

Successful Use Of Subcutaneous Infusion of Cortisol In An Adult Case Of Congenital Adrenal Hyperplasia

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Introduction

Congenital adrenal hyperplasia (CAH) is a group of a rare autosomal recessive disorders characterised by a deficiency of one of the enzymes necessary for cortisol biosynthesis. More than 90% of CAH is caused by mutations or deletions in cytochrome P450 21-hydroxylase gene. Impaired glucocorticoid synthesis results in chronic elevation of ACTH causing adrenal hyperplasia and accumulation of steroid precursors such as 17 hydroxyprogesterone (17OHP) (1). The main goal in CAH management is to replace deficient steroids in order to prevent adrenal crisis and to suppress the abnormal secretion of androgens.

In addition to mineralocorticoid (fludrocortisone), different glucocorticoids can be used i.e.. prednisolone, dexamethasone or hydrocortisone twice or thrice a day is used. However, adequate and balanced replacement therapy with glucocorticoid is sometimes difficult to obtain. This is because of a number of factors such as patient tolerance, adverse effects and drugs pharmacokinetics and bioavailability (2).

Clinical presentation & results

- In this case report, we present a 40 year old lady with a long standing history of congenital adrenal hyperplasia, which was not adequately controlled with conventional doses of oral glucocorticoid.
- With good compliance on hydrocortisone 15mg (morning) and 5 mg (late afternoon) her average 17 OHP was high in the morning at 21 nmol/L and during the day ranged between 2.9-4.9 nmol/L. Adjusting hydrocortisone doses and timings was not tolerated because of significant weight gain, stomach upset, anxiety and difficulty sleeping after the evening dose.
- Instead, prednisolone and dexamethasone (with different doses of 0.5mg -4mg twice a day) were tried but caused depression and intolerance. The 17 OHP profile on dexamethasone was again significantly high in the morning at 47-56 nmol/L. The patient blamed the exacerbation of depression requiring hospital admission on dexamethasone and refused to take it again.

Management

- Using a continuous and variable subcutaneous hydrocortisone infusion (CSHI) via an insulin pump device, we achieved rapid control of her CAH, attained normal cortisol circadian and 17 OHP profiles and significantly improved her quality of life. Average daily hydrocortisone dose was 12-17.5 mg/day, which produced on average 24-h serum cortisol and 17 OHP concentrations of 302.08 nmol/L and <2.3 nmol/ml, respectively.
- The hydrocortisone basal rate via pump was adjusted to mimic the normal cortisol circadian rhythm (Fig.1).
- Quality of life was assessed on both HC tablets vs. CSHI, using standard SF-36 health survey. This showed a far better score with CSHI than HC tablets.

