Original article

Effect of interval after surgery on *in vitro* fertilization/ intracytoplasmic sperm injection outcomes in patients with stage III/IV endometriosis

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Keywords: endometriosis; infertility; fertilization in vitro; surgery

Background For patients with severe endometriosis, the spontaneous pregnancy rates have been reported to be near 0 due to extreme distortion of normal pelvic anatomy. Surgery is one of the treatment options; however, if patients failed to conceive after surgery, *in vitro* fertilization (IVF) is effective. The objective of this retrospective study was to determine the clinical characteristics of IVF/ intracytoplasmic sperm injection (ICSI) in patients with stage III/IV endometriosis, and to determine the impact of the interval from surgery to IVF/ICSI on outcome.

Methods One hundred and sixty patients who were diagnosed with stage III/IV endometriosis underwent IVF /ICSI cycles between February 2004 and June 2009 were enrolled. The mean interval from surgery to IVF, number of oocytes retrieved, fertilization rate, implantation rate, embryos transferred, and good embryos transferred were compared between two age groups (≤35 years and > 35 years).

Results The mean interval from surgery to IVF was (37.9±28.9) months for the group ≤ 35 years of age and (57.6±39.7) months for the group >35 years of age. Twenty-five IVF/ICSI cycles (12.8%) were performed during the first year after surgery, and 34.9% IVF/ICSI cycles were performed 2 years after surgery. No significant differences existed between the two groups with respect to the fertilization rate, implantation rate, number of embryos transferred, number of good embryos, clinical pregnancy rates, live birth rates, and cumulative clinical pregnancy rates (P >0.05). The probability of cumulative clinical pregnancies was 75%, 50%, and 25% ((29.0±4.8), (61.0±7.6), and (120.0±16.9) months after surgery, respectively).

Conclusions For infertile patients with stage III/IV endometriosis, the optimal time to conceive by IVF/ICSI is <2 years after surgery; nevertheless, most of the patients took a longer time to conceive.

Chin Med J 2010;123(16):2176-2180

Endometriosis is one of the most challenging diseases for gynecologists who treat infertile women. The incidence of endometriosis in women with subfertility ranges from 20%–30%. For patients with severe endometriosis, the spontaneous pregnancy rates have been reported to be near 0% due to distortion of normal pelvic anatomy.[1] Thus, surgery is one of the options to improve fecundity.[2] If patients fail to conceive after surgery, *in vitro* fertilization (IVF) is an effective treatment option.[1] In patients with endometriosis-associated infertility, surgery followed by IVF–ET is more effective than surgery alone.[3]

In practice, the interval from surgery to IVF varies greatly, and is determined by various factors, such as the expectation for children, the economic burden and tubal patent condition. Whether or not the interval of time after surgery will influence the success rate of IVF is of clinical importance. In this retrospective study, we determined whether or not the interval from surgery to IVF had an influence on IVF outcome of infertile patients with stage III/IV endometriosis, and discuss the role of the physician in counseling patients after surgery.

METHODS

Patients and grouping

One hundred sixty infertility patients with stage III/IV endometriosis who had undergone laparoscopic or transabdominal cystectomy between February 2004 and June 2009 at the Reproductive Medical Center of Peking University Third Hospital prior to IVF/ intracytoplasmic sperm injection (ICSI) were retrospectively identified. The severity of endometriosis was determined based on the American Fertility Society Classification (1985).[4] Exclusion criteria included significant male factors, or women with polycystic ovarian syndrome (PCOS), hydrosalpinges, and uterine fibroids. Among the 160 patients, 68 underwent frozen embryo transfer (FET) treatment cycles. All subjects were divided into two age groups (≤ 35 years and >35 years). There were 114 women in the younger age group and 46 women in the older age group. This study was approved by the Ethics

DOI: 10.3760/cma.j.issn.0366-6999.2010.16.003

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Table 1. Characteristics of patients and parameters of controlled ovarian hyperstimulation in two different age groups (mean ± SD)

