

also improved during the OLE. In GRACE, patients who switched to placebo during the randomized-withdrawal phase experienced a deterioration in blood pressure. When relacorilant treatment was resumed in the OLE, their blood pressure improved. Improvements in body weight, glycemic control, and other cortisol-related comorbidities that were observed in the GRACE study were maintained in the OLE. Relacorilant was well tolerated in the OLE, consistent with the parent studies. No new safety signals were identified during up to 6 years of treatment. Long-term treatment with relacorilant led to significant and durable cardiometabolic improvements in patients with hypercortisolism and was well-tolerated.

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JOINT2362

Initial findings of the study into the health status of adults with CAH in the UK and Ireland – CaHASE2

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Background

Congenital adrenal hyperplasia (CAH) is one of the commonest forms of primary adrenal insufficiency with an incidence of about 1 in 15,000. Previous studies have highlighted the suboptimal health status and care provision in adults with CAH and these were associated with significant co-morbidities. In 2023, we implemented CaHASE2 (<https://www.endocrinology.org/clinical-practice/research-projects/cahase-2/>) to develop a strategy for prospective collection of longitudinal data. Our recent CAH service evaluation suggested significant differences in the approach to CAH patients.

Aim

To identify specific unmet needs in the care of people living with CAH, through standardised phenotyping across all participating centres.

Methods

In September 2023, PIs agreed a minimal dataset for the collection of real-world data for participating centres. The data is collected using the international CAH registry (I-CAH; <https://sdmregistries.org/>). CaHASE2 was launched in November 2023.

Results

To date, 351 adults (213 females, 138 males) with CAH have been recruited and 1213 clinic visits were available for analysis. There is a preponderance of younger to middle-aged adults in the currently available datasets (median age 42 years, range 23–88). Preliminary analysis suggests a temporal change in glucocorticoid choice over time with an increased use of hydrocortisone and a decreased use of prednisolone. Analysis of 17OHP concentrations shows that a significant proportion of patients are overtreated. A significant proportion of patients are overweight or obese. Currently 18 centres are actively recruiting and 5 are awaiting local approval to use the I-CAH registry. The data will be analysed in 12-month cycles, to assess the current level of care provision and inform the development of CAH standards. In addition, we will establish a report that will provide centres with information about their local care provision in relation to other centres.

Conclusions

The CaHASE2 project will provide important information about the health status of adults with CAH and how this might be related to differences in health care provision. Ultimately, such data should lead to a higher degree of equality of service provision in all parts of the UK and Ireland.

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JOINT3812

is imaging alone sufficient for lateralising PA in younger patients?

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Background

The role of adrenal vein sampling (AVS) in younger patients with primary aldosteronism (PA) remains debated. Endocrine Society (ES) Guidelines suggest that AVS may be avoided in patients ≤ 35 years with marked PA (aldosterone > 831 pmol/l, spontaneous hypokalaemia), and a solitary adrenal lesion consistent with an adenoma. While some centres adopt this approach, others, including ours, perform AVS routinely on all patients with PA. However, imaging alone may misclassify laterality in a significant proportion of younger patients.

Aim

To assess the accuracy of imaging alone in distinguishing unilateral from bilateral PA in patients ≤ 35 years and evaluate the added diagnostic value of AVS.

Method

We retrospectively analysed 364 patients who underwent AVS for PA between 2011 to 2024, including 39 patients aged ≤ 35 years. Of these, 38 underwent either CT or MRI prior to AVS. Two radiologists independently reviewed imaging blinded to AVS results, while two endocrinologists blinded to imaging findings analysed AVS. Concordance between imaging and AVS was assessed.

Results

The mean age was 32 years, with 60% female. Median hypertension duration was 1.5 years (IQR: 1–5 years). All patients had biochemically confirmed PA with spontaneous hypokalaemia and were on two to three antihypertensive medications. AVS was successful in all cases. Among 39 patients, four were excluded due to inconclusive AVS results and missing imaging data. In the remaining 35, imaging identified unilateral adenomas (6–25 mm) in 82.9% (29/35) patients, bilateral adenomas in 8.6% (3/35), and normal adrenal glands in 8.6% (3/35). Among 29 unilateral cases on imaging, 13.8% (4/29) had discordant AVS findings, indicating bilateral disease. Discordant cases had lateralisation index < 2 (range: 1.3–2.0) and/or contralateral suppression index > 1 , suggesting bilateral PA. Only one discordant case met ES criteria for marked PA, while the other three had milder disease. All discordant cases were managed medically, while 86.2% (25/29) underwent unilateral adrenalectomy, with histological confirmed adenoma.

