José Gonçalves Franco Júnior, Ricardo Luiz Razera Baruffi, Ana Lúcia Mauri, Cláudia Guilhermino Petersen, Márcia Siste Campos, João Batista Alcântara Oliveira.

Donation of oocytes as treatment for infertility in patients with premature ovarian failure. Awarded the "Nicolau de Moraes Barros" prize for gynecology

Work carried out at Centro de reprodução Humana da Fundação Maternidade Sinhá Juqueira.

A total of 7 cycles of embryo transfer by oocyte donation were performed on 5 patients with premature ovary failure (POF). All donors were under 35 of age and the recipients average age was 38.6 years. For synchronization between donor and recipient a semi programmed menstrual cycle was used by means of oral contraceptive followed by ovarian stimulation of donor with clomiphene citrate and human menopausal gonadotrophin. The recipients were easily adjusted to the donors by a flexible model of gradually increasing doses of estradiol valerianate. The average number of oocytes donated was 3.14 and average embryo cleavage rate was 80.2%. The average number of embryos transferred was 2.57. Embryo implantation rate was 22.2%. Clinical gestations occurred in 57.1% of the cycles.
This series is probably the first one in Brazilian literature on oocyte donation as treatment for infertility in patients with premature ovarian failure.

UNITERMS: Oocyte Donaion, Premature Ovarian Failure.

Premature ovarian failure (POF) is defined as the cessation of menstrual cycles before age 40 (1), and it occurs in approximately 1% of all women (18). These patients generally present the classical symptoms of amenorrhea, high gonadotrophins and decrease of estrogen plasmatic levels.

During puberty these patients had adequate ovarian function. The etiology of this condition has not yet been clarified, but an autoimmune origin is suspected, as there is evidence of antibodies to ovarian cells which produce steroids, gonadotrophins or its recipients. Mignot et al. (16) studied the presence of antibodies in POF patients and, although unable to identify any specific immunological factor, they verified that 92% of the patients presented autoantibodies.

Rebar et al. (20) reported that in limited cases, POF is not permanent, as evidenced by the spontaneous return of menstrual cycles and even of pregnancies. These patients showed estradiol levels above normal in menopause, and LH levels were higher than FSH levels. However, until the present, no one cause for steroidogenesis, and consequently for failure of the ovulating process, has been singled out.

On the other hand, the cessation of ovarian function as consequence of surgical removal of the ovaries, or even of serious pelvic infection, can bring about a clinical and laboratory condition identical to that of POF.

Until very recently there was no solution to infertility in POF patients, but oocyte donation is now the indicated monitored reproduction method to solve the problem. The first gestation resulting from oocyte donation in a POF patient ended in miscarriage (23).

Some months later, however, Lutjen et al. (12) reported a pregnancy and subsequent birth of a child from an anonymously donated oocyte. Later on, several other

Address for correspondence: Dr. J. G. Franco Jr.
Centro de Reprodução Humana da Maternidade Sinhá Junqueira
R. Dr. Alberto Gonçalves, 1500 – CEP.14085-100
São Paulo – SP – Brazil

authors reported having successfully employed this method (1,8.21).

At present, oocyte donation is indicated not only for infertility treatment in POF patients (premature menopause, ovarian agenesis, bilateral oophorectomy), but also when ovarian functions may be present, such as in repeated failure in collection of oocytes, failure "in vitro" fertilization and even when there is a risk of genetic disease such as in Huntington's chorea.

Patients without ovarian function need exogenous steroids to prepare the endometrium for embryo implantation. Initially steroids were employed, cyclically and steadily, with estradiol periodically raised in the attempt to imitate the usual increases of the follicular phase in a menstrual cycle (12). After menstrual bleeding had begun, a daily dose of estradiol valerianate (EV) was administered, starting with 1 mg/day and progressively increasing to 6 mg in mid-cycle. Daily, as of the 15th day, a progesterone vaginal suppository was introduced (day 15:25 mg. day 16: 50 mg and from day 17 on: 100 mg) until the 26th day of the cycle. Steroids were then suspended, thus bringing on menstruation, and a new cycle was started. In this second cycle various doses of estradiol, progesterone, follicle stimulating hormone (FSH) and luteinizing hormone (LH) were administered, and on the 21st day of the cycle,or exactly 7 days after administration of progesterone, an endometrial biopsy was performed to observe secretion changes and endometrial structure (17). The patient was kept on these hormone replacement cycles until oocyte donation became possible. Synchronization between donor and recipient would be set to happen with the transfer of embryos between the 15th and the 20th day of the recipient's artificial cycle (the ideal was considered between the 17th and 20th days). If this could not be the case, the embryos would be frozen and reserved for transfer during a subsequent cycle.