Items	Total (n=160)	≤35 years (n=114)	>35 years (n=46)	P values
Age (years)	33.4±3.9	31.4±2.8	37.9±1.7	0.000*
Duration of infertility (years)	4.4±2.9	5.2±3.7	7.1±4.7	0.000*
Interval from surgery to IVF/ICSI (months)	43.9±33.7	37.9±28.9	57.6±39.7	0.000*
Basal FSH (IU)	9.6±4.4	9.4±3.9	10.0±5.3	0.317
Primary infertility (n (%))	106 (66.3%)	76 (66.7%)	38 (65.2%)	0.861
Bilateral tubal patency (n (%))	90 (56.3%)	63 (55.3%)	27 (58.7%)	0.692
Unilateral tubal patency (n (%))	29 (18.1%)	24 (21.1%)	5 (10.9%)	0.130
Endometrioma recurrence rate (n (%))	88 (40.4%)	64 (42.1%)	24 (36.4%)	0.427
Basal E_2 (pmol/ml)	126.5±59.9	129.7±64.9	119.2±46.4	0.237
IUI prior to IVF/ICSI (n (%))	17 (14.3%)	12 (15.6%)	5 (13.8%)	0.800
Total FSH/HMG (IU)	3758±1413.4	3615.5±1436.2	4086.4±1311.8	0.023*
Days of stimulation (days)	10.4±2.0	10.3±1.8	10.4±2.4	0.787
E_2 levels on hCG day (pmol/ml)	10.4±2.0	10.3±1.8	10.4±2.4	0.336

*P <0.05.

Committee of Peking University Third Hospital.

Ovarian stimulation protocol

All women received a short down-regulation ovarian stimulation protocol. In brief, GnRH-α was administered from day 2 of menstruation (diphereline 0.1 mg; Beaufour, Ipsen, France). Ovarian stimulation started on day 3 with 225 IU daily of rFSH (Gonal-F, 75IU; Serono, Italy). Serial ultrasound scans were performed during ovarian stimulation. When at least 2 follicles reached a maximum diameter of 17–18 mm, 10 000 IU of human chorionic gonadotropin (hCG) (Profasi, 5000 IU per ampoule; Serono) was administered subcutaneously. Ultrasound-guided transvaginal oocyte retrieval was performed 35–36 hours later.

A normal fertilization rate was defined as the number of embryos with two pronuclei 24 hours after fertilization divided by the total number of all oocytes (IVF cycles) or MII oocytes (ICSI cycles). Embryos were classified according to the proposed criteria;[5] specifically, embryos with < 20% overall fragmentation (grade 1 or 2), together with > 6 blastomeres on day 3 were considered as good embryos. Embryo transfer was performed on day 3. Chemical pregnancies were indicated by an increased serum β-hCG concentration 14 days after embryo transfer, and clinical pregnancies were confirmed by sonographic demonstration of a gestational sac 30 days after embryo transfer. The implantation rate was defined as the number of gestational sacs divided by the total number of transferred embryos.

The luteal phase was supported with the daily intramuscular administration of 60 mg of progesterone (Shanghai General Pharmaceutical Company Ltd., China), beginning on the day after oocyte retrieval. Patient follow-up was carried out either by clinical appointments or by telephone interview.

Statistical analysis

Data are expressed as the mean± standard deviation (SD) or percentage. Statistical analysis was performed with a t-test for parametric data or a χ^2-test for categorical data. The crude probabilities of clinical pregnancies were calculated using Kaplan-Meier survival analysis (KMSA) which is a method of generating tables and plots of survival or hazard functions for event history data (time to event data). All statistical calculations were performed with SPSS 13.0. A P <0.05 was considered statistically significant.

RESULTS

Characteristics of patients in different groups

The clinical characteristics of patients in the two age groups at the time of IVF/ICSI are presented in Table 1. There were no significant differences between the two age groups with respect to basal FSH (day 2), basal E_2, the length of the stimulation phase, and E_2 levels of hCG day. The infertility period and interval from surgery to IVF/ICSI were longer in the older group (>35 years of age) than the younger group (≤35 years of age). The total gonadotropin requirement was higher in the older age group (Table 1).

Among the 160 patients, bilateral tubal occlusion was demonstrated in 41 patients (25.6%); bilateral or unilateral tubal patency existed in 90 (56.3%) and 29 patients (18.1%), respectively. Intrauterine insemination was attempted in 17 patients (14.3%) with at least 1 patent tube after surgery. Endometriomas recurred in 88 patients (40.4%) prior to IVF/ICSI. A second laparoscopic or transabdominal cystectomy was performed in 19 patients, and transvaginal ultrasound-guided aspiration of ovarian endometriomas was performed in 10 patients prior to IVF/ICSI; another 10 patients underwent aspiration of ovarian endometriomas during oocyte retrieval (Table 1).

