Fertility preservation in breast cancer patients: IVF and embryo cryopreservation after ovarian stimulation with tamoxifen

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BACKGROUND: Breast cancer chemotherapy commonly causes premature ovarian failure and infertility. Because increased estrogen levels are thought to be potentially risky in breast cancer patients, natural cycle IVF (NCIVF) has been used to preserve fertility and treat infertility in these women. METHODS: Twelve women with breast cancer received 40–60 mg tamoxifen for 6.9 ± 0.6 days beginning on days 2–3 of their menstrual cycle (15 cycles), and had IVF (TamIVF) with either fresh embryo transfer (six cycles) or cryopreservation (nine cycles). They were compared to a retrospective control group (n = 5) who had natural cycle IVF (NCIVF, nine cycles). RESULTS: Cycle cancellation was significantly less frequent in TamIVF, compared with NCIVF (1/15 versus 4/9, P < 0.05). Compared with NCIVF, TamIVF patients had a greater number of mature oocytes (1.6 ± 0.3 versus 0.7 ± 0.2, P = 0.03) and embryos (1.6 ± 0.3 versus 0.6 ± 0.2, P = 0.02) per initiated cycle. TamIVF resulted in the generation of embryo(s) in every patient (12/12) while only three out of five patients had an embryo following NCIVF. Two out of six patients in TamIVF, and 2/5 in NCIVF conceived. One patient in the TamIVF group delivered a set of twins. After a mean follow up of 15 ± 3.6 months (range 3–54), none of the patients had a recurrence of cancer. CONCLUSIONS: Tamoxifen stimulation appears to result in a higher number of embryos and may provide a safe method of IVF and fertility preservation in breast cancer patients.

Key words: breast cancer/fertility preservation/IVF/ovarian stimulation/tamoxifen

Introduction

Breast cancer is the most common malignancy in women of reproductive age, and of the 180 000 new cases in the USA each year, 25% occur before menopause and 15% are diagnosed in the reproductive age group (<45 years of age) (Hankey et al., 1994; Higgins and Haffty, 1994; Bines et al., 1996). These young women are most commonly treated with modified radical mastectomy or lumpectomy, followed 4–6 weeks later by combination chemotherapy including cyclophosphamide [cyclophosphamide, methotrexate and 5-fluorouracil (CMF)]; or Adriamycin and cyclophosphamide (AC); with or without taxol] (Hortobagyi, 2001; National Institute of Health Consensus Development Panel, 2001). Cyclophosphamide is an alkylating agent and its adverse effects on reproduction have been well established. Women receiving cyclophosphamide are four times more likely to develop ovarian failure, compared with controls (Meirow and Nugent, 2001). One study has shown that the likelihood of immediate ovarian failure with CMF and AC regimens increases with age, being 78 and 38% respectively, for a 40 year old breast cancer patient (Goodwin et al., 1999). Because each course of chemotherapy will result in the loss of a significant portion of ovarian reserve (Meirow et al., 2001), even those who do not immediately become menopausal following chemotherapy are likely to experience infertility and early menopause (Meirow, 2000; Poniatowski et al., 2001). Further hurdles exist for women who have remained fertile after the completion of chemotherapy. Although clinical data are lacking, many experts do not recommend pregnancy for at least a 2–5 year recurrence-free interval after breast cancer diagnosis and treatment (Gallenberg and Loprinzi, 1989; Del Mastro et al., 1997; Gemignani et al., 1999). By the time this 2–5 year period has passed, many more patients who have not immediately experienced menopause after chemotherapy will become infertile due to ageing and diminished ovarian reserve.

As the awareness of the adverse effects of breast cancer chemotherapy on reproduction increases, many patients are seeking assisted reproductive strategies to preserve their fertility. Ovarian cryopreservation and transplantation are experimental strategies that have been used to restore ovarian

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Tamoxifen and IVF in breast cancer

Tamoxifen is a non-steroidal triphenylethylene anti-estrogen that was originally synthesized in the UK as a contraceptive (Harper and Walpole, 1966). It was then found to stimulate follicle growth and used as an ovulation induction agent in Europe (Klopper and Hall, 1971), while a related compound, clomiphene, became a commonly used ovulation induction agent in the USA (Charles et al., 1966). It was then discovered that tamoxifen had suppressive effects on breast carcinoma (Jordan, 1976), and it became a drug of choice in breast cancer treatment and prophylaxis worldwide (Early Breast Cancer Trialists Collaborative Group, 1992; Mourits et al., 2001).

