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DETERMINATION OF ANDROGEN EXCRETION IN SHORT DURATION TIMED URINE SAMPLES

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SUMMARY

Urine samples collected over a timed period of short duration (between 3–5 h) were analyzed for levels of 17-keto-steroids (17KS) and testosterone glucuronide (TG), and correlated to levels determined in 24 h urine collections. The correlation coefficient for 17KS excretion was statistically significant ($r = 0.95$, $P < 0.001$) at a level that the data suggest short duration timed (SDT) urines could justifiably be utilized in place of 24-h urines. Although the correlation coefficient for TG excretion was also statistically significant ($r = 0.73$, $P < 0.01$), there was sufficient discordant values on an individual basis to suggest that the use of SDT urines for TG excretion in the clinical situation is generally not warranted. However, the data for TG excretion indicate that SDT urines might be utilized in large clinical studies involving group data, such as longitudinal studies of puberty.

INTRODUCTION

Recent studies have demonstrated that gonadotropin levels determined in overnight urine collections or short duration timed (SDT) urine collections can be correlated with 24-h urinary excretion or serum concentrations of gonadotropins [1, 2]. In fact, investigators are utilizing serial SDT urines to evaluate gonadotropin function during various phases of pubertal development [3]. The ability to determine gonadal steroids in the same urines being utilized for evaluation of gonadotropins might often be useful. Although androgenic steroids are secreted in an episodic and diurnal fashion, the variations are not marked. This study was undertaken to determine if SDT urines could be utilized to assess urinary excretion of testosterone glucuronide (TG) and 17-ketosteroids (17KS).

MATERIALS AND METHODS

Urine was collected from 35 volunteers of both sexes whose ages ranged between 4 years and 48–4/12 years. The subjects were instructed to collect a 24-h urine on an outpatient basis but to retain as a separate aliquot the first 3–5 h sample. Two of these volunteers have the adrenogenital syndrome (compensated 21 hydroxylase deficiency). One is a 25 year old male who admittedly was not on glucocorticoid therapy for several months prior to his urine collection. The other patient is a 5 year old female being treated with 15 mg of hydrocortisone per day.

Urinary excretion of 17KS was determined by a modification of the method of Drekter and associates [4]. Urinary TG was determined in 16 male patients by double antibody radioimmunoassay, modifying the procedure of Rudd and associates [5]. In brief, after enzymatic hydrolysis, 5 ml of urine were extracted with diethyl ether and then purified by cellulose acetate thin layer chromatography and alumina chromatography prior to assay. The anti-testosterone antibody utilized in the assay has less than 25% cross reactivity with 5α-dihydrotestosterone. Trace amounts of radioactive T were carried through the procedure to determine recovery.

RESULTS

The correlation of SDT urines and 24-h urines for excretion of 17KS is depicted in Fig. 1. The correlation coefficient ($r = 0.95$, $n = 35$) was highly significant with a $P < 0.001$. The male adrenogenital patient excreted 1663 μg 17KS/h in his SDT urine as compared to 1223 μg 17KS/h in his 24-h urine.

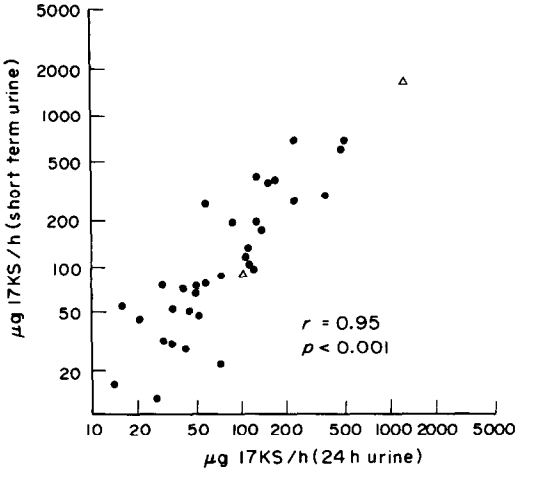

Fig. 1. Correlation between 17KS values obtained in SDT urines and 24 h urines in 35 matched samples. Open triangles (△) represent patients with the adrenogenital syndrome.

