

Development of novel non-invasive strategies for monitoring of treatment control in patients with congenital adrenal hyperplasia

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Introduction and Objectives

Monitoring of glucocorticoid treatment in congenital adrenal hyperplasia (CAH) is currently suboptimal, relying on blood tests which are traumatising in children and young persons (CYP). Evidence indicates a crucial role of 11-oxygenatedC19 androgens in the pathogenesis of CAH. We aimed to explore the use of 11-oxygenatedC19 androgens in developing non-invasive monitoring tests by establishing the correlation between plasma and salivary androgens in CYP with CAH.

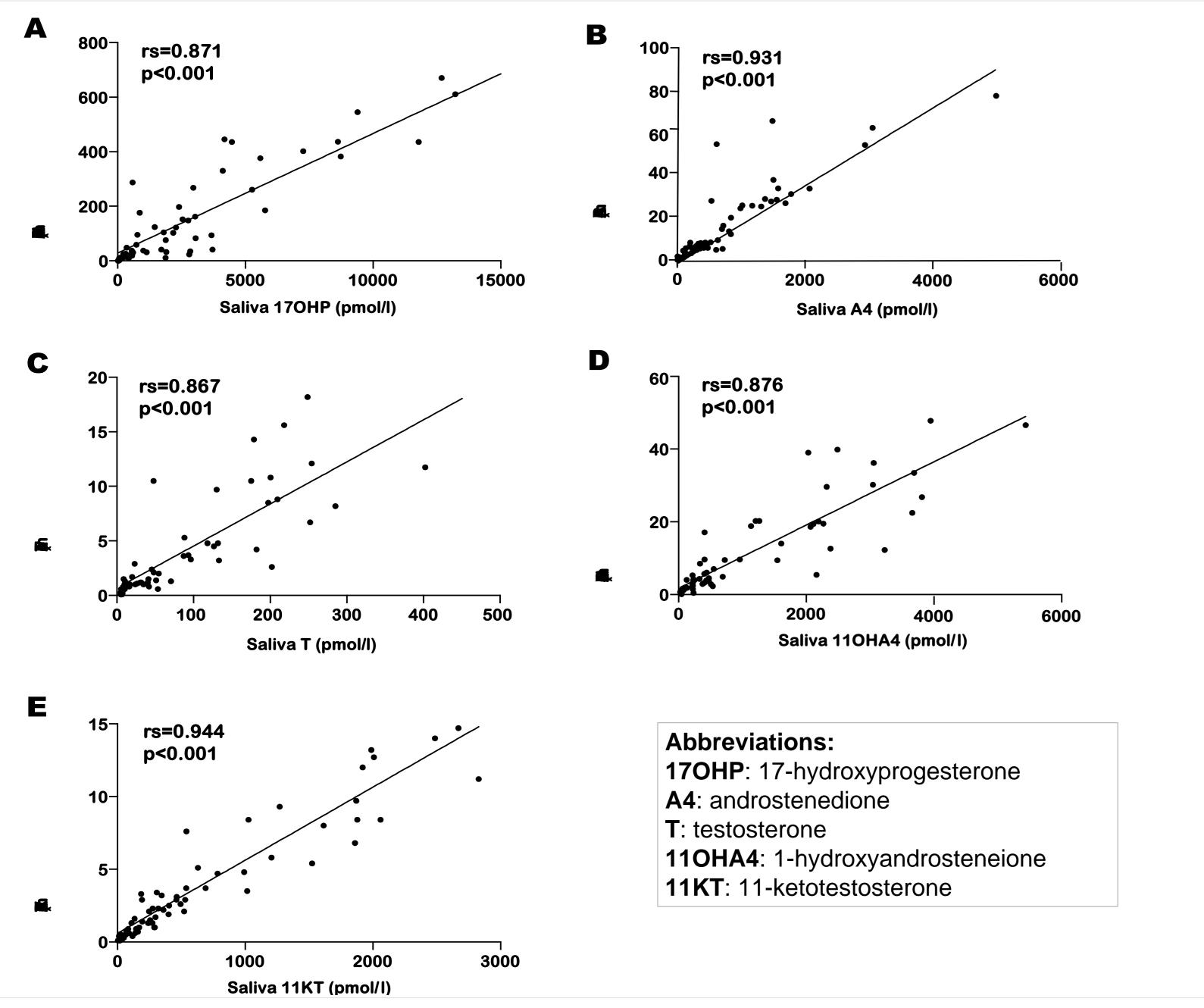
Conclusion

Salivary concentrations correlate well with plasma concentrations for androgens used as markers of therapy control in CAH. The best correlations were found for adrenal-derived 11-oxygenatedC19 androgen

