Extraction Prior to Enzyme Immunoassay Gives Reliable Salivary Estradiol Monitoring during Estrogen Therapy

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Abstract

Saliva analysis is a convenient, non-invasive and rapid method for assessing estradiol (E2) levels. However, particularly in postmenopausal women, the low salivary E2 levels are often near or below the sensitivity of available assays, compromising both accuracy and precision. We present results using an extraction step prior to E2 assay, which concentrates the sample to increase sensitivity and removes potentially interfering substances.

Morning saliva samples were obtained from premenopausal (mid-luteal phase, n=4,651) and postmenopausal women (n=1,770) not taking hormones, and from postmenopausal women receiving oral conjugated equine estrogens (Cenestin, n=119; Premarin, n=439), oral micronized E2 (Estrace, n=145; compounded E2, n=1618), transdermal E2 patches (Climara, n=623; Vivelle, n=1619); or topical E2 cream (compounded E2, n=107). E2 levels were determined by an automated enzyme immunoassay (EIA) after solid phase extraction.

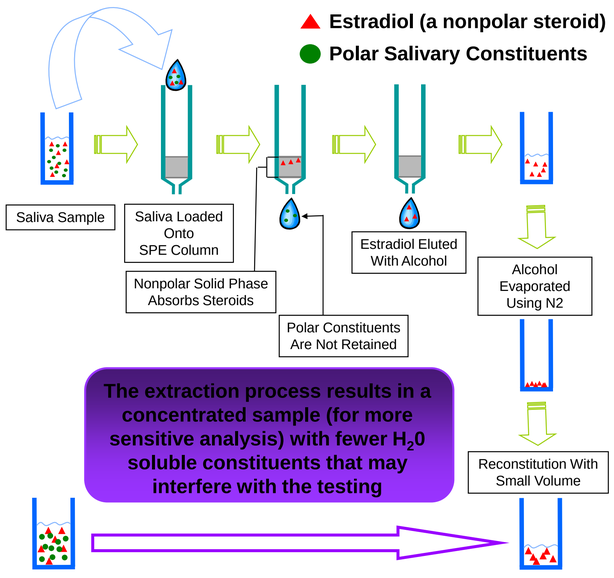
The functional sensitivity of the assay was determined to be 0.8 pg/ml, compared with >2 pg/ml without extraction.

Results are shown in the tables below:

Salivary E2 levels corresponded with the hormone dosage, suggesting a reliable assessment of unbound E2 levels with each formulation, dosage and type of estrogen therapy.

Extraction prior to EIA in an automated assay dramatically increased precision and accuracy at low concentrations. Omitting the extraction step may have contributed to poor serum versus saliva correlations in other studies. This method may therefore allow reliable monitoring of estrogen therapy without the need for expensive and inconvenient blood tests.

Solid Phase Extraction (SPE)



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

Median (Mean) Salivary E2 without Estrogen Therapy

Premenopausal 1.9 (2.3) pg/mL

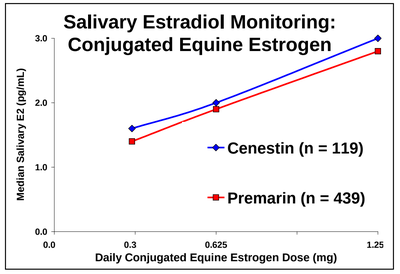
Postmenopausal 1.0 (1.3) pg/mL

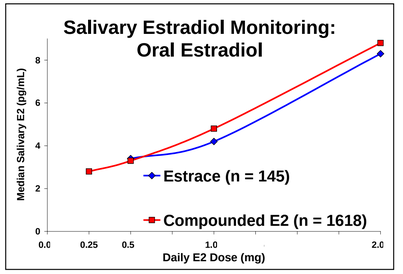
Median Salivary E2 During Estrogen Therapy

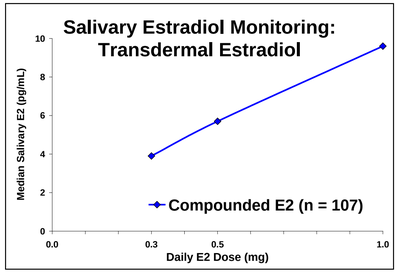
Therapy	Dosage (mg/day)	Median Salivary E2 (pg/mL)	Therapy	Dosage (mg/day)	Median Salivary E2 (pg/mL)
Cenestin[1]	0.3	1.6	Premarin[1]	0.3	1.4
	0.625	2.0		0.625	1.9
	1.25	3.0		1.25	2.8
Estrace[2]	n/a	n/a	Compounded E2[2]	0.25	2.8
	0.5	3.4		0.5	3.3
	1.0	4.2		1.0	4.8
	2.0	8.3		2.0	8.8
Climara[3]	0.025	1.2	Vivelle[3]	0.025	1.2
	0.05	1.4		0.05	1.2
	0.1	1.7		0.1	1.5
Compounded E2[4]	0.3	3.9			
	0.5	5.7			
	1.0	9.6			

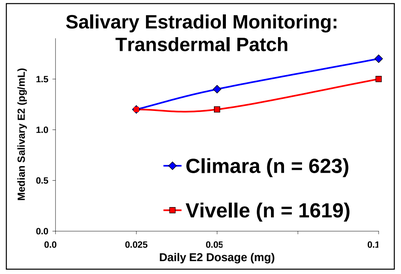
[1]Oral Conjugated Equine Estrogens; [2]Oral E2; [3]E2 Patch; [4]Topical Cream

Results: Linear, Dose-Dependent Relationships with Therapy

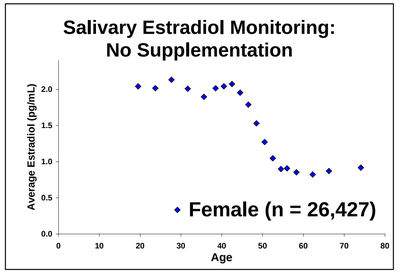








Data from ZRT's database of test results accumulated over the past four years illustrate the sensitivity of the estradiol assay to clearly differentiate premenopausal and postmenopausal estradiol levels. This differentiating power is enhanced by the use of an extracted method.



Conclusions

Our results demonstrate the clinical utility of an extracted EIA method for analysis of salivary estradiol. Monitoring of estrogen therapy ensures that levels do not exceed the normal physiological levels seen in premenopausal women, since excessive circulating estrogen has potential cardiovascular and cancer risks. This method allows clinicians to take advantage of the convenience of saliva testing, with the sensitivity required to assess the extremely low estradiol levels found in the patient population most likely to require monitoring of estrogen therapy.

References

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