Pregnancy outcome after multifetal reduction via early transvaginal embryo aspiration: Mansoura fertility care unit experience

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ABSTRACT

Objective: To evaluate the pregnancy outcome after multifetal pregnancy reduction (MFPR) via early transvaginal embryo aspiration.

Design: Prospective clinical study

Material and Methods: The study included 30 patients with high-order multifetal gestations (more than 3 fetuses), Pregnancies included, before reduction: 22 quadruplet gestations (group 1) and 6 quintuplets (group 2), and 2 sextuplets (group 3). All pregnancies were reduced to twins. The primary outcome measures included procedure complications while the secondary ones were pregnancy outcomes.

Results: The procedure was successfully completed in all cases. Miscarriage occurred in 2/30 patients (6.6%). Preterm delivery occurred in 20/30 cases (66.6%). The incidence of early pregnancy complications and neonatal outcomes in reduced pregnancies were similar to that of the control group. However, the cesarean section rate of reduced twin pregnancies was significantly higher (P < 0.05).

Conclusion: Early transvaginal embryo aspiration is a safe, effective and simple operation. It is associated with reduced perinatal morbidity and mortality as well as minimal maternal complication.

Key words: High order pregnancy, multifetal embryo reduction, early transvaginal embryo aspiration.
pregnancy, involves injection of NaCl or KCl solution near to or inside the fetal heart and/or amniotic fluid aspiration (12). This method entails a greater technical difficulty, with miscarriage rates ranging from 10.6% to 40% (13) and pre-term labor ranging from 20% to 64% (14).

The transvaginal technique is performed between the 7th and 11th weeks, by injecting NaCl (12) or KCl solution into the fetal thorax (15). The injection of such substances into the embryo or fetal thorax is not a risk free procedure as cases of anencephaly (16), limb amputation (17) and total pregnancy loss (18) have been described.

The transvaginal technique has been performed with total or partial embryo aspiration. Single embryo tissue aspiration was compared with KCl solution injection (15), and showed a lower miscarriage rate (8.8% and 30% respectively). Coffler et al., 1999 reported a 6.7% miscarriage rate (19). Furthermore, transvaginal embryo puncture aspiration without injecting substances was reported to have low incidence of miscarriage 5.3% and 7.4% respectively (20,21). The aim of the present study is to evaluate the pregnancy outcome after MFPR via early transvaginal embryo aspiration.

**MATERIALS AND METHODS**

After taking the approval of Ethical and Scientific Committee of Mansoura University, all the patients were counseled in details about the procedure, type and duration of anesthesia, possible complications, chance of success and the possible need for follow up therapy. A written and verbal consent was obtained from all the participating couples. The procedure was performed in Fertility Care Unit, Mansoura University Hospital in the period from August, 2003 to June, 2006.

The study included 30 patients with high-order multifetal gestations (more than 3 fetuses), 17 of them received their infertility therapy in our unit and 13 were referred from private clinics. Ten pregnancies resulted from controlled ovarian stimulation and IUI, 11 pregnancies resulted from ovulation induction with gonadotrophins (n=10) or clomiphene citrate (n= 1) and the other 9 pregnancies following IVF/ET therapy.

Pregnancies included, before reduction: 22 quadruplet gestations (group 1) and 6 quintuplets (group 2), and 2 sextuplets (group 3). All pregnancies were reduced to twins by transvaginal ultrasound-guided embryo aspiration which was done as an outpatient procedure under short general anesthesia using Propofol 1%. The mean gestational age at reduction was 7.5 weeks (range 7.0- 8.0 weeks).

As a preliminary step before undergoing the procedure, patients were subjected to transvaginal ultrasound evaluation to verify viability, to detect embryos with inappropriate smaller crown–rump length (CRL) and to select the gestational sacs that will be chosen for reduction.

**Technique**

With the patient in Lithotomy position and under short general anesthesia using Propofol 2-3 mg/kg (Diprivan® 1% ampoule w/v, AstraZeneca UK Limited). Vaginal cleansing with a povidone-iodine solution (U.S.P 7.5% W/V, Nile pharmaceutical company, Cairo, Egypt) was performed. The patient received i.v. antibiotic prophylaxis; Amoxycillin 500 mg and flucloxacillin 500 mg (Fluomox® 1000mg vial, Epico, Egypt)

The ultrasound machinery used was the Digital Sonace 5500 equipped with a 7.5 MHz transvaginal transducer and puncture guide. The uterus was scanned, and the configuration and the position of each gestational sac relative to the uterine cavity and to each other were identified.