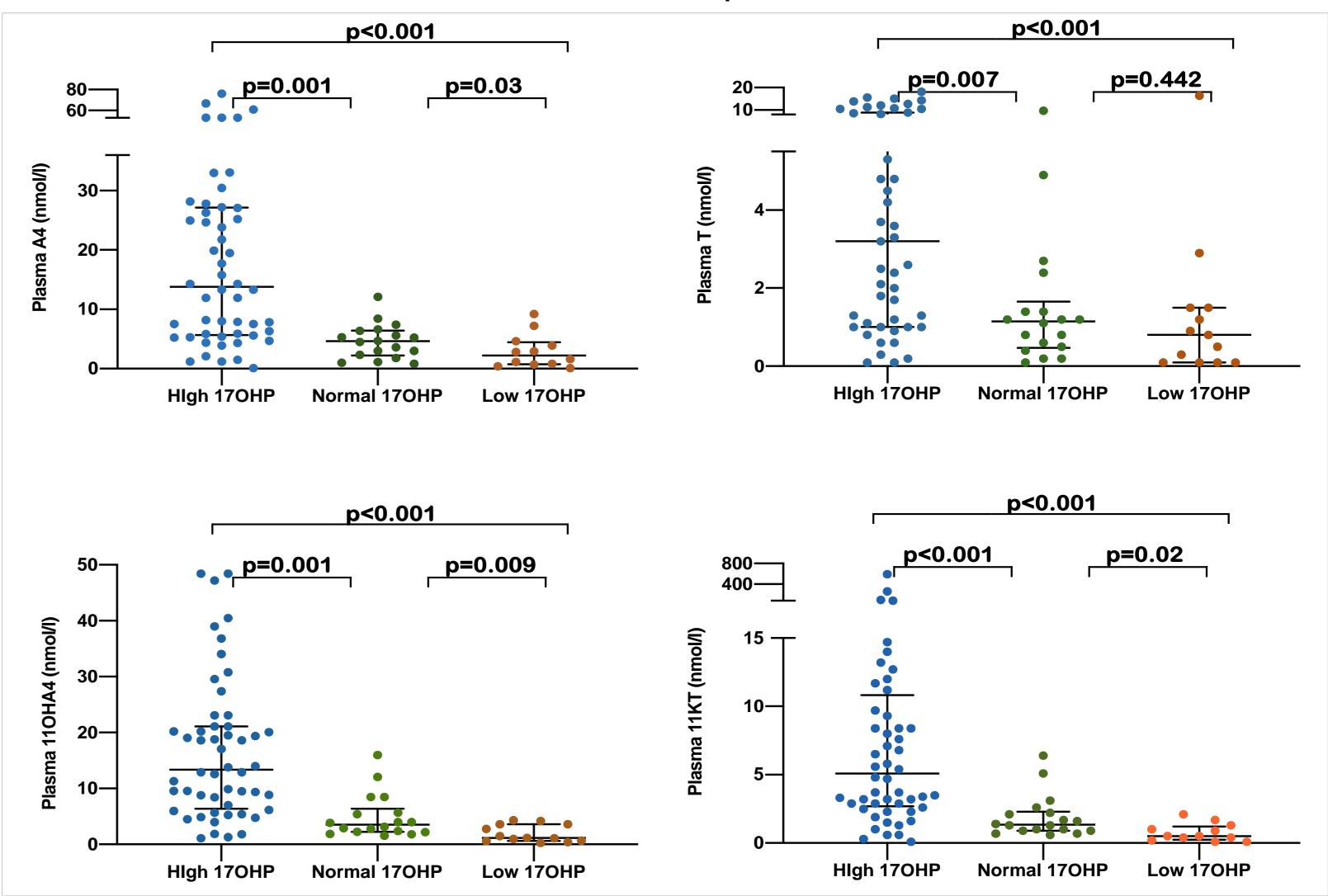
11-ketotestosterone as well as 17-hydroxyprogesterone and androstenedione. This novel combination of salivary steroid hormones can serve as non-invasive monitoring tool to help improve the medical management and outcomes in CAH.