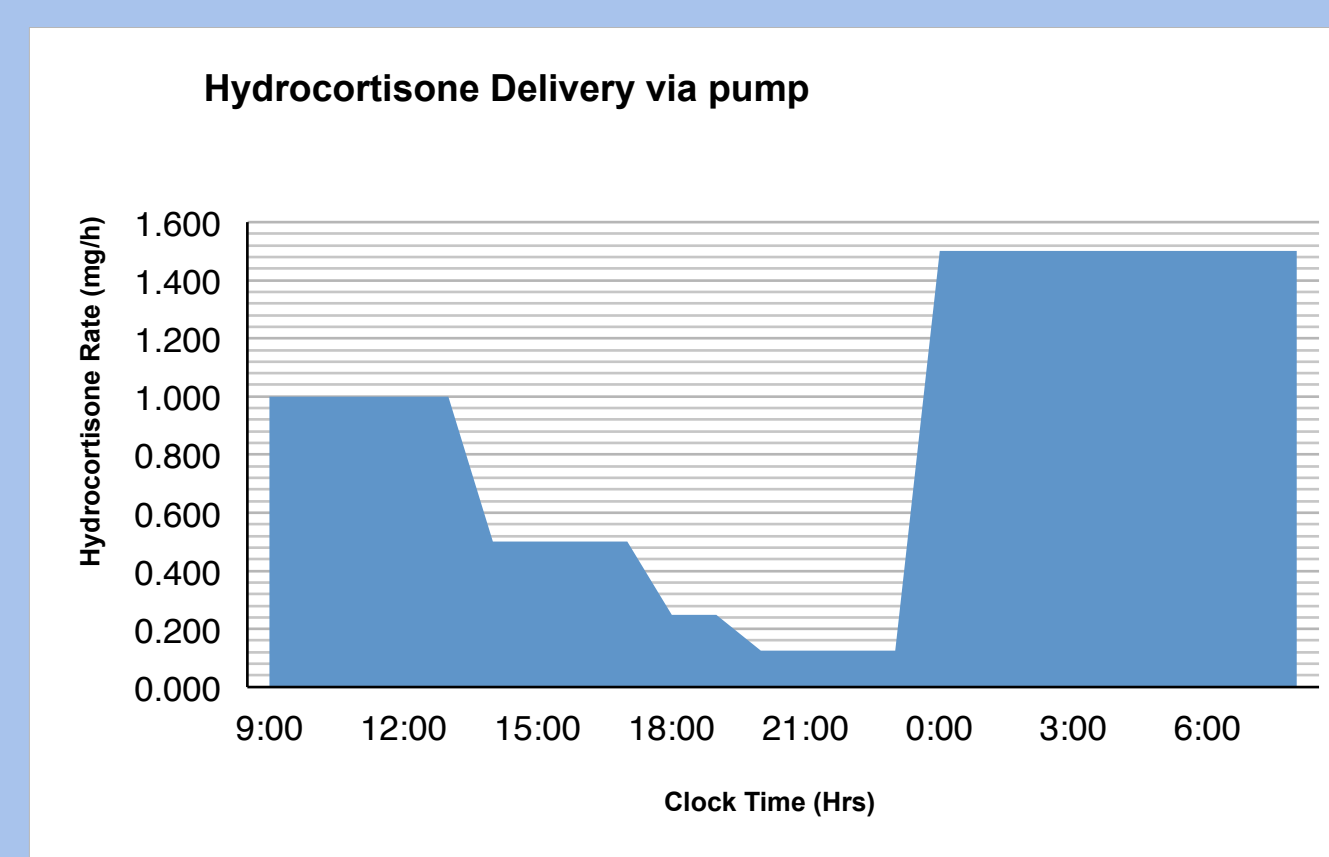


Fig.1 HC delivery via pump

Discussion

- Conventional oral hydrocortisone dosing does not mimic normal cortisol circadian rhythm. Various pharmacokinetic studies suggest a wide variation in cortisol bioavailability (range: 26–91%). This is thought to be secondary to considerable individual variations in gut absorption effects, first-pass clearance at the liver, or both (Patel et al. 1984) (2). A number of factors influence the first-pass hepatic clearance such as gender, age, puberty and liver disease, because they affect the hepatic enzyme activity (3). In addition, some studies also suggest that oral hydrocortisone may result in supraphysiological cortisol levels, especially following the evening dose, due to decreased hydrocortisone clearance and increased bioavailability (4)
- In this case, CSHI produced rapid restoration of the normal cortisol circadian rhythmicity and optimised the 17 OHP day profile (Fig.2 & Fig.3)

