FREE COMMUNICATION

Session 31 – Psychology/Counseling

Tuesday 29 June 2004 10:00–11:30

O-127 Pharmacological treatment of anxiety in women undergoing IVF: results of a prospective, randomized, double-blinded study

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Purpose: Evidence has shown that IVF is a most stressful and emotionally demanding procedure for the infertile women. Psychosocial and counseling interventions have been shown effective in reducing the negative affect of infertility; but pregnancy rates were unlikely to be affected. Since fluoxetine shows some key safety advantages over other compounds in pregnant women, we evaluated effect of this drug in women undergoing their first IVF; to date there are no studies using pharmacological interventions.

Material and methods: 78 nonobese infertile women, free of previous psychiatric treatments, undergoing their first IVF treatment were invited to participate in this approved IRB and NCER project. 62 (79%) patients, aged 23 to 39 yr, agreed to participate and were randomized by a computerized program to receive either oral folic acid (FA) 5 mg/day or fluoxetine hydrochloride 20 mg/day initiated in the preceding treatment cycle luteal phase. These drugs were blinded to both clinicians and the patients, and were administered up to the day of embryo transfer. The women received questionnaires that assess State (S) and Trait (T) anxiety in four phases of the treatment considered as the highest levels of stress: a) before initiation of ovulation (10 days); b) before egg retrieval; c) before embryo transfer, and d) day of the pregnancy test. The data were analyzed with repeated measures analysis of variance and p<0.05 was considered significant.

Results: 2 women in the FA and 5 patients in the fluoxetine group failed to respond to all questionnaires. 9 women discontinued Fluoxetine due to side effects and were considered drop-offs. Serum levels of fluoxetine and norfluoxetine on the day of oocyte retrieval obtained in sampled patients were 180.3±44.5 ng/mL. The average±SD of the scores obtained in each one of the 4 phases are shown in Table1.

<table>
<thead>
<tr>
<th>Material and methods</th>
<th>Results</th>
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<tr>
<td>STAI-S</td>
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<td>STAI-T3</td>
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<td>N=30</td>
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<td>43.1±10.7</td>
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<td>41.9±11.9</td>
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<td>39.9±8.2</td>
<td>41.7±8.6</td>
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<td>41.6±10.4</td>
<td>42.8±8.5</td>
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Discussion: The findings of this trial showed baseline STAI-S levels within the normative test range. Moreover, there were no significant variations on the STAI-S and STAI-T scores at intervals of high anxiety during IVF, implying that short course antidepressive drug intervention neither diminished feelings of anxiety nor the general level of anxiety the women felt in general. Furthermore, reduced compliance in the fluoxetine group could be caused the known possibility by initial worsening of symptoms due to SSRI. Notwithstanding, the data obtained in this socio-culturally homogeneous population strengthens the recommendation of caution before using fluoxetine for alleviating anxiety for patients treated with IVF.

O-128 Infertility, HIV and parenthood motives in South Africa

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Introduction: HIV/AIDS and infertility represent two major reproductive health problems in the developing world. This study explored motives for parenthood and strength of desire for a child among HIV negative patients and their attitudes regarding infertility treatment of HIV positive clients. Previous research in our community has shown that many infertile couples experience considerable social pressure, and at times the need to demonstrate fertility has appeared as important as the need for the actual child. It was thus hypothesized that the motive for wanting a child may influence attitudes towards reproduction in the presence of HIV infection.

Methods: 50 HIV negative infertile couples (100 informants) from a culturally diverse urban community in South Africa who presented to a tertiary institution participated in the study. A standardized questionnaire previously developed in a European setting was administered. This instrument contains 18 individual questions codifying 6 parenthood motives (happiness, well-being, parenthood, identity, continuity and social control) and scales are utilized to measure the strength of desire for a child. In addition, knowledge regarding HIV/AIDS and reproduction and attitudes towards infertility treatment of HIV positive clients were explored. Statistical analysis included factor analysis and Mantel-Haenszel Chi-Square test.

Results: Couples gave many reasons for wanting children. Motives in the realm of social control, although least frequently mentioned, were still endorsed by many of the informants. There was no gender difference in the strength of desire for a child but most informants misjudged their partners' intensity of desire. The majority of participants (88%) opposed infertility treatment in HIV positive, sero-discordant couples and many (47%) did so in sero-discordant couples. These attitudes did not appear to be influenced by motives or strength of desire for a child but they reflected the negative perspective that informants had regarding the outlook for survival of HIV infected adults and children. Factor analysis demonstrated that the 18 individual motives could not be grouped into the six larger categories of parenthood motives as in the original studies. This indicates that infertility and parenthood are constructed differently in our population.