In this study, we prospectively studied tamoxifen as an ovarian stimulating agent for IVF, embryo cryopreservation and embryo transfer in breast cancer patients. These were compared with a retrospective group of patients, who had undergone natural cycle IVF (NCIVF). Tamoxifen has been used for the treatment of anovulatory patients for many years (Suginami et al., 1993; Crosignani et al., 1999) but it has never been used as an ovarian stimulant in IVF cycles. Our aim was to develop a safe ovarian stimulation protocol specific to breast cancer patients. We hypothesized that tamoxifen stimulation would result in higher numbers of embryos compared with NCIVF, while theoretically shielding breast cancer cells against estrogen.

Materials and methods

This study was approved by the Institutional Review Board at the Weill Medical College of Cornell University. Patients were referred by their medical or surgical oncologists, and those with stage IV cancer were excluded. Patients were started on 40 mg/day of tamoxifen (AstraZeneca, Washington, DC) on the second or third day of their menstrual cycle, after baseline FSH, LH, and estradiol (E2) levels were obtained. After 5 days of tamoxifen administration, ultrasound and the E2, FSH and LH measurements were performed. If on that ultrasound, no ovarian follicle development >10 mm was noted, the dose was increased to 60 mg. Patients were monitored with ultrasound and E2, FSH and LH measurements every 1–2 days, until the day of oocyte retrieval. When the leading follicles reached 14 mm, urinary LH testing was additionally performed four times a day to detect a premature LH surge. If an LH surge was suspected prior to follicle maturity, a GnRH antagonist (250 μg, Antagon; Organon Inc., West Orange, NJ, USA) was administered concurrently with 150 IU of hMG (Pergonal; Serono, Norwell, MA, USA), to maintain follicle growth. In the latter case, tamoxifen was continued until administration of hCG (Profasi; Serono, Norwell, MA, USA). When the leading follicle reached a mean diameter of 17 mm, 10 000 IU of hCG was administered i.m., and the oocyte retrieval was performed 36 h later. IVF was performed via ICSI, as reported previously (Palermo et al., 1996). Embryos were frozen at the 2-pronuclear stage. In cases where patients had a history of breast cancer and were suffering from infertility, the same protocol was used, except the embryos were transferred on the third day following oocyte retrieval. For each patient, peak E2 was determined on the day of hCG administration; if the cycle was cancelled, the highest estradiol level prior to cancellation was considered to be the peak. Follow-up information was obtained by telephone interview with the patient and the medical oncologist to determine whether any documented recurrence occurred since the IVF treatment.

The control group was retrospectively selected from breast cancer patients who had previously undergone natural cycle IVF to freeze embryos for fertility preservation between 1992–2000. In NCIVF, no GnRH antagonist or ovarian stimulation was used, and the monitoring, ICSI and embryo cryopreservation/transfer protocols were identical to the tamoxifen group.

Statistics

To compare the percentage of cancelled cycles and the embryos generated per patient between the two groups, Fisher’s exact test was used. The Mann–Whitney test was used to compare the number of cycles per patient in each group. ANOVA was used for all other comparisons. Values of $P < 0.05$ were considered statistically significant.

Results

There were 15 cycles in 12 patients in the tamoxifen group, and nine cycles in five patients in the control group. The characteristics of all patients are shown in Table I. The mean age and baseline FSH levels between treatment and control group patients were similar. All patients reported normal menstrual cycles. There was no difference in the proportion of patients undergoing IVF after chemotherapy; one out of 12 in TamIVF, and one out of five in NCIVF underwent IVF cycle after chemotherapy ($P = 0.5$).

