Do female translocations influence the ovarian response pattern to controlled ovarian stimulation in preimplantation genetic diagnosis?

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BACKGROUND: Ovarian response in female translocation carriers is not well understood. We aimed to evaluate the impact of chromosomal autosomal balanced translocations on the ovarian response to controlled ovarian stimulation (COS) in female carriers undergoing IVF and PGD.

METHODS: In a retrospective study, we included all female translocation carriers who underwent PGD at our centre. We compared these patients to female patients from couples with male translocation carriers who underwent PGD.

RESULTS: Results from 79 cycles of PGD from 33 female translocation carriers were compared with 116 cycles from 55 male translocation carriers. No difference was observed for patient characteristics: female age, anti-Müllerian hormone or antral follicle count. No difference in COS parameters was observed for the total dose of recombinant FSH, the number of retrieved oocytes and embryos on Day 3, for unaffected and transferred embryos. For the two groups, pregnancy rate was similar per cycle (12.7 versus 20.7%, \( P = 0.208 \)). Multivariate analysis demonstrated that female translocation carriers had a significantly higher estradiol level on the day of hCG administration (+540 pg/ml, \( P = 0.05 \)).

CONCLUSIONS: This paper is the largest to report ovarian response of female translocation carriers. This study showed that the ovarian response to COS was not impaired by balanced translocation status, suggesting that female chromosomal structural abnormalities did not influence the results of COS in PGD. Thus, female carriers of balanced translocations could be considered normal responders and standard doses of gonadotrophins used for ovarian stimulation.

Key words: PGD / chromosomal autosomal translocation / female carrier / ovarian response / controlled ovarian stimulation

Introduction

Balanced chromosomal translocations affect 0.16% of the population and involve reciprocal and Robertsonian translocations (Van Dyke et al., 1983; Giardino et al., 2009). Chromosomal abnormalities occur in 5–10% of couples who experience recurrent miscarriages (Sachs et al., 1985; Campana et al., 1986; Fortune et al., 1988; De Braekeleer and Dao, 1990; De la Fuente-Cortes et al., 2009). Translocation carriers present a higher risk of reproductive complications, such as recurrent abortion, stillborn or live born fetuses with unbalanced translocations, than people without chromosomal translocations. The risk of abortion was estimated at 20–33% in couples with Robertsonian translocation carriers and 47–53% in couples with reciprocal translocation carriers (Neri et al., 1983; Ozawa et al., 2008). Thus, to avoid recurrent miscarriages or unbalanced progeny, translocation carriers may opt for a PGD with embryo biopsy and transfer of balanced embryos (Verlinsky and Kuliev, 2003). PGD represents an alternative to prenatal diagnosis, which allows an important reduction in the frequency of early pregnancy loss and a decrease in the time required to obtain an ongoing pregnancy (Otani et al., 2006; Fischer et al., 2010).

The number of realized PGD cycles for chromosomal abnormalities is increasing, with an estimated 3524 oocytes retrievals at the end of 2006 (Goossens et al., 2009) that have demonstrated the feasibility of...
PGD for the identification of unbalanced translocations in embryos (Van Assche et al., 1999; Scriven et al., 2000; Hanson et al., 2001; Melotte et al., 2004). However, ovarian function, IVF parameters and controlled ovarian stimulation (COS) response have been poorly investigated in female translocation carriers.

In male autosomal translocation carriers, severe oligospermia is often observed (Sasagawa et al., 1993; Penna Videau et al., 2001; Rao et al., 2005), probably due to meiotic disturbances that lead to cell cycle arrest and spermatogenesis impairment (Solari, 1999; Leng et al., 2009). In female translocation carriers, balanced X:autosomal translocations are also described as being associated with gonadal dysfunction and premature ovarian failure, particularly when the breakpoints fall within critical regions that are involved in the maintenance of ovarian function (Therman et al., 1990; Schlessinger et al., 2002). Some cases of balanced autosomal Roberstonian and reciprocal translocations associated with premature ovarian failure have been reported (Hens et al., 1989; Tuley et al., 1998; Burton et al., 2000; Tullu et al., 2001; Kummer et al., 2009). These few cases are insufficient to conclude that impaired ovarian function resulted in these female translocation carriers. Only one study on the ovarian response to COS during IVF was performed, and that study evaluated the ovarian response in female translocation carriers who were treated with COS and IVF–PGD. That study concluded that there was a higher proportion of low responders, suggesting an abnormal pattern of ovarian response to COS and ovarian failure (Chen et al., 2005).

