Ultrasound-guided aspiration of hydrosalpinges is associated with improved pregnancy and implantation rates after in-vitro fertilization cycles

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Introduction

The presence of hydrosalpinges appears to have a detrimental effect on in-vitro fertilization (IVF) outcomes. Several investigators have reported reduced pregnancy rates during IVF cycles in women with hydrosalpinges (Andersen et al., 1994; Kassabji et al., 1994; Strandell et al., 1994; Vandromme et al., 1995; Katz et al., 1996). Other studies have not found a reduced pregnancy rate but have noted an impaired embryo implantation rate in women with hydrosalpinges following IVF cycles (Fleming and Hull, 1996; Blazar et al., 1997). The lone study demonstrating no statistically significant effect of hydrosalpinges on IVF outcomes reported a trend towards reduced embryo implantation rates and pregnancy rates in women with hydrosalpinges (Sharara et al., 1996).

The association of hydrosalpinges with reduced pregnancy rates during IVF cycles has led some to suggest that salpingectomy be performed in these women in hopes of improving pregnancy outcomes (Strandell et al., 1994; Vandromme et al., 1995; Katz et al., 1996). Indeed two retrospective studies have suggested that surgical removal of hydrosalpinges improves IVF outcomes (Vandromme et al., 1995; Shelton et al., 1996).

The idea of performing salpingectomy before IVF cycles is controversial, however, because of the invasive nature of this intervention which precludes any possibility of subsequent tubal repair (Puttemans and Brosens, 1996).

The importance of this issue prompted us to evaluate our clinic’s experience with women who had hydrosalpinges diagnosed by ultrasound. In addition, since one of the three physicians in our programme had routinely aspirated hydrosalpinges at the time of oocyte retrieval whereas the other two had not, we were able to test the hypothesis that aspiration of hydrosalpinges leads to improved pregnancy rates in women with hydrosalpinges.

Materials and methods

We reviewed the charts of all patients with tubal factor infertility treated at the University of Iowa Assisted Reproductive Techniques programme between January 1, 1993 and December 31, 1996. The ultrasound reports and films taken during the stimulation cycle were reviewed to determine which patients had either unilateral or bilateral hydrosalpinges present on the day of human chorionic gonadotrophin (HCG) administration. We ascertained which patients had their hydrosalpinges aspirated at the time of oocyte retrieval. Because current smoking has been associated with reduced implantation and pregnancy rates (Van Voorhis et al., 1996), we also discovered by chart review whether or not patients were smoking during the stimulation cycle.

Ovarian stimulation was achieved with the same medication protocol that was previously described in detail (Van Voorhis et al., 1992). In brief, the gonadotrophin-releasing hormone agonist leuprolide acetate (1 mg s.c.) was administered from day 23 of the cycle preceding stimulation until the day of HCG administration. Follicular development was stimulated with 225 IU of follicle stimulating hormone for 3 days. Subsequent stimulation was achieved using human menopausal gonadotrophins with doses determined by ovarian response as measured by serum oestradiol levels. HCG (10,000 U) was given when at least two follicles were ≥18 mm in maximum diameter with a serum oestradiol concentration of ≥500 pg/ml. With rare exceptions, cycles were cancelled if these criteria were not met. All oocyte retrievals were accomplished by a transvaginal ultrasound-guided technique using i.v. medications for...
Analysed using Student’s t-test when a statistically significant increase in ongoing pregnancy of hydrosalpinges at the time of oocyte retrieval was associated with a reduced implantation rate observed in women with hydrosalpinges. This suggests that these factors cannot account for the reduced implantation rate (Table I). The clinical pregnancy rate and implantation rates were no different than those in women with tubal factor infertility but no hydrosalpinges (Tables I and II).

Statistical analysis
To assess differences in pregnancy and implantation rates between groups, χ²-test, with Yates’ correction for continuity, and Fisher’s exact test (when \( n < 5 \)) were used. All other differences were analysed using Student’s \( t \)-test. \( P < 0.05 \) was considered significant.

