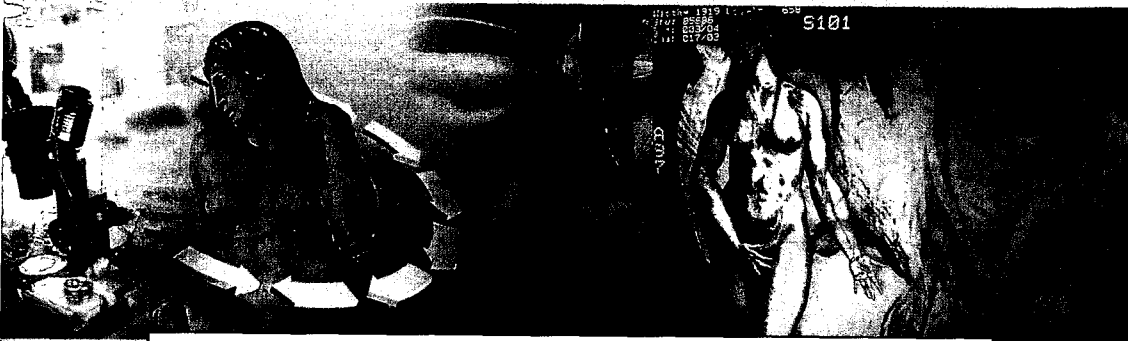


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Sera Estradiols in Women Conceiving by In Vitro Fertilization (IVF) Are not Lower in Aborters Who Conceived by IVF

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Summary

Previous data in patients conceiving without in vitro fertilization (IVF) and whose serum progesterone levels were kept >40 ng/mL found lower sera estradiol (E2) levels in those aborting after 5 weeks from conception vs those not aborting. The study presented herein evaluated sera E2 levels from mid-luteal phase to 5 weeks from fertilization in aborters vs non-aborters where serum P levels were also maintained >40 ng/mL. No frozen ETs were included. All patients with a beta-hCG level >500 mIU/mL were included. No differences were seen in sera E2 at any week when comparing the 25 aborters to the 40 non-aborters. These data are consistent with the hypothesis that the association of low serum E2 and SAB may be more a sign of an abnormal placental function rather than corpus luteum deficiency and thus only becomes apparent when the placenta begins to secrete hormones.

Introduction

A study published several years ago from our infertility center in patients conceiving without the use of assisted reproductive technology found that the serum estradiol (E2) levels were significantly lower in aborters vs non-aborters from 5 weeks from conception despite maintenance of serum progesterone (P) levels ≥ 40 ng/mL by using P supplementation (1).

This was true for women taking follicle maturing drugs as well as those who were not (1).

It was not clear from the aforementioned study whether the association of low serum E2 levels and spontaneous abortion (SAB) were related to a need for E2 secretion by the corpus luteum during the first trimester or whether the low serum E2 was merely related to deteriorating placental function (1).

The study presented here evaluated serum E2 in aborters vs non-aborters beginning from mid-luteal phase to determine if lower E2 levels would still be found in aborters. If this was found, the data would be consistent with the need for E2 as well as P by the corpus luteum of pregnancy for the establishment of an ongoing pregnancy.

Materials and Methods

This study used patients undergoing in vitro fertilization (IVF) because their data was accessible by computer. All women conceiving by IVF who subsequently aborted were prospectively matched with the first two IVF pregnancies achieved by a woman within the same two year age range, infertility diagnosis, and controlled ovarian hyperstimulation regimen, who did not abort.

Serum E2 levels were measured from mid-luteal phase (week 1 from fertilization) and weekly thereafter until 5 weeks. It was not possible to get all five levels in all patients. All patients received at least 400mg of vaginal P throughout the luteal phase and through the study period. Serial fetal ultrasounds were performed. A woman was considered as having aborted if she did not show fetal viability 5 weeks from retrieval.

Results

Ten non-aborters were eliminated because they only had the luteal phase and the 2 week serum E2 levels drawn.

The serum E2 levels in 25 women who aborted vs the remaining 40 controls is seen in Table 1. For the first 5 weeks from conception there was no week where the serum E2 was significantly lower in aborters than non-aborters.