To clarify ovarian function and ovarian response in female translocation carriers, we evaluated the ovarian response to COS and IVF–PGD in the patients treated in our PGD program. We compared the COS parameters and PGD outcomes to those of female patients from couples with male chromosomal translocation carriers who underwent PGD to investigate if the sex of the carriers influences the ovarian response and PGD outcomes.

**Materials and Methods**

**Patients**

Between January 2003 and September 2009, 88 couples were referred to our IVF unit seeking PGD for either male or female partners carrying a balanced translocation.

Because translocations involving gonosomes are thought to be associated with ovarian dysfunction, we only included female patients with autosomal translocations. The karyotypes of each patient are listed in Tables I and II for female and male carriers, respectively. All women were tested for basal hormonal level on Day 3 of a previous menstrual cycle (serum FSH and estradiol) and for ovarian reserve with anti-Mu¨llerian hormone (AMH) and antral follicle count (AFC), which was estimated for both ovaries. Only patients with an AFC $> 4$ for both ovaries or AMH $> 1$ ng/ml were included in our PGD program. Patients with polycystic ovary syndrome (PCOS) as defined by Rotterdam consensus workshop group were excluded [The Rotterdam European Society for Human Reproduction (ESHRE)/American Society of Reproductive Medicine (ASRM)-Sponsored PCOS consensus workshop group, 2004].

**Controlled ovarian stimulation**

Ovarian stimulation was achieved using one of two protocols depending on the estimated ovarian response. (i) Long protocol used 3 mg of the GnRH, triptorelin 3 mg (Decapeptyl, Ipsen, France) administered intramuscularly on the first day of the cycle. Fourteen days later, pituitary desensitization was confirmed by estradiol $< 50$ pg/ml and follicle size $< 10$ mm. Ovarian stimulation involved recombinant gonadotrophin (rFSH, Puregon, Organon, France or rFSH, Gonal-F, Merck Serono, France). For the first attempt, the physician determined the starting dose of gonadotrophins. In our reproductive centre, the starting dose of daily administered FSH varied from 150 IU to a maximum of 300 IU. The starting dose was determined according to various clinical factors, such as age, BMI, FSH on Day 3, AMH and AFC. The daily dose was kept constant during the entire ovarian stimulation because we did not perform the step-up protocol during COS. In the case of a cancelled cycle or failed attempt, for the following cycle, the dose of FSH was adapted according to the previous ovarian response to COS. (ii) The GnRH antagonist protocol used gonadotrophin stimulation starting from Day 2 with the addition of 0.25 mg/day of a GnRH antagonist (Cetrorelix, Cetrotide, Serono, France or Orgalutran, Organon, France) when the leading follicle achieved a diameter of 14 mm or when the estradiol level was $> 400$ pg/ml. The cycle was monitored by assessment of the plasma levels of LH and estradiol in conjunction with ultrasonography starting on Day 6. Additionally, 5000 IU of hCG (Human Chorionic Gonadotrophin Endo, Organon, Putaux, France) was administered when at least six follicles $> 17$ mm were observed by ultrasound and when the E2 plasma level was $> 1000$ pg/ml.

In our PGD program, due to planning organization, the GnRH long-agonist protocol was preferentially chosen for the first attempt. In the case of a cancellation and abnormal ovarian response to COS (poor response or high response), a switch from GnRH long-agonist protocol to the GnRH antagonist protocol was often implemented.

Transvaginal ultrasound-guided oocyte retrieval was scheduled 36 h after hCG administration under local or general anaesthesia.

All oocytes obtained were inseminated by ICSI to prevent residual contamination by sperm DNA. The ICSI procedure was performed in our unit as already reported. After fertilization, zygotes were cultured in specific culture media.

**Biopsy procedure**

The biopsy procedure was carried out on cleavage stage embryos on Day 3. Two blastomeres were removed from embryos that contained seven or more blastomeres. When the embryo contained less than seven blastomeres, only one blastomere was removed. Embryo biopsy was accomplished by making a hole in the zona pellucida using a Zylos laser (Hamilton-Thorn, Beverly, MA, USA). One or two blastomeres were gently aspirated with a biopsy pipette through the hole for cytogenetic analysis. Blastomeres used for PGD were checked for the presence of a nucleus.