Conclusions: This study offers insight into why couples in our community want to have children and the value they attach to them. Cultural differences in the construct of involuntary childlessness appear to exist between developing and developed world and justify further exploration. Patients not HIV infected had largely negative attitudes towards infertility treatment of HIV positive clients. Where infertility treatment of HIV positive clients is considered these negative attitudes should be addressed for the sake of both subsets of patients. Understanding motives for parenthood forms an important background to the counseling of men and women suffering from infertility.

O-129 Long term psychological outcome after IVF/ICSI

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Introduction: Long-term consequences in IVF/ICSI treatment were scarcely investigated until novel. Previous studies indicated a significant negative emotional response to unsuccessful treatment cycles. In addition, follow-up of couples proved to be a difficult task. The aim of the present cohort study was to obtain insight into psychological follow-up of couples in the years following IVF/ICSI treatment.

Material and methods: A longitudinal prospective cohort study was performed. 398 couples scheduled for the first IVF/ICSI treatment cycle were included. Couples were assessed before the start of the first treatment cycle (T1), after the last cycle (T2) and on average three years after the last treatment cycle (T3). Standardised questionnaires on anxiety and depression were sent. Furthermore, treatment outcome and spontaneous pregnancies were recorded. MANOVA’s for repeated measures with treatment outcome as factor were used to investigate differences in the course of anxiety and depression.

Results: Data on anxiety and depression at T1 and T3 were available in 298 women (77%), whereas a dataset with three assessment moments was available in 173 (44%) women. The cumulative pregnancy rate was 49%. At the time of follow-up 55% (215/389) reported a livebirth. Eleven percent (24/215) of these pregnancies were spontaneously after unsuccessful IVF/ICSI. Furthermore, 7% reported a spontaneous pregnancy following successful treatment. In the whole group (N=298) no significant effect for anxiety, but a significant time (F=6.92; p≤0.01), treatment outcome (F=5.46; p≤0.02) and interaction (time by treatment outcome) effect (F=2.30; p≤0.01) for depression were identified. Post hoc tests revealed a significant decrease in depression in women after successful treatment. No differences were found in unsuccessful women regarding pretreatment and follow-up depression levels.
In further analysing the exact course of anxiety and depression over three moments of measurement, the subgroup (N=173) again revealed a significant time, outcome and interaction effect for depression and additionally a significant interaction effect for anxiety. After successful treatment a significant decrease of both anxiety (t(=2.58; p<0.01) and depression (t(=4.79; p<0.01) between T1 and T3 was observed. However, post hoc t-tests revealed in unsuccessful women an increase in depression from T1 to T2 (t(=1.90; p=0.07), and a decrease from T2 to T3 (t(=1.94; p=0.06). Depression and anxiety scores at T1 and T3 did not differ.

Conclusions: After unsuccessful IVF/ICSI treatment a spontaneous pregnancy rate of 11% was observed. Several years after unsuccessful treatment, anxiety and depression levels, which were initially raised, were found to return to baseline levels. Successful treatment was found to result in a more positive emotional status.

O-130  The impact of hypnosis during embryo transfer
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Introduction and objectives: The procedure of embryo transfer (ET) is known as a stressful event to the patient. It is usually performed without anesthesia. Our study was aimed to investigate whether hypnosis during the ET is able to contribute in terms of successful IVF/ET outcome.

Interventions and methods: It was designed as a case-control study. Ninety-seven IVF/ET cycles with hypnosis during the ET procedure were performed. The cases from the hypnosis group were matched with 98 regular IVF/ET cycles according to the patient age, peak preovulatory estradiol level, number of oocytes retrieved and, number and quality of embryos transferred.

Result(s): The mean age of patients in the hypnosis and the control groups was of 31.8 ± 4.2 and 32.1 ± 4.6 years and the basic FSH levels were 5.9 ± 2.0 and 6.1 ± 2.1, respectively. Ovarian stimulation protocols were similar in both groups. There were comparable mean peak preovulatory estradiol levels and a similar number of mature follicles detected by ultrasound. A mean of 12.7 ± 14.2 and 12.1 ± 5.5 oocytes per retrieval in the hypnosis and the control groups, respectively, were obtained. Likewise, the following mean parameters were found similar between the groups: oocyte fertilization rate, index of embryo quality, number and quality of transferred embryos, difficulty of transfer and type of luteal support.