Laboratory and clinical outcomes

Among the 160 patients, 218 stimulation cycles resulted in 196 fresh embryo transfer cycles and 22 cancelled cycles (6 cycles with no oocytes retrieved, 10 cycles with no embryos transferred, and 6 cycles were cancelled to prevent the ovarian hyper-stimulation syndrome). Only 28 cycles (12.8%) were performed in the first year after surgery; 76 cycles (34.9%) were performed 2 years after surgery.

Table 2. IVF laboratory parameters and outcome of IVF/ICSI

Items	Total stimulation cycles	≤35 years	>35 years	*P* values
No. of stimulation cycles	218	152	66	-
No. of cancellation cycles	22	15	7	-
No. of embryo transferred cycles	196	137	59	-
Hypo-response rate (%)	9.1	5.2	18.2	0.002*
Cancellation rate (%)	10.0	9.8	10.6	0.856
No. of retrieved oocytes per cycle	8.3±5.5	8.9±5.8	6.9±4.4	0.022*
Fertilization rate (%)	73.3	72.3	75.7	0.423
No. of good embryos per cycle	2.8±3.0	2.8±2.7	2.8±3.6	0.922
Mean No. of transferred embryos	2.1±0.7	2.1±0.6	2.3±0.8	0.058
Implantation rate (%)	18.6	18.4	19.3	0.855
Clinical pregnancy rate per transfer (%)	32.7 (64/196)	29.9 (41/137)	39.0 (23/59)	0.215
Live birth rate per transfer (%)	23.5 (46/196)	23.4 (32/137)	23.7 (14/59)	0.955
Miscarriage rate (%)	18.8 (12/64)	12.2 (5/41)	30.4 (7/23)	0.099
Ectopic pregnancy rate (%)	9.4% (6/64)	9.8 (4/41)	8.7 (4/23)	0.443
No. of FET patients/cycles	68	55	13	-
FET clinical pregnancy rate (%)	38.2 (26/42)	41.8 (23/55)	23.1 (3/13)	0.342
Cumulative clinical pregnancy rate (%)	44.1 (89/202)	44.1 (63/143)	44.1 (26/59)	0.999

*P <0.05.

Women in the older group (>35 years) had a higher hypo-response rate than the younger group (≤35 years). The number of oocytes retrieved was significantly higher in the younger group (8.9±5.8) than the older group (6.9±4.4). No significant differences were found between the two groups with respect to the fertilization rate, implantation rate, number of embryos transferred, or the number of good embryos. The clinical pregnancy and live birth rates were not statistically different between the two groups. The cumulative clinical pregnancy rate was 44.1% in both groups (Table 2).

Relationship between IVF/ICSI outcomes and the interval from surgery to IVF/ICSI

The overall probability of cumulative clinical pregnancies after surgery was calculated by Kaplan–Meier survival analysis (Figure). A longer interval between surgery and IVF/ICSI was correlated with a lower probability of cumulative clinical pregnancy after surgery. The probability of cumulative clinical pregnancies was 75%, 50%, and 25% ((29.0±4.8), (61.0±7.6), and (120.0±16.9) months after surgery, respectively).

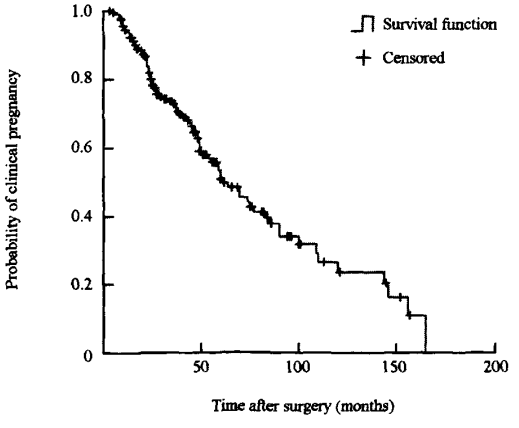

Figure. The overall probability of cumulative clinical pregnancy after surgery. Vertical tick marks represent censored observations.