**Genetic diagnosis**

Translocation cytogenetic hybridization analysis was performed on blastomeres using fluorescent in situ hybridization. The probe sets selected depended on the chromosome translocation and are detailed in Tables I and II. A minimum of three subtelomeric probes were used for reciprocal translocations and a combination of two probes for Robertsonian translocations (Munne et al., 2000). This approach cannot differentiate between normal and balanced embryos.

**Embryo transfer**

Only normal or balanced embryos were accepted for transfer, which was performed on Day 4 post-insemination.
Patients received vaginal natural micronized progesterone supplementation (Utrogestan, 200 mg, Besins, International, France) for luteal support three times a day until the pregnancy test 2 weeks later.

**Outcome parameters**

Patient characteristics are recorded and summarized in Table III: female age, BMI, hormonal status on Day 3 (FSH and estradiol) and ovarian reserve (AFC and AMH). Parameters of COS are reported in Table IV: duration of COS, dose of FSH administrated, cancellation rate, cancellation rate for poor response, estradiol level on the day of hCG administration, number of retrieved oocytes, number of embryos and the number of biopsied, unaffected and transferred embryos. The reproductive outcome was clinical pregnancy rate calculated per transfer and per cycle. Clinical pregnancy was defined as an intrauterine gestational sac with a fetal heartbeat seen at transvaginal ultrasound scan 5 weeks after embryo transfer.

**Statistical analysis**

A bivariate analysis was performed to characterize the sample and to determine the potential determinants of the two groups (female and male translocation carriers). Therefore, patient characteristics as well as clinical and biological parameters were compared for the first cycle (a Kruskal–Wallis test was performed due to the distribution of the biological variables). The $\chi^2$ test was used for factors.

For multivariate analysis, estradiol level on the day of hCG administration was chosen as the end-point to evaluate ovarian response to COS. The link between the outcome (estradiol level on the day of hCG administration) and all patient characteristics was studied to select the variables to be introduced in the multivariate analysis. To assess the correlation between two numerical covariates, a Pearson correlation coefficient was proposed with the associated $P$-value. The link between the outcome and the factors was assessed by a Kruskal–Wallis test and the variables were selected at a risk level of 20%.

While adjusting for other covariates, we then used a multivariate analysis to investigate if the sex of the translocation carriers was a determinant of the estradiol level on the day of hCG administration. The normality of the estradiol level that day was determined as the end-point to evaluate the ovarian response to COS. The particularity of the data set was that for each patient, several cycles could have been completed. This implies a correlation between the cycles of each patient and violates the hypothesis of independence between observations. This particularity has to be taken into account to have accurate estimations. Therefore, a mixed model was performed. A backwards procedure was used to select the significant covariates, step by step. All variables that were not significant at a risk level of 5% were excluded from the model. The final model determined which covariates were significant for the estradiol level on the day of hCG administration and measured the effect of the sex of the carrier. All studies were performed with R Software version 2.10.0 (http://cran.r-project.org/).

**Results**

**Patient characteristics**

The data from 195 PGD–fluorescence in-situ hybridization cycles from 88 couples with balanced translocations were evaluated; 33 patients
were female carriers (female carrier group) and led to 79 cycles and 55 patients (62.5%) from couples with male carriers (male carrier group) led to 116 cycles.

The bivariate analysis of female characteristics (Table III) showed no difference in age between the two groups (33.2 ± 3.6 and 32.6 ± 3.5 years in the female carrier group and male carrier groups, respectively, *P* = 0.532). BMI was comparable in the two groups (21.9 ± 3.4 and 22.7 ± 3.8 kg/m² in the female carrier group and male carrier groups, respectively, *P* = 0.345). No difference was observed in the basal hormonal status on Day 3. Parameters of ovarian reserve were similar in the two groups (AMH was 3.5 ± 2.2 and 3.8 ± 3.1 ng/ml, *P* = 0.547) and AFC was 13.7 ± 5.4 and 14.4 ± 5.0 (*P* = 0.355) in the female carrier and male carrier groups, respectively).