An oocyte retrieval needle (CCD Catalog # 1301001A France) 17 gauge 30 cm with 1.6 mm outer diameter was introduced through the puncture guide and was advanced briskly through the vaginal fornix and the uterine wall aligned with the biopsy needle guideline on the screen into the previously chosen embryo with the inappropriate CRL. However, in cases with all embryos having normal CRLs, the needle was introduced into the most easily accessible sac. The needle tip was positioned into the fetal echoes and suction was applied abruptly and repeatedly with a Labotect aspirator 4014 (Labotect, GmbH, Germany) adjusted to a maximum pressure of 200 mmHg until
Table 1. Type of embryo reduction and early postoperative complications

<table>
<thead>
<tr>
<th>Embryo reduction</th>
<th>Cases (n)</th>
<th>Spotting (n)</th>
<th>Vanishing embryo (n)</th>
<th>Infection (n)</th>
<th>Miscarriage ≤ 20 w (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 to 2</td>
<td>22</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>5 to 2</td>
<td>6</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>6 to 2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total no*</td>
<td>30</td>
<td>3 (10)</td>
<td>1 (3.3)</td>
<td>0</td>
<td>2 (6.6)*</td>
</tr>
</tbody>
</table>

*Values in parentheses are percentage

all or most of the embryonic parts as well as the amniotic fluid were aspirated.

Additional sacs were penetrated with the same needle without re-puncturing the vaginal mucosa and uterine wall. Disappearance of the fetal echoes completely or at least absence of fetal cardiac pulsation in any remaining fetal echo should be verified while the needle was in place. After that, the needle was withdrawn.

All the procedures were performed by the same operator (Dr. Hamed Youssef). Patients were discharged 6 hours after the procedure and the number of remaining gestational sacs with pulsating echoes was confirmed.

Postoperative antibiotic treatment, Amoxycillin 250 mg and Flucloxacillin 250 mg (Flumox® 500mg capsules, Epico, Egypt) every 8 hours for 5 days was given. Paracetamol 500 mg (Cetal® 500mg tablets, Epico, Egypt) as an analgesic was also given if needed. Follow up ultrasound examination was performed 1 week after the procedure. All patients received routine antenatal care and regular check up of the pregnancy.

Procedure complications and pregnancy outcomes were reported. The latter was compared with a matched control group included 30 non-reduced spontaneous twin pregnancies present over the same time period of the studied embryo reduction group.

Statistical analysis

Statistical analysis was performed by using SPSS (statistical package of social sciences, Chicago, IL, USA), program version 10, 1999. Data were expressed as mean ± SD. For statistical comparison, t test was used to compare mean patient age, birth weight and mean gestational age at delivery. Chi-square and Fisher, exact tests were used to compare miscarriage, early post surgical complications, malformations, neonatal mortality rates and cesarean section rates. A P-value of 0.05 was considered to be statistically significant.

RESULTS

The average patient aged 32.4 ± 3.5 years. All pregnancies (n = 30) were reduced to twins. The average time required for single embryo aspiration was 2.5 ± 0.5 minutes. All embryo reduction procedures were successfully performed in a single setting, except in two cases with sextuplets, in which selective fetal reduction were completed in two settings because of technical difficulties. In those cases, the number of embryos was reduced to 4 in the first setting, followed by reduction to twins 3 days later.

No complications were reported either due to the surgical procedure or the use of general anesthesia. The incidence of early postoperative complications after embryo reduction, are shown in Table 1. Spotting occurred in 3/30 cases (10%). Embryo vanishing after reduction occurred in one of the sextuplets cases (3.3%). No postoperative infection occurred.

Two pregnancies, 2/30 (6.6%) were lost before 24 gestational weeks. One was in the quadruplet group and the other was in the quintuplet one. The 2 patients miscarried at ten and eleven weeks gestation respectively.

Table 2 shows pregnancy outcome following selective fetal reduction. Twenty patients, 20/30 (66.6%) were delivered prematurely. In one of these patients, delivery occurred at 29 weeks with early neonatal death of both newborns. The other 19 patients (63.3%) delivered between 33 and 36 weeks. The rest 8 patients (26.6%) delivered after
Table 2. Pregnancy outcome following selective fetal reduction

<table>
<thead>
<tr>
<th>Starting no. of embryos at selective termination</th>
<th>Loss at &lt; 24 weeks</th>
<th>Gestational age at delivery (weeks)</th>
<th>Total no.</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 to 2</td>
<td>1</td>
<td>29-32</td>
<td>8</td>
</tr>
<tr>
<td>5 to 2</td>
<td>1</td>
<td>33-36</td>
<td>0</td>
</tr>
<tr>
<td>6 to 2</td>
<td>0</td>
<td>≥37</td>
<td>2</td>
</tr>
<tr>
<td>Total no *</td>
<td>2 (6.6)</td>
<td>1 (3.3)</td>
<td>19 (63.3)</td>
</tr>
</tbody>
</table>

Values in parentheses are percentages

37 completed weeks.

The incidence of early pregnancy complications and neonatal outcomes in reduced pregnancies were similar to that of the matched control group (Table 3). However, the cesarean section rate of reduced twin pregnancies was significantly higher than that of their control group (P < 0.05).

**DISCUSSION**

ART and ovulation induction continue to cause high order multiple gestation with increased perinatal morbidity and mortality as well as maternal morbidity. Selective fetal reduction has been advocated as an effective modality to reduce fetal and maternal risks associated with those pregnancies (9, 19, 21-23).