Results
When evaluating the first cycle only of treatment for women with tubal factor infertility, the presence of a hydrosalpinx on ultrasound was associated with a markedly reduced embryo implantation rate (Table I). The clinical pregnancy rate and ongoing pregnancy rate were also reduced in women with hydrosalpinges although these differences did not quite reach statistical significance. When comparing cycles of women with hydrosalpinges to those without hydrosalpinges, no differences in women’s age, parity, smoking status, number of embryos transferred or embryo grade (data not shown) were observed. There were also no differences between groups in numbers of women having embryos transferred on day 2 versus day 3 after oocyte retrieval. In addition, there were no differences in the incidence of other infertility diagnoses including low sperm counts, endometriosis, or anovulation (results not shown). This suggests that these factors cannot account for the reduced implantation rate observed in women with hydrosalpinges.

When evaluating only the first cycle of treatment, aspiration of hydrosalpinges at the time of oocyte retrieval was associated with a statistically significant increase in ongoing pregnancy and implantation rates (Table II). Comparing those women who had their hydrosalpinges aspirated versus those who did not, no differences were found in the women’s age, parity, smoking status, number of embryos transferred or embryo grade (data not shown). There was also no difference in the incidence of other infertility diagnoses. This suggests that these factors cannot account for the improved pregnancy and implantation rates found in women following aspiration of hydrosalpinges. Following aspiration of hydrosalpinges, pregnancy and implantation rates were no different than those in women with tubal factor infertility but no hydrosalpinges (Tables I and II).

Similar findings of higher implantation and pregnancy rates following aspiration were found when evaluating all cycles performed in women with hydrosalpinges (Table III). Statistical comparisons of these results could not be made since the cycles were not independent observations. Individual women had more than one cycle and many have been included in both groups depending on whether or not aspiration of their hydrosalpinges was performed.

Another variable among women with hydrosalpinges was the physician performing the IVF cycle. Since one of us routinely had aspirated hydrosalpinges at the time of oocyte retrieval (C.H.S.) and the others had not (B.J.V., D.W.S.), theoretically, differences in physician practices aside from the aspiration of hydrosalpinges could account for the differences in pregnancy rates observed. We do not believe this is the case since standard cycle protocols are always followed. In addition, yearly pregnancy rates achieved by the individual physicians in their patients have been calculated and no differences in pregnancy rates between physicians have ever been detected at any time for any other group of patients treated in our programme (results not shown).

Discussion
We have demonstrated that the presence of hydrosalpinges diagnosed by ultrasound is associated with a markedly impaired embryo implantation rate. The pregnancy rate in women with hydrosalpinges was reduced by one half compared to women with tubal disease but no hydrosalpinges, although this difference did not quite reach statistical significance \( \left( P = 0.051 \right) \). The failure to show a difference in the pregnancy rate in this group is likely to be due to the fact that approximately one-half of these women had their hydrosalpinges aspirated, which had a beneficial effect on the pregnancy rate. The reduced

<table>
<thead>
<tr>
<th>Hydrosalpinges</th>
<th>No hydrosalpinges</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( n )</td>
<td>34</td>
<td>124</td>
</tr>
<tr>
<td>Clinical pregnancies</td>
<td>6 (18%)</td>
<td>46 (37%)</td>
</tr>
<tr>
<td>Ongoing pregnancies</td>
<td>5 (15%)</td>
<td>42 (34%)</td>
</tr>
<tr>
<td>Implantation rate</td>
<td>9/129 (7%)</td>
<td>85/463 (18%)</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>33.2</td>
<td>32.8</td>
</tr>
<tr>
<td>Current smokers</td>
<td>26%</td>
<td>20%</td>
</tr>
<tr>
<td>Mean embryos transferred</td>
<td>3.7</td>
<td>3.8</td>
</tr>
<tr>
<td>Mean parity</td>
<td>0.3</td>
<td>0.6</td>
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</tbody>
</table>