### COS parameters and results

The COS parameters are summarized in Table IV. The distribution of the different types of protocol was similar in the two groups (*P* = 0.678). Bivariate analysis showed that the duration of COS was similar in the two groups (9.9 ± 1.3 days in the female carrier group and 9.9 ± 1.5 in the male carrier group, *P* = 0.444). The dose of FSH administrated was identical in the two groups (2052 and 1918 IU, respectively, *P* = 0.348). The level of estradiol on the day of hCG administration was significantly higher in the female carrier group (2781 versus 2215 pg/ml, *P* < 0.001). No difference was observed for the number of retrieved oocytes (12.7 versus 12.5, respectively, *P* = 0.870), the number of matured oocytes (10.24 versus 10.27, *P* = 0.889) and the number of embryos on Day 3 (8

### Table III Patient characteristics.

<table>
<thead>
<tr>
<th>First cycle</th>
<th>Female carriers (n = 33 patients)</th>
<th>Females from couple with male carrier (n = 55 patients)</th>
<th><em>P</em>-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female age (years)</td>
<td>33.2 ± 3.6</td>
<td>32.6 ± 3.5</td>
<td>0.532</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>21.9 ± 3.4</td>
<td>22.7 ± 3.8</td>
<td>0.345</td>
</tr>
<tr>
<td>FSH (IU/l)</td>
<td>6.2 ± 1.5</td>
<td>7.0 ± 1.9</td>
<td>0.115</td>
</tr>
<tr>
<td>Estradiol (pg/ml)</td>
<td>39.5 ± 20.6</td>
<td>42.5 ± 18.7</td>
<td>0.325</td>
</tr>
<tr>
<td>AMH (ng/ml)</td>
<td>3.5 ± 2.2</td>
<td>3.8 ± 2.1</td>
<td>0.547</td>
</tr>
<tr>
<td>AFC</td>
<td>13.7 ± 5.4</td>
<td>14.4 ± 5.0</td>
<td>0.355</td>
</tr>
</tbody>
</table>
normal responders and suggested the feasibility of PGD for these patients. Moreover, we observed a high pregnancy rate per transfer in female translocation carriers that was similar to the rate previously described (Munne et al., 2000; Lim et al., 2004; Fischer et al., 2010; Goossens et al., 2009; Keymolen et al., 2009).

To date, our study involved the largest cohort studied to analyse the COS results in female translocation carriers: 33 female translocation carriers and 79 PGD–IVF cycles. To identify abnormal ovarian response and to analyse PGD outcomes considering embryo biopsies, we compared cycles in this female translocation group to a control group of male translocation carriers who underwent PGD. Women

### Table IV COS parameters and results (all cycles).

<table>
<thead>
<tr>
<th></th>
<th>Female carriers (n = 79)</th>
<th>Male carriers (n = 116)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agonist GnRH protocol</td>
<td>57/79 (72.2%)</td>
<td>88/116 (75.9%)</td>
<td>0.6778</td>
</tr>
<tr>
<td>Antagonist protocol</td>
<td>22/79 (27.8%)</td>
<td>28/116 (24.1%)</td>
<td></td>
</tr>
<tr>
<td>Cancellation rate</td>
<td>12/79 (15.19%)</td>
<td>32/116 (26.7%)</td>
<td>0.0631</td>
</tr>
<tr>
<td>Cancellation rate for poor response</td>
<td>10/79 (12.66%)</td>
<td>21/116 (18.10%)</td>
<td>0.4114</td>
</tr>
<tr>
<td>Duration of COS (days)</td>
<td>9.9 ± 1.3</td>
<td>9.9 ± 1.5</td>
<td>0.4445</td>
</tr>
<tr>
<td>Total dose of FSH (IU)</td>
<td>2052 ± 790</td>
<td>1918 ± 758</td>
<td>0.3481</td>
</tr>
<tr>
<td>Estradiol level on the day of hCG administration (pg/ml)</td>
<td>2781 ± 1291</td>
<td>2215 ± 1559</td>
<td>0.0004</td>
</tr>
<tr>
<td>No. of retrieved oocytes</td>
<td>12.7 ± 4.6</td>
<td>12.5 ± 5.4</td>
<td>0.8703</td>
</tr>
<tr>
<td>No. of matured oocytes</td>
<td>10.24 ± 4.1</td>
<td>10.27 ± 4.7</td>
<td>0.8895</td>
</tr>
<tr>
<td>No. of fertilized oocytes</td>
<td>7.43 ± 4.1</td>
<td>6.93 ± 3.6</td>
<td>0.5702</td>
</tr>
<tr>
<td>No. of embryos on Day 2</td>
<td>7.9 ± 3.9</td>
<td>7.1 ± 3.5</td>
<td>0.3299</td>
</tr>
<tr>
<td>No of embryos on Day 3</td>
<td>8.0 ± 4.0</td>
<td>7.4 ± 3.4</td>
<td>0.6116</td>
</tr>
<tr>
<td>No. of biopsied embryos</td>
<td>5.8 ± 3.2</td>
<td>5.2 ± 3.1</td>
<td>0.1910</td>
</tr>
<tr>
<td>No. of transferred embryos</td>
<td>1.28 ± 1.5</td>
<td>1.69 ± 1.7</td>
<td>0.1413</td>
</tr>
<tr>
<td>Clinical pregnancy rate per cycle</td>
<td>10/79 (12.7%)</td>
<td>24/116 (20.7%)</td>
<td>0.2081</td>
</tr>
<tr>
<td>Clinical pregnancy rate per transfer</td>
<td>10/40 (25%)</td>
<td>24/56 (42.9%)</td>
<td>0.1125</td>
</tr>
<tr>
<td>Implantation rate</td>
<td>10/68 (14.7%)</td>
<td>32/102(31.4%)</td>
<td>0.0222</td>
</tr>
</tbody>
</table>

