

For immediate release

UK-wide study of adults with rare disease relates treatment to self-reported mental and physical health

A new study of adults with a rare congenital condition finds that how patients perceive their health relates to their weight and to the type and dose of their medication. The findings from this unique UK-wide study recently published in *EJE (European Journal of Endocrinology)* suggest that studies focussed on optimising and standardising treatment options for adults with congenital adrenal hyperplasia (CAH) represent the most pragmatic approach to improve their long-term health.

CAH is an inherited condition that results from a deficiency of the steroid hormone cortisol, a situation that is potentially fatal and one that has many other effects on physiology and health. The Society for Endocrinology formed the Congenital adrenal Hyperplasia Adult Study Executive (CaHASE) to collate data on the condition in adulthood, and the results of long-term steroid treatment, from centres across the UK. (see more info on CAH below)

151 men and women with CAH completed the Short Form Health Survey 36 (SF-36) which measures how the patient perceives their physical and mental health. They were given a physical examination (blood pressure, height, weight) and a biochemical assessment (for metabolic parameters influenced by steroid treatment such as androgens, insulin resistance, cholesterol, triglycerides) and had their medications noted. 20 controls from the general population were age- and sex-matched to each patient.

Adults with CAH were found to have significantly impaired quality of life in relation to the general population, and this was related to the type of steroid treatment they had been using to control their disease. Those on more potent steroids or those taking a combination of steroids felt that their vitality and mental health were worse (significant results).

Further analysis using a statistical tool called principle components analysis revealed that the interrelated variables of waist circumference, blood lipid levels and insulin resistance (together: 'adiposity and insulin resistance') were together significantly associated with three of the four domains of physical health and functioning assessed by SF-36 (impaired physical functioning ($p<0.001$), bodily pain ($p<0.001$), general health ($p=0.001$), and the four domains assessed together (the Physical Component Summary score ($p<0.001$)).

CaHASE found that adult patients with CAH had a poorer perception of their quality of life if they were taking more potent steroids, or a combination of steroids. Whether the more

potent/combinations of steroids are prescribed to control a more aggressive disease with a greater effect on quality of life, or whether the steroids themselves are impacting on quality of life to a greater extent, is highlighted as an avenue for further study.

CaHASE also found that markers of poor metabolic profile including increased weight and insulin resistance also associated with poorer quality of life in the physical domains. This can also be related to the steroid medication since weight gain and insulin resistance can be linked with steroid excess.

The findings of this cross-sectional study raise important questions as to why such variation in the methods of treatment, the control of CAH in adulthood and how patients perceive their quality of life exists across the UK. It suggests that further research with a view to establishing best-practice guidance is needed.

Richard Ross, Chair of the Society for Endocrinology Congenital adrenal Hyperplasia Adult Study Executive, said:

“Adults with congenital adrenal hyperplasia are quite able to lead a normal life, the only difference being that they must replace the steroid hormone cortisol that their body is unable to produce. This presents a delicate balancing act between too much and too little steroid.

“In this study we found quality of life to be worse in adults taking stronger forms of steroids, or combinations of steroids, and in those with markers of a worse metabolic profile such as weight gain around the middle and insulin resistance. Perhaps this is because they have a more aggressive form of the disease and so feel worse, but perhaps the stronger medication impacts on quality of life.

“It’s a real ‘goldilocks’ challenge to make sure that these patients get the medication that is ‘just right’. These and other findings from CaHASE have raised the choice of steroid treatment as a key research question in improving the long-term health prospects of adults with CAH. ”

Info on CAH:

CAH is an inherited condition that results from a deficiency of the steroid hormone cortisol. Cortisol enables the body to respond to stress such as illness and injury and so for undiagnosed patients, or those unable to access their steroid medication, a minor illness can be fatal. In CAH a lack of cortisol causes an over-production of male hormones known as androgens (such as testosterone) and as a consequence patients suffer from problems with growth, gender-related development in females, and fertility. To counteract this, patients are prescribed daily steroid medication to replace the cortisol and suppress the androgens. From the clinician’s perspective this provides a delicate balancing act between under-replacement

(high androgens) and over-replacement (side effects). Life-saving steroid replacement therapy was only developed 60 years ago, and a previous study by CaHASE found that only around 10% of adults with CAH are treated in specialist centres, so research is lacking on long-term care.

