

THE EFFECTS OF HYDROSALPINX ON IN VITRO FERTILIZATION-EMBRYO TRANSFER OUTCOMES

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Abstract - Hydrosalpinx (dilatation of the Fallopian tube that can be seen by hysterosalpingography, laparoscopy, and in severe cases by sonography) is one of the probable confounding factors of assisted - reproduction therapy (ART) outcomes. This cohort study is conducted to determine the effects of hydrosalpinx on IVF-ET outcomes. For this, of the total number of patients who had approached the Infertility Department of Mirza Koochak Khan Hospital in the period between Ordibehesht 1377 to Aban 1378 (April 1998 to November 1999), 392 patients had come for the IVF-ET cycles and were selected for our study. In these patients the numbers of oocytes retrieved and fertilized, the number of embryos transferred to the uterine cavity and resulting clinical pregnancy rates were measured.

51 patients who had hydrosalpinx were studied in two separate comparisons, initially with 50 patients who had tubal involvement other than hydrosalpinx and secondly with 341 patients who didn't have hydrosalpinx, but had other indications of IVF-ET. These groups had similar age distribution. The numbers of oocytes retrieved (in first comparison = 4.6 & 3.92 and in second comparison = 4.6 & 4.65) and the number of embryo obtained (in first comparison = 2.6 & 2.54 and in second comparison = 2.6 & 2.47) didn't have significant statistical differences, but despite the fact that the same number of embryos were transferred to the uterine cavity (in the first comparison = 2.53 & 2.14 and in the second comparison = 2.53 & 2.27), the clinical pregnancy rates in both comparisons were reduced by more than 50% in patients with hydrosalpinx as compared with control groups, that is group 2 & group 3 (in first comparison = 7.8% & 20% and in second comparison = 7.8% & 16.1%). We conclude that hydrosalpinx didn't result in impaired ovarian stimulation or decreased oocyte fertilization. It did however interfere with implantation and reduced to some degree the success of IVF in achieving a clinical pregnancy.

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Key Words: Hydrosalpinx, IVF-ET, clinical pregnancy rate, implantation.

INTRODUCTION

In vitro fertilization-embryo transfer (IVF-ET) has been used to treat couples with a variety of infertility

diagnoses. However, the classic indication is tubal factor infertility. The rationale for this intervention is straightforward: In the presence of abnormally functioning fallopian tubes, an effective approach to treatment would be to bypass the contribution of these structures to the reproductive process. Such circumvention should lead to high pregnancy rates with IVF-ET, as most couples with tubal factor infertility are otherwise fertile.

In recent years, however, several authors (1-11) have reported that tubal disease accompanied by hydrosalpinx resulted in poorer clinical pregnancy rates than in those patients without hydrosalpinx or those who had undergone salpingectomy. Indeed, some investigators have recommended that salpingectomy be considered in individuals with hydrosalpinx before an IVF cycle in order to maximize success (3,8)

There are several possible causes of such an active effect: 1) abnormal tubal epithelium may secrete detrimental hormones or growth factors, 2) altered uterotubal flow might affect the implantation cascade, 3) hydrosalpingeal fluid can make the endometrial environment unfavorable for implantation, and 4) adhesion tissue products might prove toxic to gametes or embryos. (4,14-18) There are several possible mechanisms to explain the toxicity of hydrosalpinx fluid for gametes and embryos: Direct flow of toxins, microorganisms, or microbial products from the dilated tube into the uterus may exert a detrimental effect on the endometrium and/or embryo (14,18). Irreversible damage to endometrium during the acute infectious tubal insult also could diminish implantation rates. Further alternation in endometrial integrin production associated with hydrosalpinx has been proposed (16). Another potential mechanism of hydrosalpinx fluid-induced toxicity is immunization to the human heat-shock protein 60KD. The production of antibodies to human heat-shock protein 60KD is increased in patients with hydrosalpinx (17). The production of proinflammatory cytokines with passage into the endometrial canal may have a deleterious effect on embryonic development and implantation. Interleukin-1 receptor antagonist has been shown to decrease implantation in mouse model (15). Other potential proinflammatory cytokines that may be detrimental to embryonic development include tumor necrosis

factor- α and β - interferone.

Fluid collection from such structures is known to increase with controlled ovarian stimulation, and this fluid empties into the uterine lumen.

Our purpose in this study was to evaluate the adverse effects of hydrosalpinx on success rate of IVF-ET in our patients.

