Does Salpingectomy Achive a Favorable Outcome Than Proximal Tubal Occlusion for Bilateral Hydrosalpinx Before IVF?

IVF Öncesi Bilateral Hidrosalpinksi Olanlarda Salpinjektomi Proksimal Tubal Oklüzyona Göre Tercih Edilen Sonuçları Verebilir mi?

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ABSTRACT Objective: Patients with bilateral hydrosalpinges treated by salpingectomy or proximal tubal occlusion before undergoing in-vitro fertilization (IVF)/intracytoplasmic sperm injection (ICSI-ET) were compared. The primary outcome measures were implantation, miscarriage, clinical and ongoing pregnancy rates after the IVF treatment. **Material and Methods:** The data of 58 patients who were treated for bilateral hydrosalpinx before sheduling for IVF treatment were reviewed retrospectively. **Results:** In comparison of the groups, statistically significant differences were found in the number of gonadotrophin ampoules administered and in the days of stimulation regarding the clinical parameters after the ICSI procedure. Although the implantation, clinical and ongoing pregnancy rates in the salpingectomy group were all higher than the proximal occlusion group they were no statistically significant (30.2% vs 24.4%, p= 0.65; 63.6% vs 56%, p= 0.76; 54.5% vs 48%, p= 0.79 respectively). Miscarriage rate was decreased in those with salpingectomy than in those with proximal occlusion which was not statistically significant either (15% versus 24%, p= 0.50). **Conclusion:** Management of hydrosalpinges by laparoscopic salpingectomy or bipolar proximal tubal occlusion yielded statistically similar responses to IVF-ET cycle outcome but a trend toward a higher implantation and clinical pregnancy rate and a lower abortion rate in salpingectomy group is approaching.

Key Words: Fallopian tube diseases; fertilization in vitro; pregnancy rate; laparoscopy

ÖZET Amaç: Bilateral hidrosalpinks nedeniyle in vitro fertilikasyon (IVF) öncesi bilateral salpinjektomi ya da proksimal tubal oklüzyon yapılan 58 kadında retrospektif olarak değerlendirilerek implantasyon, düşük oranı, klinik ve devam eden gebelik oranları araştırıldı. **Gereç ve Yöntemler:** Bilateral hidrosalpinksi saptanan 58 hastaya IVF öncesi uygulanan bilateral salpinjektomi ya da bilateral tubal oklüzyon tedavisi retrospektif olarak araştırıldı. **Bulgular:** Her iki grup arasında gonadotropin dozu ve stümülasyon tedavi süresi açısından anlamlı fark bulunurken, intrastoplazmik sperm enjeksiyonu (ICSI) işlemi sonrası karşılaştırılan klinik sonuçlar arasında istatistiksel bir fark bulunmadı. Ancak salpinjektomi grubunun implantasyon, düşük oranı, klinik ve devam eden gebelik oranları proksimal tubal oklüzyon grubundan daha yüksek olmasına rağmen istatistiksel anlamda farklı bulunmadı (sırasıyla %30.2 karşılık %24.4, p= 0.65; %63.6 karşılık %56, p= 0.76; %54.5 karşılık %48, p= 0.79). Düşük oranı salpinjektomi grubunda proksimal tubal oklüzyon grubundan daha az bulunmasına rağmen aynı şekilde istatistiksel açıdan fark bulunamadı (%15 karşılık %24, p= 0.50). **Sonuç:** IVF siklusundaki sonuçların başarısı açısından hidrosalpinksin yönetiminde bilateral salpinjektomi ile proksimal tubal oklüzyon istatistiksel açıdan benzer sonuçlar alınmaktadır. Ancak sonuçlar değerlendirildiğinde salpinjektomi gurubu yüksek bir implantasyon ve klinik gebelik oranı ile düşük bir abortus oranına sahip olma eğilimindedir.

Anahtar Kelimeler: Fallop tüp hastalıkları; tüp bebek; gebelik oranı; laparoskopi