Results

Salivary and plasma concentrations correlated well for all the five steroids measured, with the strongest correlations found for androstenedione and 11-ketotestosterone.

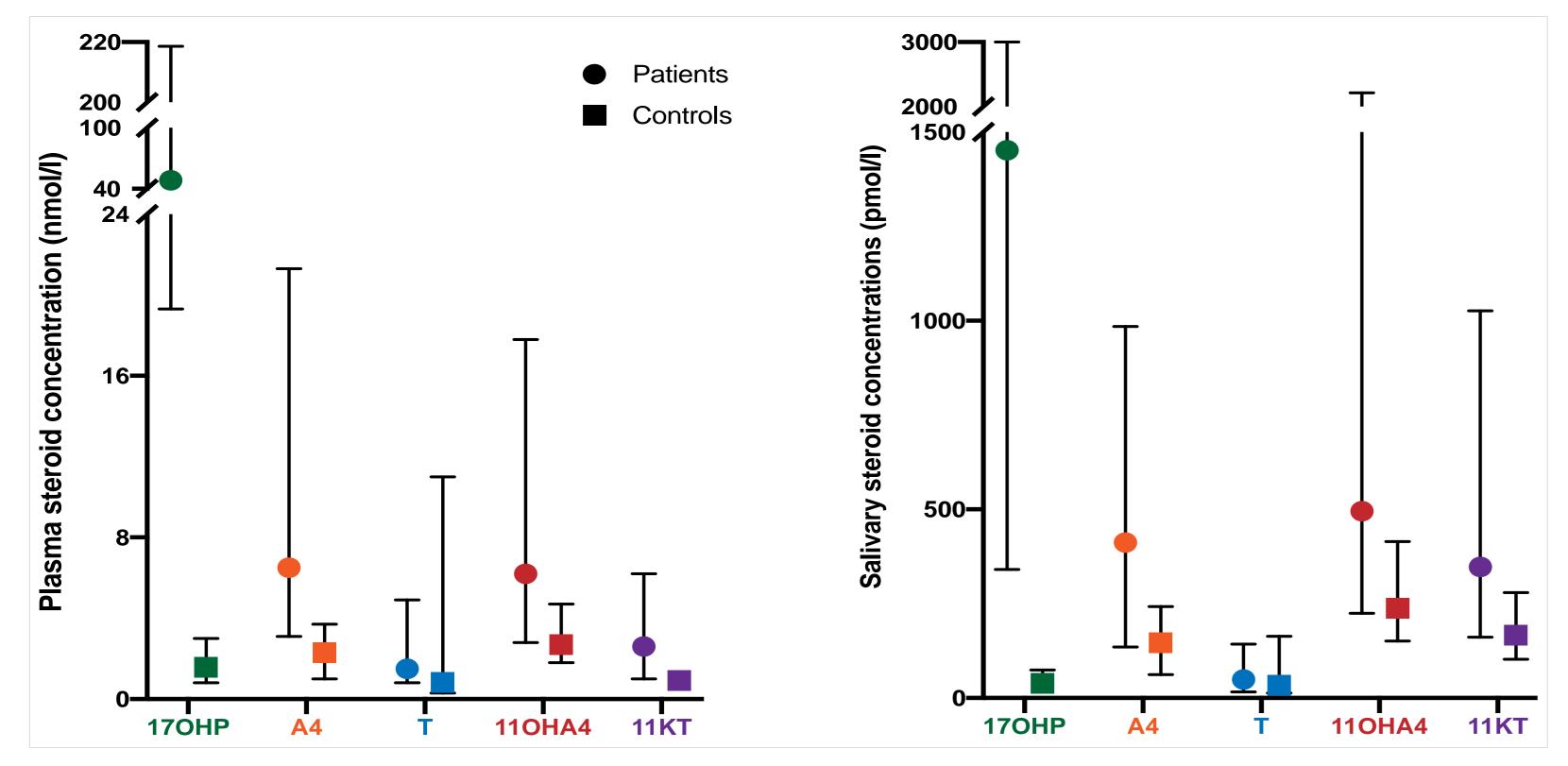


Comparing patient subgroups of treatment control based on the plasma 17OHP concentration, we found consistent overlap between groups for all the other four steroids measured in both plasma and saliva.



We found consistently strong correlations between plasma and salivary steroids when analysing patients subgroups based on age and gender. We found weaker correlations in controls: 17OHP ($r_s=0.641$, p<0.001), A4 ($r_s=0.925$, p<0.001), T ($r_s=0.787$, p<0.001), 11OHA4 ($r_s=0.828$, p<0.001), 11KT ($r_s=0.842$, p<0.001).

Plasma and salivary steroid concentrations were significantly raised in patients compared to controls for all hormones (p<0.001) with the exception of testosterone (p=0.143 in plasma and p=0.681 in saliva).



We found significant correlations among the plasma and salivary concentrations of all the steroids analysed.

Spearman correlations	Plasma 17OHP	Plasma A4	Plasma T	Plasma 110HA4	Plasma 11KT	Salivary 170HP	Salivary A4	Salivary T	Salivary 110HA4	Salivary 11KT
Plasma 170HP										
Plasma A4	r _s =0.784 p<0.001									
Plasma T	r _s =0.527 p<0.001	r _s =0.673 p<0.001								
Plasma 11OHA4	r _s =0.837 p<0.001	r _s =0.889 p<0.001	r _s =0.702 p<0.001							
