

Spontaneous Abortion Rate in Patients with Endometriosis Treated with Progesterone

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ABSTRACT: Several reports suggest that women with endometriosis have a higher risk of spontaneous abortions when left untreated; however, these studies did not control for the presence of possible luteal phase defects. This study was designed to document the frequency of spontaneous abortions in women with endometriosis and ovulation defects treated prophylactically with progesterone, compared with similar patients without endometriosis. All the women had late luteal phase endometrial biopsies dating perfectly normal. Our findings show an increase in the rate of spontaneous abortions (25.7%) in women with endometriosis as compared with the entire group (3.8%). However, when the result for the group with endometriosis is compared with the subgroup of patients at diagnostic laparoscopy not showing endometriosis, the results are similar (30%). We conclude that when properly matched groups are compared, there is no increased risk of spontaneous abortions in women with endometriosis. Since we perform laparoscopies only in women failing to conceive after a reasonable number of seemingly normal cycles, the apparently high incidence of abortions in this group may be secondary to other factors that not only may lengthen the time needed for conception but also increase the abortion risk after conception.

INTRODUCTION

THE SURGICAL OR MEDICAL TREATMENT of endometriosis has been reported to reduce considerably the risk of spontaneous abortions as compared with that in patients with endometriosis who are not treated.¹⁻³ A 52% abortion rate was reported in the untreated controls in a study by Groll³ versus 12% in the surgically treated group and 7% in the group treated with danazol. Since in these patients, with or without therapy for endometriosis, there remains a high incidence of luteal phase defects (LPD), the implication from this study was that endometriosis through some mechanism other than compromising luteal function, e.g., autoimmunity to the endometrium and ovary or

possibly through prostaglandin abnormalities, was the cause of increased risk of abortion.

If endometriosis truly causes abortions through some mechanism besides inducing LPD, then patients with endometriosis and LPD treated with progesterone (P) should abort at a higher frequency than patients with LPD treated with P but not having endometriosis.

A study was, thus, performed comparing the rate of abortions in pregnant patients with untreated endometriosis and patients without endometriosis in whom the possibility of LPD contributing to the risk of abortions was eliminated by carefully treating each patient with P and determining by late luteal phase endometrial biopsy the normal endometrial dating.

MATERIALS AND METHODS

All patients were selected from a previous study,⁴ in which prophylactic P was used in the luteal phase to see if the spontaneous abortion rate in women taking ovulation-inducing drugs could be reduced.

A total of 566 patients in this previous study were treated with P during their first trimester, beginning three days after ovulation. Laparoscopies were performed in only 110 of these patients, and this subset of pregnant patients was divided into two groups, one with endometriosis and one without. The remainder of the 456 pregnant patients were not included in this study because their conceptions occurred so quickly that a laparoscopy was not needed, and thus we could not determine which patient(s) in this group had endometriosis.

RESULTS

Eighteen patients with LPD and endometriosis aborted during the first trimester. Thus, 25.7% (18 of 70) of women with endometriosis aborted compared with 30% (12 of 40) of patients who did not have any endometriosis. The difference is not statistically significant.

The distribution of the patients with endometriosis according to stage is seen in Table I.

DISCUSSION

Normally, patients with a history of habitual abortion are not subjected to the surgical risks of a laparoscopy because tubal factors would be reasonably well excluded, and if endometriosis was present it could seem not to be inhibiting conception. How-

ever, with the data presented by Naples et al,¹ Wheeler et al,² and Groll³ indicating a high incidence of spontaneous abortions in patients with untreated endometriosis, but a markedly reduced risk when the endometriosis was treated, a physician might conclude that a laparoscopy should be included as part of the diagnostic work-up for habitual abortions. Furthermore, if endometriosis is discovered, medical or surgical therapy would then be given. Indeed, Pittaway et al⁵ also found an increased risk of spontaneous abortion in untreated endometriosis. They suggested performing a laparoscopy in women with recurrent abortions of unknown etiology and recommended that endometriosis, if found, be treated.

Our data suggest that an inherent bias in the "controlled" study of Pittaway et al is that the abortion rate in a group of previous fertile patients who now had a tubal reanastomosis was compared with that of patients with apparent infertility who needed laparoscopy and subsequently conceived. We suggest the possibility that some factor(s) that delay(s) conception also leads to a higher abortion incidence. Our data support this hypothesis, in that women who required a longer time to conceive as reflected in their need for diagnostic laparoscopy (which was performed only in those who failed to conceive within 6 months after all nontubal factors had been corrected) had a much higher incidence of abortion (30/110, or 27%) than patients conceiving quickly, i.e., within 6 months (7/456, or 1.5%). This factor would not seem to be related to endometriosis, since we found that women requiring laparoscopies, but not having evidence of endometriosis, had an incidence of spontaneous abortions (30%) similar to that of women in whom endometriosis was found (25.7%).

The surgical correction of endometriosis can result in adhesions; and therefore, if surgery is performed to prevent recurrent abortions in patients with endometriosis, it may result in secondary infertility. Danazol is expensive, has many side effects, and delays pregnancy for several months. It would be inappropriate to use it if it was not necessary. Recently, Hull et al⁶ found no significant difference in either conception or abortion rates in patients with endometriosis treated with danazol, medroxyprogesterone acetate, or placebo; and in their placebo group the abortion rate was only 14.3%.⁶ Interestingly, Kable and Yussman found that 23% of surgically treated endometriosis cases aborted,

TABLE I
Distribution, according to stage, of patients with endometriosis who aborted.

	Stage of Endometriosis				Total
	1	2	3	4	
Aborted	13	3	2	0	18
Did not abort	36	6	6	4	52
Total	49	9	8	4	70

Note: The two distributions did not differ significantly ($P = .34$).

compared with only 11% of untreated patients with endometriosis.⁷

Thus, unless proper prospective studies—yet to be performed—show a clear benefit to medical or surgical correction of endometriosis to prevent abortion, we feel that a more conservative and less risky therapeutic approach be taken, e.g., meticulous correction of LPD. This is not to negate the information provided by the data suggesting improvement in spontaneous abortions through medical or surgical treatment of endometriosis. Certain interesting questions remain, though. Why did the abortion rate drop in the same patients following treatment? Could a drug like danazol have a benefit for reducing spontaneous abortions by reducing autoimmune problems or negating an abnormal prostaglandin problem, whether endometriosis is present or not? What is the effect of placebo, i.e., the role of the psyche on subsequent abortion? Would placebo work as well?

We feel the proper study would involve proper randomization of the study group into pretreatment with danazol versus pretreatment with placebo, and would include proper matching of danazol and control groups, with consideration given to factors such as relative length of time to conception. Furthermore, to determine if danazol therapy may be effective even when endometriosis is not present, there should also be equal numbers of habitual aborters in placebo and treatment groups who do not have endometriosis, but are matched for length of time to conceive.

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