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PLASMA OESTRADIOL-17β IN NORMAL HUMAN PREGNANCY

WIGGO FISCHER-RASMUSSEN*
University Department of Obstetrics and Gynaecology, Rigshospitalet, Copenhagen, Denmark
(Department Heads: Dyre Trolle and Børge Sørensen)

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SUMMARY

Plasma oestradiol-17β concentrations in a series of normal pregnant women were measured from the 23rd to 41st week of pregnancy by a gas–liquid chromatographic method which allows the simultaneous measurement of the three classical oestrogens from a 5 ml plasma sample. The oestriol and oestrone results have been reported previously.

In addition to a clear increase in the plasma oestradiol-17β concentration as pregnancy proceeds, it was found that the spread about the means of the values for each week of pregnancy was less than for oestrone, and as much dependent on variation within the individual as between individuals. By comparison, plasma oestrone variation was greater between individuals than in individuals.

Plasma oestradiol-17β concentrations were definitely correlated with urinary excretion of oestradiol-17β.

INTRODUCTION

THE measurement of plasma oestriol and oestrone in a series of normal pregnant women has been reported previously[1, 2]. In continuation of this study, the results of plasma oestradiol-17β measurement in the same series of women are now presented. A normal range of method-specific values for the three oestrogens between the 23rd and 41st week of pregnancy is suggested in the respective studies.

EXPERIMENTAL

Material

The study comprised 21 pregnant women. Detailed description is given in the oestriol and oestrone studies[1, 2]. The average birth weight was 3250 g (2700–4100 g).

Methods

Venous blood samples were collected at one-to-two-week intervals, and at the same time the women provided 24 h urine specimens. Oestrone and oestradiol-17β excretion in the urine was measured in the Hormone Department, Statens Seruminstitut, Copenhagen, by Svenstrup's method[3].

Oestradiol-17β in plasma was measured together with oestriol and oestrone using a method described by the author[4]. The oestradiol-17β and oestrone plasma fractions were stored at −21°C until analysis could be made.

RESULTS

Table 1 gives the mean value and standard deviation of oestradiol-17β in both plasma and urine for each week from 23rd to 41st week of pregnancy. Figure 1

*Address of the author: Fagerbo 19, 2950 Vedbaek, Denmark.

Table 1. Mean value and standard deviation for plasma oestradiol-17β and for urinary oestradiol-17β (24-h sample) for individual pregnancy weeks. 21 normal pregnant women

Weeks of pregnancy	Plasma (μg/l.)	Number	Urine (mg/24 h)	Number
23	13	5	0·40	2
24	20	5	0·23	5
25	16 ± 7	7	0·21 ± 0·10	7
26	21 ± 8	9	0·26 ± 0·09	9
27	20 ± 8	15	0·27 ± 0·10	10
28	24 ± 11	16	0·27 ± 0·11	16
29	19 ± 7	15	0·27 ± 0·12	17
30	24 ± 11	15	0·29 ± 0·11	15
31	26 ± 14	16	0·29 ± 0·18	16
32	25 ± 11	14	0·30 ± 0·16	16
33	21 ± 6	14	0·22 ± 0·09	16
34	24 ± 7	15	0·31 ± 0·13	15
35	26 ± 9	16	0·33 ± 0·15	13
36	27 ± 9	20	0·35 ± 0·11	17
37	31 ± 13	16	0·36 ± 0·17	19
38	28 ± 14	17	0·41 ± 0·18	15
39	28 ± 11	13	0·41 ± 0·11	14
40	34 ± 14	9	0·34 ± 0·15	9
41	29 ± 10	7	0·36 ± 0·14	6
		244		237

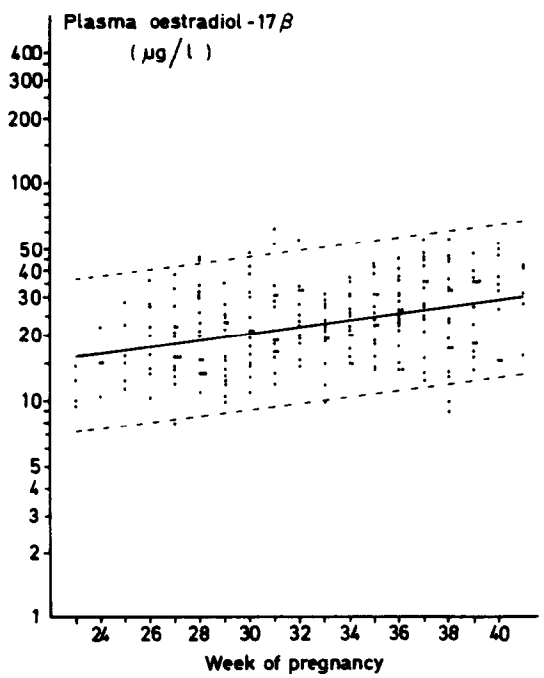

Fig. 1. Oestradiol-17β in plasma from the 23rd-41st week of pregnancy. Mean value $\pm s_{y \cdot x} \cdot t_{0 \cdot 05}$. Regression equation: Log $Y = 0{\cdot}8611 + 0{\cdot}0150 \cdot X$. $N = 244$. The correlation is significant ($P < 0{\cdot}001$).

is a semi-logarithmic scatter graph of the individual plasma oestradiol-17β concentrations against the weeks of pregnancy on the abscissa. The regression lines for the mean values, and upper and lower 95% limits for all values are appended. Clear increase of mean values as pregnancy proceeds is demonstrated ($P < 0{\cdot}001$).