MATERIALS AND METHODS

All patients who had approached the Infertility Department of Mirza Koochak Khan Hospital from Ordibehesht 1377 to Aban 1378 (April 1998 to November 1999), and according to primary evaluations and investigations were candidates for IVF-ET, were selected for our study (392 patients). Patients in whom persistent hydrosalpinx (one or both tubes enlarged and occluded distally) had been demonstrated by hysterosalpingography (HSG) and/or laparoscopy formed the group of patients having hydrosalpinx (51 patients = group 1). Other patients were also evaluated. Those patients, who had occluded fallopian tubes without hydrosalpinx, formed the group of patients having tubal involvement other than hydrosalpinx (50 patients = group 2). The patients who didn't have hydrosalpinx, but had other indications of IVF-ET, formed another group (341 patients = group 3). Age of the patients in all groups was compared using a t-test. Fisher's exact test was used to compare rates. These patients underwent induction of ovulation with same drugs (GnRH, HMG, HCG) and finally the numbers of retrieved and fertilized oocytes (numbers of embryos), the numbers of embryos transferred into the uterine cavity, and success rates of IVF-ET (only the clinical pregnancies were regarded as success) were compared with each other.

RESULTS

Group 1 (patients with hydrosalpinx) with 51 members, was compared to initially group 2 (patients with tubal involvement other than hydrosalpinx) with 50 members and then to group 3 (patients who didn't have hydrosalpinx, but had other indications of IVF-ET) with 341 members. Age distribution of patients was similar in all groups. Average age of patients in group 1 was 31 years (SD = 6.55) in group 2, 32.18 years (SD = 6); and in group 3, 30.44 years (SD = 6.24). Between groups 1 & 2, P-value, was 0.06 and between groups 1 & 3, P-value, was 0.13, so there were no significant

statistical differences between these groups (Table 1).

The number of retrieved oocytes in three groups were 4.6 (SD = 3.95), 3.92 (SD = 3.6), and 4.65 (SD = 3.72) respectively (Fig. 1), therefore by considering the P-value = 0.08 between groups 1 & 2, and P-value 0.863 between groups 1 & 3, there were no significant statistical differences between these groups.

The fertilization rate of oocytes (time numbers of obtained embryos) in three groups were 2.6 (SD = 2.37), 2.54 (SD = 2.79), and 2.47 (SD = 2.51) respectively (Fig. 2), therefore by considering the P-value = 0.85 between groups 1 & 2 and P-value = 0.584 between groups 1 & 3, there were no significant statistical differences between these groups.

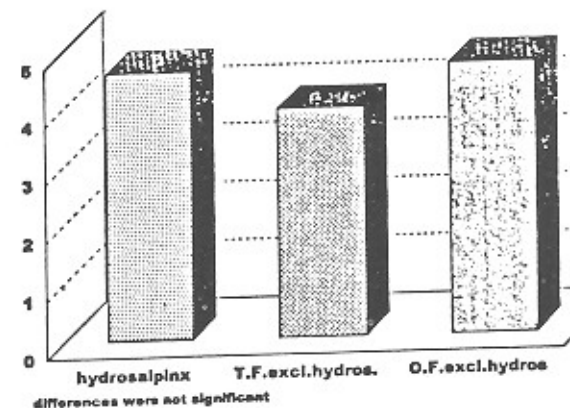


Fig. 1. Number of ovum retrieved (hydrosalpinx, tubal factors excluding hydrosalpinx, other factors excluding hydrosalpinx)

The number of embryos transferred into the uterine cavity in three groups were 2.53 (SD = 2.23), 2.14 (SD = 1.88) and 2.27 (SD = 2.09) respectively, therefore by considering P-value = 0.17 between groups 1 & 2 and P-value = 0.234 between groups 1 & 3, differences between these groups were not statistically significant.

The clinical pregnancy rate in first group was 7.8% (4 patients), in second group was 20% (10 patients), and in the third group was 16.1% (55 patients). (Fig. 3). In comparison between groups 1 & 2, P-value, was 0.08 and between groups 1 & 3 P-value was 0.13. As we can see the clinical pregnancy rate was reduced by more than 50% in patients with hydrosalpinx. Although, considering the P-value = 0.08 & 0.13, these differences did not reach statistical significance.

An interesting incidental finding was that the duration of infertility in patients with hydrosalpinx was longer than the other patients. [In group 1, was 8.58 yr. (SD = 5.25); in group 2, 6.34 yr. (SD = 5.19) and in

Table 1. Outcomes of IVF-ET in patients with and without* hydrosalpinx

Patients	Patients with hydrosalpinx: n=51 (1)	Tubal factors except hydrosalpinx: n=50 (2)	Other factors except hydrosalpinx: n=341 (3)	P-value (1&2)	P-value (1&3)
IVF outcome					
Average number of retrieved oocytes	4.6 (\pm 3.95)	3.92 (\pm 3.6)	4.65 (\pm 3.72)	0.08	0.863
Average number of obtained embryos	2.6 (\pm 2.37)	2.54 (\pm 2.79)	2.47 (\pm 2.51)	0.85	0.584
Average number of transferred embryos	2.53(\pm 2.23)	2.14 (\pm 1.88)	2.27 (\pm 2.09)	0.17	0.234
Clinical pregnancy rate	4 (7.8%)	10 (20%)	55 (16.1%)	0.08	0.13

* Patients without hydrosalpinx has defined in two ways: (2) patients who have tubal involvement other than hydrosalpinx; (3) Patients who do not have hydrosalpinx but have other indications of IVF-ET

group 3, 7.81 (SD = 5.43)], therefore by considering P-value = 0.000003 between groups 1 & 2 and P-value = 0.028 between groups 1 & 3 it had significant statistical value.