Conclusion

While imaging alone correctly lateralised PA in 86.2% of cases, 13.8% of patients with unilateral adenomas had discordant AVS findings, indicating bilateral disease. Only one discordant case met the ES criteria for marked PA, supporting AVS omission in these patients. However, AVS remains essential for those with milder PA to prevent misclassification and unnecessary adrenalectomy.

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JOINT1023

Challenges in the interpretation of cortisol response during insulin tolerance test: prevalence of secondary adrenal insufficiency and predictive factors

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Background

The insulin tolerance test (ITT) is the gold standard for assessing the integrity of growth hormone (GH) and cortisol axes. While ITT is essential for diagnosing growth hormone deficiency (GHD) and secondary adrenal insufficiency (SAI), its interpretation can be challenging due to variability in thresholds and individual responses.

Methods

This retrospective study analyzed ITTs performed at the Institute for Maternal and Child Health IRCCS “Burlo Garofolo,” Trieste, Italy, from January 1, 2019, to December 31, 2024. Tests were conducted to confirm GHD after a blunted response to arginine stimulation or for retesting at the end of GH treatment. Regular insulin (0.1 IU/kg intravenously) was administered, and adequate hypoglycemia was defined as a $\geq 50\%$ decrease in basal glucose or a nadir glucose < 40 mg/dL.

Results

Of 212 ITTs performed, adequate hypoglycemia was achieved in 186 (88%), including 157 diagnostic tests and 29 retests. The prevalence of SAI varied widely depending on the threshold used: Between 14% and 27% of individuals meeting these thresholds were not diagnosed with GHD. Peak cortisol levels positively correlated with basal cortisol ($\rho=0.490$, $P < .001$), nadir glycemia ($\rho=0.307$, $P < .001$), basal ACTH ($\rho=0.255$, $P < .001$), ACTH after hypoglycemia ($\rho=0.332$, $P < .001$), and peak GH ($\rho=0.312$, $P < .001$). No significant correlation was found with age, sex, or BMI SDS. Multivariate analysis identified lower basal cortisol ($P < .001$), lower ACTH after hypoglycemia ($P < .001$), and nadir glycemia ($P=.012$) as significant predictors of cortisol peak, with a moderate model fit ($R^2=0.354$).

Conclusions: The prevalence of SAI during ITT ranged from 13% to 80% depending on the diagnostic thresholds. Between 14% and 27% of individuals

Threshold for SAI	n (%)	Of which with no GHD
Peak cortisol <400 nmol/l	32 (17%)	6 (19%)
Delta cortisol <200 nmol/l	75 (40%)	20 (27%)
Peak cortisol <400 nmol/l and delta <200 nmol/l	24 (13%)	5 (21%)
Peak cortisol <550 nmol/l	129 (69%)	18 (14%)
Delta cortisol <250 nmol/l	102 (55%)	22 (22%)
Peak cortisol <550 nmol/l or delta <250 nmol/l	149 (80%)	28 (19%)

meeting SAI thresholds were not diagnosed with GHD, complicating interpretation. Significant predictors of cortisol peak include basal cortisol, nadir glycemia, and ACTH after hypoglycemia. These findings highlight the need to consider clinical context alongside hormonal thresholds to ensure accurate SAI diagnosis and avoid overdiagnosis.

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JOINT2537

The relationship between androgens and autistic traits: a comparative study in children with congenital adrenal hyperplasia

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Purpose

Autism Spectrum Disorder (ASD) is a neurodevelopmental condition characterized by difficulties in social interaction, communication, restricted interests, and repetitive behaviors. ASD is more prevalent in males than females, with some studies suggesting a possible association with prenatal androgen exposure. Congenital Adrenal Hyperplasia (CAH), a genetic disorder causing increased prenatal androgen levels, provides a suitable model to investigate this relationship. This study aims to evaluate the potential link between early androgen exposure and autistic traits by comparing children and adolescents with CAH to healthy controls.

Method

The study included 49 participants: 25 children diagnosed with CAH (13 males, 12 females) followed by Istanbul University-Cerrahpaşa Medical Faculty Pediatric Endocrinology Clinic, and 24 age- and sex-matched healthy controls (12 males, 12 females) aged 2–18 years. Autism symptoms were assessed using the Childhood Autism Rating Scale (CARS), the Autistic Behavior Checklist (ABC), and the Strengths and Difficulties Questionnaire (SDQ).

