Real and expected delivery rates of patients with myotonic dystrophy undergoing intracytoplasmic sperm injection and preimplantation genetic diagnosis

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BACKGROUND: This study aimed to analyse the reproductive outcome of a large cohort of myotonic dystrophy type 1 (DM1) patients undergoing ICSI and PGD. The secondary outcome parameter of this study was ovarian response as a way to express gonadal function in female DM1 patients. METHODS: Prospective cohort study. Real and expected cumulative delivery rates are descriptive. The reproductive outcome per cycle was compared with that of a control group of patients with X-linked recessive disorders. The comparative analysis of ovarian stimulation parameters in the study group versus the control group was carried out using both bivariate (crude) and multivariate (linear regression) analysis. RESULTS: Between 1995 and 2005, 205 cycles of ICSI and PGD were carried out for DM1 in 78 couples. The real cumulative delivery rate (max 6 cycles) overall was 46%. The expected overall cumulative delivery rate was 72%. Multivariate analysis did not show a significant difference in total dose of gonadotrophins used for ovarian stimulation between Group A (in which the female partner was affected) and a control group. CONCLUSIONS: This study shows that ICSI and PGD for DM1 offer good reproductive outcome, both in cumulative terms and per treatment cycle. There is no evidence of impaired gonadal function in female DM1 patients.

Keywords: ICSI; PGD; myotonic dystrophy; DM1; delivery rate

Introduction

Myotonic dystrophy type 1 (syn: dystrophia myotonica type 1; DM1; Steinert’s disease; OMIM #160900) is an autosomal dominant disorder, with an incidence of 1/8000. The genetic defect is an unstable expansion of a CTG trinucleotide repeat at the 3’ end of the DMPK gene located on chromosome 19q13.3 (see Human Gene Organisation), which was cloned in 1992 (Brook et al., 1992; Mahadevan et al., 1992). Expansion of the trinucleotide repeat is frequently observed after parent-to-child transmission, but extreme expansions are not transmitted through the male line. This explains anticipation, that is, an increase in severity in successive generations and the occurrence of the severe, often lethal, congenital form almost exclusively in the offspring of affected women (Harper et al., 1992).

DM1 patients are progressively affected to various degrees by myotonic dysfunction, cardiorespiratory and ophthalmological (cataract) problems (Machuca-Tzili et al., 2005; Cho and Tapscott, 2007). Other features of myotonic dystrophy include frontal balding and a characteristic haggard facial appearance due to atrophy of masseter, sternocleidomastoid and temporalis muscles (Image 1). An increased risk of obstetric complications for female carriers has been reported, predominantly associated with the congenital type of myotonic dystrophy in the fetus, resulting in polyhydramnios and fetal akinesia (O’Brien and Harper, 1984; Jaffe et al., 1986; Rudnik-Schönenborn and Zerres, 2004). Pregnancies in which the fetus is affected by congenital DM1, present with non-immune hydrops fetalis (Stratton and Patterson, 1993), reduced fetal movements and joint contractures may be visible at prenatal ultrasound. Muscle hypotonia may lead to severe respiratory distress after birth, and may result in neonatal death.

Clinical classification can be based on time of onset of the disease (Table I) (Rudnik-Schönenborn and Zerres, 2004). The clinical severity and prognosis of DM1 is highly variable,
This prospective cohort study was carried out in a series of consecutive patients presenting for PGD to exclude DM1. The study aimed to analyse the reproductive outcome in terms of real and expected cumulative delivery rate, as well as outcome per treatment cycle and embryo transfer. In addition, we investigated the difference in reproductive outcome between females affected by DM1 and a control population of patients with X-linked recessive disorders without any impact on ovarian function known to be associated with the genetic disorder and with the same theoretical risk of having 50% of transferable embryos affected.

Materials and Methods

The study design was a prospective cohort study at a tertiary referral centre for ICSI and PGD.

Patients

Consecutive couples at risk of transmitting DM1 to their offspring were treated between 1995 and 2005. The initial consultation of the couples consisted of combined genetic and reproductive assessment and counselling, as well as psychological advice if and when required. For female patients, cardiological reports were requested, or the patient was referred for preconceptional assessment. Treatment with ovarian stimulation and ICSI/PGD plus PGD was initiated upon completion of the genetic test development.

