ABSTRACT

This research will be registered in http://www.clinicaltrials.gov/.

Accuracy of Dexcom G6® and FreeStyle Libre® sensors in Standardized Hypoxemia conditions:
FOX study

Poitiers University Hospital is the sponsor of this research.

Brief summary:
In this project, the major aim is to evaluate accuracy of 2 CGMS: Dexcom G6® and FreeStyle Libre® in standardized hypoxemia conditions (artificial normobaric hypoxia).

Detailed description:
Patient self-monitoring of blood glucose (SMBG) and A1C are available to health care providers and patients to assess the effectiveness and safety of a management plan on glycemic control. Data indicate similar on A1C and similar safety with the use of Continuous glucose monitoring (CGM) compared with SMBG
Implementation of routine use of CGM was shown to lead to an improved glycemic control

Additionnaly, the use CGM devices like FreeStyle Libre® and Dexcom G6®, was demonstrated to be associated with a substantial benefit in prevention of hypoglycemia in T1D and T2D patients

Mackenzie et al. reported that acute hypoxia improves glucose tolerance in T2D patients using arterialized-venous blood technique for BG monitoring. However, really few is known in patient during acute/chronic hypoxemia. These conditions are of peculiar interest since they can be frequently encountered by patient with diabetes during short stay in altitude or even during prolonged severe medical conditions such as chronic heart failure or chronic obstructive pulmonary disease.

The actual gold standard for monitoring of BG is capillary SMBG for routine monitoring and venous BG for physiological exploration. One can easily perceive the limitation of traditional venous BG-based strategies compared to CGM strategy with no calibration.

CGM systems are electrochemical glucose biosensor based on glucose oxidase method that maybe sensitive to tissue hypoxia. They are reliable tools for BG monitoring in normoxia. Our purpose is to demonstrating the good performance and calibration of these CGM sensors in hypoxemia conditions.

Primary outcome: Mean absolute relative difference (MARD)

Secondary outcomes: Safety and tolerability of acute hypoxia (arterial blood oxygen saturation ($Sp0_2$) and Lake Louise Questionnaire)

Study design:
The overall study duration for each participant will be 3 or 4 days.
Visit 0: inclusion
Visit medical examination to check pulmonary and coronary status.
Visit 1: protocol day
Eligibility criteria:

- inclusion criteria:

All the population :

- women or man
- social security scheme
- no history of respiratory diseases (childhood asthma, respiratory allergies, exercise asthma, exertional dyspnea)
- signature of informed consent before any study-related procedure

Patients with diabetes:

- type 1 diabetes mellitus or type 2 diabetes mellitus (ADA definition)
- [18 ; 75] years
- stable treatment > 3 months
- no retinopathy
- no neuropathy (10g filament test)
- no complication of diabetes (cardiovascular diseases)

Healthy volunteers:

- [18 ; 40] years
- No diabetes
- No acute/long term > 3 months drug use outside contraception
- BMI : [18,5 – 29,9] kg/m^2

- exclusion criteria :

- Active smoking
- Pregnancy or breast-feeding
- Known allergies to patches or skin disinfectants used during the study
- Skin lesions, irritation, redness, edema, in the possible application of the sensor sites that may interfere with the placement of the device of the detection accuracy of test results
- Major cardiovascular complications such as coronary heart disease, unstable or stable angina, myocardial infarction, ventricular arrhythmias, and atrial fibrillation in the last 3 months
- Decompensated congestive heart failure
- Chronic respiratory disease
- Chronic renal failure with glomerular filtration rate <45ml/min/1,73m^2
- Anomaly during respiratory function tests
- Discovery of coronary anomaly requiring medical management
- Oxygen saturation ≤94%
- Therapy with systemic corticosteroid products
- Severe hypertension (180 mmHg systolic or 110 mmHg diastolic blood pressure
- Any concomitant disease or condition that may interfere with the possibility for the patient to comply with or complete the study protocol
- Anemia Hb<12g/dl
- Persons under enhanced protection i.e. minors, persons deprived of liberty by judicial or administrative decision
- Acute or chronic situation that in any way affect safety or conducting the study

Group: Healthy volunteer and diabetes patients will be exposed to hypoxia with CGM

Interventions: Acute hypoxia will be induced by a normobaric hypoxic chamber. Arterial blood oxygen saturation (SpO_2) and heart rate (HR) will be continuously monitored by pulse index oximetry. The signal will be recorded on a Biopac acquisition chain (BIOPAC Systems, Goleta, California, USA).
Two medical devices for continuous interstitial glucose measurement are used compared to venous glucose measurement. Interstitial and venous (blood catheter) glucose will be recorded every 15 minutes for a total of 3 hours.

Number of subjects: 30 (15 patients with diabetes and 15 healthy volunteers)

Statistical analysis: Repeated measures mixed-model analyses will be applied to assess MARD between FSL and Dexcom G6 sensor (i.e glucose oxidase) and venous BG (PCA Hexokinase).
For each patient and intervention, CGM readings were paired with blood glucose values measured simultaneously every 15 min.
Overall accuracy and accuracy during euglycemia (70-180 mg/dl) and hyperglycemia (>180 mg/dl) as well as during exercise will be assessed by calculating the MARD between sensors and venous BG.
In addition, Clarke Error Grid Analysis will be applied to quantify the clinical accuracy of CGM.
Values are expressed as mean ± standard error of the mean, unless specified otherwise.

Conditions : Hypoxia ; Diabetes mellitus, type 1 ; Diabetes mellitus, type 2

Key-words: *diabetes ; hypoxia ; CGM ;*