Results

The total CARS score was significantly higher in the CAH group compared to the control group ($P < 0.001$). The CAH group also had higher scores in the following CARS subtests: Relating to People ($P = 0.027$), Body Use ($P = 0.031$), Visual Response ($P = 0.017$), Listening Response ($P = 0.028$), Taste/Smell ($P = 0.033$), Verbal Communication ($P = 0.049$), Activity Level ($P < 0.001$), and Intellectual Response ($P = 0.003$). However, there was no significant difference between the groups in motor skills, language skills, and general autism scores ($P > 0.05$). When the participants were evaluated with ABC, it was found that the sensory behavior score ($P = 0.037$) was higher, and the relating behavior score ($P = 0.001$) was lower in the CAH group compared to the control group. This finding indicates difficulties in social communication. In the SDQ assessment, emotional problems ($P = 0.043$), behavioral issues ($P = 0.043$), hyperactivity/attention deficit ($P = 0.025$), and peer relationship problems ($P = 0.001$) were significantly higher in the CAH group. The general difficulties score was also higher, indicating an increased psychosocial risk. No correlation was found between current androgen levels (17-OH, DHEA-S, 1,4) and CARS and ABC scores ($r < 0.4$).

Conclusion

Children diagnosed with CAH had higher scores regarding autism symptoms and had more difficulties with social communication. Additionally, increased behavioral and attention problems were observed in these children, which indicates emotional fragility. No direct correlation between androgen levels and autism symptoms was found, but it is thought that there might be indirect effects of prenatal androgen exposure. Further investigations are needed, with broader samples required to clarify this relationship.

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JOINT3950

Adrenal dysfunction and cardiometabolic comorbidities associated with weight cycling in postmenopausal conditions

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Overweight and obesity are major public health issues. ~20% of overweight people achieve sustainable weight loss with a risk of repeated weight loss and regain. Obese patients exhibit high plasma leptin levels, but are resistant to its anorectic action. Leptin, and other adipokines, directly regulates adrenal aldosterone biosynthesis, while aldosterone has been implicated in obesity-induced suppression of adiponectin, an insulin sensitizing adipokine, suggesting a central role for aldosterone in the development of overweight-associated comorbidities. Interestingly, aldosterone levels are associated with the development of metabolic syndrome. Weight cycling is associated with fluctuations in blood pressure, heart rate and glomerular filtration, leading to increased risk of developing metabolic syndrome, type-2 diabetes, chronic kidney disease and heart failure, inducing higher mortality, particularly in women. The menopausal transition is associated with a 60% increase in the incidence of metabolic syndrome, which is associated with higher cardiovascular mortality. We hypothesize that adrenal dysfunction, in a postmenopausal context may play a role and has a lasting impact on the increased cardiometabolic risk induced by weight cycling. The aim of our study was to evaluate the impact of weight cycling on adrenal gland function and the impact on the development of cardiometabolic complications in postmenopausal conditions. We established an experimental protocol in which female mice were either ovariectomized (OVX, post-menopause) or not (non-OVX, pre-menopause) and subjected to three weight cycles of high fat diet/standard diet (Yoyo) or maintained on a standard diet throughout. At the end of each phase of the weight cycling protocol, blood samples were collected to assess various metabolic parameters and perform steroid profiling. A variety of tissues (adrenal, heart, adipose tissue...) were collected for further analyses. The yoyo diet led to a greater weight gain in OVX mice compared to non-OVX mice. After ovariectomy, mice exhibited higher fasting blood glucose and circulating leptin levels, an effect that was exacerbated in response to Yoyo diet. Additionally, OVX mice on Yoyo diet chow impaired glucose tolerance and insulin resistance. These mice developed heart failure with preserved ejection fraction, which was prevented by the use of the mineralocorticoid receptor antagonist, finerenone. Surprisingly, OVX mice on Yoyo diet displayed an increase in adrenal gland weight, accompanied by significant morphological and functional remodeling of the adrenal cortex. The absence of estrogen leads to cardiometabolic disorders that are worsened by the Yoyo diet, as well as adrenal dysfunction, which could, in turn, contribute to the worsening of cardiometabolic comorbidities.

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JOINT1699

Chronotherapy with once-daily osilodrostat is safe and effective in Cushing's syndrome and restores circadian profile improving quality of life and sleep

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