Urine steroid profiles: what can they do for me?

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Introduction

Assessment of urine steroid profiles (USPs) is a powerful test for investigating adrenal steroid disorders. Unlike most biochemical testing, USP analysis is very labour intensive, and full interpretation requires qualitative and quantitative assessment of the profile. For some disorders steroids must be identified manually, therefore adequate clinical information is essential to provide a complete report. Clinical indications for USP analysis are limited, typically including ambiguous genitalia, salt-losing states, virilisation, hypertension, and adrenal tumours. In 2017 we moved to a gas chromatograph-tandem mass spectrometer (GC-MS/MS), which has improved the specificity and throughput of the method.

Here we present a review of USPs from the last 12 months to assess requesting patterns. We also present data from the new instrument examining the utility of steroid ratios for the diagnosis of late onset congenital adrenal hyperplasia due to 21-hydroxylase deficiency (LOCAH).

Requesting patterns

USP requests received between May 2017 and 2018 were extracted from the laboratory database. Clinical details were grouped according to possible condition and assessed for relevance to the following: 1) ambiguous genitalia, 2) salt-losing states, 3) adrenarche / virilisation, 4) hypertension, 5) adrenal tumour.

Requests categorised by age and gender are shown in Table 1. Clinical details received for these requests are shown in Figure 1. The majority of requests (~35%) were made to exclude LOCAH in the work up of adrenarche or polycystic ovarian syndrome, depending on the age of the patient.

Table 1 Total number of USP requests from May 2017-2018, categorised by age and gender.

Age range	≤12 weeks	3 months – 1 year	1 – 10 years	11 – 16 years	≥16 years	Totals
Female	10	2	89	23	121	245
Male	14	21	41	24	44	144
Unknown	4	0	0	0	0	4
Totals	28	23	130	47	165	393

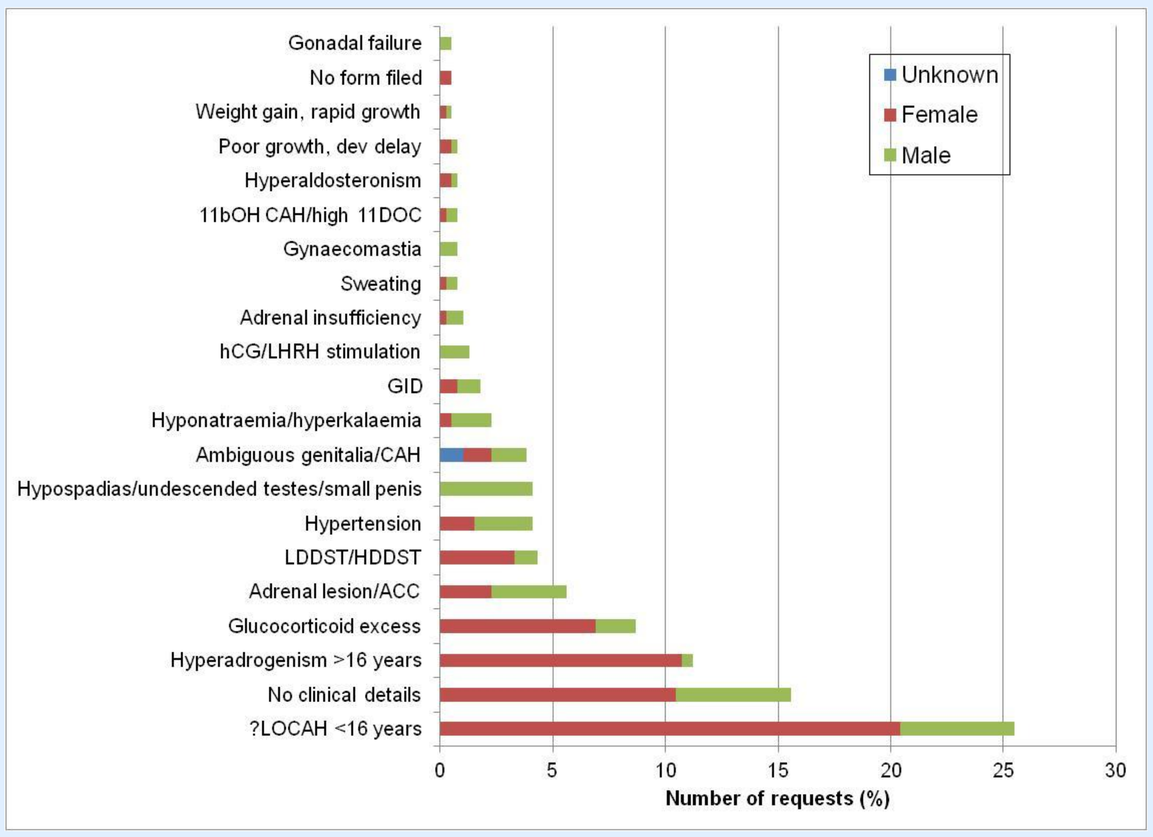

Figure 1 Clinical details/reason for request (≥2 requests).

Most USP requests were made appropriately. However, 22% of requests were sent either without or with inappropriate clinical details. Inappropriate requests included GID, hCG/LHRH test, poor growth/developmental delay, glucose tolerance test, COPD, unwell, diabetes, alkalosis, bladder stones.

The more common disorders of adrenal steroid metabolism tend to be relatively apparent when reviewing steroid profiles. However, some conditions require close examination of the profile to make an exclusion, and without clinical details we cannot know to look for these conditions.

