

CITATION: “Laparoscopic evaluation following failure to achieve pregnancy after ovulation induction with clomiphene citrate,” *Fertility and Sterility*, December 2003.

HIGHLIGHTS: Some physicians have suggested that an X-ray image of the fallopian tubes is a sufficient diagnostic tool when a woman with irregular or absent ovulation fails to become pregnant after a trial of fertility pills (clomiphene citrate). If the tubes appear to be open, patients may then undergo more months of hormonal therapy, followed by *in vitro* fertilization if pregnancy still is not achieved. But new research indicates that many women with infertility due to ovulation problems who do not become pregnant after using the fertility pill clomiphene citrate should undergo a laparoscopy prior to further treatment. Laparoscopic evaluation provides much better images, is far more useful in identifying anatomical abnormalities, and can enable many patients to avoid the cost and frustration of months of unneeded treatment.

SPECIALISTS: LAPAROSCOPY CAN HELP INFERTILE WOMEN AVOID MONTHS OF UNNECESSARY TREATMENTS

LOS ANGELES (Feb. 23, 2004) – Researchers in obstetrics and gynecology and reproductive endocrinology at Cedars-Sinai Medical Center and the University of Alabama at Birmingham suggest that specialists should consider the routine use of laparoscopic evaluation when women are unable to become pregnant after four cycles of the “fertility pill” clomiphene citrate.

They made their recommendation after reviewing 92 patient cases over an eight-year period.

Some physicians have in the past few years forgone laparoscopy, relying only on a special X-ray image of the fallopian tubes. If the tubes appear to be open, patients then may undergo up to six cycles of additional hormone therapy (gonadotropin injections), followed by *in vitro* fertilization if pregnancy still has not been achieved.

The X-ray procedure, called a hysterosalpingogram, fills the uterine cavity with a dye that flows into the fallopian tubes unless a blockage is present. The resulting X-rays enable physicians to see abnormalities in the tubes, or areas of polyps, scar tissue or fibroid tumors in the uterine cavity – some of the conditions that can cause infertility or reduced fertility. These images, however, lack the accuracy and diagnostic specificity available with chromotubation – the injection of a colored fluid – used during a laparoscopic evaluation.

“Laparoscopy is the gold standard for diagnosing intrapelvic adhesions or tubal disease. By taking advantage

of this procedure after a four-cycle trial of clomiphene citrate we may diagnose abnormalities earlier rather than later,” said Ricardo Azziz, MD, MPH, MBA, Chair of Cedars-Sinai’s Department of Obstetrics and Gynecology and Executive Director of the Androgen Excess Society, an international research organization.

“Using the laparoscope, we also often can treat fertility-inhibiting conditions immediately with minimally invasive surgical procedures. In cases when surgical correction is not possible, the laparoscopic findings will guide us to perform *in vitro* fertilization earlier than later. In either case, the use of laparoscopic techniques can allow many patients to avoid needless cycles of treatments and the related emotional stress and financial burden,” said Dr. Azziz, who holds The Helping Hand of Los Angeles Chair in Obstetrics and Gynecology at Cedars-Sinai.

Prior to joining Cedars-Sinai, Dr. Azziz served as Professor in the Department of Obstetrics and Gynecology and in the Department of Medicine at the University of Alabama at Birmingham. Currently he is also Professor and Vice-Chair of the Department of Obstetrics and Gynecology, and Professor in the Department of Medicine at The David Geffen School of Medicine at the University of California, Los Angeles. He and his colleagues published the results of their review in the December 2003 issue of the journal *Fertility and Sterility*.

Before any treatment is started, women who seek help because they have been unable to become pregnant due to irregular or absent ovulation typically undergo a pelvic examination and hysterosalpingogram, and the partner’s sperm count is analyzed. If there is no obvious abnormality, ovulation induction with clomiphene citrate is often one of the first treatment options used. If pregnancy has not been achieved after four ovulatory cycles, most specialists in reproductive endocrinology have routinely used laparoscopy to search for anatomical abnormalities. Only in recent years have some specialists suggested forgoing this examination.

Of the 92 cases reviewed in this study, 32 patients (34.8 percent) had a “positive” laparoscopy, defined as findings of advanced stages of endometriosis, a tumor, pelvic adhesions, and/or disorders of the fallopian tubes. Besides these significant abnormalities, more than 29 percent had stage I or stage II endometriosis, which, according to some studies, also may be associated with reduced fertility and may respond to laparoscopic surgery. Only 35.9 percent of patients had a completely normal pelvis.

Analyzing patient demographic data, medical histories, and laparoscopic results, the study’s authors attempted to determine if certain factors could help predict which patients would be at high risk for pelvic disorders. They found a higher frequency of endometriosis among women who had painful menstrual periods and those who had previously used natural contraception. Pain during intercourse and the previous use of natural contraception were associated with the presence of tumors (endometriomas). Women who had previously been pregnant and those who had used oral contraceptive pills had a reduced number of pelvic adhesions, while those who had never been pregnant and those who had never used oral contraceptives had a higher incidence of pelvic adhesions.

About 91 percent of the patients in the study had at least one predictor for intrapelvic disease, and almost 40 percent of those with predictors had a positive laparoscopy, compared with only 12.5 percent of those without predictors.

Of those experiencing pain during intercourse, nearly 52 percent had a positive laparoscopy, compared to only 27 percent of women without pain. Patients with no prior history of using oral contraceptives had a 64.3 percent likelihood of a positive laparoscopy, compared with 29.5 percent of women who had used birth control pills. Sixty-four percent of women who had never used contraceptives had positive findings, compared with

only 30 percent of those who had used birth control measures.

While these correlations between clinical features and surgical findings were noted, there were no features that could be used to absolutely predict the presence of significant surgical findings. The investigators concluded that laparoscopy should be used routinely after treatment with four cycles of clomiphene citrate, although the technique may be delayed if there are no identifiable predictors for intrapelvic disease.

“Laparoscopy continues to be a useful tool in the workup of an infertile couple,” Dr. Azziz said. “Using a set of predictors for intrapelvic disease appears to be a valid approach in developing diagnostic and treatment options, although many women with intrapelvic abnormalities may have no identifiable predictors. Together, these techniques may help many couples avoid months of needless therapies.”

Cedars-Sinai is one of the largest nonprofit academic medical centers in the Western United States. For the fifth straight two-year period, it has been named Southern California's gold standard in health care in an independent survey. Cedars-Sinai is internationally renowned for its diagnostic and treatment capabilities and its broad spectrum of programs and services, as well as breakthroughs in biomedical research and superlative medical education. It ranks among the top 10 non-university hospitals in the nation for its research activities.

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