### Table V Results of multivariate analysis: determinants of estradiol level on the day of hCG administration.

<table>
<thead>
<tr>
<th>Fixed effects</th>
<th>Value</th>
<th>Std. Error</th>
<th>t-value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Intercept)</td>
<td>2029.99</td>
<td>310.56</td>
<td>6.53</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Female from couple with male carrier</td>
<td>−540.11</td>
<td>271.56</td>
<td>−1.99</td>
<td>0.0503</td>
</tr>
<tr>
<td>AMH</td>
<td>193.96</td>
<td>63.19</td>
<td>3.1</td>
<td>0.0028</td>
</tr>
<tr>
<td>Random effects (Std dev Confidence Intervals)</td>
<td>Lower Estimate Upper</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Random effect (Intercept)*</td>
<td>526.11</td>
<td>788.58</td>
<td>1181.97</td>
<td></td>
</tr>
<tr>
<td>Random effect (Residual)*</td>
<td>1057.17</td>
<td>1220.94</td>
<td>1410.08</td>
<td></td>
</tr>
</tbody>
</table>

*These parameters were introduced to consider the link within the cycles of each couple. The parameters are only needed to estimate fitted values. The fixed effect interpretation does not change.

### Discussion

The main findings of our study were that female translocation carriers had a normal pattern of response to COS and that translocation did not influence the ovarian response in an IVF–PGD procedure. These results led us to consider female translocation carriers as normal responders and suggested the feasibility of PGD for these
The aim of our study was to characterize the COS pattern of female translocation carriers, leading us to conduct our analysis in two steps. First, we performed a comparison of patient characteristics and COS parameters using a bivariate analysis. Then, we conducted a multivariate analysis to identify the factors that influence ovarian response and, in particular, the effect of sex of the carrier on the estradiol level on the day of hCG administration. These results suggest that female translocation carriers presented a good ovarian response with higher estradiol level on the day of hCG administration (+540 pg/ml in female carriers). The observation of a higher estradiol level on the day of hCG in female translocation carrier was unexpected, while patients characteristics, COS parameters and number of retrieved and mature oocytes were similar in the two groups. According to our knowledge, two factors could lead to a higher level of estradiol on the day of hCG: the type of protocol, with higher estradiol level in agonist protocol (Albano et al., 2000; Borm and Mannaerts, 2000; European and Middle East Orgalutran Study Group, 2000) and patients with PCOS profile (MacDougall et al., 1993). In our study, the distribution of the type of protocol used was similar in the two groups and multivariate analysis with adjustment on type of protocol confirmed higher estradiol level on the day of hCG in female translocation carrier. Then, in our study, due to exclusion of PCOS patients, higher estradiol level on the day of hCG could not be explained by the presence of PCOS patients. The reason and the link between an increased steroidogenesis and female translocation carrier were unclear and remain to be confirmed and elucidated. The absence of increased ovarian deficiency or poor results in IVF–PGD in female translocation carriers was also reported by Keymolen et al. (2005). They reported results from 10 years of PGD experience for Roberstonian translocations with 76 couples and 124 cycles and found similar numbers of oocytes (14.4 in female carriers and 14.6 in male carriers) as well as similar pregnancy rate per cycle and per transfer regardless of the sex of the carrier. They concluded that the sex of the carrier had no effect on controlled ovarian response and PGD outcomes.