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Notes for Editors:

This research will be published in the June 2013 issue of *European Journal of Endocrinology* **168**; 887-893, [DOI: 10.1530/EJE-13-0128](https://doi.org/10.1530/EJE-13-0128). The abstract is reproduced below. A copy of the final Open Access paper can be obtained ahead of publication from the Society for Endocrinology press office (details below)

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For more information: contact the Society for Endocrinology press office

Toby Stead

Public & Media Relations Executive
Tel: +44 (0)1454 642 252
Email: toby.stead@endocrinology.org

Paul MacKenzie-Cummins

Communications and Public Relations Manager
Mob: +44(0)7453 755 057
Tel: +44 (0)1454 642 772
Email: paul.mackenzie-cummins@endocrinology.org

The Society for Endocrinology is Britain's national organisation promoting endocrinology and hormone awareness. For general information, please visit our website: <http://www.endocrinology.org>

For more information on CAH, endocrinology and hormones please visit You & Your Hormones (www.yourhormones.info), the Society for Endocrinology's public information website.

More information on CaHASE can be found at the [Society for Endocrinology website](http://www.endocrinology.org).

ABSTRACT

Quality of life in adults with congenital adrenal hyperplasia relates to glucocorticoid treatment, adiposity and insulin resistance: United Kingdom Congenital adrenal Hyperplasia Adult Study Executive (CaHASE)

Thang S Han¹, Nils Krone², Debbie S Willis³, Gerard S Conway¹, Stefanie Hahner⁴, D Aled Rees⁶, Roland H Stimson⁵, Brian R Walker⁵, Wiebke Arlt², Richard J Ross⁷, the United Kingdom Congenital adrenal Hyperplasia Adult Study Executive (CaHASE)

¹ Department of Endocrinology, University College London Hospitals, London, UK; ² School of Clinical and Experimental Medicine, Centre for Endocrinology, Diabetes and Metabolism, University of Birmingham, Birmingham, UK; ³ Society for Endocrinology, Bristol, UK; ⁴ Endocrinology and Diabetes Unit, Department of Medicine I, University of Würzburg, Würzburg, Germany; ⁵ Endocrinology Unit, Queen's Medical Research Institute, Centre for Cardiovascular Science, University of Edinburgh, Edinburgh, UK; ⁶ Institute for Molecular and Experimental Medicine, Centre for Endocrine and Diabetes Sciences, Cardiff University, Cardiff, UK; ⁷ Academic Unit of Diabetes, Endocrinology and Metabolism, University of Sheffield, Room 112, Floor M, Royal Hallamshire Hospital, Glossop Road, Sheffield S10 2JF, UK

Context

Quality of life (QoL) has been variously reported as normal or impaired in adults with congenital adrenal hyperplasia (CAH). To explore the reasons for this discrepancy we investigated the relationship between QoL, glucocorticoid treatment and other health outcomes in CAH adults.

Methods

Cross-sectional analysis of 151 adults with 21-hydroxylase deficiency aged 18–69 years in whom QoL (assessed using the Short Form Health Survey), glucocorticoid regimen, anthropometric and metabolic measures were recorded. Relationships were examined between QoL, type of glucocorticoid (hydrocortisone, prednisolone and dexamethasone) and dose of glucocorticoid expressed as prednisolone dose equivalent (PreDEq). QoL was expressed as z-scores calculated from matched controls (14430 subjects from UK population). Principal components analysis (PCA) was undertaken to identify clusters of associated clinical and biochemical features and the principal component (PC) scores used in regression analysis as predictor of QoL.

Results

QoL scores were associated with type of glucocorticoid treatment for vitality ($P=0.002$) and mental health ($P=0.011$), with higher z-scores indicating better QoL in patients on hydrocortisone monotherapy ($P<0.05$). QoL did not relate to PreDEq or mutation severity. PCA identified three PCs (PC1, disease control; PC2, adiposity and insulin resistance and PC3, blood pressure and mutations) that explained 61% of the variance in observed variables. Stepwise multiple regression analysis demonstrated that PC2, reflecting adiposity and insulin resistance (waist circumference, serum triglycerides, homeostasis model assessment of insulin resistance and HDL-cholesterol), related to QoL scores, specifically impaired physical functioning, bodily pain, general health, Physical Component Summary Score ($P<0.001$) and vitality ($P=0.002$).

Conclusions

Increased adiposity, insulin resistance and use of prednisolone or dexamethasone are associated with impaired QoL in adults with CAH. Intervention trials are required to establish whether choice of glucocorticoid treatment and/or weight loss can improve QoL in CAH adults.