The spread of plasma oestradiol-17β values about the mean was notably less than for oestrone. Treating the results for oestradiol-17β as the plasma oestrone results were treated[2], showed that variation in individuals (s) was ± 7 μg/l. Similarly, variations between individuals were calculated from the standard deviations of the mean ordinates of the individual regression lines in weeks 28, 32, and 36. Means ± standard deviations in these weeks were 19 ± 7, 22 ± 6, and 26 ± 7 μg/l., indicating that variation between individuals is not greater than variation within the individual.

Figure 2 shows the correlation between plasma and urinary oestradiol-17β

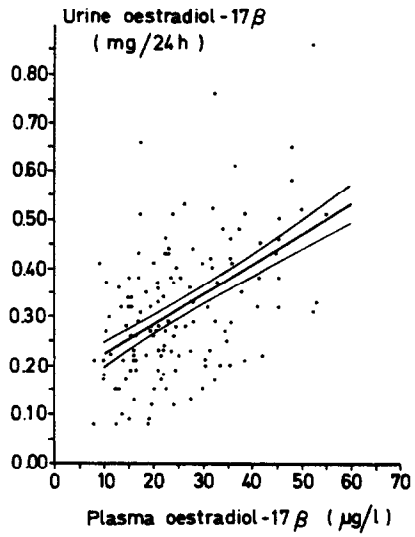

Fig. 2. Correlation between oestradiol-17β in plasma and urine. Regression line ($Y = 0{\cdot}1606 + 0{\cdot}0062 \cdot X$) shown with 95% confidence intervals. $N = 198$. The correlation is significant ($P < 0{\cdot}001$).

values, which are plotted against each other. The regression line and 95% confidence intervals are appended. A significant correlation is demonstrated ($P < 0{\cdot}001$).

DISCUSSION

A significant increase in "total" oestradiol-17β concentrations in plasma as pregnancy proceeds is demonstrated, supporting the findings of other authors [5, 6]. Variation in and between individuals was less than found in the oestrone study of the same women[2]. The standard deviations (Table 1) are of the same percentage order as found by other authors in determinations of unconjugated oestradiol-17β in plasma of pregnant women[7]. Other authors suggest that the individual and daily variation in plasma oestradiol-17β is less than that in oestriol and oestrone[8].

Plasma oestradiol-17β shows a profile similar to that of plasma oestriol in cases of "high risk" pregnancy[9], and may therefore be a useful parameter of the foeto-placental unit function. This is of great practical interest, since rapid methods of measurement of plasma oestradiol-17β by competitive protein binding and radioimmunoassay are under development[7, 10, 11].

Table 2 compares the findings of different authors in plasma oestradiol-17β studies near term. Where whole blood was used, correction is made on the basis of a 40% haematocrit value[12], and the results expressed for plasma. The first part of the table contains results for "total" oestradiol-17β – that is, oestradiol-17β extracted after hydrolysis. Values from this present work for weeks 39 and 40 (Table 1) are given. The second part of the table concerns determinations of "free" (unconjugated) oestradiol-17β alone. Probably the greater part of oestradiol-17β in plasma of pregnant women is free, but results differ, as the following percentages have been given: 81%, 66%, and 27%[13, 14, 15].

In most earlier studies acid hydrolysis and colorimetry were used to determine total plasma oestradiol[6, 8, 16–18]. However, in one instance fluorometry was used[5] and in another enzyme hydrolysis combined with gas–liquid chromatography[15].

Mean values for total oestradiol-17β in late pregnancy found in the present study are comparable with those of two other studies[15, 16], but otherwise relatively high. In this connection, it is stressed that the method of the current study[4] includes correction for analysis loss based on the recovery of a known quantity of tritium labelled oestradiol-17β added before hydrolysis. Roy and Brown[18] record a recovery of approximately 59%. Only one of the cited studies[8] includes, in the method, correction for analysis loss. The difference

Table 2. Different authors' determinations of oestradiol-17β in plasma or blood late in pregnancy. Mean values and range (μg/l)

Investigators	Period of pregnancy	Number of women	Mean	Range	Biological fluid
Total oestradiol-17β:					
Roy and Mackay[6]	37th–42nd week	29	12·3 (20·5)	7–20 (12–33)	Blood Plasma*
Smith and Arai[16]	37th–43rd week	4	29	17–46	Plasma
Schwers[17]	Term	12	12·7	4·8–25·2	Plasma
Rado *et al.*[8]	Labor	4(5)	19	12–33(81)	Plasma
Ittrich *et al.*[5]	9th month	5	13 (22)	5–23 (8–38)	Blood Plasma*
Touchstone and Murawec[15]	3rd trimester	pool	30·6		Plasma
Present investig.	39th–40th week	22	30·5	14–52	Plasma
Free oestradiol-17β:					
Svendsen and Sørensen[19]	39th–40th week	12	12·9	1·6–23·3	Plasma
Mead *et al.*[20]	40th–41st week	5	15·0	6·7–26·0	Plasma
Korenman *et al.*[7]	36th–40th week	41	15·7 ± 5·6		Plasma
Abraham *et al.*[11]	Term	6	20	14–27	Serum

*Based on a haematocrit value of 40%.

between the mean found in the current study and this latter may depend on the few individuals studied in the latter. The values in parentheses [8] were found in a twin pregnancy.

The second section of Table 2 gives, as mentioned, the results of investigations for free oestradiol-17β. Widely different methods were used: double isotope dilution [19], gas–liquid chromatography with electron capture detection [20], competitive protein binding [7], and radioimmunoassay [11]. Notwithstanding, there is reasonable agreement between the results. If it is presumed that the free fraction of plasma oestradiol-17β is 50% or a little more, then the results of these four studies and the present one – mean values and upper limits – are in particularly good agreement.

A review of the relevant literature concerned with plasma oestrogen analysis during pregnancy seems to indicate that, of individual oestrogen studies, findings for oestradiol-17β are the most uniform, irrespective of method.

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