DISCUSSION

Fecundity of patients with stage III/IV endometriosis after surgery

Stage III/IV endometriosis has significant effects on fertility because of marked anatomic distortion and adhesions. It has been reported that the spontaneous pregnancy rate is as low as near 0% with severe distortion of pelvic anatomy.[6-10] Surgery is generally the treatment of choice to correct distorted pelvic anatomy and excise endometriomas, and can improve pregnancy rates in comparison to no treatment or medical therapy.[9]

In women with advanced stages of endometriosis, the spontaneous pregnancy rate after laparoscopic surgery in the first 6 months (23%) has been reported to be significantly greater than in the following 6 months. This finding suggests that IVF should be proposed as soon as patients fail to conceive spontaneously and within a maximum of 1 year from the time of laparoscopic surgery.[10]

In the current study, the probability of cumulative clinical pregnancies after surgery was calculated with the Kaplan–Meier survival analysis based on the interval of time between surgery and attempted IVF cycles. The probability of cumulative clinical pregnancies was 75%, 50%, and 25% from surgery, respectively. Thus, the ideal interval in which to conceive by IVF/ICSI is <2 years after surgery. Considering the low response rate to controlled ovarian hyperstimulation was significantly higher in patients >35 years of age, patients should attempt IVF/ICSI as early as possible. Given the fact that the current study was retrospective, it will be interesting to compare the results of a prospective, randomized, control study to follow the fecundity of patients after surgery to better understand the exact effects of the interval of time after surgery and patient age with IVF outcome.

Present status of IVF/ICSI for infertile patients with stage III/IV endometriosis

Even though IVF is currently considered an effective

treatment in women with endometriosis, the percentage of women who undergo IVF after surgery is not high. A recent study from Italy reported that only 33% patients attempted IVF 3 years after surgery for endometriosis, and as high as 51% of patients never attempted IVF, even where the IVF treatment cycles were entirely supported by the public health system. One of the reasons proposed for this low rate is that gynecologists are usually not engaged in assisted reproductive technology. Therefore, patients may fail to receive the detailed counseling and adequate information regarding IVF, which prevents them from making an informed and shared decision on treatment alternatives with clinicians.[11]

In this study, only 12.8% of IVF/ICSI cycles were performed in the first year following surgery and 34.9% of IVF/ICSI cycles were performed 2 years after surgery for infertile women with stage III/IV endometriosis. The mean interval from surgery to IVF was (37.9±28.9) months for patients < 35 years of age, and (57.6±39.7) months for patients > 35 years of age. Most of the stage III/IV endometriosis patients' attempted expectant management longer than they had been advised. For those patients with at least 1 patent tube, only 17 patients (14.3%) attempted intrauterine insemination prior to IVF/ICSI. These results may indicate that surgeons fail to recognize the importance of patient follow-up and fertility guidance for infertile patients with stage III/IV endometriosis.

Understanding endometriosis associated with infertility after surgery and providing fertility guidance

For patients with stage III/IV endometriosis, the risk of ovarian deficiency after a cystectomy for an endometrioma needs to be considered.[12] Both endometrioma-related injuries and surgery-mediated damage may be involved in ovarian deficiency. In fact, bilateral disease with laparoscopic removal of endometriomas from both ovaries has a 2.4% risk of premature ovarian failure.[13-15] Thus, these patients should be cognizant of the optimal time of fertility.[16] In this study, despite the common concept that the fecundity of the younger group (≤35 years) should be better than that of the older group (>35 years),[17] the clinical pregnancy and live birth rates showed no significant differences between the two age groups, so the diminished fecundity of younger women after surgery should not be ignored.

At the same time, endometriosis is a recurrent and progressive disease. The recurrence rate of endometriosis has been estimated to be 21.5% at 2 years and 40~50% at 5 years.[18] Young age and stage III/IV endometriosis appear to be the factors associated with the high recurrence risk for endometriosis.[19] The present study showed that 40.4% of endometriomas recurred prior to IVF/ICSI in these stage III/IV patients. Thus, the time-dependent diminution of fecundity may be related to a detrimental effect of the disease on fertility. It was also reported that stage III/IV endometriosis worsens the cumulative pregnancy and live-born rates.[9,20] Therefore, patients should be advised to start trying to conceive immediately after surgery.