We report our experience with 30 women who underwent early transvaginal selective embryo aspiration (mean 7.5 weeks gestation, range 7.0 – 8.0 weeks). All pregnancies were reduced to twins.

Table 3. Comparison of reduced twin pregnancies and the control group

<table>
<thead>
<tr>
<th>Complication / outcome</th>
<th>Reduced n = 30</th>
<th>Control n = 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient age (years)*</td>
<td>32.4 ± 3.5</td>
<td>32.1 ± 3.2</td>
</tr>
<tr>
<td>Miscarriage (n)</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Malformation (n)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Gestational age at delivery</td>
<td>35.3 ± 3.2</td>
<td>36.6 ± 2.6</td>
</tr>
<tr>
<td>Delivery (weeks)*</td>
<td>2308 ± 492</td>
<td>2315 ± 481</td>
</tr>
<tr>
<td>Birth weight (gm)*</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Neonatal death (n)</td>
<td>22/28 (78.6)</td>
<td>12/28 (42.85)</td>
</tr>
</tbody>
</table>

* Values are expressed as mean ± SD.
  * Values in parentheses are percentages.
  * P< 0.05

Transvaginal technique has been performed with total or partial embryo aspiration. Single embryo tissue aspiration was compared with KCl solution injection and showed a lower miscarriage rate 8.8% and 30% respectively (15). Another study reported a 6.7% miscarriage rate (19), this compared favorably to 6.6% in our study. However in the collaborative study which was performed by Evans et al., 1996 the miscarriage rate was 11.7% (24).

In our series, performing selective termination in two settings in the 2 sextuplets cases did not increase the risk of pregnancy loss. This finding was also reported by others (19).

Spotting occurred in 3/30 cases (10%) and was self limited in the following week with rest without affecting the outcome of pregnancy. No reported postoperative infection. Actually, our low rates of spotting (10%), miscarriage (6.6%) and absence of infection could be explained by minimal manipulations (single needle entry) and the use of pre and post operative antibiotics. These results are comparable to that reported by Ibérico et al., 2000; miscarriage (7.4%), spotting (11.4%) and infection (1.34%). However, they perform an intracardiac embryo puncture until asystolia is verified without injecting any substance or aspirating any embryonic tissues or amniotic fluid (21).

A potential disadvantage of transvaginal aspiration at 7-8 weeks gestation would be too early interference i.e. before the natural phenomenon of "vanishing twins" could occur. The whole pregnancy may be endangered if additional embryos were lost spontaneously after selective reduction to the desired number of fetuses. However, there is controversy over when spontaneous reabsorption may occur. While some reports point to weeks 9 through 12 (25,26), other
studies reported that 90% of the vanishing cases occur up to the 7th week and never after week 13 (27).

In the present study, embryo vanishing occurred in one patient (3.3%) among sextuplets reduced to twins during the 10th week. This patient continued her pregnancy with the remaining embryo. This result is comparable to that of Ibérico et al. (2000), reporting embryo vanishing in four patients (3%) among those reduced to twins, 3 of them before the 9th week and the other one during the 11th week (21). The observed low incidence of embryo vanishing after reduction in our study might be explained by the fact that the embryo with the smallest CRL is the one that reduced. According to Stern and Coulam, 1992, 79% of compromised cardiac activity and low development among 6 week old embryos end in spontaneous reabsorption, in contrast, only 8% of those with an adequate size for their gestational age resulted in a vanishing embryo (28).

Sebire et al., 1997 reported that when fetal tissue was left in place following incomplete aspiration, this could result in an inflammatory reaction, with prostaglandin and cytokine secretion, thus increasing the severe preterm labor rate and risk of maternal coagulopathy (14). However these did not occur in our patients since only one case (3.3%) in who total aspiration could not be performed delivered at 29 weeks (Table 2).

In our study, most of the cases 19/30 (63.3%) delivered between 33-36 weeks and only 8/30 cases (26.6%) delivered after 37 weeks (Table 2). The mean gestational age at delivery was 35.3 weeks (Table 3) similar to 35.7 weeks reported by Coffler et al. (19) and to 35.6 weeks in the collaborative study (24).

When we compared reduced pregnancies with their respective control group (Table 3), only the CS rate among reduced group was significantly higher (P < 0.05%). However, CS rate in our series (78.6%) is considered to be high in comparison to that reported by Coffler et al. (55.8%) (19), in view of patients request difference and prolonged periods of infertility. As regards the other parameters, no significant was found which could be attributed to the limited number of cases included and the consequent lack of statistical power.

**CONCLUSION**

Early transvaginal ultrasound guided embryo aspiration is a feasible and safe option for the management and prevention of medical and obstetric risks associated with higher order multiple pregnancies resulting from ART and ovulation induction therapy. It could be offered to all patients with 4 or more fetuses in which early reduction to twins should be attempted since the obstetric risks and outcome are acceptable provided that the procedure is carefully planned and performed. Finally, full support should be given to the couples both before and after the procedure.

**REFERENCES**

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