Plasma 11KT	r _s =0.816 p<0.001	r _s =0.806 p<0.001	r _s =0.691 p<0.001	r _s =0.923 p<0.001						
Salivary 170HP	r _s =0.877 p<0.001	r _s =0.825 p<0.001	r _s =0.530 p<0.001	r _s =0.838 p<0.001	r _s =0.779 p<0.001					
Salivary A4	r _s =0.749 p<0.001	r _s =0.931 p<0.001	r _s =0.705 p<0.001	r _s =0.843 p<0.001	r _s =0.790 p<0.001	r _s =0.866 p<0.001				
Salivary T	r _s =0.618 p<0.001	r _s =0.746 p<0.001	r _s =0.867 p<0.001	r _s =0.753 p<0.001	r _s =0.738 p<0.001	r _s =0.693 p<0.001	r _s =0.807 p<0.001			
Salivary 110HA4	r _s =0.749 p<0.001	r _s =0.765 p<0.001	r _s =0.644 p<0.001	r _s =0.876 p<0.001	r _s =0.811 p<0.001	r _s =0.804 p<0.001	r _s =0.758 p<0.001	r _s =0.728 p<0.001		
Salivary 11KT	r _s =0.785 p<0.001	r _s =0.841 p<0.001	r _s =0.701 p<0.001	r _s =0.932 p<0.001	r _s =0.944 p<0.001	r _s =0.826 p<0.001	r _s =0.869 p<0.001	r _s =0.802 p<0.001	r _s =0.861 p<0.001	
Strength of correlation:			r _s >0.8			r _s =0.6-0.8			r _s =0.4-0.6	

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Methods

We recruited 78 CAH patients (43 females, (12.87+/-3.04 years)) from 13 centres in the United Kingdom and 62 controls. Using liquid chromatography tandem mass spectrometry, we measured plasma and salivary concentrations for 17-hydroxyprogesterone, androstenedione, testosterone, 11-hydroxyandrostenedione and 11-ketotestosterone. We used Spearman correlations to analyse the relationship between plasma and salivary steroids.