Baseline characteristics, such as age, body mass index (BMI), early follicular phase FSH levels, parity and treatment and outcome data on a control group of patients undergoing PGD for X-linked recessive disorders without any impact on ovarian function known to be associated with the genetic disorder and with the same theoretical risk of having 50% of transferable embryos affected, were registered in the same way as in the index group.

Ovarian stimulation and oocyte retrieval

Controlled ovarian hyperstimulation (COH) was carried out in an agonist protocol, using GnRH analogues for pituitary desensitization (buserelin, Suprefact; Hoechst, Frankfurt, Germany), combined with human menopausal gonadotrophins (Menopur, Ferring Pharmaceuticals A/S, Copenhagen, Denmark) or recombinant FSH (Puregon, NV Organon, Oss, The Netherlands) (Van de Velde et al., 1998), or an antagonist protocol using recombinant FSH combined with a GnRH antagonist (ganirelix, Orgalutran, NV Organon) (Kolibianakis et al., 2004). The starting dose of gonadotrophins was determined according to the patient’s age and/or previous response to ovarian stimulation (range 75–450 IU). Human chorionic gonadotrophin (hCG) (10 000 IU, Pregnyl; NV Organon, Oss, The Netherlands) (Van de Velde et al., 1998) or recombinant FSH (Puregon, NV Organon, Oss, The Netherlands) (Van de Velde et al., 1998; Van Landuyt et al., 2005). Regardless of the sperm quality, ICSI was the method of choice rather than classical IVF to prevent DNA contamination with sperm in PCR-based PGD (Liebers et al., 1998). Fertilization is assessed 16–18 h after ICSI. Further development is evaluated in the morning of Day 2 and again.

<table>
<thead>
<tr>
<th>Type</th>
<th>Age at onset</th>
<th>Main features</th>
<th>CTG repeats</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>&gt;50 years</td>
<td>Cataracts, mild weakness, myotonia, muscle weakness, fatigue</td>
<td>50–100, 100–1000</td>
</tr>
<tr>
<td>Adult</td>
<td>10–50 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Childhood</td>
<td>1–10 years</td>
<td>Hypotonia, learning difficulties, limited motor skills</td>
<td>500–2000</td>
</tr>
<tr>
<td>Congenital</td>
<td>Prenatal-birth</td>
<td>Respiratory distress, sucking difficulties, hypotonia, joint contractures, psychomotor retardation</td>
<td>1000–5000</td>
</tr>
</tbody>
</table>

From Rudnik-Schöneborn and Zerres (2004).
on Day 3, when embryos were evaluated before biopsy. According to the number of anucleate fragments, the embryos were subdivided into Grades A, B, C and D as described previously (Vandervorst et al., 2000). From the 6-cell stage onwards, embryo biopsy is performed on Day 3 of culture. The embryo is immobilized with a holding pipette, the zona pellucida is then breached using an acid solution (tyrode’s solution) or laser assisted using two or three laser pulses of 5–7 ms of a non-contact 1.48 μm diode laser system (Fertilase; Octax, Herbron, Germany) as previously described (De Vos and Van Steirteghem, 2001). A biopsy pipette is introduced through the hole and one or two blastomeres are carefully aspirated. Each blastomere is placed in a cell lysis buffer (Sermon et al., 2004). In the control group of X-linked conditions, ICSI was used for fertilization.

Genetic diagnosis
The PCR procedures were performed as previously described (Sermon et al., 2001). Direct analysis of the CTG repeat was used for fully informative couples, i.e. when the healthy allele of the affected parent differs from the two alleles of the healthy parent. For semi-informative couples (the affected parent and healthy parent share one healthy allele, the second allele of the healthy parent is different) or not informative couples (the healthy allele of the affected parent and the two alleles of the unaffected parent are the same), the triplet-primed PCR (TP-PCR) protocol was applied. A conclusive diagnosis of unaffected embryos was assigned only if and when two blastomeres gave the same negative result for the disorder (Sermon et al., 1998a,b, 2001).

