The Effectiviness of Hydrosalpinx Treatments in Patients that Need Assisted Reproductive Techniques

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Abstract

DIE WIRKSAMKEIT VON METHODEN ZUR BEHANDLUNG VON HYDROSALPINX FÜR DIE ASSISTIERTE REPRODUKTION

Bekanntlich halbiert sich bei Patientinnen mit tubarer Pathologie insbesondere im Fall von Hydrosalpinx die Erfolgsrate von Verfahren der assistierten Reproduktion, wie beispielsweise der In-vitro-Fertilisation.

Theorien zur Erklärung der schlechten Resultate konzentrieren sich auf eine embryotoxische Wirkung der Hydrosalpinx-Flüssigkeit, eine Beeinträchtigung der Endometrium-Rezeptivität oder ein mechanisches Hindernis für die Einnistung auf der Endometriumoberfläche durch die Hydrosalpinx-Flüssigkeit.

Ziel dieser Analyse ist es, die verschiedenen Behandlungsmöglichkeiten zur Beseitigung der Hydrosalpinx-Flüssigkeit vor einer In-vitro-Fertilisation zu evaluieren.

Zu diesem Zweck wurde Literatur zu diesem Thema, die im Zeitraum zwischen Januar 1997 und September 2007 veröffentlicht wurde, aus den Datenbanken MEDLINE und EMBASE abgerufen und ausgewertet. Die entsprechenden Quellen sind im Literaturverzeichnis angeführt.

Die Ergebnisse erlauben folgende Schlussfolgerungen:

Eine Salpingektomie vor der In-vitro-Fertilisation ist die einzige Methode, die sich bei der Wiederherstellung der Fruchtbarkeitsrate von Patientinnen mit Hydrosalpinx als wirkungsvoll erwies. Nach einer randomisierten, kontrollierten Studie ist eine proximale Tuben-Okklusion ebenfalls zielführend.

Andere vorgeschlagene Behandlungsverfahren, wie eine transvaginale Ableitung der Hydrosalpinx-Flüssigkeit, bieten keinen Nutzen.

Die grundlegenden Mechanismen, welche für die niedrigen Einnistungsraten und die schlechte Entwicklung des Embryos verantwortlich sind, werden nicht erklärt.

INTRODUCTION

Several retrospective studies collected in meta-analysis have shown that patients with hydrosalpinx who are subjected to in vitro fertilization (IVF) showed a lower rate of pregnancy and childbirth by up to 50 % and twice the rate of spontaneous abortion compared with other patients without this pathology who were also subject to assisted reproduction techniques [1–2].

The main theory behind this mechanism suggests that the hydrosalpinx fluid (HF) plays an important role in causing these results. Hydrosalpinx may affect the likelihood of pregnancy by the hydrosalpingueal embryotoxic effect of the fluid that leaks out continuously to the endometrial cavity, causing endometrial abnormalities, making the implantation[3–11] and embryo development hostile, or simply producing detached embryos by mechanical drag effect produced by filtration[12–18]. Other theories have included simultaneous damage to the endometrium at the time of onset of tubal infection [12-22], impairment of ovarian function and oocyte quality due to the influence of toxic inflammatory substances transported through blood or the lymphatic system[23–24, 25–37].

Despite the existing information, so far, a pattern of treatment related to this topic has not been set.

In the last decade, numerous studies have demonstrated the concern about the presence of hydrosalpinx and its management in patients who will be undergoing IVF.

Thus, two polls on the management of hydrosalpinx prior to IVF conducted at centers performing assisted reproduction techniques (ART) in Europe - the first held in England in 2004 and another in France in 2006 – reported the following:[38–39]

The British survey shows that of 117 centers performing ART, 88 centers responded (75%), of which 80 (91%) stated that they discussed with patients the effect of hydrosalpinx on the outcome of IVF. Ten centers (12%) did not recommend treatment of hydrosalpinx prior to IVF, while 30 (36%), 27 (33%) and 16 (19%) recommended treatment mildly, strongly and very strongly respectively. Treatment options offered by physicians were laparoscopic salpingectomy (75%), salpingectomy by laparotomy (45%), salpingostomy (40%), proximal tubal occlusion (34%), aspiration of fluid from the hydrosalpinx by transvaginal sonography (TVS) during aspiration of oocytes (23%), and aspiration of the hydrosalpinx fluid TVS before follicular aspiration (10%). Only 28% of hospitals had protocols for hydrosalpinx management.

The French survey was conducted at 100 sites registered in ART, 82 centers answered the questionnaire, 67% of which had between 10 and 20 years of experience in infertility. 33% of IVF units had a surgery specialised in infertility and hydrosalpinx management had been discussed with all staff prior to IVF. Eighty (98%) of the eighty-two centers that responded indicated that they previously discussed the effects of hydrosalpinx on IVF outcomes, six centers (7.5%) did not suggest a specific treatment, while 12 (15%), 53 (66%) and 9 (11.3%) suggested a treatment mildly, strongly and very strongly respectively.