To overcome the problem of synchronizing cycles between donor and recipient a second model of steroid administration was developed, consisting of the extension of the recipient's follicular phase. In this case progesterone was administered only on the day, or day before collecting the donor's oocytes (1). Serhal & Craft (22), however, suggest that endometrium receptivity for implanting might not be dependent on the dose of estradiol or progesterone; estradiol was thus administered during two to four weeks and progesterone introduced the day before collecting the oocytes. Transformations in the endometrium could usually be observed under a common microscope after 3 to 7 days of administering progesterone; during that same period, electronic microscopy identified modifications in endometrial cells characteristic of endometrial receptivity (17).

Devroey et al. (6,7) also suggest that an efficient system of cryo-freezing the embryos could solve the problems of synchronization between donor and recipient. The embryos from the donor's oocytes would be frozen upon collection and unfrozen at the appropriate moment of the recipient's cycle.

The use of artificial menstrual cycles for transferring embryos from donated oocytes made it possible to study the so-called endometrial receptivity "window" and the successful implanting of an embryo. In lower mammals this "window" is open for only a few hours (24), while in primates it may last up to 3 days (10). From a practical point of view, gestations in patients without ovary function would result from the transfer of embryos to an endometrium which had been exposed to the action of progesterone from 1 to 4 days, as long as it had already been developed by the estrogens.

Twelve days after embryo transfer, HCG is commonly detected, and steroid supplementation maintained until the trophoblastic tissue is able to sustain pregnancy. It is believed that the placenta usually starts production of progesterone around the 7th week of pregnancy. In patients without ovary function, therefore, steroid supplements should theoretically last up to 5 weeks after embryo transfer (4). However, opinions differ, as to the ideal moment to interrupt administration of estradiol and progesterone. Some authors recommend fixed doses of steroids for a determined period, while others base administration on plasmatic levels for final setup (1,8). Estradiol and progesterone administration is frequently interrupted after an average of 12 weeks (interval of 7 to 19 weeks).

The aim of this work was to present, in detail, a successful oocyte donation program for infertility treatment in POF patients; also, to introduce an original synchronization donor-recipient model with oral contraceptives, which reduced the operational costs of the program considerably.

PATIENTS AND METHODS

1. Donors

A total of 7 infertile patients under 35 years of age in perfect health , with negative syphilis and HIV tests, spontaneously accepted to donate their excess oocytes to 5 recipients with POF who were submitted to a program of "in vitro" fertilization.

Ethical and legal rules have not yet been established in Brazil as a guideline for human reproduction centers in their oocyte donation programs. The Federal Council of Medicine plans to issue such guidelines very soon, and it is likely that they will include guarantees for the anonymity of the donors and preclude any profit or commercial motives (# 1358/92 Resolution). In special medical situa-

tions, however, information concerning the donors could be provided, but exclusively to physicians, without the identification of the donor. The clinics, centers or services which use oocyte donation should keep a permanent record of general clinical data, including donors' phenotype characteristics and samples of their cell material.

2. *Ovary stimulation of donors and collecting of oocytes*

In every case in the present project, the menstrual cycle was partially controlled by oral contraceptive of low hormonal dosage (30 μg of ethynyl-estradiol and 75 μg of gestodene beginning on the first day of the menstrual cycle which preceded the planned in "vitro" fertilization (Fig.1). Medication continued until the Monday (last day of use of oral contraceptive) previous to beginning the planned ovary stimulation process. Ovary stimulation was always performed the Saturday following suspension of oral contraceptive. The pill was generally prescribed for a minimum of 21 days and a maximum of 28.