Conclusions

Since these data failed to demonstrate any association of SAB with low sera E2 levels from mid-luteal phase to 5 weeks from conception, the best conclusion is that the low sera E2 levels seen in aborters later than 5 weeks is related to placental deterioration rather than corpus luteum malfunction. This is an important distinction because in the former instance sup-

Table 1 - Range () and median sera E2 levels (pg/mL) in aborters (AB) vs non-ABs conceiving following IVF from mid-luteal to 5 weeks from fertilization

	Luteal Phase	Week 2	Week 3	Week 4	Week 5
AB (n=25)	(n=19) (292-2372) 1100	(n=21) (29.5-1509) 581	(n=22) (227-2866) 823	(n=20) (298.5-3840) 961.7	(n=18) (99-7384) 1071.5
Non-AB (Ctrls) (n=40)	(n=34) (256-4920) 1044	(n=36) (34-2203) 321	(n=40) (89-2357) 421	(n=36) (166-4109) 475.5	(n=29) (132-3268) 733

plementation of exogenous E2 would not seem likely to help prevent a pregnancy loss. In contrast, if waning corpus luteum function was responsible, the possibility exists that maintenance of pregnancy prior to significant placental contribution is dependent on higher P and E2 levels and therapy aimed at only maintaining adequate serum P levels may be insufficient.

There are, however, some concerns about the conclusion that the association of SAB and low E2 level is related to placental deterioration. In contrast to the previous study, no difference in E2 levels were seen with the group aborting vs not aborting at 5 weeks from conception. The first study exclusively used patients not having assisted reproductive technology whereas all patients in this study had IVF. Thus, the possibility exists that the controlled ovarian hyperstimulation, by creating multiple corpora lutea, maintain sufficient E2 levels through the first 5 weeks from conception. If subsequent evaluation of E2 levels after 5 weeks in patients conceiving with IVF fail to confirm the previous data, then the study needs to be repeated with non-IVF patients to see if a problem with corpus luteum failure to adequately secrete enough E2 might contribute to causing SABs.

Another way of interpreting the data could be that with excessive controlled ovarian hyperstimulation, as manifested by the higher serum E2 levels, some factors produced by the ovaries may cause a greater chance of SAB. Thus some patients who may have aborted because of lower sera E2 levels could have been masked by others with this hyperstimulation factor that is associated with higher sera E2 levels. There have been in fact, some studies suggesting that the hyperstimulation regimen negatively affects implantation (2-4).

The possibility exists that early corpus luteum failure is not the cause of SAB but rather delayed E2 production by the placenta in the presence

of normal waning of corpus luteum function. This is an important distinction from placental deterioration because if the mechanism is delayed rather than deteriorated placental function then possibly estrogen supplementation could be remedial.

If anything, there was a trend in this study for the higher sera E2 levels to be found in the aborter group. Thus, it seems to be a safe conclusion that supplementing hyperstimulated patients conceiving on a retrieval cycle with supplemental E2 in addition to P is not likely to help reduce subsequent SAB at least those that occur by 5 weeks. It will still be of interest to see if those aborting subsequent to 5 weeks from fertilization have lower sera E2 levels than non-aborters.

References

1. CHECK JH, LURIE D, DAVIES E, VETTER B. Comparison of first trimester serum estradiol levels in aborters versus nonaborters during maintenance of normal progesterone levels. *Gynecol Obstet Invest* 34:34:206-210, 1992.
2. PAULSON RJ, SAUER MV, LOBO RA. Embryo implantation after human in vitro fertilization: importance of endometrial receptivity. *Fertil Steril* 53:870-874, 1990.
3. CHECK JH, O'SHAUGHNESSY A, LURIE D, FISHER C, ADELSON HG. Evaluation of the mechanism for higher pregnancy rates in donor oocyte recipients by comparison of fresh with frozen embryo transfer pregnancy rates in a shared oocyte programme. *Hum Reprod* 10:3022-3027, 1995.
4. CHECK JH, CHOE JK, KATSOFF D, SUMMERS-CHASE D, WILSON C. Controlled ovarian hyperstimulation adversely affects implantation following in vitro fertilization-embryo transfer. *J Assist Reprod Genet* 16:416-420, 1999.

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