Steroid ratios

We reviewed 151 steroid profiles generated using the GC-MS/MS from children aged 3 months-10 years. The dataset contained 99 profiles with no abnormalities, 33 with probable adrenarche, 16 with non-specific findings and 3 cases of LOCAH. Urine quantities of the three classical markers of LOCAH (17-hydroxypregnanolone (17P), pregnanetriol (P3) and 11-oxopregnanetriol (11oxoP3) are shown in Figure 2. There was a clear difference in 17P and P3 values between the LOCAH and non-LOCAH groups. The most specific marker, 11oxoP3, was not measurable in any of the non-LOCAH cases.

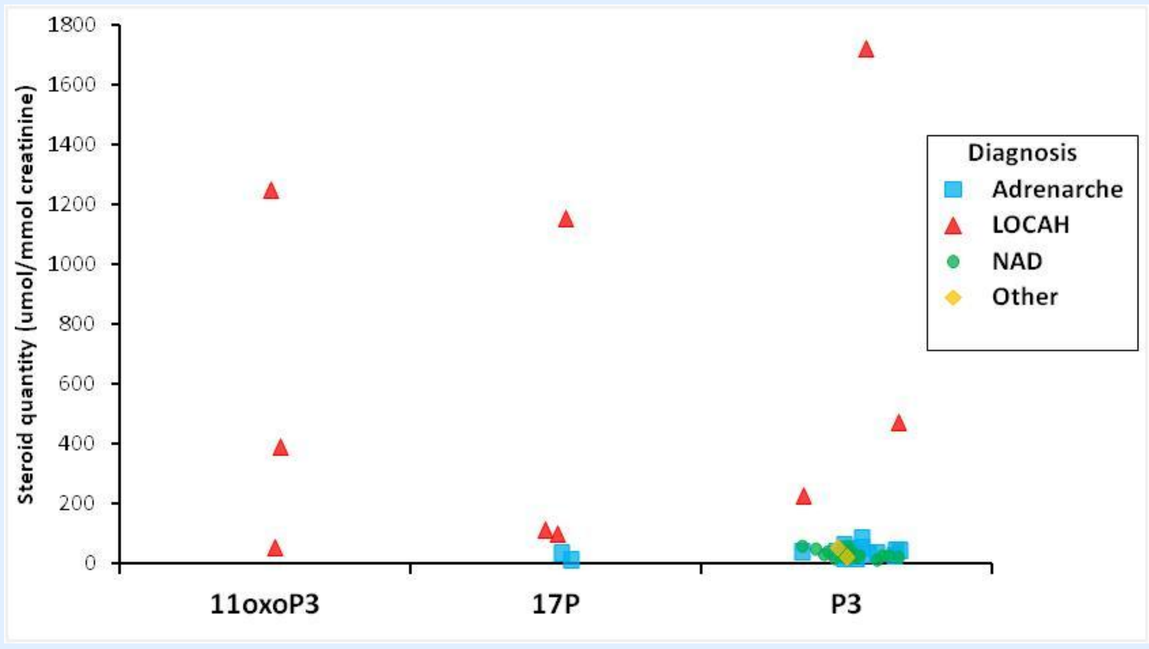

Figure2 Steroid concentrations and diagnoses.

Ratios of 17P, P3, and 11oxoP3 to three glucocrticoids (tetrahydrocortisone (THE), tetrahydrocortisol and allo-tetrahydrocortisol (THFs)) were calculated according to Lucas-Herald *et al.* [1] Steroid ratios could only be calculated where all steroids were measurable and were available for 54/151 cases (2 for 11oxoP3, 4 for 17P and 48 for P3).

Table 3 shows the number of results exceeding the age-specific reference interval for each diagnosis. The classical markers of LOCAH were elevated in all cases of LOCAH, as were the ratios (where available). One non-LOCAH patient had a raised 17P ratio, and 6 had a raised P3 ratio (though P3 itself was only raised in 4 cases).

Table 2 Number of results exceeding age-specific reference interval for each steroid and ratio.

Diagnosis (totals)	11oxoP3	17P	P3	11oxoP3 (THE+THFs)	17P (THE+THFs)	P3 (THE+THFs)
Adrenarche (33)	0	1	2	0	1	1
LOCAH (3)	3	3	3	2	2	2
NAD (99)	0	0	0	0	0	5
Other (16)	0	0	2	0	0	0

In agreement with previous studies, these data suggest steroid ratios do not offer any advantages over steroid quantification for diagnosis of LOCAH due to 21-hydroxylase deficiency. Raised 17P and P3 alone may indicate other conditions depending on the age of the patient, such as PCOS, mid-luteal phase sampling, or pregnancy. 11oxoP3 is the most specific marker of LOCAH, especially in conjunction with 17P and P3.

Conclusions

1) Most urine steroid profile requests received in Glasgow are appropriate., but adequate clinical information is essential to provide helpful interpretation.
2) In agreement with Lucas-Herald *et al*, steroid ratios generated by the GC-MS/MS do not appear to offer significant advantages over steroid quantification in the diagnosis of LOCAH due to 21-hydroxylase deficiency.

We are in the process of assessing the utility of steroid ratios in other clinical scenarios, in particular in adults for the differentiation of adrenal adenoma and carcinoma.

References

1. Lucas-Herald AK, Rodie M, Lucaccioni L, *et al. Int J Pediatr Endocrinol.* 2015; 10: DOI 10.1186/s13633-015-0007-1

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