In the control group of X-linked conditions (Group C), two blastomeres were taken for analysis. PGD in Group C was carried out using a FISH procedure, allowing for analysis of chromosomes X and Y, and depending on the availability of the fluorochromes at the time of analysis, for chromosome 18, for chromosomes 13 and 21 and at even later stages also for 16 and 22 in the second round (Multivision PGT Probe Panel; Vysis, Downers Grove, IL, USA).

Embryo transfer procedure
If available one or more unaffected embryos were transferred into the uterus on Days 3–5 post-insemination. As in regular IVF cycles, the age of the patient, the rank of trial and embryo quality determined the number of embryos transferred. For Belgian patients, the number of embryos for transfer was restricted according to age and rules laid out by federal law from July 2003 onwards. Supernumerary unaffected embryos were cryopreserved subject to consent by the patient.

Luteal phase supplementation consisted of intravaginal administration of 600 mg of natural micronized progesterone daily (Utrogestan, Besins, Brussels, Belgium).

Outcome parameters
The embryological data were analysed on a per cycle basis, and compared with a control group of patients for whom no known fertility problem was documented, undergoing PGD–FISH for gender selection on the basis of X-linked disorders, and who were expected to have the same genetic risk of having an affected embryo (50%) as the patients in the myotonic dystrophy group.

The reproductive outcomes (clinical pregnancy rate, cumulative delivery rate, mean number of oocytes, mean number of embryos for biopsy and mean number of embryos transferred) were calculated on a per patient basis.

A biochemical pregnancy was defined as two consecutive positive rising (>15 IU/ml) serum hCG levels. A clinical pregnancy was defined as an intrauterine gestational sac seen at transvaginal ultrasound scan at least 5 weeks after embryo transfer. An ongoing pregnancy was defined as a clinical pregnancy with a fetal heartbeat at ≥12 weeks (Boduelle et al., 2002). In these cases, and without any exception, the couple was advised to undergo prenatal diagnosis in order to confirm the preimplantation diagnosis.

A spontaneous abortion was defined as a pregnancy loss before 20 weeks of gestation. A stillbirth was an intrauterine or intrapartum death of a child born at a gestation of ≥20 weeks or with a birthweight of ≥500 g. A preterm delivery was defined as a delivery at 34 weeks’ gestation or later, and before 37 weeks’ gestation. A premature delivery was defined as a delivery before 34 weeks’ gestation (Boduelle et al., 2002). The live birth delivery rate was defined as the number of live birth deliveries expressed per 100 initiated cycles, aspiration cycles or embryo transfer cycles (Zegers-Hochschild et al., 2006). The reproductive outcome parameters in this study are reported per OR and per embryo transfer. The real cumulative delivery rate is the observed number of deliveries born at a gestation of ≥20 weeks or with a birthweight of ≥500 g, over a maximum of six treatment cycles per patient. The expected cumulative delivery rate using Kaplan–Meier analysis takes into account drop-out patients over a maximum of six treatment cycles, and calculates the cumulative delivery rate had they not discontinued the treatment (Hull, 1992; Osmanoagolu et al., 1999).

Statistical analysis
The comparative analysis of ovarian stimulation parameters in the study group versus the control group was carried out using both bivariate (crude) and multivariate (linear regression) analysis. The unpaired t-test was used for statistical analysis of embryological data. The chi-square test was used for comparison of per cycle and per embryo transfer pregnancy rates. Cumulative delivery rates were calculated by life-table analysis using the Kaplan–Meier procedure (Hull, 1992; Osmanoagolu et al., 1999). The sample size allowed for descriptive cumulative analysis only. Cumulative delivery rates are expressed as cumulative percentage probabilities with 95% confidence intervals (95% CI). The maximum number of cycles per patient included was six. Transfers of frozen-thawed embryos were not included in the analysis. SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

Results
Patient characteristics
Between 1995 and 2005, 205 cycles of ICSI and PGD were carried out for DM1 in 78 couples. In 54 couples, the female partner was affected (Group A), versus 24 couples with the male partner affected (Group B). The patient characteristics did not differ significantly between the two groups (Table II). The control group (Group C) consisted of 78 patients with X-linked recessive disorders without any impact on ovarian function known to be associated with the genetic disorder and with the same theoretical risk of having 50% of transferable embryos affected.

