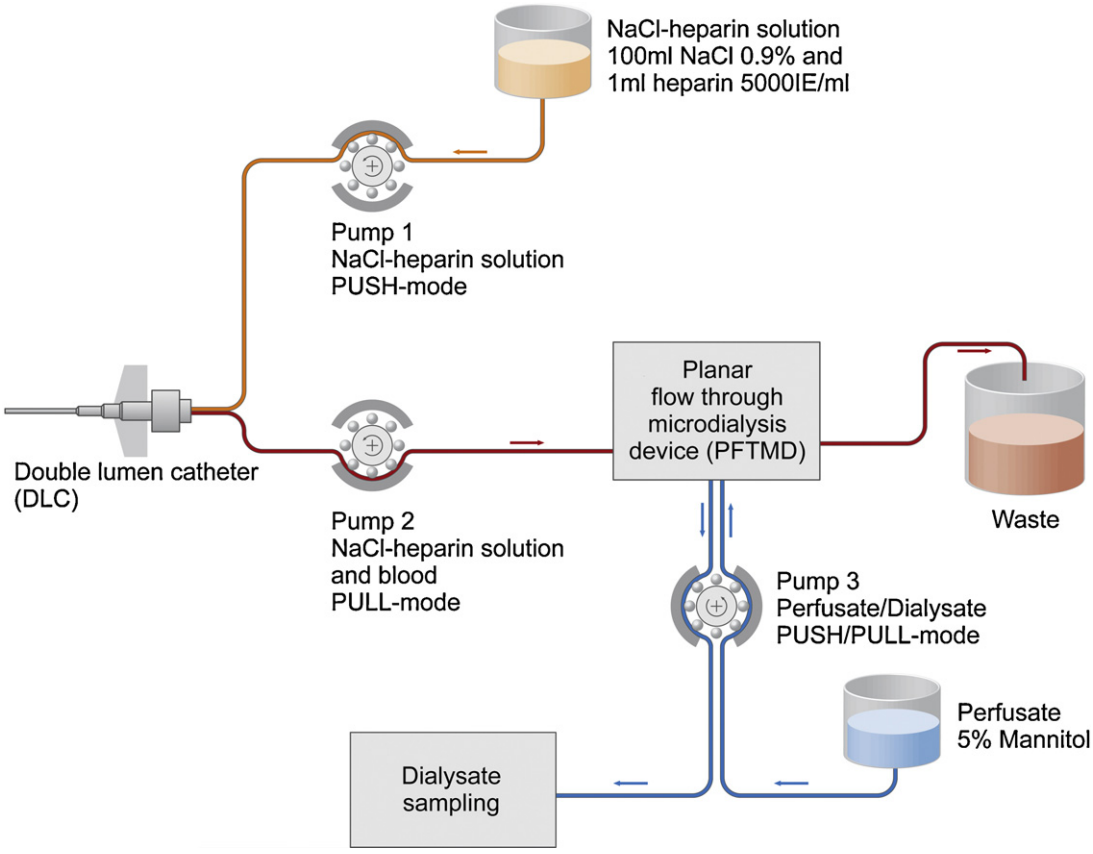

Fig. 1 – Schematic set-up of the extracorporeal vascular microdialysis approach. NaCl–heparin solution is pumped to the double lumen catheter where it mixes with blood. NaCl–heparin/blood mixture is further pumped to the planar flow through microdialyser. 5% mannitol is used as perfusate. Dialysate is collected in a sampling vial for further analysis.