We have observed 54 clinical pregnancies out of 98 cycles (55.1%) among hypnosis IVF/ET cycles and 30 out of 97 (30.9%) in the control cycles. The difference was found statistically significant (p<0.01). Although, the duration of infertility was found different between the groups: 4.7 ± 3.1 and 7.4 ± 4.3 for the hypnosis and regular IVF/ET patients, respectively, and there was more primary infertility cases among the control group patients, the multiple logistic regression analysis resulted in a significant odds ratio of 2.07 in favor of the hypnosis group.

Conclusions: This study suggest that use of hypnosis during ET may significantly contribute to the successful IVF/ET cycle outcome in terms of increased clinical pregnancy rates. In addition, the patients attitude to the treatment was more favorable.

O-131  Postpartum psychological functioning following ART
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Introduction: There is emerging Australian evidence that ART conception may increase women’s risk of early parenting difficulties. Research into the impact of infertility and infertility treatment on postpartum mood and early mothering is limited and characterized by methodological flaws. The aims of this study are to compare aspects of childbirth and early mothering following ART in a representative sample with existing knowledge of women who have conceived spontaneously and to quantify the impact of infertility and ART on postpartum psychological functioning.

Material and methods: This prospective longitudinal study recruited participants from a consecutive cohort of women with an ultrasound verified viable intrauterine pregnancy at 6 weeks gestation from two ART centres in Melbourne between July and December 2001. The study used mailed questionnaires in early and late pregnancy and 3, 8 and 18 months postpartum. Three months postpartum the questionnaire assessed childhood, maternal physical and emotional health, and infant health and behaviour. It incorporated the Edinburgh Postnatal Depression Scale (EPDS), the Profile of Mood States (POMS), the Intimate Bonds Measure (IBM) and the Vulnerable Personality Scale (VPS). A score reflecting burden of infertility and treatment (BIT) was calculated using 7 factors: maternal age, cause and length of infertility, number of embryo transfers, previous pregnancy losses and live births and use of donor gametes.

Results: Of the eligible 238 women 181 (76%) agreed to participate in the study. By 3 months postpartum 5 had dropped out of the study and 4 had lost the pregnancy leaving a sample of 172. Of these, 166 (96%) completed and returned the questionnaire. Compared with community samples these women were older (34.5 vs 29.8, p<0.001), more likely to have experienced a caesarean section delivery (51% vs 23%, p<0.001), to have had twins (18% vs 3%, p<0.001), to feel anxious about baby care when leaving the hospital (20% vs 6%, p<0.001) and less likely to be breastfeeding at 3 months (64% vs 72%, p<0.015). The prevalence of depressive symptomatology as measured by a score of >12 on the EPDS was comparable to community samples. EPDS score reported in late pregnancy, the baby’s sleep pattern and the VPS, IBM and BIT scores were entered into regression analysis. Together these variables explained 34% of the variance in EPDS at 3 months postpartum. EPDS in pregnancy, baby’s sleep pattern and VPS made significant independent contributions to the variance. Although no correlation was found between the BIT score and measures of postnatal mood, higher BIT scores significantly increased the likelihood of women being dissatisfied with the intra and postpartum care (p=0.015) and of utilization of specialized postnatal services (p=0.04).

Conclusion: A number of differences on aspects of birth and early mothering were found between women in this study and community samples. The degree of difficulty involved in conceiving as calculated by the BIT score can help identify women who may need additional support during childbirth and in the early postpartum following ART.

O-132  ART twins: parenting and child development
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Introduction: Risks associated with multiple births in terms of perinatal mortality, neonatal problems and disability are high and have been well documented both for naturally conceived and assisted reproduction children. However, little is known about the consequences of multiple births following IVF and ICSI for parent-child relationships or the psychological development of the child. Studies of naturally conceived twins show that the high level of stress experienced by parents has an adverse effect on family relationships. In addition, naturally conceived twins have consistently been found to show delayed language development and to obtain lower scores on verbal intelligence and reading tests. The present investigation is the first study of the nature and extent of difficulties in parenting and child development in a large, nationally representative sample of IVF and ICSI families with 3-5-year-old twins.

