P2-14 CLINICAL AND HORMONAL EVOLUTION OF ALDOSTERONE SYNTHASE DEFICIENCY: IS COMPLETE REMISSION POSSIBLE?

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BACKGROUND

Aldosterone synthase deficiency (ASD);

- Autosomal recessive
- Biallelic mutations of the ***CYP11B2*** gene
- The patients are presented with symptoms of severe salt-wasting
- The need for treatment decreases with the increasing age
- Adult patients are usually asymptomatic without having mineralocorticoid therapy
- Data are scarce regarding clinical and biochemical outcomes

OBJECTIVE

Assessment of the growth and steroid profiles of patients at the time of diagnosis and after discontinuation of treatment.

DESIGN AND METHOD

- Children with clinical diagnosis of ASD
- Multicenter study
- Growth and treatment characteristics were recorded
- Plasma adrenal steroids were measured using **LC-MS/MS**
- Genetic diagnosis was confirmed by *CYP11B2* gene sequencing and *in silico* analyses

RESULTS

✓ Sixteen patients from 12 families were included (8 females; median age at presentation:3.1 months, range:0.4-8.1)

✓ The most common symptom was poor weight gain (56.3%)

✓ Median age of onset of fludrocortisone treatment was 3.6 months (0.9-8.3)

✓ Catch-up growth was achieved at median 2 months (0.5-14.5) after treatment.

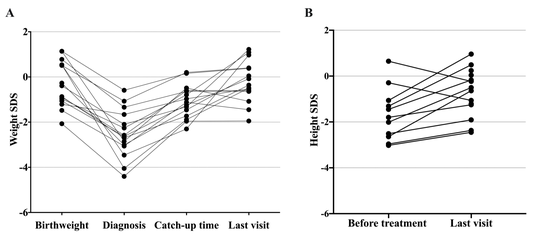
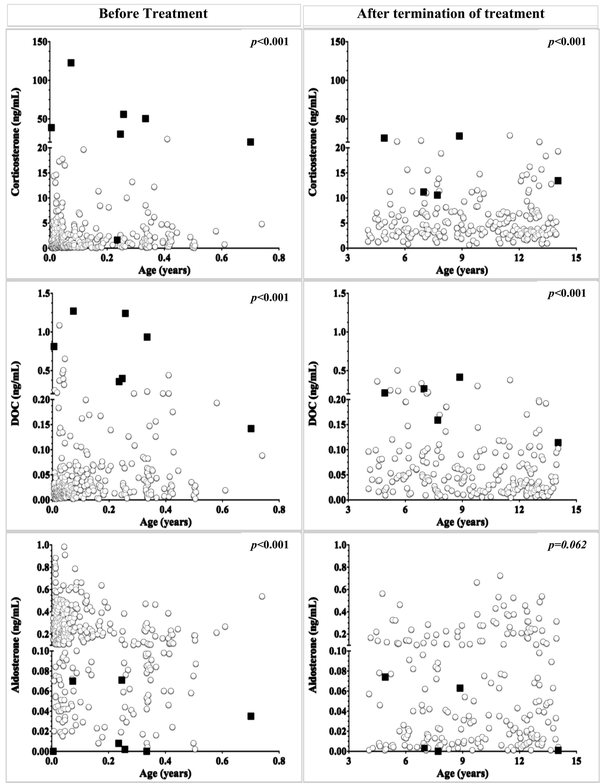


Figure 1. Plots of weight and height SDS values of patients with ASD over time.
A. Change in weight SDS values in patients with ASD before and after treatment showing individual patterns of catch-up growth (p=0.0002),
B. Change in height SDS values of patients between before treatment and last visit (p=0.027).

The mean weight and height of the patients were -0.2±0.9 [median: -0.4, range: -2.0 – 1.2] and -0.7±1.0 SD [median: -0.6, range: -2.5 – 1.0] at the last visit, respectively, compared to -2.5±1.0 [median: -2.6, range: -4.4 – (-0.6)] and -1.7±1.1 [median: -1.8, range: -3.0 – 0.7] at diagnosis



✓ Fludrocortisone could be stopped in five patients at a median age of 6.0 years (2.2-7.6)

✓ Comparison of steroid hormone profiles of the patients at dignosis and after their treatment could be terminated demonstrated the followings;

- ✓ Corticosterone (p=0.014) and DOC (p=0.027) concentrations were significantly lower in the latter,
- ✓ No statistically significant difference was found between aldosterone levels (p=0.974) and corticosterone/aldosterone ratios (p=0.876)
- ✓ Corticosterone, DOC, and corticosterone/aldosterone ratios were higher and aldosterone concentrations were lower in patients both at diagnosis and after their treatment could be terminated

✓ We identified six novel (p.Y195H, c.1200+1G>A, p.F130L, p.E198del, c.1122-18G>A, p.I339_E343del) and four previously described *CYP11B2* variants

✓ The most common variant was p.T185I (40%)

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Figure 2. Adrenal steroid hormones of the patients with ASD.
DOC, corticosterone and aldosterone concentrations of ASD patients before treatment and after termination of treatment compared to control group

CONTACT INFORMATION

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CONCLUSIONS

✓ Fludrocortisone treatment is associated with a rapid catch-up growth and control of electrolyte imbalances in ASD

✓ Decreased mineralocorticoid requirement over time can be explained by the development of physiological adaptation mechanisms rather than improved aldosterone synthase activity

✓ As complete biochemical remission cannot be achieved, a long-term surveillance of these patients is required