Aspiration of hydrosalpinges

Analgesia. In some women, hydrosalpinges were aspirated using an ultrasound-guided technique until the hydrosalpinges were completely drained. This was performed after follicles had been aspirated on each side. Hydrosalpinx fluid was kept separate from the retrieved oocytes and was discarded without culturing the fluid. All patients, whether or not hydrosalpinges were aspirated, were given a single dose of prophylactic i.v. antibiotics. All mature oocytes were inseminated in vitro and embryos were cultured for 2 days (before July 1, 1995) or for 3 days (after July 1, 1995) before being transferred to the uterus. All patients were seen for a post-operative appointment and pregnancy test ~2 weeks after oocyte retrieval.

We defined a clinical pregnancy as the presence of an intrauterine gestational sac on ultrasound and an ongoing pregnancy as a pregnancy beyond 20 weeks gestation. Implantation rate was defined as the number of fetuses with cardiac activity divided by the number of embryos transferred. Prior to transfer, embryo cell number and grade were determined under an inverted microscope using standard grading criteria (Veeck, 1991).
fashion and there are no differences in pregnancy rates achieved as aspects of the IVF cycles were performed in a standardized factors do not account for the differences we found. All other smoking status, suggesting that these potential confounding diagnoses, number of embryos transferred, embryo quality or differences in age, parity, incidence of other infertility dia- gnees aspirated versus those who did not, there were no hydrosalpinges at the time of oocyte retrieval was associated other two did not, we were in a position to analyse the effect hydrosalpinges at the time of oocyte retrieval whereas the current smokers when comparing women with hydrosalpinges not explain the impaired outcomes for women with hydro- salpinges although there were no differences in percentages of their treatment cycle, this potential confounding factor could Although a high percentage of women were smoking during an IVF cycle is associated with reduced embryo implantation and pregnancy rates (V an V oorhis et al., 1990). Smoking during an IVF cycle is associated with reduced embryo implantation and pregnancy rates since simple removal of the fluid by aspiration appears to have a therapeutic effect. The mechanism of the impaired implantation needs to be further explored but may include adverse effects by hydrosalpinx fluid on endometrial and or embryo development (Mukherjee et al., 1996).

Our clinical experience suggests that aspiration of hydrosalp-inges is a safe treatment for improving IVF outcomes. We found that ultrasound-guided aspiration of hydrosalpinges is easily performed using i.v. sedation at the time of oocyte retrieval. Per our programme policy, all patients had a 10 day course of doxycycline within 3 months of having an IVF cycle. In addition, all patients have prophylactic antibiotics (usually a cephalosporin) given after oocyte retrieval. Under these conditions we believe that hydrosalpinx aspiration is safe, based on the fact that no patients had a flare of pelvic inflammatory disease or peritonitis following the procedure.

How to treat patients with hydrosalpinges who are trying to conceive with IVF has recently been debated. Several authors have suggested that a salpingostomy or a salpingectomy be performed prior to the IVF cycle (Strandell et al., 1994; Marchbanks et al., 1990). Although a high percentage of women were smoking during their treatment cycle, this potential confounding factor could not explain the impaired outcomes for women with hydrosalpinges since there were no differences in percentages of current smokers when comparing women with hydrosalpinges to those with tubal disease but no hydrosalpinges.

Because one physician in our programme routinely aspirated hydrosalpinges at the time of oocyte retrieval whereas the other two did not, we were in a position to analyse the effect of this intervention on IVF outcomes. We found that aspirating hydrosalpinges at the time of oocyte retrieval was associated with significantly improved embryo implantation and pregnancy rates. Indeed, the implantation and pregnancy rates achieved in women who had their hydrosalpinges aspirated did not differ from women with tubal disease but no hydrosalpinges. When comparing the women who had their hydrosalp-inges aspirated versus those who did not, there were no differences in age, parity, incidence of other infertility dia- gnees, number of embryos transferred, embryo quality or smoking status, suggesting that these potential confounding factors do not account for the differences we found. All other aspects of the IVF cycles were performed in a standardized fashion and there are no differences in pregnancy rates achieved in patients treated by the individual physicians when analysing programme-wide data.

