Salivary Levels of Estrogens and Progesterone During and After Pregnancy

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Introduction

Adequate production of estrogens (estradiol, estrone, estriol) and progesterone by the corpus luteum and placenta are essential for a successful pregnancy. Insufficient production of progesterone by the corpus luteum during the first trimester often results in miscarriage, whereas low placental estriol during later stages of pregnancy is associated with fetal distress. A non-invasive method to monitor hormone levels throughout pregnancy, particularly during the first trimester, could help identify hormonal deficiencies (e.g. low progesterone) that increase risk for miscarriage, and lead to therapeutic interventions, such as progesterone supplementation, for women with unrecognized luteal insufficiency. Very little salivary reference data has been published to date for sex steroids during pregnancy.

Method

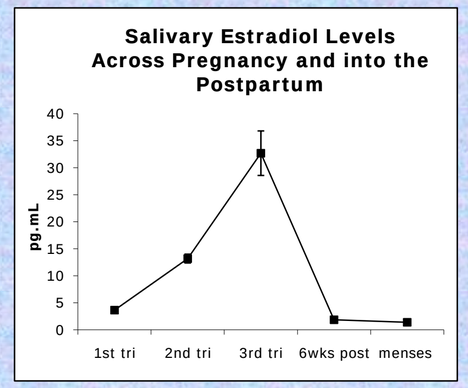
To establish normal ranges for salivary sex-steroids during and after pregnancy, saliva was collected and hormones tested from 45 healthy pregnant women 12, 24, and 37 weeks after their last menstrual period, postpartum at 6 weeks, and once menstruation had resumed (between days 2-8 of the first menstrual cycle). Saliva was tested for estradiol, estrone, estriol, and progesterone using a C-18 column chromatography extraction and enzyme-immunoassay (EIA) procedure previously described (Glaser et al., Gynecol Obstet Invest 2008; 66: 111-118).

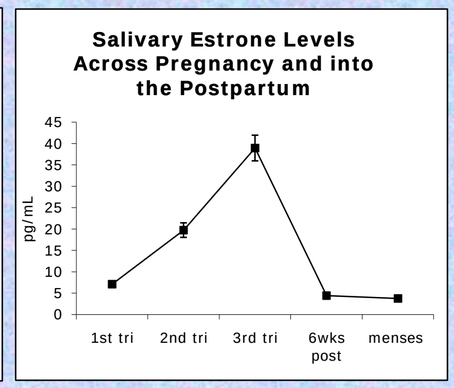
Results

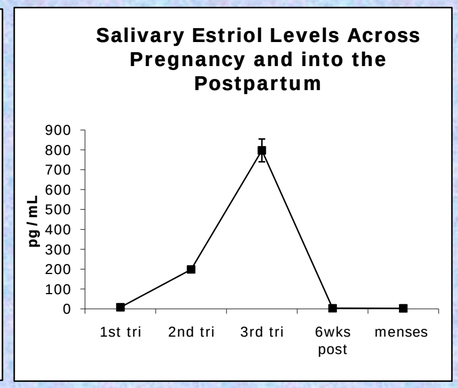
Mean (standard error of the mean) salivary hormone levels (pg/mL) at the five time points are shown in the table and graphs below:

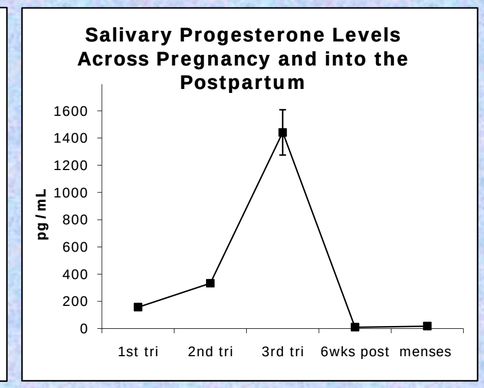
	Estradiol	Estrone	Estriol	Progesterone
1st trimester	3.65 (0.18)	7.11 (0.4)	8.40 (0.8)	157.27 (9.79)
2nd trimester	13.19 (0.82)	19.75 (1.7)	198.33 (8.82)	332.85 (22.77)
3rd trimester	32.69 (4.12)	38.95 (3.0)	797.37 (57.26)	1441.05 (166.46)
6 weeks postpartum	1.85 (0.31)	4.42 (0.22)	3.24 (0.19)	9.63 (1.61)
1st menses	1.39 (0.11)	3.75 (0.16)	2.59 (0.24)	17.38 (7.54)

Mean postpartum levels of salivary estradiol, estrone, and estriol were similar to the lower mid-luteal ranges (1.3-3.3, <7.0, and 1.6-5 pg/mL respectively) according to saliva test data from >50,000 premenopausal women not using exogenous hormones (ZRT Laboratory data).