Patients received on average $6.9 \pm 0.6$ days of tamoxifen (range 5–12 days) at a mean dose of 48.3 (40–60 mg). The comparison of cycle characteristics between the treatment and control groups is shown in Table II. Even though the difference in the number of follicles >17 mm and the oocytes retrieved did not reach significance between treatment and control groups, the total number of mature oocytes was higher in the tamoxifen group ($P = 0.03$). This resulted in a significantly higher number of embryos/retrieval, in the tamoxifen treatment group, compared with natural cycle (1.6 versus 0.6 respectively; $P = 0.02$). Peak estradiol levels were also significantly higher in the tamoxifen group, reflecting the growth of a greater number of mature follicles. This was consistent with the finding that the
tamoxifen group experienced a trend towards a higher number of follicles >17 mm on the day of hCG administration \(P = 0.07\) (NS). When cycles where a GnRH antagonist and hMG were given \((n = 5)\) were compared to those without GnRH antagonist and hMG administration \((n = 10)\), there was no difference in peak estradiol levels \([405.8 \pm 45.6 \text{ pg/ml} \text{ versus } 460.7 \pm 43.6 \text{ pg/ml}, P = 0.45\) (NS)], number of mature oocytes recovered \([1.4 \pm 0.2 \text{ versus } 1.7 \pm 0.4, P = 0.64\) (NS)], or embryos generated \([1.4 \pm 0.2 \text{ versus } 1.7 \pm 0.4, P = 0.64\) (NS)].

In the tamoxifen group, nine patients attempted one cycle, and three attempted two cycles of IVF. Of these 12 patients in the TamIVF group, eight intended embryo cryopreservation in nine cycles, prior to chemotherapy; and four patients attempted pregnancy with fresh embryos in six cycles, after being ‘cured’ from breast cancer. In the former group, a 24 year old patient (patient 8 in Table I) had received prior chemotherapy but she underwent embryo cryopreservation with TamIVF before her second chemotherapy due, to recurrent cancer. In the latter group, two patients had two IVF cycles each, and two patients underwent one IVF cycle. Two of these patients had received radiotherapy for breast cancer 3 years before IVF treatment (patients 11 and 12 in Table I) and the other two did not receive any adjuvant therapy after surgery (patients 1 and 5). IVF indications were tubal factor (patient 1), male factor (patient 11) and unexplained infertility (patients 5 and 12). All patients were disease free and were ‘cleared for pregnancy’ by their oncologists. Patient 1 conceived a singleton pregnancy during the second attempt, following the transfer of four embryos. However, this pregnancy resulted in a spontaneous abortion at 8 weeks. Patient 5 conceived a twin pregnancy on the second attempt, following the transfer of two embryos, and delivered a healthy boy and girl. None of the patients with frozen embryos has, as yet, undergone embryo transfer.

In the control group (NCIVF), one patient attempted one cycle and four patients attempted two cycles each. The mean number of cycles per patient was similar between the TamIVF and NCIVF groups \((1.25 \text{ versus } 1.8\) respectively; \(P = 0.08\). In NCIVF, two patients had four cycles for embryo cryopreservation prior to chemotherapy, and three patients intended to have fresh embryo transfer after being cured from cancer in five cycles. Among these, patient 15 (Table I) attempted IVF because of male factor infertility, which resulted in a term pregnancy. This patient had received chemotherapy 8 years before undergoing IVF. Patient 12 also attempted pregnancy with fresh embryos 18 months after cancer diagnosis, conceived, and delivered a healthy girl. She had only received radiotherapy. In total, of the fresh transfer cycles, 2/6 in TamIVF, and 2/5 in NCIVF resulted in a pregnancy. In NCIVF, one patient attempted pregnancy after thawing two previously frozen embryos, but did not conceive.