These treatment options were proposed by the doc-

tors: medical treatment (22%), aspiration of hydrosalpinx fluid by TVS with or without medical treatment (12.9%) and surgical treatment (64.9%). Only 11% of hospitals had protocols for hydrosalpinx management.

These results show great variations in the management of hydrosalpinx prior to IVF, with different treatment options that may be questionable. Many of these options related to removing fluid from the hydrosalpinx have not been adequately evaluated with the exception of salpingectomy by laparoscopy, which was subject to a randomised controlled study conducted by Strandell in 1995. Therefore, any surgery to interrupt communication to the uterus may prevent leakage of this fluid and improve pregnancy[40] rates.

The objective of this review is to apply the treatment options that are discussed in the literature, but focusing on those that remove the tubal fluid before in vitro fertilization (IVF) is performed.

METHODOLOGY

A review of the literature on the subject in the databases MEDLINE and EMBASE for the past ten years, from January 1997 to September 2007 was carried out. The language used for the review was English. The keywords used for searching the database were: hydrosalpinx, tubal disease, IVF, ICSI, result, treatment, surgery, salpingectomy, salpingostomy, before pregnancy, next to and after pregnancy, prevention, implementation, toxic, embryo culture.

All key words were used in combination with »hydrosalpinx«. A total of 126 articles were found related to the subject.

After that, the articles were evaluated and were given a score relative to their objective, methodology, type of study and type of review.

Finally, 54 articles selected for review were used which were related to randomised controlled trials, retrospective and observational, and case reports.

So far, only a research paper from 1999 dealing with the management of hydrosalpinx visible on ultrasound before IVF shows an increase in pregnancy rate after salpingectomy prior to the Assisted Reproduction Technique.[5]

RESULTS OF DIFFERENT TREATMENT OPTIONS

Treatment of hydrosalpinx with salpingectomy before IVF, is the only method that has been evaluated in a prospective, randomised, controlled and sufficiently large study, providing a high level of evidence for recommendations. Proximal ligation has also been evaluated in a small prospective randomised study. Like the transvaginal aspiration, this method has been evaluated in small retrospective studies therefore their level of evidence is lower.

Salpingectomy:

A Scandinavian multicenter study compared the laparoscopic salpingectomy versus non-surgical intervention before the first IVF cycle, and showed significant improvement in pregnancy rates and birth after salpingectomy in patients with hydrosalpinx, which were large enough to be visible during the ultrasound examination[5]. The clinical pregnancy rate was 45.7% versus 22.5%, P = 0.029, and the delivery rate 40% versus 17.5%, P = 0.038. The delivery rate increased 3.5-fold in patients with sonographically visible hydrosalpinx after bilateral salpingectomy (P = 0.019). The difference in the final result was not statistically significant in the total study population of 204 patients, which included patients with hydrosalpinx that were not visible by ultrasound, showing that the benefit of salpingectomy is only evident if the hydrosalpinx is fluid-filled.

A review by Cochrane in 2002 was based on three randomised controlled trials, including the Scandinavian one, and concluded that laparoscopic salpingectomy should be considered in all women with hydrosalpinx to be subjected to IVF[41]. This recommendation of salpingectomy is concerned with the unnecessary removal of fallopian tubes that can be repaired, as there are arguments in favour of performing tubal microsurgery in patients with hidrosalpinx.[42] Performing In Vitro Fertilization (IVF) should be a complementary strategy for tubal disease, since it has been shown that approximately one third of women with hydrosalpinx have a good prognosis of spontaneous pregnancy after reconstructive surgery[43].

Risk of complications after salpingectomy.

The effects of salpingectomy on ovarian function were discussed, because so far there are no conclusive studies on the problem, no significant difference was found in the response to hormonal stimulation or oovocitary recovery used in cycles after surgery; on average 0.7 fewer follicles are recovered compared with the cycle previous to the surgery intervention.[44]

From these results, we cannot conclude that patients with low ovarian reserve, have a higher risk of damaging their ovarian response after salpingectomy.

Tubal ligation.

Proximal tubal occlusion of the fallopian tube has been suggested as an alternative to salpingectomy, particularly when dense adhesions are so extreme as to hinder that process.

Occlusion of the tube serves the purpose of disrupting the fluid flow to the endometrial cavity, leaving the hydrosalpinx in place, which may cause difficulty in aspiration of oocytes. The procedure is often accompanied by the realisation of a window or hole in the distal hydrosalpinx for it to drain the fluid, but this opening usually closes early.