Although the decision to undergo ART is determined by personal preference and ethical consideration or economic situations of the patients, physician guidance is still very important. For patients with stage III/IV endometriosis associated with infertility, a comprehensive evaluation of fecundity should be made according to age, the basal hormonal levels of the patients, and the expectation for a baby. The advantages and disadvantages should also be fully discussed with the patient. Any decision for expectant guidance or an expedient attempt IVF should be carefully considered.

In conclusion, for infertile patients with stage III/IV endometriosis, the optimal time for IVF/ICSI should be <2 years after surgery. In order to achieve a better clinical outcome, a following-up system should be established to give the patients timely guidance. Surgeons should keep in mind that the objectives of surgery are not only to remove endometriomas or alleviate symptoms, but also to shorten the time interval to conception.

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(Received April 30, 2010)
Edited by CHEN Li-min

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刊名： 中华医学杂志（英文版） ISTIC SCI

英文刊名： CHINESE MEDICAL JOURNAL

年，卷(期)： 2010，123(16)

被引用次数： 0次

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相似文献(10条)

1. 外文期刊 Hull. MG. Williams. JA. Ray. B. McLaughlin. EA. Akande. VA. Ford. WC The contribution of subtle oocyte or sperm dysfunction affecting fertilization in endometriosis-associated or unexplained infertility: a controlled comparison with tubal infertility and use of donor spermatozoa.

This study aims to determine the relative contribution of oocyte and/or sperm dysfunction to the reduction of fertilization rates in vitro in cases of minor endometriosis and prolonged unexplained infertility. The results of in-vitro fertilization (IVF) treatment with ovarian stimulation have been compared between couples with the above conditions and women with tubal infertility (as control for oocyte function) and the use of donor spermatozoa (as control for sperm function). Fertilization and cleavage rates using husband's spermatozoa were significantly reduced in endometriosis couples (56%, n = 194, P < 0.001) and further significantly reduced in couples with unexplained infertility (52%, n = 327, P < 0.001) compared with tubal infertility (60%, n = 509). Using donor spermatozoa the rates were the same as using husband's spermatozoa in tubal infertility (61%, n = 27) or endometriosis (55%, n = 21) but significantly though only partly improved with unexplained infertility (57%, n = 60, P < 0.02). In unexplained infertility, a significantly increased proportion of couples experienced complete failure of fertilization and cleavage in a cycle (5-6% versus 2-3%). However, complete failure was not usually repetitive, and the affected couples did not account for the overall reduction in fertilization and cleavage rates, which remained significantly lower in the rest of the unexplained and endometriosis groups. Implantation and pregnancy rates appeared similar in all groups. The benefit of IVF treatment in cases of minor endometriosis and prolonged unexplained infertility is due to superabundance of oocytes obtained by stimulation. The reduction in natural fertility associated with endometriosis appears to be at least partly due to a reduced fertilizing ability of the oocyte. In unexplained infertility, there is distinct impairment due to otherwise unsuspected sperm dysfunction but probably also oocyte dysfunction.

2. 外文期刊 Berube. S. Marcoux. S. Langevin. M. Maheux. R Fecundity of infertile women with minimal or mild endometriosis and women with unexplained infertility. The Canadian Collaborative Group on Endometriosis.

OBJECTIVE: To assess whether infertile women with minimal or mild endometriosis have lower fecundity than women with unexplained infertility. DESIGN: Prospective cohort study. SETTING: Twenty-three infertility clinics across Canada. PATIENT(S): Three hundred thirty-one infertile women aged 20-39 years. INTERVENTION(S): Diagnostic laparoscopy for infertility. Infertile women with minimal or mild endometriosis (n = 168) were compared with women with unexplained infertility (n = 263). Both groups were managed expectantly. The women were followed up for 36 weeks after the laparoscopy or, for those who became pregnant, for up to 20 weeks of the pregnancy. MAIN OUTCOME MEASURE(S): Fecundity refers to the probability of becoming pregnant in the first 36 weeks after laparoscopy and carrying the pregnancy for > or = 20 weeks. The fecundity rate is the number of pregnancies per 100 person-months. RESULT(S): Fecundity was 18.2% in infertile women with minimal or mild endometriosis and 23.7% in women without endometriosis (log-rank test). The fecundity rate was 2.52 per 100 person-months in women with endometriosis and 3.48 per 100 person-months in women with unexplained infertility. The crude and adjusted fecundity rate ratios were 0.72 and 0.83 (95% confidence interval = 0.53-1.32), respectively. CONCLUSION(S): The fecundity of infertile women with minimal or mild endometriosis is not significantly lower than that of women with unexplained infertility.