Our results confirm two previous reports demonstrating that the presence of hydrosalpinges diagnosed by ultrasound is associated with impaired pregnancy and implantation rates (Andersen et al., 1994; Katz et al., 1996). The fluid in a hydrosalpinx is likely to be the factor that impairs implantation and pregnancy rates since simple removal of the fluid by aspiration appears to have a therapeutic effect. The mechanism of the impaired implantation needs to be further explored but may include adverse effects by hydrosalpinx fluid on endometrial and or embryo development (Mukherjee et al., 1996).
is necessary to achieve IVF pregnancy rates comparable to those in women without hydrosalpinges.

Ultrasound-guided aspiration of hydrosalpinges has been previously reported. A study from Egypt reported the outcomes of 32 women who had their hydrosalpinges aspirated the month before beginning an IVF stimulation (Aboulghar et al., 1990). Results were compared with 32 women who did not have an aspiration procedure performed. They found that aspiration led to a greater ovarian response to stimulation and they noted greater numbers of embryos for transfer after aspiration of the hydrosalpinges. Pregnancy rates were also higher in women after hydrosalpinx aspiration although this difference failed to reach statistical significance. Russell et al. (1991) also reported a single case in which aspiration of hydrosalpinges was performed the month prior to an IVF stimulation cycle which resulted in an ongoing pregnancy. Only one other study has reported the aspiration of hydrosalpinges at the time of oocyte retrieval. As part of a larger study on the effects of hydrosalpinges on IVF outcomes, Sharara et al. reported that a subset of seven women having eleven IVF cycles had hydrosalpinges aspirated at the time of oocyte retrieval with no morbidity resulting (Sharara et al., 1996). These cycles resulted in two ongoing pregnancies and three miscarriages. No further detail is given to compare this subset of women with others in the study. None of our patients who conceived after aspiration of hydrosalpinges suffered a miscarriage.

The rapidity with which hydrosalpinx reaccumulate appears to be quite variable. Bloechle et al. (1997) recently reported a patient whose hydrosalpinges were aspirated at the time of oocyte retrieval, yet within 3 days reaccumulation of hydrosalpinges fluid and development of a large serometra were noted. Following aspiration of the serometra, embryos were transferred but no pregnancy resulted. These authors concluded on the basis of one case that aspiration of hydrosalpinges is not useful. We have recently attempted to determine the rapidity of hydrosalpinx fluid reaccumulation by performing repeat ultrasound studies. Based on a limited number of observations, we find that it is uncommon for reaccumulation to occur in the 3 days between oocyte retrieval and embryo transfer. However, we have seen reaccumulation of fluid 14 days after aspiration, even in women with ongoing pregnancies. By 24 days after aspiration, we have noted reaccumulation of hydrosalpinx fluid in 50% (3/6) of women with ongoing pregnancies. This suggests that hydrosalpinges reaccumulate fluid at different rates but that fluid present even 14 days after aspiration does not preclude an ongoing pregnancy. The rapidity of hydrosalpinx fluid reaccumulation is another variable that needs to be assessed in a prospective fashion. Very rapid reaccumulation may prevent implantation whereas slower rates of reaccumulation appear to be more common and allow for embryo implantation and ongoing pregnancies.

Our study is the first to directly evaluate the IVF outcomes in comparable populations of women with hydrosalpinges who either did or did not have their hydrosalpinges aspirated during the IVF cycle. Although we recognize the inherent weaknesses of a relatively small retrospective study as compared to prospective randomized trials, our results suggest that aspiration of hydrosalpinges is an efficacious practice. We suggest that advising patients to have a salpingectomy or salpingostomy prior to IVF cycles may be premature until these treatments have been shown to result in better outcomes than can be achieved by simple aspiration.

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References


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