Materials and methods: 293 families with twins and a matched group of 928 families with singletons, recruited in France through a national organisation established to follow up children conceived by assisted reproduction, were compared on the Parenting Stress Index, the Edinburgh Depression Scale and the Golombok Rust Inventory of Marital Satisfaction to assess stress associated with parenting, depression and marital satisfaction respectively. Behavioural and emotional problems in the child were assessed using the Strengths and Difficulties Questionnaire (SDQ), and developmental delay was assessed using the Denver Developmental Questionnaire.

Results: Mothers of twins were found to show higher levels of parenting stress and depression, but not marital problems, than mothers of singletons. Twins showed significantly lower levels of emotional problems and peer problems, and significantly higher levels of cognitive and motor development, than singletons.
### Session 33 – Paramedical Free Communications 2 (Mixed Topics)

#### O-135 In vitro follicle interaction can influence oocyte maturation in co-cultured pairs of preantral mouse ovarian follicles

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**Introduction:** It has been suggested that follicles might secrete factors that have a direct impact on neighbouring follicles. In vitro culture of follicles offers the possibility to check whether there are direct interactions between follicles. We investigated oocyte maturation after co-culture of different- or like-sized preantral mouse ovarian follicles. Pairs of follicles were cultured in physical contact or separate from each other. Individually cultured follicles served as control.

**Materials and methods:** Preantral mouse follicles were isolated mechanically from ovaries of 14-day-old C57bl/6j x CBA/Ca F1 female mice. Follicles with a diameter ≤ 110µm (small) or > 110-160µm (large) were cultured in α-MEM media with 5% heat inactivated fetal bovine serum, 5 µg/ml insulin, 10 µg/ml transferrin, 5 ng/ml selenium and 100 µl/ml recombinant FSH (Puregon, Organon). Different-sized or like-sized large follicles being in physical contact or not, were cultured in 20 µl droplet under oil for 10 days with medium refreshments every other day. Survival rate and antrum formation were evaluated. On day 10 hCG was administered. On day 11 “in vitro ovulated” mucified cumulus-oocyte-complexes (COCs) were collected. The percentage of MII oocytes was scored.

**Results:** A total of 420 small follicles and 1148 large follicles were obtained: 340 different-sized follicles were cultured as pairs in contact and 352 separate. 212 large like-sized follicles were cultured as pairs in contact and 204 separate; 74 small and 386 large follicles were cultured individually as controls. Co-culture of different-sized follicles in contact gave 98.8% survival, 60.7% antrum formation and 60.7% mucified COCs of which 48.0% contained MII oocytes. The non-contact co-culture of different-sized follicles gave comparable results (97.7%; 55.8%; 61.9% and 49.8% MII oocytes). Co-culture of large like-sized follicles in contact gave 92.5% survival, 60.7% antrum formation and 79.1% mucified COCs of which 57.8% contained MII oocytes. The non-contact co-culture of like-sized follicles gave comparable results (95.1%; 64.9%; 82.5% and 56.1% MII oocytes). Individual culture of small follicles gave 79.7% survival, 28.8% antrum formation and 50.8% mucified COC of which 26.1% MII oocytes. Individual culture of large follicles gave 96.4% survival, 59.4% antrum formation and 87.6% mucified COCs of which 65.9% MII oocytes.

**Conclusion:** The yield of mature oocytes from individual culture of large follicles was significantly higher compared to culture of small or different-sized follicles. It was also consistently higher than in culture of large-like sized follicles.

**Conclusions:** The highest percentage of MII oocytes was obtained in individual culture of large preantral follicles. Co-culture of different-sized follicles did not show a maturation stimulant to the small follicles. When like-sized follicles were cultured together either in contact or separate, inhibition is suggested. These results support the idea of direct follicle-to-follicle interaction.

#### O-136 Blastocyst development of mouse embryos after exposure to hypo- and hyper-osmotic solutions is influenced by zona drilling

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**Introduction:** Cryosurvival of biopsied multicellular human embryos is reduced. In these embryos, blastomere damage is more frequently observed close to the site where the opening was made. For biopsied embryos, the protective function of the zona pellucida during freezing and thawing may have changed. In the past, the osmotic sensitivity of embryos at different stages of development has been tested. So far, however, this was performed...