Ovary stimulation was accomplished with two daily doses of clomiphene citrate 50 mg, for five days. On the same day administration of hypophysis gonadotrophins (150 IU of FSH = 150 IU and LH = 150 IU) was started at 48-hour intervals. A daily dose of dexamethasone 0.5 mg was also administered from the first day (at night, before sleep) of ovary stimulation until embryo transfer.

On the eighth day of stimulation the patient's follicle development was evaluated by ultrasonography (with an ATL, Ultramark 4 model) with a 5.0 Mhz vaginal transducer. When a minimum of two or more follicles of 17 mm had been obtained and there was no discharge of endogenous LH (LH levels by immunoenzymatic assay < 5 mIU/ml), approximately 10,000 IU of HCG were administered by intramuscular injection. Aspiration follicular puncture was carried out 34 to 36 hours after HCG, under sedation with etomidate (Hypnomidate). Vaginal asepsis was performed with Ringer's solution and a 17G

Start ovary stimulation in donor

Stop on a Monday
Menstruation

Dexamethasone 0.5 mg /day
BLOCKAGE   1st 2nd 3rd 4th 5th 6th 7th 8th
    5-day interval

                            CLOMIPHENE CITRATE
                            100 mg from 1st to 5th day
                            150 IU of HMG every other day
Oral contraceptive   7th and 8th day
                            Start ultrasound control

Figura 1 – Semi-programmed scheme for ovary stimulation in oocyte donors.

needle was inserted by means of the vaginal transducer until it penetrated the follicle; follicular liquid was then collected by direct aspiration with a 5 ml Discardit syringe. The follicles were not washed.

The oocytes were identified in the follicular liquid and classified for maturity, according to Marrs et al. (13). They were then placed in Nunc plates with Menezo B2 (Api-System)] enriched with 10% of the patient's serum. Between four and six hours after oocyte collection, approximately 50,000 to 150,000 mobile spermatozoids per ml from the recipients' husband, prepared by the ascendent migration technique, were added to the culture where the donor's excess oocytes had been placed. Embryos were identified 56 hours after insemination in order to avoid any meeting of donor and recipient at or near the center (embryo transfer is usually carried out 48 hours after insemination). The embryos obtained were classified as follows: Degree I: blastomeres with over 50% fragmentation; Degree II: blastomeres with 10% to 50% fragmentation; Degree III: irregular blastomeres with less than 10% fragmentation; Degree IV: embryos with 1 to 3 regular blastomeres and no fragmentation; Degree V: embryos with 4 or more regular blastomeres and no fragmentation. The embryos were then placed in pure serum from the recipient and transferred through a Frydman catheter to a site 0.5 cm from the fundus of uterus. The transfers were performed with the patient in dorsal decubiti; she was, then, requested to remain at the clinic during another three hours mandatory rest.

3. *Donor-recipient synchronization*

Synchronization obeyed the steps for stimulating the donor described above. In other words, when the donor started with oral contraceptive (on the 1st day of menstruation), the recipient began taking EV/2 mg dose/day. The donor would then stop taking the oral contraceptive always on a Monday. At this point the recipient's EV dose was increased to 4 mg per day. Likewise, on the 1st day of ovary stimulation of the donor, the recipient's EV dose was raised to 6 mg per day. The next step in adjusting recipient and donor was when ultrasound signalled for administration of HCG in the donor, at which point a daily dose of progesterone was being given to the recipient and lowering EV to 4 mg daily. On the day of embryo transfer, progesterone was increased to 100 mg/day until confirmation or not, of pregnancy (Table 1). If pregnancy occurred, EV was raised to 8 mg per day and hormonal substitution maintained for a minimum of 12 weeks and a maximum of 15 weeks. Doses for hormone replacement were based on circulating steroid levels, and an attempt was made to keep estradiol levels at ≥ 2000 pg/ml and progesterone at ≥ 50 ng/ml (9).
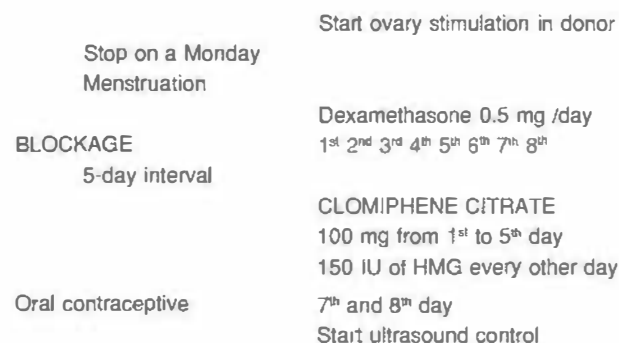
Table 1
Steps in synchronizing donor and recipient