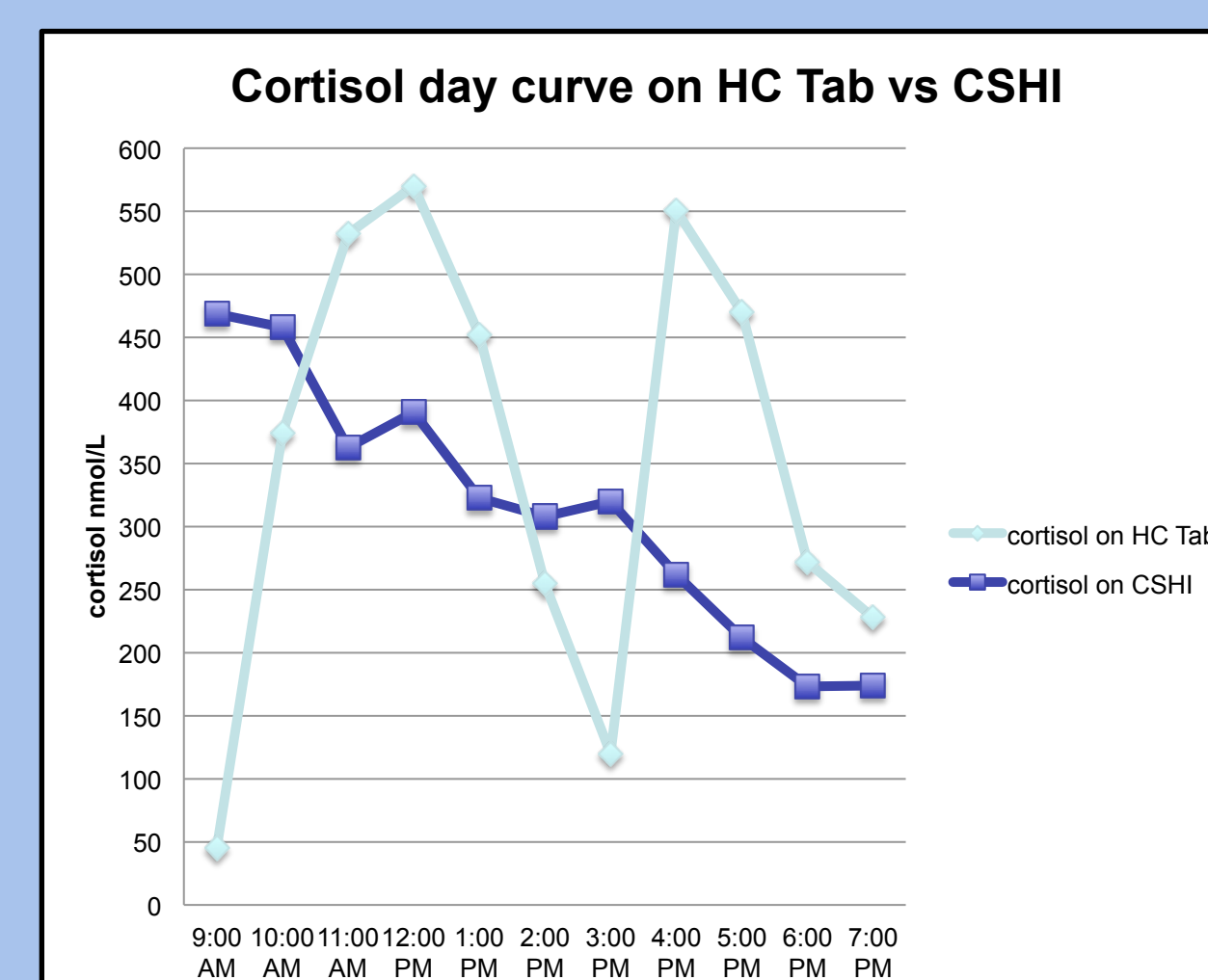


Fig.2: Cortisol day curve on HC Tab vs. CSHI

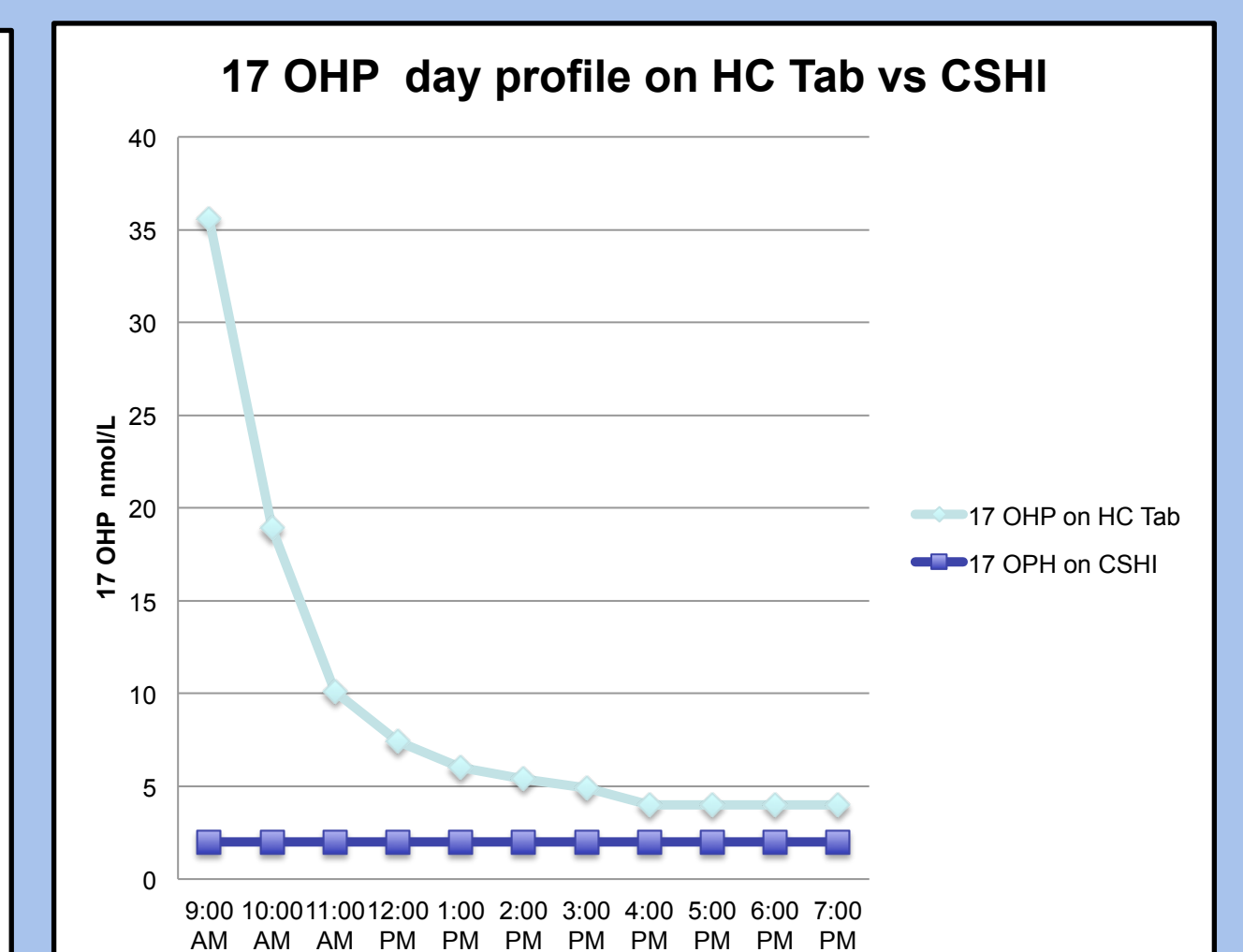


Fig.3: 17 OHP day profile on HC Tab vs. CSHI

Conclusions

- Adequate control of CAH with oral hydrocortisone or other glucocorticoid may sometimes be difficult due to the adverse effects and the variability in pharmacokinetic and bioavailability of the oral dose.
- Continuous subcutaneous infusion of hydrocortisone may prove a valuable adjunct therapy for CAH, as it is safe and effective, particularly in patients who are intolerant to oral glucocorticoid and have variable drug pharmacokinetics and bioavailability.

References

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