The comparative analysis of the dosage of gonadotrophins used for ovarian stimulation does not reveal any significant differences between Group A and Group C in terms of age, BMI, parity, basal FSH values, infertility status (documented infertility), number of days stimulated, number of cumulus oocyte complexes (COC) retrieved and total dose of gonadotrophins administered (Table III). Multivariate analysis (linear regression) correcting for age, BMI, basal FSH values, parity and fertility status did not show a significant
difference in total dose of gonadotrophins used for ovarian stimulation between Group A and Group C.

Analysis of the embryological data did not show a significant difference between any of the groups in terms of number of oocytes at retrieval, number of metaphase II oocytes, number of 2PN oocytes and number of embryos for biopsy (Table IV), except for the number of cryopreserved embryos, which showed a significant difference ($P = 0.032$) due to a significant difference between Group A and Group B.

The embryo quality, as expressed as the ratio of top quality embryos of $>/C21$8 cells at Day 3 analysis, did not show any significant differences between Group A and Group B. The sperm quality as expressed by sperm concentration and motility was not significantly different between Group A and Group B (Table IV). In Group A, surgically retrieved sperm was used in one patient, versus four patients in Group B.

The clinical pregnancy rate (CPR), ongoing pregnancy rate (OPR) and live birth delivery rate (LBDR) overall (Groups $A+B$) per OR and per embryo transfer is illustrated in Table V. The CPR, OPR and LBDR were not significantly different between Group A and Group B. The overall (Groups $A+B$) CPR, OPR and LBR was not significantly different to the results in Group C (Table V). The spontaneous abortion rate was 4.2% in Group A, 1.7% in Group B and 6.6% in Group C (NS). There were no extra-uterine pregnancies reported in the study population. The real cumulative delivery rate (max 6 cycles) overall was 46%. The expected cumulative delivery rate was 72% (Fig. 1a). The real and expected cumulative delivery rate in Group A was 41% and 81%, respectively, compared with 58% and 72%, respectively, in Group B (Fig. 1b).

**Obstetric outcome**

Forty-one deliveries led to the birth of 49 children overall (Groups $A+B$), 31 in Group A and 18 in Group B. The twin pregnancy rate was 19.5% overall, 19.2% in Group A and 20.0% in Group B. The mean gestational age at delivery was 38.5 weeks. In Group C, 45 children were born [24 singletons, 9 twins (twin delivery rate 26.5%) and 1 triplet (triplet delivery rate 2.9%)]. The mean birth weight of the children born in Group C was 2916.2 g (SD 690.0), and the gestational age 36.9 (SD 4.1) weeks. The mean birth weight for singletons and twins in Group C was 3102.4 g (SD 559.6) and 2572.9 (SD 521.1), respectively. The mean gestational age at delivery for singletons and twins was 38.2 (SD 2.5) weeks and 34.5 (SD 4.9) weeks, respectively.
There are no significant differences between any of these results. Per ET 23.8% 35.7% 23.4%  Live birth delivery rate 26 15 34 Per ET 25.7% 35.7% 24.1% Ongoing pregnancy rate 28 15 34 Per OR 19.3% 25.0% 19.2% Clinical pregnancy rate 32 16 45 Per ET 29.4% 38.1% 31.0% Mean # biopsied embryos 5.7 (SD 3.6) 5.4 (SD 3.3) 6.3 (SD 4.0)  Mean # top quality embryos 3.3 (SD 3.0) 3.2 (SD 3.1) 3.7 (SD 2.9)  Mean # transferred embryos 1.3 (SD 0.9) 1.4 (SD 0.9) 1.1 (SD 0.9)  Mean # cryopreserved embryos 0.3 (SD 0.9) 0.1 (SD 0.4) 0.8 (SD 1.4)  There is no significant difference between the embryological results except for the number of cryopreserved embryos, which showed a significant difference (P = 0.032) due to a significant difference between Group A and Group B. SD, standard deviation.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>DM1 group total</th>
<th>Group A</th>
<th>Group B</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td># patients</td>
<td>78</td>
<td>54</td>
<td>24</td>
<td>78</td>
</tr>
<tr>
<td>COC</td>
<td>12.9 (SD 7.6)</td>
<td>12.2 (SD 6.3)</td>
<td>14.6 (SD 9.9)</td>
<td>13.1 (SD 7.6)</td>
</tr>
<tr>
<td>Metaphase II</td>
<td>11.0 (SD 6.4)</td>
<td>10.4 (SD 5.7)</td>
<td>12.2 (SD 7.7)</td>
<td>11.3 (SD 6.4)</td>
</tr>
<tr>
<td>2PN</td>
<td>8.4 (SD 5.2)</td>
<td>8.0 (SD 4.6)</td>
<td>9.5 (SD 6.3)</td>
<td>8.8 (SD 5.4)</td>
</tr>
<tr>
<td>Mean sperm conc (10^6/ml)</td>
<td>51.0 (SD 36.2)</td>
<td>51.3 (SD 67.9)</td>
<td>54.7 (SD 44.2)</td>
<td></td>
</tr>
<tr>
<td>Mean sperm motility</td>
<td>53.6% (SD 20.8)</td>
<td>43.0% (SD 28.8)</td>
<td>47.1% (SD 21.4)</td>
<td></td>
</tr>
<tr>
<td>Mean # biopsied embryos</td>
<td>5.7 (SD 3.6)</td>
<td>5.4 (SD 3.3)</td>
<td>6.3 (SD 4.0)</td>
<td></td>
</tr>
<tr>
<td>Mean # top quality embryos</td>
<td>3.3 (SD 3.0)</td>
<td>3.2 (SD 3.1)</td>
<td>3.7 (SD 2.9)</td>
<td>3.5 (SD 2.9)</td>
</tr>
<tr>
<td>Mean # transferred embryos</td>
<td>1.3 (SD 0.9)</td>
<td>1.4 (SD 0.9)</td>
<td>1.1 (SD 0.9)</td>
<td></td>
</tr>
<tr>
<td>Mean # cryopreserved embryos</td>
<td>0.3 (SD 0.9)</td>
<td>0.1 (SD 0.4)</td>
<td>0.8 (SD 1.4)</td>
<td></td>
</tr>
</tbody>
</table>