3. 外文期刊 Omland. AK. Tanbo. T. Dale. PO. Abyholm. T Artificial insemination by husband in unexplained infertility compared with infertility associated with peritoneal endometriosis.

There have been numerous inconclusive studies examining the differences between unexplained and peritoneal endometriosis-associated infertility. Hence, the choice of artificial reproductive technique may be difficult. This prospective study compares outcome in couples with unexplained infertility and with minimal or mild endometriosis-associated infertility, undergoing treatment

with ovarian stimulation combined with artificial insemination by husband. No differences were found between the unexplained infertile and the endometriosis group as to patient characteristics, response to ovarian stimulation and semen qualities. There was a significantly higher total pregnancy rate, with more multiple gestations, in the unexplained infertile compared with the endometriosis group. The difference in outcome could reflect differences in pathogenesis and aetiology for the two groups.

4.外文期刊 Skrzypczak J.Szczepanska M.Puk E.Kamieniczna M.Kurpisz M Peritoneal fluid cytokines and sICAM-1 in minimal endometriosis: search for discriminating factors between infertility and/or endometriosis.

OBJECTIVE:: To evaluate cytokine levels (IL-1beta, TNF-alpha, IL-6, IL-8), soluble intercellular adhesion molecule-1 (sICAM-1) and number of macrophages in peritoneal fluid (PF) of women with no minimal endometriosis and associated (or not) infertility in order to discriminate between infertility and/or endometriosis. STUDY DESIGN:: Cytokines and sICAM-1 were measured by using quantitative enzyme-linked immunosorbent assay (ELISA) while the macrophages were identified by May-Grunwald-Giemsa and non-specific esterase staining and presented as medians. The measurements were performed in 78 women belonging to four selected subgroups according to their endometriosis and/or infertility status. Statistical analysis was performed using Kruskal-Wallis non-parametric ANOVA test. Additionally, discriminant function analyses were performed. RESULTS:: We have found the most elevated macrophage numbers in the groups of women with endometriosis. IL-1beta did not present any statistically significant values differentiating the analysed subgroups. IL-6 (110.0pg/ml) and TNF-alpha exhibited the highest concentrations (statistically significant) in a group of fertile women with endometriosis. IL-8 clearly differentiated between the subgroups with infertility and sICAM-1 was statistically significantly elevated in the subgroups of infertile women. In the forward discriminant analysis, when subdividing the studied population according to its infertility status (we considered macrophages, IL-8 and IL-6 in order of probability values), we have found striking probability value of 92% for the correct classification into an infertile population. CONCLUSION:: Out of the range of the analysed factors we have found only the sICAM-1 to be singled out between the standard discriminant analysis and the forward one. However, this important flagging molecule might be of considerable value for discrimination between different types of pathology at the level of immune effector function. The increased

5.外文会议 J. Donnez.J. Squifflet.C. Pirard.P. Jadou Surgical Options for Endometriosis Associated Infertility

This manuscript is a review of the efficacy of medical and surgical treatment of endometriosis-associated infertility and pelvic pain.Endometriosis is the cause of pelvic pain (dysmenorrhea, dyspareu-nia) and infertility in more than 35% of women of reproductive age. Complete resolution of endometriosis is not yet possible but therapy has essentially three main objectives: 1) to reduce pain; 2) to increase the possibility of pregnancy; 3) to delay recurrence for as long as possible.It could be concluded that a consensus will probably never be reached on minimal and mild endometriosis. Nevertheless, because the Canadian study reported a large number of cases, we strongly support the view that visible endometriosis must be removed at the time of surgery.In cases of moderate and severe endometriosis-associated infertility, the combined approach (operative laparoscopy with GnRH-a) must be considered as "first-line" treatment. The mean pregnancy rate of 50% reported in the literature following surgery provides scientific proof that operative treatment should first be undertaken to give our patients the best chance of conceiving naturally.