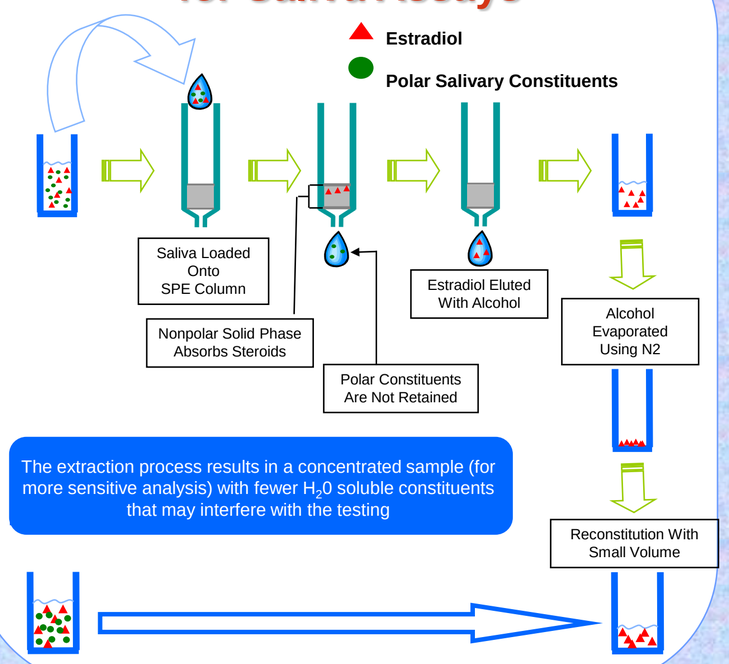








Extraction Procedure for Saliva Assays



The extraction process results in a concentrated sample (for more sensitive analysis) with fewer H_20 soluble constituents that may interfere with the testing

Conclusion

We have shown that saliva is a viable matrix for accurately monitoring sex steroid hormones throughout pregnancy and postpartum. The ranges established here should allow for a simple means of monitoring sex hormone profiles in pregnant women at risk. As salivary steroid levels represent the free or bioavailable fraction of these unconjugated steroids, which are approximately 2-3% of serum values representing the total amount of circulating hormone, there has been some controversy concerning the reliability of saliva assays compared to serum assays. However, numerous correlation studies (see table below) find that salivary levels can reliably predict serum levels. Saliva has advantages over conventional serum testing in that the collection is simple, convenient and non-invasive. Moreover, sampling can be carried out at home and sent directly to the testing laboratory as a practical alternative to frequent clinic visits.

Analyte	Correlation (r)	Reference
Progesterone	.90	Meulenberg PM, Hofman JA. Salivary progesterone excellently reflects free and total progesterone in plasma during pregnancy. *Clin Chem* 1989;35:168-72.
Progesterone	.98	Price DA, Astin MP, Chard CR, Addison GM. Assay of hydroxyprogesterone in saliva. *Lancet* 1979;2:368-9.
Estradiol	.77	Belkien LD, Bordt J, Möller P, Hano R, Nieschlag E. Estradiol in saliva for monitoring follicular stimulation in an in vitro fertilization program. *Fertil Steril* 1985;44:322-7.
Estradiol	.82	Worthman CM, Stallings JF, Hofman LF. Sensitive salivary estradiol assay for monitoring ovarian function. *Clin Chem* 1990;36:1769-73.
Estriol	.90	Lachelin GC, McGarrigle HH. (1984). A comparison of saliva, plasma unconjugated and plasma total oestriol levels throughout normal pregnancy. *Br J Obstet Gynaecol* 1984;91:1203-9.
Estriol	.97	Vining RF, McGinley R, Rice BV. (1983b) Saliva estriol measurements: an alternative to the assay of serum unconjugated estriol in assessing fetoplacental function. *J Clin Endocrinol Metab* 1983;56:454–60.
Estrone	.79	Folan J, Gosling JP, Finn MF, Fottrell PF. Solid-phase enzymoimmunoassay of estrone in saliva. *Clinical Chemistry,* 1989;35:569-72.

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