Step	Donor	Recipient
Coupling	1st.day pill	2 mg EV
Monday	Stop pill	4 mg EV
Saturday	1st.day stimulation	6 mg EV
Friday		Ultra sound
HCG	10,000 IU	4 mg EV + 50 mg P4
Embryos transfer	48 hours	56 hours
On transfer day		4 mg EV + 100 mg P4
Pregnancy		8 mg EV + 100 mg P4

4. Recipients

Case 1 – AP, age 35, infertile for the last 8 years. In 1975 she was submitted to a left oophorectomy for post-miscarriage infection and in 1985 developed POF. An exploratory laparotomy was performed two years later with biopsy of the right ovary, which showed absence of follicles (in the anatomopathological test). Husband's sperm count revealed azoospermia. Clinical and gynecological examination results were normal. At pre-treatment uterus measured 6.5 cm and ultra-sound showed no uterine alterations. HIV tests showed negative for both husband and wife. The patient became pregnant after the second series of embryos transfer (a total of 5 embryos were produced: Degree I, I; Degree III, 2; Degree IV, 2) from donated oocytes and sperms.

Case 2 – AL, age 41, married 3 years, with clinical and laboratory diagnosis of premature menopause for 2 years. Clinical and gynecological examinations normal. Presently taking hormone medication. Uterine cavity measured 6.5 cm. Ultra-sound on the day previous to donor's arrival for control indicated an 11 mm endometrium with "3 line" pattern. Husband showed normal sperm count. Syphilis and HIV tests for both were negative. The first embryo transfer resulted in pregnancy (total of 2 embryos: Degree IV = 1; Degree V = 1).

Case 3 – MK, age 31, married 10 years with secondary infertility. In 1985 she developed POF after bilateral salpingo-oophorectomy by endometriosis. Presently undergoing hormone treatment. Uterine cavity measured 6.5 cm and showed no alterations under ultra-sound. Husband's sperm count normal. Syphilis and HIV tests were negative for both. The first embryo transfer resulted in pregnancy (total of 3 embryos: Degree II=3).

Case 4 – DH, age 42, married 7 years. Sought treatment for POF at the center 3 years ago after ovarian sur-

gery for endometriosis. Showed high level of gonadotrophins (FSH = 59.5 mIU/ml. LH = 47 mIU/ml) and low plasmatic estradiol levels (16.3 pg/ml). Uterine cavity measured 5.0 cm. Husband's sperm count was normal. She became pregnant after the second embryo transfer (total of 4 embryos: Degree III = 1; Degree IV = 2; Degree V = 1). Endometrium measured 9.0 mm, hyperecogenic pattern two days before embryo transfer.

Case 5 – MM, age 44, married for 14 years. Amenorrhea for 10 years after taking Enduxan as therapy for polymyositis. Clinical and gynecological exams normal. Uterine cavity measured 7.0 cm. Ultrasound performed the day before donor's arrival identified an endometrium 10 mm thick with "3 line" pattern. First embryo transfer failed.

RESULTS

The results obtained are shown in Table 2. The recipients had an average age of 38.6 years. The average number of oocytes donated was 3.14; average cleavage rate was 80.2%, and average number of embryos transferred, 2.57. The rate of embryo implantation was 22.2%. Clinical gestation, defined by ultra-sound on the 6th week, with identification of gestational sac and embryo with heart beats, occurred in 57.1% of the cycles.

DISCUSSION

The results obtained in this series of oocyte donations for correcting infertility in POF patients are encour-

Table 2
Oocyte donation program: age of recipients, number of oocytes donated, cleavage rates, number of embryos transferred and clinical pregnancies (series of 7 cycles).