Similarly, the ninth report of the ESHRE PGD consortium published data from January to December 2006 on 3524 oocytes retrieval PGD cycles for chromosomal abnormalities (Goossens et al., 2009). Only PGD outcomes were studied, and the results were analysed according to the sex of the carrier and the type of translocation. The clinical pregnancy rate per cycle was similar regardless of the sex of the carrier and the type of translocation. Due to the absence of information about COS parameters in that study, it could only be concluded that the sex of the carrier had no effect on the pregnancy rate. However, only retrieved oocytes cycles were recorded without any data concerning cancellation rate.

Subsequently, Munné et al. (2000) analysed 47 PGD cycles with 35 translocation carriers. Even if no data were available on ovarian reserve and COS parameters, they did not notice any effect of the sex of the carrier on the pregnancy rate.

Our results are in contrast with a previous study (Chen et al., 2005) that analysed ovarian patterns in PGD for female translocation carriers. They chose the estradiol level on the day of hCG administration as the end-point and considered all patients with an estradiol level <1500 pg/ml to be low responders. They found a higher rate of low responders in female translocation carriers than in females.
from couples with the male translocation carriers (42.6 versus 23.8%, \(P = 0.49\)). Low estradiol level on the day of hCG administration is often used as a marker of poor ovarian response to COS even if the cut-off varies among studies and remains poorly established (Keay et al., 1997; Tarlatzis et al., 2003). In our study, we chose to cancel the cycle when the estradiol level on the day of hCG administration was <1000 pg/ml or when the number of follicles was <6. However, the higher cut-off chosen by Chen et al. (>1500 pg/ml) could lead to an over-classification of some mild or normal responders as low responders. Different poor-response criteria could explain the higher rate of poor responders in our study and the differences with the present study. Nevertheless, when investigating ovarian response, the mean number of oocytes retrieved in the female carrier group (16.3) was elevated and higher than the number we observed (12.7), suggesting an adequate ovarian response in patients who reached oocyte retrieval (Chen et al., 2005).

Our study showed that female translocation carriers were normal responders to COS with standard doses of gonadotrophins (2052 IU per COS). Actually, the number of oocytes obtained was 12.7 and led to 5.8 embryos and 1.28 unaffected embryos that were suitable for transfer. This rate of balanced embryos was similar to that already observed in previous studies of embryo PGD analysis (Munné et al., 2000; Lim et al., 2004; Otani et al., 2006; Fischer et al., 2010; Keymolen et al., 2009) and oocyte polar body analysis (Durban et al., 2001). The higher rate of aneuploidy involving other chromosomes than those implicated in translocation was also described in oocytes from female translocation carrier (Pujol et al., 2003). The impact of COS on balanced embryo and aneuploidy rates in translocation carriers is unknown. In patients undergoing IVF for infertility, Baart et al. (2007) compared mild and standard stimulation on embryo aneuploidy rate and demonstrated that mild stimulation was associated with a decreased aneuploidy rate but a similar pregnancy rate. These observations suggested an association between dose of gonadotrophins and aneuploidy oocyte rate. With PGD cycles, using high dose of gonadotrophins would be theoretically interesting to obtain high number of oocytes and embryos. However, impact of high dose on aneuploidy rate in oocytes and embryos from translocation carrier is unknown. In our study, we used a standard protocol of COS with a standard dose of FSH, allowing the observation of an adequate ovarian response and sufficient available embryos for transfer. To decrease the balanced translocation rate and because female translocation carriers were good responders with standard doses of gonadotrophins, one could hypothesize that there are benefits associated with standard stimulation. However, its efficiency could be evaluated in PGD cycles.

**Conclusion**

Female translocation carriers had an adequate ovarian response to COS for IVF–PGD. The presence of translocations did not influence the ovarian response to COS. In practice, female translocation carriers requiring an IVF–PGD had to be considered normal responders and could receive standard doses of gonadotrophins for COS. More studies are necessary to confirm these results and to evaluate the efficiency of standard stimulation on COS results and IVF–PGD outcomes.

**Authors’ roles**

C.D., T.A.: conceived the study, collected and interpreted the data, drafted and revised the manuscript critically. C.D., H.D., B.H., L.R.: COS and cycle monitoring. C.C.: performed statistical analysis. S.H.: involved in embryo culture and biopsy. T.A.: cytogenetic analysis, review and design of the study. All authors have approved the final manuscript.

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