URINARY EXCRETION OF DEHYDROEPIANDROSTERONE IN NORMAL AND ABNORMAL LATE PREGNANCY AND IN NON-PREGNANT WOMEN

By

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ABSTRACT

The urinary excretion of dehydroepiandrosterone (DHA) in 10 healthy women during the last month of pregnancy (mean m = 0.43 mg/24 h; standard deviation sd = ±0.13) was found to be as high as that in 7 patients with chronic hypertension or with toxaemia of pregnancy (m = 0.40 mg/24 h; sd = ±0.13). The values were significantly (P < 0.01) decreased in 6 women in late pregnancy with intrauterine foetal death (m = 0.20 mg/24 h; sd = ±0.10), in two cases of pregnancy with anencephalic foetuses (0.30 and 0.25 mg/24 h, resp.) and in 11 healthy non-pregnant women (m = 0.26 mg/24 h, sd = ±0.10). The method used involved separation of free non-conjugated Zimmermann chromogens from the urine by extraction with benzene, mild hydrolysis of the urine, column chromatography on silica gel and colorimetric determination as Zimmermann chromogen. It is assumed that the increased excretion of DHA in the two groups of late pregnant women with intact pregnancy as compared with non-pregnant women may be caused by the biosynthesis of DHA in the foetal adrenals. The unchanged values of DHA in the two groups of women during late pregnancy with intrauterine foetal death or with anencephalics may reflect the interrupted biosynthesis of DHA.

Dehydroepiandrosterone (3β-hydroxy-androst-5-en-17-one, DHA) and its sulphate (DHAS) are known to be important precursors for the formation of
oestrogens in the foeto-placental unit in pregnancy. In this paper the urinary excretion of DHA is described in healthy pregnant women and in those with disorders of pregnancy as well as in non-pregnant women.

MATERIAL AND METHODS

Patients. – The urinary excretion of DHA was determined in 10 healthy pregnant women and in 7 women with toxaemia of pregnancy or with chronic hypertension. The determination was carried out in the 10th month of pregnancy. All these women gave birth to living children. Determinations were also done in 6 women in late pregnancy with intrauterine death of the foetus and in two women in late pregnancy with a subsequently confirmed anencephalic foetus and also in 11 healthy non-pregnant women.

Separation of free Zimmermann chromogens (Dässler 1965). – A urine specimen large enough for hydrolysis was extracted twice with half its volume of benzene.

Hydrolysis (Fotherby 1959). – One fifth of a 24-h-urine was refluxed with half its volume of benzene for 6 h. After cooling, shaking and separation of the benzene, the extraction was repeated with the same volume of benzene. The combined benzene layers were washed with \(\frac{1}{10}\) volume of 3 N NaOH and distilled water and then evaporated to dryness.

Chromatography (Goldzieher & Axelrod 1962). – Column chromatography was carried out with 2 g of silica gel (Merck No. 7734). DHA runs in the fraction containing the \(C_{19}O_2\)-steroids.

Colour reaction. – Colorimetric determination was carried out according to a modified method of Zimmermann (1955) using 0.3 ml of ethanol, 0.3 ml of 2 % m-dinitrobenzene in abs. ethanol (w/v) and 0.3 ml of 3 N KOH and extraction of the chromogen with 1.5 ml of ether (Dässler 1965). The optical density was read at 440, 510 and 580 nm on a VSU 2 spectrophotometer from VEB Carl Zeiss Jena, DDR. Corrected optical densities were calculated (\(E_{\text{corr}} = E_{510} - \frac{1}{2} (E_{440} + E_{580})\) minus an \(E_{\text{corr}}\) blank value produced by solvents and reagents used in chromatography and colorimetry). \(E_{\text{corr}}\) blank = 0.020. Ten µg of DHA showed an \(E_{\text{corr}}\) value of 0.075. The values reported were not corrected for losses.

RESULTS

1. The mean urinary excretion of DHA in 10 healthy late pregnant women was as high as in 7 patients with toxaemia of pregnancy or suffering from chronic hypertension, but it was found to be significantly \((P < 0.01; t\)-test\) higher than the mean found for 11 non-pregnant women (Table 1).