Recipient	Age	Oocytes donated	Cleavage rates %	Embryos transferred	Clinical pregnancy
AP	35	2	50	1	negative
AP	35	5	80	4	positive
AL	41	2	100	2	positive
MK	31	3	100	3	positive
DH	42	3	66	2	negative
DH	42	4	100	4	positive
MM	44	3	66	2	negative

aging (incidence of clinical pregnancy of 57.1% per cycle of uterine embryo transfer, and 22.2% embryo implantation rate, which is at least twice that obtained in our usual IVF program). This rate of pregnancy, however, is similar to the 57.9% mentioned by Balmaceda et al. (3) after uterine transfer, and the 53.8% obtained by Formigli et al. (9) using oocytes donation by more invasive technique such as gamete intra-fallopian transfer (GIFT). Nevertheless, they differ from those described by Asch et al. (2), who referred to 75% success applying GIFT on 8 POF patients using oocytes donation.

The record of "in vitro" fertilization and embryos transfer by oocytes donation in the United States (14) showed that 498 patients received 547 transfers (there are no references to type: uterine or tubal), 160 having resulted in clinical gestations (29%) and 122 deliveries (22%).

The present data on oocytes donation programs for POF patients using "in vitro" fertilization with embryo transfer to the uterus or tubes present higher rates of clinical gestations than in patients with normal ovary function submitted to the same techniques for correction of infertility (19). This fact was also observed in our "in vitro" fertilization program, which showed rates of 27.5% of clinical gestations per cycle in 1992, far lower than that obtained in cases of oocyte donation in the same institution that same year. As a reason for this fact, it is speculated that stimulation of the endometrium or of the tubal epithelium by hyper stimulation of the ovaries could be a negative factor toward the chances of obtaining pregnancy.

On the other hand, the ideal site for the transfer of embryos obtained by oocyte donation is discussed. Some authors state that the embryos generated "in vitro" and transferred to the tubes produced high rates of implantation when compared to those transferred directly to the uterus (6,25). The main arguments are related to better conditions for embryo development in the tubes and in the perfect timing for the embryos to enter the uterus. Although the theoretical arguments have a physiological basis, the data which support the superiority of tubal transfer are retrospective, non-randomized and fail to analyze other fundamental variables such as the age of the patients and embryos quality.

Balmaceda et al. (3) confirm high rates of pregnancy in an oocyte donation program and report in a prospective study that in the cycles of hormone replacement with uniform endometrium stimulation there is no advantage in transferring the embryo to the fallopian tube rather than to the uterus. As a result, 23 (54.7%) gestations were obtained for a total of 42 patients. In the group with uterine transfers 12 out of a total of 22 patients (54.5%) became

pregnant, while 11 gestations were obtained in 20 patients (57.9%) using tubal transfers. They also mention that embryo quality and endometrial receptivity would seem to be more important variables than the moment for transferring the embryo to the uterus.

In our service, patients submitted to the fertilization "in vitro" program for correcting infertility are the source of the donated oocytes. Since synchronization between donor and recipient is a critical step for success, the preliminary results made it clear that a semi-programmed cycle regulated by oral contraceptives is an efficient means to this objective. Besides this, its low operational cost and the possibility of preparing more than one donor for the same period, with enough time to prepare recipients, are important aspects.

Controlling hormone replacement in the recipient is one of the aspects cited as being of major importance. Some authors attempt to give great importance to prior adjustment of the ideal estradiol and progesterone doses to be administered later, in the embryo transfer cycle, including an obligatory hormone evaluation by endometrial biopsies. In the present series all previous laboratory or histological evaluations were dispensed with for determining hormone replacement doses, before or during the embryo transfer cycle. Only ultrasonography analyses of endometrial thickness (ideal: ≥ 6 mm) and of endometrial pattern (ideal: 3 lines) were the basis for adjusting hormone replacement doses. Since the endometrial receptivity window in humans consists of 3 to 5 days of exposure of the endometrium to progesterone (15), the 4th day was established in this present project as the best moment for transferring the embryo to the recipient. Pregnancy rates obtained in this series of oocyte donations in POF patients seem to support this protocol.