6.外文期刊 Meden-Vrtovec.H.Tomazevic.T.Verdenik.I Infertility treatment by in vitro fertilization in patients with minimal or mild endometriosis.

PURPOSE: To estimate the clinical effectiveness of in vitro fertilization treatment in patients with minimal or mild endometriosis (stages I and II) in comparison to the patients with tubal infertility in terms of fertilization, pregnancy and livebirth rates. METHODS: Retrospective analysis of the outcome of IVF-ET in 612 cycles of the patients with endometriosis (389 stimulated with HMG/HCG and 223 co-treated with GnRH-a) and in 7,339 cycles of the patients with tubal infertility (5,520 stimulated with HMG/HCG and 1,819 co-treated with GnRH-a). RESULLTS: Regardless of the type of ovarian stimulation, the fertilization rate per treated cycle was practically the same in both groups (endometriosis 81.4% vs tubal infertility 84.2%; p = 0.07). However, in the endometriosis group the pregnancy rate was higher (25.3% vs 18.9%; p = 0.000), and so was the livebirth rate (19.0% vs 14.2%; p = 0.003). Considering the type of ovarian stimulation, the fertilization rate in the endometriosis group was almost the same in the HMG/HCG (81.2%) and in the GnRH-a co-treated cycles (81.6%), and did not differ from that in the tubal infertility group (83.6% in the HMG/HCG vs 85.9% in the GnRH-a cycles). In the GnRH-a co-treated cycles the pregnancy rate and the livebirth rate were not significantly higher in the endometriosis group than in the tubal infertility group (27% and 20.2% vs 22.2% and 17.5%). In the HMG/HCG stimulated cycles the pregnancy rate was significantly higher in the endometriosis than in the tubal infertility group (24.3% vs 17.7%; p = 0.004), and so was the livebirth rate (18.4% vs 13.0%; p = 0.008). CONCLUSION: In patients with minimal or mild endometriosis the IVF-ET procedure is at least as effective as in patients with tubal infertility.

7.外文期刊 Wang H.Gorpudolo N.Behr B The role of prolactin- and endometriosis-associated infertility.

This review will address the current understanding of the relationship between prolactin (PRL) and endometriosis-associated infertility. Although the exact mechanisms of action of hyperprolactinemia in patients with endometriosis-associated infertility have not been clearly established, this report reviews results from relevant studies in the literature. These include serum PRL levels in endometriosis-associated infertility, PRL receptors in ectopic endometriotic tissues, basal PRL levels after TSH and Danazol (isoxazolic derivative of the synthetic steroid 5alpha-ethinyl-testosterone) therapy, peritoneal fluid and nocturnal serum PRL levels in endometriosis, infertility, and luteal phase PRL concentrations in patients with endometriosis. TARGET AUDIENCE: Obstetricians & Gynecologists, Family Physicians. LEARNING OBJECTIVES: After completion of this article, the reader should be able to explain the relationship between prolactin- and endometriosis-associated infertility, relate endometriosis with infertility, and summarize two ways in which prolactin and endometriosis may be linked in the pathophysiology of infertility.

8.外文期刊 Werbrouck E.Spiessens C.Meuleman C.D'Hooghe T No difference in cycle pregnancy rate and in cumulative live-birth rate between women with surgically treated minimal to mild endometriosis and women with unexplained infertility after controlled ovarian hyperstimulation and intrauterine insemination

OBJECTIVE: The association between infertility and minimal to mild endometriosis is controversial and poorly understood. The

clinical pregnancy rate (PR) per cycle after controlled ovarian hyperstimulation (COH) with or without intrauterine insemination (IUI) is reportedly lower in women with surgically untreated minimal to mild endometriosis than in women with unexplained infertility. It is possible that prior laparoscopic removal of endometriosis has a positive effect on the clinical PR after COH and IUI. Therefore, we tested the hypothesis that after COH and IUI the PR per cycle and the cumulative live-birth rate (CLBR) are equal or higher in women with recently surgically treated minimal to mild endometriosis when compared with women with unexplained infertility. DESIGN: A retrospective, controlled cohort study. SETTING: Leuven University Fertility Centre, a tertiary academic referral center. PATIENT(S): One hundred seven women treated during 259 cycles with COH and IUI including patients with endometriosis (n = 58, 137 cycles) and unexplained infertility (n = 49, 122 cycles). All patients with endometriosis had minimal (n = 41, 100 cycles) or mild (n = 17, 37 cycles) disease that had been laparoscopically removed within 7 months before the onset of treatment with COH and IUI. INTERVENTION(S): Controlled ovarian hyperstimulation using clomiphene citrate (23 cycles) or gonadotrophins (236 cycles) in combination with IUI. MAIN OUTCOME MEASURE(S): Clinical PR per cycle and CLBR within four cycles of treatment with COH and IUI. RESULT(S): The clinical PR per cycle was comparable in women with minimal or mild endometriosis (21% or 18.9%, respectively) and in women with unexplained infertility (20.5%). The CLBR within four cycles of COH and IUI was also comparable in women with minimal endometriosis, mild endometriosis, and unexplained infertility (70.2%, 68.2 %, 66.5%, respectively). CONCLUSION(S): The data from our study suggest that COH and IUI shortly after laparo