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It has been demonstrated that in-vitro fertilization (IVF) patients with hyrosalpinx have decreased pregnancy rates as compared with control individuals. Theories explaining the mechanisms for the impaired out-

come of in-vitro fertilization mainly focusing on the hydrosalpingeal fluid. Hydrosalpinx, especialy when it is bilateral and visible by ultrasonography, impacts negatively on pregnancy and implantation rates after IVF cycles.[1,2] Hydrosalpinges fluid has embryotoxic effects on embryogenesis.[3] The retrograde flow of tubal fluid may disturb intrauterine embryo development. Endometrial receptivity may be detoriated by the reduced expression of cytokines and integrins important to implantation. But the mechanism of reduced implantation and embryo development is still not clearly explained. Treatments to improve the results of is based on interruption of the leakage of hyrosalpinx fluid into the uterine cavity. Salpingectomy has been suggested as a method to overcome the negative influence of the hydrosalpingeal fluid on implantation and embryo development.[4] There is a wide variation in the management of hydrosalpinx prior to IVF treatment and many treatment options may be questionable, as they are not yet based on evidence.[5] On the other hand, in patients with hydrosalpinges, ultrasonograpy is mandatory before ET to detect newly developed hydrometra. Aspiration of the uterine fluid is unlikely to help because of rapid reaccumulation of hydrometra.[6] Cryopreservation of the embryos for future transfer after the hydrosalpinx is removed or ligated is recommended.[7] Patients with tubal pathologies such as hydrosalpinx pregnancy rate is reduced by half compared with patients without hydrosalpinx. Notably, there are also substantial increases in both early pregnancy loss and ectopic pregnancies in patient's ART cycles with hydrosalpinges.[8] Treatments proved in restoring birth rates involved laparoscopic salpingectomy, proximal tubal ligation and transvaginal drainage. Preferred treatment option with either surgical or medical therapies. How should hydrosalpinx be managed? Selection of the surgical method, either proximal occlusion or salpingectomy, depending on patients' clinical findings, differ in outcome. The aim of this study is to assess the pre-IVF surgical interventions and to compare the impact of the two surgical methods depending on the patient's clinical findings and cycle outcomes.

MATERIAL AND METHODS

Data was collected restrospectively from patients selected for IVF-ICSI cycles prepared at Suzan Woman's Health Care Center coordinated with Memorial, American Hospital's and Anatolia IVF Center's between January 2001 and November 2008. All women who referred to the investigators' unit routinely provided an informed consent for their clinical data to be used for researches purposes. The patients with poor ovarian reserve (described by FSH >20 IU/L on the day 3 of the menstrual cycle) and patients azospermia were excluded from the study. Women with bilateral hydroslapinx who were treated with either a laparoscopic salpingectomy or a laparoscopic proximal tubal occlusion before intracytoplasmic sperm injection (ICSI) were chosen for the study. A surgical correction of the tubes was performed in total of fifty eight patients with bilateral hydrosalpinges who were candidates for IVF treatment.

The diagnosis of hydrosalpinges was based on the presence of histerosalpingogram and transvaginal pelvic ultrasonography findings. Hysterosalpingogram of bilateral hydrosalpinges was represented by tubular convoluted structures on both sides of the uterus and no intraperitoneal spillage of contrast was demonstrated. Bilateral hydrosalpinges was defined on tranvaginal ultrasonography as bilaterally sonolucent fluid-filled fallopian tubes. Tubular structure separate from ovary with incomplete septations which may be anechoic or hypoechoic on transvaginal ultrasound imaging finding.

OVARIAN STIMULATION

The patients were stimulated with standart long protocol or flexible antagonist protocol.

Long GnRH agonist protocol: 0.1 mg/day leuprolide acetate (Lucrine, Abbot) sc was commenced on the 20th day of the menstrual cycle and 150-450 IU/day depending on the anticipitated ovarian response. Human chorionic gonadotropin (HCG) 10.000 IU was administered to trigger oocyte maturation when there were at least 3 follicles measuring greater than or equal to 17 mm in the mean diameter.

Flexible GnRH antogonist protocol :FSH injections at doses varying between 150 and 450 IU/day were commenced on the second day of menstruel bleeding. 0.25 mg GnRH antogonist (Cetrotide, Serono) injections were started when the leading follicle reached a mean diameter at 10 mm. Patients were received 10.000 IU of HCG as soon as > or = 3 follicles > or = 17 mm were present on ultrasound.

Oocyte retrieval was performed 36 hours after HCG administration. Fertilization was achieved universally by ICSI in all couples.

DEFINING CHARACTERISTICS OF TOP QUALITY EMBRYO

On day 3 of culture, the quality of the embryos was evaluated. The group of 'excellent' quality consisted of grade I embryos which had 6-8 cells, without fragmentation, equal sized blastomers with an absence of multinucleation . Embryo transfers were performed under direct ultrasound guidance on the third day after ICSI.

DEFINITIONS OF THE CLINICAL PARAMETERS

A clinical pregnancy was determined by the visualization of an embryo with cardiac activity at 5th week after the transfer of the embryos. Miscarriages rate was classified as the loss of the pregnancy till twelfth week of gestation. The primary outcome measures were the total amount of gonadotropin used , days of stimulation, miscarriage rate, implantation rate, clinical and ongoing pregnancy rates.