If the recipient conceives, hormone replacement can be performed steadily or in alternation, according to steroid rates in the blood. Efforts are usually made to keep hormone levels close to those which occur in normal pregnancies: estradiol > 2000 pg/ml and progesterone > 50 ng / ml (9). In the present series of oocyte donations, plasmatic estradiol rates served as a guide for EV replacement, which varied from 8 mg to 12 mg per day. Progesterone was almost always kept at 100 mg daily. Hormone evaluations were needed to adjust dosage.

One of the points which demands further analysis is the moment to discontinue hormone replacement. Csapo et al. (5) showed that fetus/placenta hormone production occurs between the 7th and 8th week of gestation. Hormone therapy could, therefore, be interrupted during this period. Nevertheless, a fall in steroid rates in the blood could indicate a return to therapy. In the present program, the general rule for discontinuing hormone medication was

15 weeks, except in cases where the placenta had clearly taken on steroid production before this time.

This series would seem to be the first to be published in Brazilian literature on oocyte donation in treating infertility in POF patients.

REFERENCES

1. ASCH, R.; BALMACEDA, J.; ORD,T.; BORRERO, C.; CEFALY,E.; GASTALDI,C.& ROJAS,F.—Oocyte donation and gamete intrafallopian transfer as treatment for premature ovarian failure. Lancet, I: 687, 1987.

2. ASCH, R. H.; BALMACEDA, J.; ORD,T.; BORRERO, C.; CEFALY, E.; GASTALDI, C. & ROJAS, F.—Oocyte donation and gamete intrafallopian transfer as treatment for premature ovarian failure. Fertil Steril, 49: 263-267, 1988.

3. BALMACEDA, J. P.; ALAM, V.; ROSZJTEIN, D.; ORD, T.; SNELL, K. & ASCH, R. H. – Embryo implantation rates in oocyte donation : a prospective comparison of tubal versus uterine transfers. Fertil Steril, 57: 362-365, 1992.

4. CAMERON, I. T.; ROGERS, P. A. W.; CARO,C.; HARMAN, J.; HEALY, D. L. & LEETON, J. F. – Oocyte donation : a review. Br J Obstet Gynaecol, 96: 893-899, 1989.

5. CSAPO, A. I.; PULKKINEN, M. O. & WEIST, N. G.—Effects of lureectomy and progesterone replacement therapy in early pregnant patients. Am J Obstet Gynecol, 115: 759, 1973.

6. DEVROEY, P.; CAMUS, M.; VAN DELL ABBEEL, E.; VAN WAESBERGHE, L.; WISANTO, A. & VAN STEIRTEGHEM, A. C. – Establishment of 22 pregnancies after oocyte and embryo donation. Br J Obstet Gynaecol, 96: 900-906, 1989.

7. DEVROEY, P.; STAESSEN,C.; CAMUS, M.; DEGRAUWE, E.; WISANTO, A. & VAN STEIRTEGHEM, A. C. – Zygote intrafallopian transfer as a successful treatment for unexplained infertility. Fertil Steril, 52 : 246-249, 1989.

8. FEICHTINGER, W. & KEMETER, P. – Pregnancy after total ovariectomy achieved by ovum donation. Lancet, II: 722-723, 1985.

9. FORMIGLI, L.; ROCCIO, C.; BELOTTI, G.; STANGALINI, A.; COGLITORE, M. T. & FORMIGLI, G. – Oocyte donation by gamete intra-fallopian transfer to amenorrhoeic and cycling patients given replacement steroids. Hum Reprod, 4: 772-776, 1989.

10. HODGEN, G. D. – Surrogate embryo transfer combined with estrogen-progesterone therapy in monkeys : implantation, gestation and delivery without ovaries. JAMA, 250: 2167-2171, 1983.

11. JAFFE, R. B. – The menopause and perimenopausal period. In Reproductive Endocrinology. Edited by S.S.C. Yen, R.B. Jaffe. Philadelphia, W.B. Saunders, 406, 1986.

12. LUTJEN, P. J.; TROUNSON, A. O.; LEETON, J. F.; FINDLAY, J. K.; WOOD, E. C. & RENOU, P. M. – The establishment and maintenance of pregnancy using "in vitro" fertilization and embryo donation in a patient with primary ovarian failure. Nature, 307: 174-175, 1984.