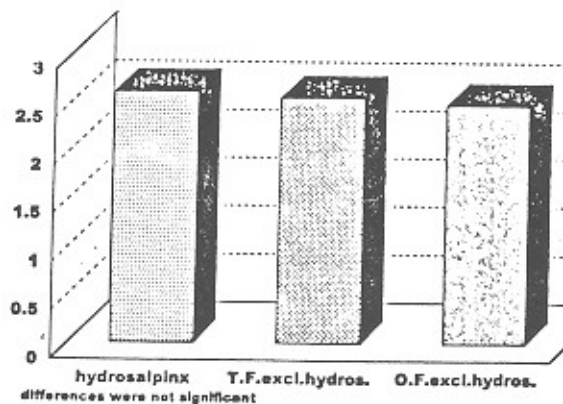


Fig. 2. Number of embryo (hydrosalpinx, tubal factors excluding hydrosalpinx, other factors excluding hydrosalpinx)

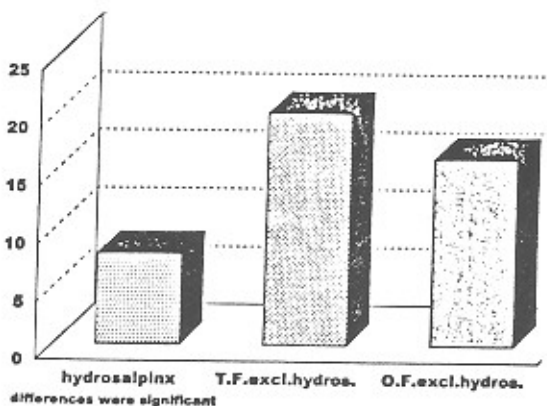


Fig. 3. Results of embryo transfer (hydrosalpinx, tubal factors excluding hydrosalpinx, other factors excluding hydrosalpinx)

DISCUSSION

On the basis of the limited data available, this study shows that hydrosalpinx is associated with a reduced chance of implantation. The pregnancy rate for the patients with hydrosalpinx was less than half that of patients without hydrosalpinx. In our study the difference in clinical pregnancy rate doesn't reach statistical significance like most of the studies conducted in this respect till now. Although the 95% confidence interval indicates that the underlying difference in our sample may be as high as 8-13%. In a population where the true rates of clinical pregnancy and hydrosalpinx are similar to those observed in our study, approximately 1700 patients would be required to detect a significant difference with 80% power.

Our results combined with those previously reported seem to confirm that neither response to stimulation nor rate of fertilization are responsible for the diminished clinical pregnancy rates observed in patients with hydrosalpinx. In contrast, implantation rates, which were lower in the presence of hydrosalpinx, likely led to reduced clinical pregnancy rates. Lessey and coworkers (8) reported a lower quantity of a histochemically detected adhesion molecule (VB3 vitronectin receptor) normally present at the time of implantation in a group of 14 patients with hydrosalpinx. Additionally, they reported that in five patients who underwent surgical correction of the hydrosalpinges, return to nominal expression of this same integrin was demonstrated.

An alternative hypothesis suggests that the tubal fluid contained in hydrosalpinges exerts a negative impact on implantation by exposing the endometrium and/or embryo to a biochemically altered environment.

Palmer (13) showed that pregnancy outcome was poor in the presence of chronic progressive inflammation. David & Czernobilsky (12) showed that the hydrosalpinx wall was fibrotic and the epithelial lining was impaired. The fluid had low levels of protein and bicarbonate with fluctuating pH levels between 7.2 and 7.7, suggesting passive transudation rather than active secretion. Furthermore, correcting the high pH of the fluid did not change the results. Also it has been shown (6,9) that the hydrosalpingeal fluid is toxic for the embryo, although if this fluid is diluted too much, it

will lose its toxicity; to exert its toxic effects, the fluid should have at least 75% of primary concentration (18).

Although the distal end of a hydrosalpinx is blocked, the proximal end is usually in free communication with the uterine cavity, which may allow a direct flow of microorganisms, toxic debris, and lymphocytes into the uterus. Cytokines, prostaglandins and other agents also may be transferred directly to the endometrium. Anecdotal reports suggest that such a mechanism may be important clinically.

Oehninger and coworkers (6,10) showed that the best results in IVF-ET were obtained in patients with pure mechanical factor (bilateral tubal ligation).

Time effects of salpingectomy on the results of IVF-ET have not yet been elucidated and we need further research to confirm the effects.

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