SURGICAL INTERVENTION

The salpingectomy incision was made with a monopolar needle on the mesenteric border as close as the tube in order to not to jeopardize the blood supply of the ovary. Tip of the vascular structures on the mesenter of the tube was cauterized as pinpoint at the edge of tubal entery.

The proximal tubal occlusion was performed by identification proximal entry of the fallopian tube to the uterine corn and a monopolar cauterization with cutting modes was applied on the 10 mm segment of the tuba.

STATISTICAL ANALYSIS

The parametric variables were analyzed by upaired student's *t*-test and non-parametric variables were analyzed by Chi-square test. *p* value less than 0.05 was considered statistically significant.

RESULTS

A total of 58 cycles were included in the study. The groups are similar in age, day 3 FSH, LH, estradiol blood levels. The estradiol level on hCG day, the number of oocytes, the number of transferred top quality embryos and endometrial thickness was also similar in the both groups (Table 1). However statistically significant differences were found in the number of gonadotrophin ampoules administered and in the days of stimulation (10.3 days vs 8.9 days p= 0.006, 3010 IU vs 2495 IU p= 0.008) (Table 2). Clinical results did not reveal significant differences between the two groups. Implantation, clinical and ongoing pregnancy rates in the salpingectomy group were all higher than the pxoximal occlusion group which were not statistically significant ((30.2% vs 24.4%, p= 0.65; 63.6% vs. 56%, p= 0.76; 54.5% vs 48%, p= 0.79 respectively) (Table 3). Miscarriage rate was decreased in those with salpingectomy than in those with proximal occlusion

TABLE 1: Comparison of the clinical variables of the patients with hydrosalpinges treated either by salpingectomy or proximal tubal occlusion.

	Salpingectomy group (n= 33)	Proximal tubal occlusion group (n= 25)	P
Age (mean years) ±SD	30.9 ± 5.5	31.9 ± 5.8	0.55
day_3 E2 (pg/mL) ±SD	39.06 ± 9.5	34.05 ± 9.7	0.07
LH (IU/L) ±SD	6.06 ± 1.6	7.23 ± 3.5	0.12
FSH (IU/L) ±SD	6.3 ± 3.4	7.4 ± 3.5	0.28
E2 on the day of hCG (pg/mL) ±SD	2035.06 ± 990.7	2180.55 ± 1188.3	0.64
Endometrial thickness (mm) ± SD	9.62 ± 1.43	10.32 ± 1.67	0.12

Metric variables were analysed by unpaired Student's t-test. p<.05 was considered statistically significant.

TABLE 2: Comparison of the IVF results of the patients with hydrosalpinges treated either by salpingectomy or proximal tubal occlusion.

	Salpingectomy group (n= 33)	Proximal tubal occlusion group (n= 25)	P
Days of stimulation ±SD*	10.3 ± 1.8	8.9 ± 1.3	0.006
Total amount of gonadotropin used (IU ±SD)*	3010 ± 725.0	2495 ± 501.2	0.008
Total oocytes collected*	11.1 ± 5.2	11.0 ± 5.9	0.91
MII proportion of oocytes % **	79.4	81.3	0.61
Fertilized oocytes %**	73.8	75.7	0.54
Mean top quality embryo transferred ±SD*	2.5 ± 0.6	2.45 ± 0.8	0.69

* Metric variables were analysed by unpaired Student's t-test. p<.05 was considered statistically significant.

**Non-parametric variables were analyzed with Chi-square test p<.05 was considered statistically significant.

TABLE 3: Clinical outcomes of the patients with hydrosalpinges treated either by salpingectomy or proximal tubal occlusion.

	Salpingectomy group (n= 33)	Proximal tubal occlusion group (n= 25)	p
Implantation rate	30.2% (23 /76)	24.4% (12/49)	0.61
Clinical pregnancy rate	63.6% (21/33)	56.0% (14/25)	0.76
Ongoing pregnancy rate	54.5% (18/33)	48.0% (12/25)	0.79
Miscarriage rate	15.0% (5/33)	24.0% (6/25)	0.50

Non-parametric variables were analyzed with Chi-square test p<.05 was considered statistically significant.

which was not statistically significant either (15% versus 24%, p= 0.50).