Three retrospective studies have found that the procedure produces results comparable to those obtained after salpingectomy and improves outcomes when compared with non intervention[45–47].

TABLE 1.

Clinical pregnancy rates per embryo transferred in three retrospective studies comparing the tubal ligation and salpingectomy with no surgery in patients with hydrosalpinx before IVF.

Author, Year of publication	Salpingectomy N/n (%)	Tubal Ligation N/n (%)	No Surgery N/n (%)
Murray et al., 1998 [35]	9/23 (39)	9/15 (60)	4/47 (8.5) P < 0.05
Stadtmauer et al., 2000 [43]	7/15 (47)	22/30 (73)	2/15 (13) P<0.05
Surrey and Schoolcraft, 2001 [44]	16/28 (57)	7/15 (47)	—

TABLE 2.
Clinical pregnancy per embryo transferred in two retrospective studies of transvaginal aspiration of hydrosalpinx fluid prior to IVF, made in a single cycle.

	Treatment Group		
Author, Year of publication	Aspiration n/n (%)	No aspiration n/n (%)	P de Value
Sowter et al., 1997 [46]	6/30 (20.0)	3/18 (16.73)	1.0
Van Voorhis et al., 1998 [47]	5/16 (31.3)	1/18 (5.6)	0.13

In a recent randomised, controlled study of 115 patients with hydrosalpinx 50 were treated prior to IVF via tubal ligation, 50 via salpingectomy and 15 had no treatment. Both surgical methods showed a high significance in pregnancy rates (37.8 and 55.3%) compared with women who had not undergone the procedure (7.1%) analysed on the basis of an intention to treat (P = 0.049). Although the study is underpowered, the results confirm the findings of previous retrospectives studies, suggesting that proximal occlusion is effective[48]. However further studies are required to conclude that proximal occlusion is as effective as salpingectomy to increase the pregnancy rate.

Taking into account the technical aspects of surgery in complicated cases due to severe adhesions and the potential risk of vascular injury, proximal ligation is an alternative to be recommended.

Transvaginal fluid aspiration

Transvaginal aspiration hydrosalpinx fluid guided by ultrasound has been recommended as a treatment option to remove the hydrosalpinx fluid. However, if the procedure is performed before ovarian stimulation, there is a high risk of reaccumulation. Even if it is done at the time of follicular aspiration, the risk of recurrence is already high at the time of transfer.

In two retrospective case-control studies, evaluating the procedure found no benefits[49–50]. (Tabel 2)

In the clinical situation in which the patient develops tubal fluid during ovarian stimulation, transvaginal aspiration at the time of follicular aspiration may be an alternative, but the best option is to freeze embryos and carry out subsequent surgery before transferring thawed embryos. Another phenomenon that sometimes occurs with hydrosalpinx is the presence of fluid in the uterine cavity (hydrometra). Some retrospective studies have shown that the presence of hydrometra at the time of transfer is a sign of poor prognosis[51]. Aspiration of the uterine fluid is unlikely to be beneficial because there is rapid accumulation of hydrometra[52].

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Treatment with antibiotics

The use of antibiotics has been presented as a simple treatment option to overcome the negative effects of hydrosalpinx, based on the theory of persistent tubal infection. Antibiotic treatment has never been prospectively evaluated, however, to date, only one retrospective study has suggested that the use of doxycycline during the IVF cycle may minimise the deleterious effect of hydrosalpinx[53].

Other suggested handling

A retrospective study has suggested the use of natural cycle with the intention of preventing ovarian hyperstimulation and subsequent enlargement of hydrosalpinx [54].

In the study 72 patients with hydrosalpinx undergoing natural cycle IVF showed a significant rate of pregnancy rate compared with patients undergoing ovarian hyperstimulation (n = 49, 18% versus 7%, $P < 0.05$). This result is biased by the selection of patients for the chosen treatments. However, the poor results obtained in cycles where freezing and thawing occurs contradicts the potential benefit of natural cycles.

The suggestion to increase the number of transferred embryos to counteract the adverse effect of hydrosalpinx has not been shown to be an effective management, therefore, should not be considered, as efforts are aimed in reducing the rate of multiple pregnancies, and the trend is to transfer a single embryo.

CONCLUSIONS

Patients with hydrosalpinx who will be undergoing IVF, already have a poor prognosis following previous tests. Its negative influence is not fully understood, and is an area that needs further investigation. However, it has been shown that laparoscopic salpingectomy before IVF, is effective in restoring birth rates and should be recommended if the hydrosalpinx is visible by the ultrasound examination

Ligation or section of the tuba at the isthmus is a suitable alternative if salpingectomy is difficult. Other suggested treatments need to be evaluated in randomised controlled trials.

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