Between patient and inter-time point variability in salivary cortisone: cortisol ratios.

Green J\textsuperscript{1}, Lancaster G\textsuperscript{2}, Titman A\textsuperscript{3}, Peak M\textsuperscript{3}, Newland P\textsuperscript{4}, Collingwood C\textsuperscript{4}, Chesters C\textsuperscript{4}, Moorcroft T\textsuperscript{5}, Hawcutt D\textsuperscript{6}, Didi M\textsuperscript{1}, Couriel J\textsuperscript{7}, Blair J\textsuperscript{1}

\textsuperscript{1}Departments of Endocrinology, \textsuperscript{2}Research, \textsuperscript{3}Biochemistry and \textsuperscript{7}Respiratory Medicine, Alder Hey Children’s NHS Foundation Trust, \textsuperscript{4}Liverpool Postgraduate Statistics Centre, Lancaster University, \textsuperscript{5}NIHR Clinical Research Network: Children, North West Coast \textsuperscript{6}Molecular and Clinical Pharmacology, University of Liverpool

INTRODUCTION

- Salivary biomarkers are attractive diagnostic tools for paediatric practice.
- Cortisol is rapidly converted to cortisone in the salivary gland by eleven beta hydroxysteroid dehydrogenase type 2 (11\textbeta-HSD2) (Figure 1).
- Salivary cortisone (SCn) is reported to be a better measure of plasma cortisol than salivary cortisol (SCl) and measurements of SCI may not be necessary, reducing cost and sample volumes.
- 11\textbeta-HSD2 activity is subject to genetic variability, and may become saturated at high cortisol concentrations.
- Variability in 11\textbeta-HSD2 activity can be examined by studying the ratio of SCI to SCn between individuals and over time.

PATIENTS AND METHODS

- Inter and intra-individual variability in SCI:SCn was examined in 756 early morning saliva samples collected on 3 consecutive days (D1,D2,D3) from 269 (160M) children age 10yrs (5-15) with asthma, reported previously\textsuperscript{(1)}.
- Box-Cox transformations were applied to yield normally distributed data. Pearson correlation and variance component models were used to investigate intra and inter-individual variability.

RESULTS

- Mean SCI:SCn ratio for all samples was 0.177 (range 0.0274 – 3.57).
- There was a moderate correlation between SCI:SCn on D1 vs D2, D1 vs D3 and D2 vs D3: 0.512, 0.580 and 0.585 respectively.
- 56\% of overall variation was explained by between patient variation and 44\% by inter-time point measurement error.

CONCLUSION

- Statistically significant relationships are observed between measurements obtained from the same individual over time, and between individuals.
- However, the observed level of variability could influence clinical decision making for individual patients. These observations may indicate genetic heterogeneity in our population and/or saturation of 11BHSD2 at higher levels of SCI.
- We continue to measure both biomarkers on serial samples to mitigate these effects.

REFERENCE

\textsuperscript{1}Early morning salivary cortisol and cortisone, and adrenal responses to a simplified low-dose short Syntacthen test in children with asthma. Clin Endocrinol. 2014;80:376-83.

\textsuperscript{1}Figure 1: Conversion of cortisol to cortisone in the salivary gland