9.外文期刊 Goker EN.Ozcakir HT.Terek MC.Levi R.Adakan S.Tavmergen E Controlled ovarian hyperstimulation and intrauterine insemination for infertility associated with endometriosis: a retrospective analysis.

OBJECTIVE: To evaluate the efficacy of controlled ovarian hyperstimulation and intrauterine insemination for infertility associated with endometriosis. MATERIAL AND METHODS: A retrospective analysis of 260 patients with the only diagnosis of endometriosis, or male factor, or tubal factor, or unexplained infertility were performed: a total of 56 patients with different stages of endometriosis, a control group consisting of 38 patients with male factor infertility, a group of 26 patients with tubal factor infertility and a group of 140 patients with others (unexplained infertility, ovulation disorders, cervical factor). Pregnancy rate, hormone levels, endometrial thickness and number of follicles were analyzed. RESULTS: Clinical pregnancy rates per patient were similar between endometriosis, male factor, tubal factor, and others including unexplained infertility, ovulation disorders and cervical factor groups (10.7%, 5.4%, 11.5%, 17.9%, respectively; p>0.05). Clinical pregnancy rates per patient were not effected between the 2 subgroups of endometriosis as minimal to mild and moderate to severe [5.1% (2/39) versus 23.5% (4/17), p=0.19]. CONCLUSION: Endometriosis did not affect the clinical pregnancy rate per patient compared to the other infertility factors. Endometriosis of various stages have no effect on the success of controlled ovarian hyperstimulation combined with intrauterine insemination.

10.外文期刊 Omland.AK.Fedorcsak.P.Storeng.R.Dale.PO.Abyholm.T.Tanbo.T Natural cycle IVF in unexplained, endometriosis-associated and tubal factor infertility.

BACKGROUND: To elucidate possible differences between unexplained and minimal peritoneal endometriosis-associated infertility, we studied their outcome in natural cycle IVF (NIVF). METHODS: A prospective cohort study was carried out on unexplained (33 couples), minimal peritoneal endometriosis-associated (30 couples) and tubal factor (24 couples) infertility in 223 NIVF cycles, using human chorionic gonadotrophin (HCG) for ovulation induction. RESULTS: During the first NIVF attempt, follicular and luteal phase oestradiol, FSH, LH and progesterone concentrations, as well as endometrial thickness and follicular diameter were similar among the three groups. Periovulatory follicular growth monitored from day of HCG administration to oocyte aspiration was significantly lowered in unexplained infertility compared with minimal endometriosis-associated and tubal factor infertility. The fertilization rate, clinical pregnancy rate per initiated cycle, per successful oocyte retrieval and per embryo transfer, in minimal endometriosis (80.0, 10.4, 16.0 and 23.5% respectively) were similar to that in tubal factor infertility patients (68.6, 5.8, 11.4 and 16.0%) but significantly higher (P < 0.05) than that of the unexplained infertility group (62.2, 2.6, 5.4 and 8.7%). CONCLUSIONS: The significant reduction in follicular periovulatory growth, fertilization and pregnancy rates in unexplained infertility compared with minimal peritoneal endometriosis patients may be explained by sub-optimal follicular development with possibly reduced oocyte quality, intrinsic embryo quality factors or by impaired implantation. From a clinical point of view, NIVF is less suited to unexplained infertility treatment, but might represent an interesting treatment option for minimal peritoneal endometriosis-associated infertility.