13. MARRS, R. P.; SAITO, H.; YEE, B.; SATO, F. & BROWN, J. – Effect of "in vitro" culture techniques upon oocyte fertilization and embryo development in human "in vitro" fertilization procedures. Fertil Steril, 41: 519-524, 1984.

14. MEDICAL RESEARCH INTERNATIONAL, The Society for Assisted Reproductive Technology – "In vitro" fertilization / embryo transfer in the United States : 1990 results from the IVF-ET registry. Fertil Steril, 57: 15-24, 1992.

15. MELDRUM, D.R.; WISOT, A.; HAMILTON, F.; GUTLAY-YEO, A. L.; MARR, B. & HUYNH, D. –Artificial agonadism and hormone replacement for oocyte donation. Fertil Steril, 52: 509-511, 1989.

16. MIGNOT, M. H.; SCHOEMAKER, J.; KLEINGELD, M.; RAMANATH RAO, B. & DREXHAGE, H. A – Premature ovarian failure. I : The association with autoimmunity. European Journal of Obstetrics & Gynecology and Reproductive Biology, 30: 67-72, 1989.

17. MURPHY,C.R.; ROGERS,P.A.W.; LEETON,J.F.; HOSIE, M.; BEATON, L. & MACPHERSON, A.- Surface ultrastructure of uterine epithelial cells in women with premature ovarian failure following steroid hormone replacement. Acta Anat, 130: 348-350, 1987.

18. OSKARSSON, T.; EDGAR, D. H.; WHALLEY, K. M. & MILLS, J. A. – Clinical and biochemical pregnancy in two recipients without ovarian function following gamete intrafallopian transfers using oocytes from a single donor. Scot Med J,35: 114-115, 1990.

19. PAULSON, R. J.; SAUER, M. V. & LOBO, R. A. – Embryo implantation following human "in vitro" fertilization : importance of endometrial receptivity. Fertil Steril, 53: 870-874, 1990.

20. REBAR, R. W.; ERICKSON, G. F. & YEN, S. S. C. – Idiopathic premature ovarian failure : clinical and endocrine characteristics. Fertil Steril, 37: 35-37, 1982.

21. ROSENWAKS, Z.; VEECK, L. L. & HUNG-CHING, L. – Pregnancy following transfer of "in vitro" fertilized donated oocytes. Fertil Steril ,45: 417-420, 1986.

22. SERHAL, P. & CRAFT, I. – Simplified treatment for ovum donation. Lancet, I: 687-688, 1987.

23. TROUNSON, A. O.; LEETON, J.F.; BESANKO, M.; WOOD, E. C. & CONTI, A. – Pregnancy established in an infertile patient after transfer of a donated embryo fertilized "in vitro". Br Med J, 286: 835-838, 1983.

24. WU, J. T. & CHANG, M. C. – Effects of progesterone and estrogen on the fate of blastocysts in ovariectomized pregnant ferrets : preliminary study. Biol Reprod, 7: 231-237, 1972.

25. YOVICH,J.L.; BLACKLEDGE, D.G.; RICHARDSON,P.A.; MATSON, P.L.; TURNER, S.R. & DRAPER, R. – Pregnancies following pronuclear stage tubal transfer. Fertil Steril 48: 851-857, 1987.

RESUMO

Um total de 7 ciclos de transferência de embriões provenientes da doação de oócitos foram realizados em 5 pacientes portadoras de insuficiência ovariana precoce. As doadoras possuíam idade inferior a 35 anos, e as receptoras, apresentavam idade média de 38.6 anos. No esquema de sincronização entre doadora e receptora usou-se um ciclo semiprogramado com pílula, seguido de estimulação da doadora com citrato de clomifeno e gonadotrofina menopausal humana. As receptoras foram facilmente acopladas com as doadoras através de um modelo flexível de doses crescentes de valerianato de estradiol. O número médio de oócitos doados foi de 3.14, a taxa de clivagem embrionária média de 80.2%, sendo o número médio de embriões transferidos de 2.57. A taxa de implantação embrionária foi de 22.2%. As gestações clínicas ocorreram em 57,1% dos ciclos.

Provavelmente, essa série é a primeira apresentada na literatura nacional sobre a doação de oócitos no tratamento da infertilidade em pacientes com insuficiência ovariana precoce.