

Intra-individual biological variation in sweat chloride concentrations

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Background. The sweat test (ST) remains the main test for Cystic fibrosis (CF) diagnosis and it is now also used to evaluate the function of the CFTR protein in basal conditions and under the influence of CFTR modulators. However it is not yet well-defined the biological variability of the test, both among different individuals (inter-individual) and within the same individual at different times and under different conditions (intra-individual).

Hypothesis and objectives. The project aims to study intra-individual sweat chloride (Cl) biological variability both in subjects with CF and in healthy people and to assess its possible correlation to different variables (diet, seasons, menstrual cycle).

Methods. 35 out of 36 selected subjects (6 to 18 years) have been enrolled in a multicentre prospective clinical study and divided into 3 cohorts: patients with CF, patients with CFTR-Related Disorder (CFTR-RD), healthy volunteers. Each subject have to perform 8 ST at different times: at least 2 tests for each period, autumn-winter (A/W) and spring-summer (S/S), on hyposodic diet and on free diet (for CF patients all tests on free diet) and, in menstruating females, at least 1 test during both mid-cycle and pre-menstrual phase.

The statistical analysis of the collected data will clarify the intra-individual variability for each group.

Results. At the end of summer only 5/35 patients have completed all tests. From an interim descriptive analysis of collected data we can observe: in healthy subjects the intraindividual variability seems to be not related to any analyzed factor; no patient with CF have Cl values <60mEq/l at any time; 2 patients with CFTR-RD and 1 healthy male have at least 1 value >60

mEq/l; 9/11 CF patients have at least one Cl value >150 mEq/l; hyposodic diet seems to be related to slight lower value of Cl in patients with CFTR-RD; only in CF patients Cl values in the period A/W are lower than values collected in S/S; in CF patients mid-cycle tests are associated to higher Cl values.

Spin-off for research & clinical purposes. These preliminary results suggest the following considerations:

1. Considering the high frequency of Cl values >150 mEq, are they really not physiological as reported in international guidelines?
2. May the variability of Cl observed on hyposodic diet in CFTR-RD patients reflect CFTR dysfunction suggesting possible variations also in CF patients not evaluated in this study for ethical reasons?
3. May the variability of Cl in seasons in CF reflect the hydration status of patients?
4. May the observed variations during the menstrual cycle in CF patients reflect changes in CFTR function induced by hormones and related inflammation?

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