There are no significant differences between any of these results.

**Table IV. Reproductive outcome: embryological data.**

**Table V. Reproductive outcome: pregnancy rates.**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>DM1 group total</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>54</td>
<td>24</td>
<td>78</td>
<td></td>
</tr>
<tr>
<td>Cycles with oocyte retrieval (OR)</td>
<td>145</td>
<td>60</td>
<td>182</td>
<td></td>
</tr>
<tr>
<td>Cycles with embryo transfer (ET)</td>
<td>109</td>
<td>42</td>
<td>145</td>
<td></td>
</tr>
<tr>
<td>Clinical pregnancy rate</td>
<td>32</td>
<td>16</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>Per OR</td>
<td>22.1%</td>
<td>26.7%</td>
<td>24.8%</td>
<td></td>
</tr>
<tr>
<td>Per ET</td>
<td>29.4%</td>
<td>38.1%</td>
<td>31.0%</td>
<td></td>
</tr>
<tr>
<td>Ongoing pregnancy rate</td>
<td>28</td>
<td>15</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Per OR</td>
<td>19.3%</td>
<td>25.0%</td>
<td>19.2%</td>
<td></td>
</tr>
<tr>
<td>Per ET</td>
<td>25.7%</td>
<td>35.7%</td>
<td>24.1%</td>
<td></td>
</tr>
<tr>
<td>Live birth delivery rate</td>
<td>26</td>
<td>15</td>
<td>34</td>
<td></td>
</tr>
<tr>
<td>Per OR</td>
<td>17.9%</td>
<td>25.0%</td>
<td>18.7%</td>
<td></td>
</tr>
<tr>
<td>Per ET</td>
<td>23.8%</td>
<td>35.7%</td>
<td>23.4%</td>
<td></td>
</tr>
</tbody>
</table>

There are no significant differences between any of these results.

**Discussion**

Over a period of 12 years, we assessed the outcome of 205 ICSI–PGD cycles in 78 couples at risk of transmitting DM1 to their offspring because either the female or the male partner was affected. In parallel, we evaluated the outcome of couples undergoing PGD with sex selection to avoid transmission of X-linked diseases, to be used as a control group. The main findings of this study were (i) that women affected by myotonic dystrophy do not need a higher dosage of gonadotrophins for ovarian stimulation, confirming previous reports of unaltered gonadal function in affected females, and (ii) that reproductive outcome is adequate in terms of expected cumulative delivery rate. The strength of this study is that it analyses reproductive outcome and gonadal function in the largest reported cohort of ICSI and PGD cycles in women affected by myotonic dystrophy.