DISCUSSION

Salpingectomy improves the PR per transfer in patients with hydrosalpinges. Many of the studies concluded that bilateral salpingectomy due to hydrosalpinges restores a viable pregnancy as well as implantation rate cost effectively before IVF treatment compared to controls.[9-11]

Our results show that the technic of bilateral salpingectomy had a higher implantation, clinical and ongoing pregnancy than the technic of bilateral proximal tubal occlusion but we were not able to show that at a statistically significant level. The results of cumulative cycles in the strandell's randomized controlled study strengthen the recommendation for a laparoscopic salpingectomy prior to IVF in patients with ultrasound-visible hydrosalpinges.[12] Many author offered laparoscopic salpingectomy in cases where hydrosalpinges are large enough to be visible on ultrasound.[13,14] We think that it is not sufficient to say that only hyrosalpinges visible on ultrasound are associated with reduced implantation and pregnancy rates after IVF as mentioned. Because if there is not a fluid accumulation in the broadened tubal lumen, it is not possible to scan it's echogenecity on ultrasound. We still don't know the cutoff limit of the luminal enlargement for hydrosalpinges on HSG. Consequently, in undetermined cases laparoscopic surgery has a place in the diagnosis and management of hydrosalpinx.[15]

Pre-in-vitro fertilization salpingectomy is the only method that has proved effective in explaning reduced implantation and embryo development awaits further research.[12] On the other hand, patients underwent proximal tubal occlusion before IVF displayed significantly increased implantation, clinical and ongoing pregnancy rates compared with those with no surgical intervention and demonstrated implantation, clinical and ongoing pregnancy rates comparable to those underwent salpingectomy as in our twenty women's treatment.[16] So proximal tubal occlusion may be realised as an alternative approach in the case of salpingec-

tomy is technically difficult or not feasible. Procedures such as salpingectomy or proximal tubal occlusion to circumvent the passage of hydrosalpinx fluid into the uterine cavity may have beneficial effects on the developmental environment for embryos in vivo.

Laparoscopic salpingectomy should be considered for all women with hydrosalpinges due to undergo IVF.[17] But this is not the case for the women who had severe pelvic adhesions. Cauterization of hydrosalpinges before in vitro fertilization is an effective surgical method.[18] Proximal tubal cauterization is effective than salpingectomy in reversing the adverse effects of hydrosalpinges in women who had severe pelvic adhesions. Because it has easy and exact surgical applicability in the adhesive cases, the obstructed group may be favorable for the pregnancy rates and the complications than the inappropriately salpingectomized group

We could say that the validity of routine salpingectomy for hydrosalpinx is appropriate in selected individuals. The presence of a hydrosalpinx does not impair the number of embryos transferred but seems to impair the implantation process.[19] It interfered with implantation and reduce to some degree the success of IVF in achieving an ongoing pregnancy.[20] In the mean time authors hypothesize that this may be due to leakage of fluid into the uterine cavity which may disturb the recetivity of the endometrium and/or the developing embryos.

Studies compared the cost-effectiveness of the salpingectomy prior to IVF after a failed cycle shows that intervention strategy seems reasonable.[11] On the other hand, proximal tubal occlusion, when performed in women with bilateral hydrosalpinges before their IVF treatment, represents a potentially beneficial surgical procedure, increasing significantly the chances for successful implantation. clincal and ongoing pregnancy. Proximal tubal occlusion may be viewed as a valid alternative when salpingectomy is technically difficult or not feasible.[21] Regarding the ovarian stimulation and response the technic of proximal occlusion may be the treament of choice. Prophylactic salpingectomy before an IVF cycle in women with hydrosalpinx may compromise ovarian response to stimulation without affecting pregnancy rates.[22] Salpingectomy diminish the ovarian reserve by compromising network of ovarian blood supply. Considering the follicular pool ,this detrimental effect may not realise in the normal or high responders but it may display significant difference in poor or subnormal responders. Howerer regarding the rate of implantation, clinical and ongoing pregnancy, effects of salpingectomy is also favorable than proximal tubal occlusion in poor responders. Our findigs suggest that salpingectomy in women with hydrosalpinx may compromise ovarian response to stimulation without affecting pregnancy rates.

The best treatment approach of hydrosalpinges seems to be salpingectomy. However, in patient who has severe salpingeal adhession, tubal occlusion is the prefered operative procedure in terms of operative technical aplicabablity and so far the pregnancy rate. In our retrospective collected data proximal occlusion was performed on severe pelvic adhesion cases which may be vieved as a valid alternative when salpingectomy was technically difficult or not feasible. It is as effective as salpingectomy on the outcome of IVF but using the salpingectomy technic prior to IVF-ET in the setting of hydrosalpinges has become more common and favorable in terms of the standard of care. This monocentric study must be confirmed by other similar studies to allow for a definitive evidence.

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