In the tamoxifen group, only 1/15 cycles were cancelled due to spontaneous ovulation, a day prior to oocyte retrieval. This patient attempted a second cycle, which resulted in cryopreservation of an embryo. In all other cycles in the tamoxifen group, at least one embryo was generated. Thus, all 12 patients in the tamoxifen group had one or more embryos for cryopreservation or fresh transfer. There was no difference in cycle cancellation rates between those who used GnRH antagonists and those who did not \((P = 0.5)\). In the control group, 4/9 cycles were cancelled \((P < 0.05)\), and an embryo was generated in only 3/5 patients \((P = 0.07)\). In two cycles, patients ovulated prior to retrieval; in one, follicle growth halted at an early stage and in the other no fertilization occurred. A 44 year old patient (patient 11) underwent three consecutive IVF cycles. Interestingly, the first two unstimulated cycles did not yield an embryo, while the third cycle with tamoxifen resulted in an embryo. Patient 12 underwent NCIVF at ages 38 and 39, followed by a TamIVF at the age of 42, which all resulted in the generation of a single embryo.

Mean follow-up after the completion of the IVF procedures was 15 ± 3.6 months (range 3–54). All patients were recurrence free, and had survived at the time of this report.

### Table I. Age at first IVF, cancer stage and adjunctive treatment type of tamoxifen treated (TamIVF) and natural cycle (NCIVF) patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Cancer Stage</th>
<th>Adjunctive treatment</th>
<th>TamIVF</th>
<th>NCIVF</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>42</td>
<td>DCIS</td>
<td>None</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>39</td>
<td>II</td>
<td>AC&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>36</td>
<td>II</td>
<td>AC+T&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>42</td>
<td>II</td>
<td>AC+T&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>38</td>
<td>DCIS</td>
<td>None</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>40</td>
<td>II</td>
<td>CMF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>37</td>
<td>II</td>
<td>AC&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>24</td>
<td>IIIB</td>
<td>AC+T&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>29</td>
<td>II</td>
<td>AC+T&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>36</td>
<td>II</td>
<td>AC&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>44</td>
<td>DCIS</td>
<td>RT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>38</td>
<td>I</td>
<td>RT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>37</td>
<td>III</td>
<td>AC&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>40</td>
<td>I</td>
<td>CMF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>39</td>
<td>I</td>
<td>CMF+RT</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Age at first IVF cycle; when patients underwent multiple cycles, age at the time of IVF cycle was used for comparing NCIVF and TamIVF.

<sup>a</sup>IVF cycle performed before chemotherapy
<sup>b</sup>IVF cycle performed after chemotherapy
<sup>c</sup>Had received CMF 2 years prior; second chemotherapy was given due to recurrence

DCIS = ductal carcinoma in situ; A = Adriamycin; C = Cyclophosphamide; T = Taxol; M = Methotrexate; F = 5-fluouracil; RT = radiotherapy; CMF = cyclophosphamide, methotrexate and 5-fluouracil.

### Table II. Comparison of cycle characteristics and embryo yield between tamoxifen treated (TamIVF, 12 patients, 15 cycles) and natural cycle (control, NCIVF, five patients, nine cycles) patients

<table>
<thead>
<tr>
<th>Variable (years)</th>
<th>TamIVF</th>
<th>NCIVF</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>37.9 ± 1.4</td>
<td>40 ± 0.9</td>
<td>NS</td>
</tr>
<tr>
<td>Baseline FSH (mIU/ml)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>11.5 ± 1.2</td>
<td>9.5 ± 2.3</td>
<td>NS</td>
</tr>
<tr>
<td>Peak E&lt;sub&gt;2&lt;/sub&gt; (pg/ml)</td>
<td>442.4 ± 32.6</td>
<td>278 ± 39.9</td>
<td>0.006</td>
</tr>
<tr>
<td>Total follicles</td>
<td>1.3 ± 0.2</td>
<td>1.3 ± 0.3</td>
<td>NS</td>
</tr>
<tr>
<td>Mature follicles</td>
<td>1.2 ± 0.11</td>
<td>0.9 ± 0.1</td>
<td>0.07</td>
</tr>
<tr>
<td>Total oocytes</td>
<td>1.8 ± 0.3</td>
<td>1.7 ± 0.7</td>
<td>NS</td>
</tr>
<tr>
<td>Mature oocytes</td>
<td>1.6 ± 0.3</td>
<td>0.7 ± 0.2</td>
<td>0.03</td>
</tr>
<tr>
<td>Total embryos</td>
<td>1.6 ± 0.3</td>
<td>0.6 ± 0.2</td>
<td>0.02</td>
</tr>
</tbody>
</table>

<sup>a</sup>Normal value <20 mIU/ml.