There was no difference in terms of ovarian response following stimulation with exogenous gonadotrophins, between the female affected DM1 patients and a control group, corrected by linear regression for all documented factors with a potential influence on ovarian response (Table III). The only factor showing a correlation with ovarian response in terms of number of oocytes retrieved and total dose of gonadotrophins used was the age of the patient (P = 0.012). These findings are in contrast with those reported in a recent small series of patients by Feyereisen et al. (2006), who suggest that ovarian response is lower than in controls. They base their findings on an observed significant delay in day of hCG and a higher prevalence of poor quality embryos in the DM1 group. Remarkable is the high cancellation rate (38%) per started cycle in this study, leading to a small study population, and the poor reproductive results. Our findings do seem to support those by Sagel et al. (1975), who report normal function of the pituitary-ovarian axis. They claim, however, that women with myotonic dystrophy show a tendency to develop loss of libido, oligo- and amenorrhoea and an increased risk of spontaneous abortion. These findings have so far not been substantiated by other studies. Our study results do not support any effect of loss of Six5 gene expression on female fertility, contrary to the negative effect already elucidated in male DM1 patients where a decrease in Six5 gene expression has been associated with deficient spermatogenesis and a progressive decrease in testicular mass with age (Sarkar et al., 2004).

There was a trend for poorer sperm quality in our study group of male affected DM1 patients, yet no significant difference was observed. The ratio of reported male factor infertility was higher in the male affected group of our study and testicular sperm was used more often in this group, but did not significantly influence success rates presumably because of the by-pass effect of ICSI. The findings of this study should therefore not be extrapolated to the DM1 population attempting spontaneous conception. Indeed, affected males are reported to have an increased risk of fertility problems, with an 80% incidence of hypogonadism, raised FSH levels and lower testosterone levels, and sperm quality is on average worse than in non-affected men. Secondary sexual development is usually normal (Sagel et al., 1975; Sarkar et al., 2004). Our study shows acceptable reproductive results in DM1 patients undergoing IVF/ICSI and PGD, both in terms of cumulative expected and crude delivery rates. Recognizing the limitations of these observations in terms of sample size, these findings should nevertheless be accepted as important as this comprises the largest cohort of DM1 patients having undergone ICSI and PGD. Further analysis of larger cohorts is required to assess the effect of genetic selection on...
cumulative results; this effect so far seems limited as the expected cumulative delivery rate of 72% is close to the 79% expected cumulative delivery rate reported in our non-PGD ICSI population (Osmanogaoglu et al., 1999). The clinical and ongoing pregnancy rate, as well as delivery rate per cycle, is similar to that of a control group of patients with X-linked recessive disorders without any impact on ovarian function known to be associated with the genetic disorder and with the same theoretical risk of having 50% of transferable embryos affected.

There were no reports of perinatal mortality in our study group, confirming that PGD by selecting unaffected embryos may contribute to a safer obstetric and perinatal outcome for these patients. This can, however, only be accepted if the implications of reproductive treatment including physical consequences, financial cost and potential false negative results at genetic analysis are justified by appropriately high reproductive outcomes. Despite PGD for DM1 having become more accurate by double-cell analysis and multiplex markers, the finding of one false negative result, diagnosed at prenatal diagnosis by AC, is a reason to continue counselling patients on the risk of a false negative diagnosis and on the possibility to have CVS or AC once an ongoing pregnancy has been achieved.

In conclusion, this study shows that IVF/ICSI and PGD for DM1 offer good reproductive outcome, both in cumulative terms and per treatment cycle. There is no evidence of impaired gonadal function of female DM1 patients. These data are highly useful in counselling couples affected by DM1 on the

Figure 1: (a) Expected (n) versus real (l) cumulative delivery rate (percentage) study group total (female + male affected Steinert patients) (n = 78); (b) expected cumulative delivery rates for Group A (n) and Group B (l).
reproductive aspects of their condition and the success rates with PGD.

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