2. The urinary excretion of DHA in 6 late pregnant women with intrauterine foetal death and in two late pregnant women each with an anencephalic foetus, was found to be significantly \((P < 0.01)\) lower than in the group of women with normal pregnancy and as low as in healthy non-pregnant women (Table 1).

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The amount of DHA found after hydrolysis in the urine of non-pregnant women and in the urine of women in late pregnancy under normal and abnormal conditions (m = mean; sd = standard deviation; r = range; n = number of patients; a₁ and a₂ = single observations). All values are indicated as mg/24 h.

<table>
<thead>
<tr>
<th>Non-pregnant women</th>
<th>Healthy late pregnant women</th>
<th>Chronic hypertension or toxaemia of pregnancy</th>
<th>Intrauterine foetal death in late pregnancy</th>
<th>Pregnancy with anencephalic foetus</th>
</tr>
</thead>
<tbody>
<tr>
<td>n = 11</td>
<td>n = 10</td>
<td>n = 7</td>
<td>n = 6</td>
<td>n = 2</td>
</tr>
<tr>
<td>m = 0.26</td>
<td>m = 0.43</td>
<td>m = 0.40</td>
<td>m = 0.20</td>
<td>a₁ = 0.25</td>
</tr>
<tr>
<td>sd = ±0.10</td>
<td>sd = ±0.13</td>
<td>sd = ±0.13</td>
<td>sd = ±0.10</td>
<td>a₂ = 0.30</td>
</tr>
<tr>
<td>r = 0.13–0.42</td>
<td>r = 0.30–0.70</td>
<td>r = 0.29–0.50</td>
<td>r = 0.11–0.37</td>
<td></td>
</tr>
</tbody>
</table>

**DISCUSSION**

Lauritzen (1968) observed almost the same range of DHA excretion in pregnant and in non-pregnant women. Kotásek et al. (1967) found the urinary excretion of DHA in healthy late pregnant women to be less than 60 per cent of that in healthy non-pregnant women. Moreover, a reduced average urinary excretion of DHA was found in late toxaemia of pregnancy with a total absence of DHA in 25 of 27 cases (Kotásek et al. 1967). The observations described in this paper differ both qualitatively as well as quantitatively from these results. This may be due first of all to the different methods used.

Our findings point to an increased urinary excretion of DHA in the group of healthy pregnant women and in the group of women with toxaemia of pregnancy as compared to the non-pregnant women. This is in agreement with the suggestion that major quantities of DHAS are produced by the foetus (Diczfalusy 1968) as well to the observation of an increasing level of DHA in the urine of one woman during early pregnancy (Adlercreutz et al. 1967).

Lamb et al. (1967) following removal of the foetus at midpregnancy and in situ perfusion of the placenta with ³H-labelled DHAS and ¹⁴C-labelled DHA, demonstrated a small transfer of DHAS and DHA and/or their metabolites to the maternal circulation. For the most part DHAS and DHA were metabolized to phenolic steroids. Hence, there is reason to assume that the increased level of DHA found in the urine of late pregnant women with intact pregnancy may be derived from foetal DHAS or DHA.

The excretion of DHA in cases of intrauterine foetal death in late pregnancy was found to be as low as in non-pregnant women. This may be due
to the fact that in these cases the foetus no longer produces DHAS. Moreover, in late pregnant women who gave birth to an anencephalic newborn some days after the estimation of DHA, the urinary excretion of this steroid was observed to be as low as in women with foetal death and in non-pregnant women. This may be in agreement with the observation that the concentration of DHAS in the cord plasma of anencephalic foetuses and in the peripheral blood of mothers bearing anencephalic foetuses was nil or very low as compared with the values of healthy women with normal pregnancy (Easterling et al. 1966). In anencephalics the adrenals are generally hypoplastic (Frandsen & Stakemann 1964) and thus probably produce little, if any, of this steroid. Thus it appears that the urinary excretion of DHA in late pregnant women with intrauterine foetal death and in late pregnant women with an anencephalic foetus is at the same level as in non-pregnant women, but not as high as in women with an intact pregnancy.

REFERENCES


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