Dear Sir,

I read with interest the manuscript ‘What is the optimal medical management of infertility and minor endometriosis: Analysis and future prospects’ (Cahill, 2002). Dr Cahill concludes that the body of evidence supports the concept that some women’s fertility potential is adversely affected by this disorder. He presents data however that suggest that the association of endometriosis and infertility may be related to oocyte dysfunction possibly related to reduced LH concentrations in follicular fluid (Cahill et al., 1995; Verpoest et al., 2000) or glucocorticoid abnormalities in the follicular fluid (Smith et al., 2002). These abnormalities seem to be negated for the most part by correcting follicular maturation (Deaton et al., 1990; Mahmood et al., 1991; Fedele et al., 1992; Tummon et al., 1997).

Thus one question facing the infertility specialist is whether first to try therapy aimed at improving ovulation in patients where there is suspicion of endometriosis, or suggest concomitant laparoscopic ablation of endometriotic implants? Our normal policy, up to recently, has been to present data from a study we published in 1987 where we took patients who failed to conceive after at least eight cycles of ovulatory therapy where the patients appeared to make mature follicles, have normal post-coital tests, release the oocyte and have in-phase endometrial biopsies and patent Fallopian tubes, and subjected them to their first laparoscopy (Nowroozi et al., 1987). However, we only fulgurated the implants in women with mild endometriosis with even social security numbers and then placed them back on the same therapy that failed prior to surgery. In the next 8 months, 61% of 69 women conceived where the endometriosis was removed, but only 18% of 54 women with mild endometriosis which was untreated conceived despite repeat ovulation therapy (Nowroozi et al., 1987).

Dr Cahill in his manuscript seemed to agree that laparoscopic removal of endometriotic implants can improve fertility since he quoted a Canadian co-operative study which subsequently confirmed our conclusions (Marcoux et al., 1997). However, we would also make the women aware of a different study we performed. This study showed that women suspected of having endometriosis based on clinical symptoms and signs, and increased serum CA-125 levels (O’Shaughnessy et al., 1993) did not show any lower pregnancy rate in their first 6 months of ovulatory therapy compared with women without suspected endometriosis and normal CA-125 (Check et al., 1997). Thus we advise patients that, based on our data, we think that only a minority of women with endometriosis will actually improve their infertility by laparoscopically treating their endometriosis. We advise them of the risks of laparoscopy and surgery in general and leave the decision on proceeding or deferring laparoscopy up to the patient who must weigh the fear of surgical complications against the fear that they will delay conception by not treating the endometriosis.

Thus our patients are basically advised that laparoscopic removal of endometriosis may or may not help their infertility status but the implication is that it cannot hurt. From reading Dr Cahill’s article I think the same conclusions could be made. However some recent observations have made me consider that possibly the thought that laparoscopic ablation of endometriotic implants cannot adversely affect infertility, may not be true.

Dr Cahill referred to the study using donor oocytes by Sung et al. (1997) that endometriosis does not have an adverse effect on the endometrial environment based on finding no reduction in pregnancy rates in recipients with endometriosis. Sung et al. (1997) concluded therefore that since it is known that endometriosis is associated with some reduction in fertility potential, that its main adverse effect is on the oocyte (which is also consistent with Dr Cahill’s paper). However, we have recently evaluated in a shared donor oocyte system whether the recipient of oocytes from donors with endometriosis have lower pregnancy and implantation rates than those women receiving oocytes from women without endometriosis. The study, which was recently presented at the 2002 American Society for Reproductive Medicine meeting, showed that oocytes taken from donors with endometriosis (and thus possibly exposed to follicular fluid with an abnormal hormonal content) provided pregnancy rates at least as good, or better than, oocytes from donors without endometriosis. The respective clinical and viable pregnancy rates and implantation rates were 73.1, 61.5, and 37.8% for the endometriosis group versus 54.9, 47.2, and 29.5% for recipients receiving oocytes from donors without endometriosis. These data plus other observations have made us reconsider whether to suggest as the next step laparoscopy in women who have failed to conceive despite normal sperm–mucus interactions and bilateral tubal patency by hysterosalpingography and ovulatory defects seemingly corrected.

Our infertility clinic sees a lot of women with incipient ovarian failure. Anecdotally we rarely see patients with family histories of early menopause, but a history of endometriosis in the patient is the most common association. This led to the question as to whether the auto-immune nature of endometriosis may be associated with a greater likelihood of auto-immune damage to the ovary or could prior treatment of even mild disease by fulguration or laser ablation lead to damage to oocytes? Since infertile donors willing to share their oocytes with or without endometriosis have to demonstrate normal day 3 serum FSH levels and have a normal clomiphene challenge test, possibly we would have not found the oocytes with such good fertility potential had we retrieved them from donors with...
endometriosis with decreased oocyte reserve. We question whether there would be a difference in follicular fluid hormonal content in women with decreased ovarian reserve but with or without endometriosis? We have found that younger women with elevated day 3 serum FSH levels do have respectable pregnancy rates compared with older patients (Check et al., 1998) but still the outcome is lower than expected for a population with normal serum FSH.

Though we were probably the first group to demonstrate that the laparoscopic treatment of mild endometriosis can improve pregnancy rates in a select group of women (Nowroozi et al., 1987), nevertheless these new considerations have modified my recommendations to infertile couples. I now advise them that laparoscopic therapy not only poses a rare but possible risk of surgical complications, but it might possibly make the infertility problem more resistant to therapy by further decreasing oocyte reserve. We ask the patient to give these thoughts some consideration as to whether they want to include laparoscopy with intent to treat endometriosis if present as part of their initial infertility management.

On the other hand, if they fail to conceive after 6–8 months of ovulatory therapy, should they proceed to laparoscopy or go straight to IVF? Dr Cahill’s brilliant paper points out that success rates in IVF for women with minor endometriosis are generally comparable with other female diagnostic factors (Mills et al., 1992; Hull et al., 1998). Thus, more and more, I am leaning in the direction of steering women who fail after reasonable ovulatory therapy to trying IVF–embryo transfer and foregoing laparoscopy. However, for those with limited economic resources, we still recommend laparoscopy (which is covered by insurance) with hope of improved fertility by resuming ovulatory therapy once endometriotic implants are removed.

I would greatly appreciate Dr Cahill’s opinion as to what role decreased ovarian reserve plays in the etiology of infertility related to endometriosis and is he aware of any data supporting or refuting this hypothesis? Could a lower number of oocytes and somewhat higher serum FSH level explain differences in hormonal content of follicular fluid? Where in the diagnostic/therapeutic spectrum does Dr Cahill recommend laparoscopy and possible surgical removal of endometriotic implants?

References


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