

# Variations in Blood Glucose and their Impact on various Blood Parameters in Healthy Subjects

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**Introduction:** Various minimally- and non-invasive (NI) methods for *in-vivo* glucose monitoring have been suggested and developed. A number of the NI methods measure glucose indirectly, e.g. the impedance spectroscopy (IS). Indeed, it is well known that glycemic excursions lead to changes in the electrolyte balance across membranes in blood, interstitial fluid (ISF) and cells. The resulting changes in the dc/ac conductivity and tissue permittivity of the skin and underlying tissue in different frequency ranges can be measured using IS. The aim of our study was to evaluate the effect of an extended hyperglycaemic period on various blood parameters in healthy subjects.

**Methods:** Eight blood parameters (BG, Na<sup>+</sup>, K<sup>+</sup>, Ca<sup>2+</sup>, Cl<sup>-</sup>, Mg<sup>2+</sup>, urea, osmolality) were measured periodically during a glucose clamp (BG level was increased rapidly from euglycemic to hyperglycemic values and back to euglycemic values) in 19 healthy subjects (10 male and 9 female, age 36±5 years, BMI 22.7±2.9 kg/m<sup>2</sup>) using the glucose clamp technique with the Biostator. The single experiments lasted about 10 h in total; the duration of the hyperglycemic episode was 3 h. In total more than 1000 blood samples were collected to monitor changes in the 8 parameters while BG was kept constant at the different levels. To assess the correlation between changes in the electrolyte levels (as well as urea & osmolality) and glucose, Spearman correlation coefficients  $r_s$  were calculated.

**Results:** During the three BG levels (euglycemia 82±3, hyperglycemia 302±17, euglycemia 89±6 mg/dl) changes in Na<sup>+</sup> levels from 145±2.6 to 140±2.6 to 145±2.5, Cl<sup>-</sup> levels of 106±15 to 103±13 to 108±15 mmol/L and K<sup>+</sup> levels of 4.1±0.24 to 4.61±0.35 to 3.86±0.23 mmol/L were measured. For five blood parameters  $r_s$  showed significant ( $p<0.05$ ) and strong ( $r_s>0.6$ ) monotonic correlations with glucose: Na<sup>+</sup> 0.890; K<sup>+</sup> 0.743; Ca<sup>2+</sup> 0.604; Cl<sup>-</sup> 0.812; osmolality 0.668 and charge 0.842.

A simple linear multiple regression analysis applied to the full data set (data of all patients combined) and taking into account the 5 blood parameter with the most significant correlations yields a global model with a predictive power, showing a strong correlation between predictions and measurements of  $R^2 = 0.936 \pm 0.038$  for the 19 subjects.

**Conclusion:** This study confirms a systematic correlation between changes in BG and the blood parameters. It suggests that monitoring of glucose changes is feasible by measuring the effects induced by changes in electrolytes, at least under these controlled clinical-experimental conditions. It remains to be confirmed if this also enables NI monitoring of glucose changes under daily life conditions with its various confounding factors.