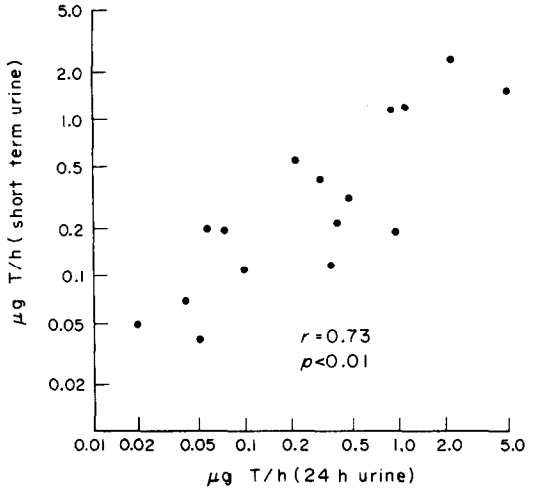

Fig. 2. Correlation between T glucuronide values obtained from SDT urines and 24 h urines in 16 matched samples from male patients.

The treated female patient excreted 88 μg 17KS/h in her SDT urine as compared to 107 μg 17KS/h in her 24-h urine.

The correlation of SDT urines and 24-h urines for TG is depicted in Fig. 2. The correlation coefficient was also statistically significant ($r = 0.73$, $n = 16$, $P < 0.01$). However, analysis of individual urine values revealed discordant results in 7 of the 16 male patients. There were 3 SDT urine values twice as great as the 24-h values and 4 SDT urine values only half as great.

DISCUSSION

Urinary TG levels have been found to be of value in evaluating testicular function, especially in conjunction with administered human chorionic gonadotropin [6]. The data from the present study revealed intermittent discordant values for TG excretion in SDT urines as compared to 24-h urines. This information, coupled with the knowledge that TG excretion is a reflection of a variety of factors including adrenal androgens and liver metabolism as well as gonadal function, would suggest that TG excretion in SDT urines should not be utilized as a means to evaluate clinical situations suggesting hyperandrogen or hypoandrogen conditions. However, the data also demonstrate that TG levels in SDT urines correlate to levels determined in 24-h urines at a degree of statistical significance comparable to those reports correlating SDT urinary gonadotropin levels to 24-h urinary gonadotropin levels [1, 2]. It is in this context that SDT urinary TG values might be useful. Plasma levels of T have been demonstrated to fluctuate not only diurnally but cyclically over a period of days as well [7]. In large clinical investigative studies, such as longitudinal studies of puberty, in which either serial or large numbers of SDT urines are being collected for gonadotropin levels, determination of TG levels may be enlightening.

The diurnal rhythm of 17KS excretion was demonstrated by Pincus in 1943 [8], who cautioned against the use of "short-interval collections of urine for clinical routine studies". Although Pincus demonstrated that there is a significant difference in 17KS excretion when fractional urines collected during sleep are compared to fractional urines during the day, a later study by Pincus [9] demonstrated no statistically significant difference between morning urines compared to day urines. In fact, recalculation of his data, using the time intervals stated, revealed that there is no significant difference between the mean 17KS excretion determined in 4-h morning samples (13.8 ± 6.88 mg/24 h) and the mean 17KS excretion determined in 24-h urines (11.2 ± 5.14 mg/24 h).

The present study indicates that the degree of correlation between SDT urines and 24-h urines for 17KS excretion is so highly significant that utilization of SDT urines could justifiably be substituted for 24-h urines. The use of SDT urines would facilitate the study of various virilizing disorders, especially in childhood and specifically in the newborn with ambiguous genitalia. Furthermore, the management of certain disorders, such as the adrenogenital syndrome, require periodic evaluation of 17KS excretion and SDT urines would facilitate surveillance of such disorders.

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