<sup>d</sup>Day of hCG administration.

NS = not significant.
Discussion

There are ~180 000 new cases of breast cancer annually in the USA alone, and 15% of these women are of reproductive age (Hankey et al., 1994; Higgins and Haffty, 1994; Bines et al., 1996; Goodwin et al., 1999). As a result, it has been estimated that >25 000 women are possibly exposed to gonadotoxic chemotherapy and may immediately or subsequently suffer from ovarian failure and infertility. Here we report a novel use of tamoxifen to perform ovarian stimulation in an attempt to preserve fertility and treat chemotherapy-related infertility via IVF embryo cryopreservation, and embryo transfer after breast cancer diagnosis. We exploited tamoxifen’s dual action as an ovarian stimulating drug and an anti-neoplastic agent, to increase the yield of embryos compared with natural cycle IVF. We demonstrated that a higher number of embryos could be obtained in breast cancer patients with tamoxifen stimulation. Strikingly, we found that women with breast cancer who previously underwent oocyte retrieval and IVF without stimulation (natural cycle) had a relatively poor yield, with only 3/5 patients’ IVF cycles resulting in embryo formation. In contrast, we were able to obtain at least one embryo in every patient in the tamoxifen group. Thus, tamoxifen helped a higher proportion of patients to potentially preserve their fertility and attempt pregnancy.

There were five cycles where GnRH antagonists were used to prevent a spontaneous LH surge in TamIVF. In these cases, follicle growth was maintained with hMG administration. One can question whether this was responsible for the improved outcome. However, there was no difference in peak estradiol, number of mature oocytes recovered, and embryos generated between the patients who used GnRH + hMG and those who did not. This is not surprising because we used GnRH antagonists only during the last 1–2 days of stimulation, after follicles were recruited. Interestingly, we had excluded a rectal cancer patient who had NCIVF for embryo cryopreservation prior to chemo- and radiotherapy, and who used GnRH antagonists and hMG. This patient’s peak estradiol was 198 pg/ml; only one mature oocyte was obtained but the cycle was cancelled due to failed fertilization. It is still possible, however, that the difference in cycle cancellation rates between NCIVF and TamIVF was at least partly due to antagonist use. Thus we see antagonist use as an integral part of our protocol. Because of lack of a flare-effect (Reissmann et al., 1995), antagonists are more suitable for breast cancer patients than the GnRH agonists.

Another estrogen agonist/antagonist drug related to tamoxifen is clomiphene. However, we chose tamoxifen because of the extensive clinical experience in the treatment of breast cancer with this agent, and laboratory evidence that it has a better suppressive effect on cell proliferation and tumorigenesis (Math et al., 1984). Another advantage of tamoxifen is that, in contrast to clomiphene, it does not antagonize endometrial development (Marttunen et al., 2001). Clomiphene’s antagonistic effect can result in suboptimal endometrial development for embryo implantation in some patients (Cook et al., 1984; Fritz et al., 1987; Massai et al., 1993). Even though no published study has compared tamoxifen to clomiphene vis-à-vis IVF success rates, tamoxifen at least does not appear to alter implantation rates, as has been suggested for clomiphene (Gerhard and Runnebaum, 1979; Messinis and Nillius, 1982; Boostanfar et al., 2001). In those patients undergoing fresh embryo transfer, this may prove to be another advantage of TamIVF.

We also report the occurrence of pregnancy and live birth after tamoxifen stimulation, IVF and embryo transfer. This is, to our knowledge, the first report of IVF pregnancy after tamoxifen stimulation. However, because most patients in the tamoxifen group cryopreserved their embryos and have not yet undergone embryo transfer, and, in contrast, most patients in the NCIVF group had a fresh embryo transfer, we are not yet able to compare pregnancy rates between these two protocols.

Of the two patients who conceived in the tamoxifen group, one miscarried at 8 weeks of pregnancy. This patient was 42 years old, and her risk of spontaneous abortion was already high due to her age. The other patient recently delivered a healthy set of twins. Thus, we could not provide long-term data on the effects of tamoxifen on pregnancy outcome. However, tamoxifen has been used extensively for ovulation induction in anovulatory patients in other countries (Gerhard and Runnebaum, 1979; Ruiz-Velasco et al., 1979; Messinis and Nillius, 1982), and recently in the USA (Boostanfar et al., 2001) without any adverse effects on fetal development. Moreover, one study reported lower miscarriage rates with tamoxifen, compared with clomiphene (Wu, 1997). These studies also show comparable pregnancy rates between tamoxifen and clomiphene stimulated patients and indicated that tamoxifen was better tolerated. Concerns have been raised regarding the safety of tamoxifen administration in women attempting pregnancy, based mainly on studies in laboratory animals (Furr et al., 1976; Sweet and Kinzie, 1976; Sadek and Bell, 1996; Halakivi-Clarke et al., 2000) and a few case reports of dissimilar anomalies (Cullins et al., 1994; Tewari et al., 1997) which did not establish a cause–effect relationship. In contrast, the long-term experience with tamoxifen, and its close relative clomiphene, in ovulation induction does not suggest a teratogenic effect. Moreover, when used for the purpose of ovarian stimulation, the drug is discontinued prior to ovulation or oocyte retrieval. In the case of IVF, early stage embryos are not exposed to tamoxifen as fertilization takes place in vitro. Further support giving evidence for the safety of tamoxifen use in assisted reproduction is found in a previous study that showed a lack of detrimental effects of tamoxifen on oocyte and early embryo development (Fisk et al., 1989). In that study, volunteers undergoing tubal ligation procedures were given 80 mg of tamoxifen on the day before oocyte retrieval. Even though tamoxifen was detected in substantial amounts in follicular fluids of patients, there was no statistical difference in fertilization rates in vitro between tamoxifen-treated patients and controls (80 and 68% respectively). In addition, the morphological characteristics of the oocytes, the rates of cleavage and the concentrations of estradiol, progesterone and androstenedione in follicular fluid were similar in the two groups. These results suggest that even high-dose tamoxifen does not adversely affect the final stages of maturation or the fertilization and early cleavage of human oocytes. Consistent
with the latter study, there has been one published case report of a male fetus exposed to tamoxifen throughout the entire pregnancy. Even though the birth was premature, no congenital anomalies were noted (Isaacs et al., 2001). Based on this evidence, it appears that the short-term administration of tamoxifen for ovarian stimulation does not pose a risk to the fetus, and in fact it has been used extensively for ovulation induction in Europe and elsewhere. However, because of the long half-life of tamoxifen, women who are on long-term tamoxifen therapy may have higher serum levels of tamoxifen, and should not conceive while taking this drug.

Peak estradiol levels were higher in the TamIVF than the NCIVF and this may raise concerns regarding stimulation of breast cancer cells. When patients are placed on long-term tamoxifen therapy for breast cancer treatment and prophylaxis, mean estradiol levels are chronically elevated, and can be much higher than the peak levels reported in our study (Shushan et al., 1996; Klijn et al., 2000). Yet, tamoxifen reduces breast cancer incidence in these patients, indicating that this drug can even block the effects of supraphysiological levels of estrogen on breast tissue. Nevertheless, aromatase inhibitor drugs have recently been used in ovulation induction (Fisher et al., 2002), and we are conducting a prospective study to test their value for fertility preservation in breast cancer patients as they may not result in a rise in estradiol levels.

Short-term use of tamoxifen for ovarian stimulation and embryo transfer or cryopreservation appears to be a feasible method of fertility preservation in breast cancer patients. However, this study had several limitations; the NCIVF group was retrospective and small, and the follow-up of cases with TamIVF was relatively shorter. Long-term follow-up will be required to determine the pregnancy rates with cryopreserved embryos after TamIVF. To maximize the patients’ future chance of pregnancy, women of reproductive age with breast cancer should be referred to an appropriate assisted reproduction centre as soon as the diagnosis is made in order to enable patients to discuss their options for fertility preservation.

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References


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