Half-dose depot triptorelin in pituitary suppression for multiple ovarian stimulation in assisted reproduction technology: a randomized study*

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BACKGROUND: Pituitary suppression by depot GnRH agonist may be excessive for ovarian stimulation in assisted reproduction technology. This study compares the efficacy of standard and half-dose depot triptorelin in a long protocol. METHODS: A total of 180 patients were randomized into two groups using sealed envelopes. Pituitary desensitization was obtained in group 1 (90 patients) with half-dose (1.87 mg) triptorelin depot in the mid-luteal phase of their menstrual cycle, and in group 2 (90 patients) with full-dose (3.75 mg) triptorelin. RESULTS: There was no premature LH surge, with LH levels being lower in the full-dose group (1.04 ± 0.05 versus 0.7 ± 0.06 IU/l on the day of hCG). The number of FSH ampoules used was lower in group 1 (42 ± 2 versus 59 ± 3). The numbers of mature oocytes (10.1 ± 0.54 versus 7.4 ± 0.55), of fertilized oocytes (8.24 ± 0.35 versus 6.34 ± 0.37) and of embryos (7.8 ± 0.36 versus 5.9 ± 0.37) were significantly higher in group 1. No significant differences were found in pregnancy (38.8 versus 25.3%), implantation (22.6 versus 13.8%) or abortion (6.1 versus 5.0%) rates. Cumulative pregnancy (fresh plus frozen embryo transfers: 56.8 versus 35.4%) rate was significantly higher in group 1. CONCLUSION: A half-dose of depot triptorelin can be successfully used in ovarian stimulation for IVF and produce a higher number of good quality embryos with a good chance of implantation.

Key words: GnRH-agonist/half-dose/IVF/ovarian stimulation/triptorelin

Introduction

The use of GnRH agonists in women undergoing controlled ovarian stimulation (COS) with gonadotrophins for IVF provides some well-known benefits. These include prevention of a premature LH surge and luteinization, eliciting a lower cancellation rate (Caspi et al., 1989) and improvement of follicular recruitment, allowing recovery of a larger number of oocytes (Liu et al., 1992). Depot GnRH agonist formulations have been welcomed both by patients and physicians, because of the convenience of single administration. The currently available products were prepared for treatment of endometriosis or uterine fibroids, the objective being to achieve persistently high levels of pituitary desensitization for a protracted period of time. In COS, however this strong pituitary suppression has the drawback of inducing a slower and more muted ovarian response requiring a higher number of gonadotrophin ampoules (Ben-Rafael et al., 1991).

Some authors have suggested that it might be enough to induce just partial pituitary desensitization in assisted reproductive techniques and have suggested protocols that use reduced doses of short-acting GnRH agonist (Feldberg et al., 1994; Olivennes et al., 1996; Janssens et al., 2000; Dal Prato et al., 2001). In a previous study (Dal Prato et al., 2001) we showed that reduced daily doses of short-acting triptorelin induce a lower level of pituitary suppression, which is nevertheless sufficient for ovarian stimulation in young women. However, although this treatment is shorter and requires a smaller amount of gonadotrophins, no significant improvement in IVF cycle outcome has been reported when compared with depot formulation.

Other studies have evaluated the effects of reducing depot formulation doses. Both full-dose (3.75 mg) and half-dose (1.87 mg) of GnRH agonist triptorelin seem to be equally effective in pituitary desensitization, with similar duration times for both desensitization and recovery (Balasch et al., 1992), but it remains to be determined which of the two doses provides the best clinical outcome in IVF treatment. Recently, a randomized trial (Yim et al., 2001) showed that half-dose long-acting GnRH agonist is enough for the prevention of an LH surge in patients stimulated with hMG, but it does not improve IVF outcome in spite of the lower suppression. Since the presence of LH in the gonadotrophin formulation may compensate for low levels of endogenous LH during ovarian stimulation (Fleming et al., 1996), it would be of interest to check the effect of half-dose long-acting GnRH agonist in patients stimulated with FSH only.

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The aim of this study was to compare the clinical efficacy of standard and half-doses of the depot GnRH agonist triptorelin, in long luteal protocol, prior to ovarian stimulation with highly purified FSH in IVF or ICSI.

Materials and methods

Protocol
A total of 180 women undergoing COS for IVF or ICSI were enrolled in the trial. The study was approved by our institutional review board. All subjects were undergoing their first IVF treatment and were aged between 25 and 38 years with infertility caused by tubal, idiopathic or male factors. Active endometriosis, previous ovarian surgery, or FSH levels >15 IU/l on day 3 of the menstrual cycle were exclusion criteria.

Eligible patients who agreed to participate were randomized into two treatment groups.

Pituitary desensitization was obtained in group 1 (90 patients) with a half-dose (1.87 mg) triptorelin depot (Decapeptyl 3.75; Ipsen, Italy) in a single i.m. injection in mid-luteal phase (day 21) of the menstrual cycle preceding treatment, and in group 2 (90 patients) with standard full dose (3.75 mg) in the mid-luteal phase of the menstrual cycle preceding treatment. At the onset of menses, patients in both groups began gonadotrophin stimulation as described elsewhere (Dal Prato et al., 2001). Briefly, they received 4 ampoules (3001U) per day of highly purified urofollitropin (Metrodin HP 75; Serono, Italy) for 2 days and 2 ampoules (150 IU) per day for 4 days. The dose was then adjusted according to the individual response as assessed by 17β-oestradiol (E2) assay and ultrasound scanning performed every other day. Metrodin HP was chosen, as a drug containing merely FSH, because it was the only option allowed by our local health authority for the first IVF attempt, without charging the whole cost of the medication to patients.

hCG (Profasi HP; Serono, Italy), 10,000 IU, was administered when at least three follicles reached a maximum diameter of 20 mm, of which at least one was >23 mm. E2 levels were only used as an indication for coating, when they were >3000 pg/ml, for the prevention of ovarian hyperstimulation syndrome (OHSS). Cycles in which less than three follicles developed were discontinued. Transvaginal oocyte retrieval was performed under ultrasound guidance 36 h after hCG administration.

Two days after oocyte retrieval, a maximum of two embryos in women aged <35 years and three in women aged >35 years were replaced into the uterine cavity via the transcervical route. All remaining embryos presenting adequate morphology were cryopreserved for future use.

Luteal phase support was sustained with natural progesterone in oil (Prontogest; AMSA, Italy), 50 mg i.m. daily from day 1 after oocyte retrieval.

Pregnancy was defined as the presence of one or more gestational sacs detected on ultrasound scan performed ≥4 weeks after embryo transfer. Biochemical pregnancies (a rise of ± hCG with no further evidence of a gestational sac on ultrasound scan) were not considered.

Parameters evaluated

The primary endpoint was the total number of oocytes retrieved from patients who received hCG. The following secondary endpoints were also recorded: number of FSH ampoules, number of days of stimulation, 17β-oestradiol (E2) at hCG administration, LH on day 7 of stimulation and at hCG administration, progesterone at hCG administration, number of follicles at hCG administration, number of mature oocytes, fertilization rate, number of cleaved and grade 1 embryos, number of embryos transferred or frozen, number of clinical pregnancies, miscarriages and multiple pregnancies.

Sample size

Sample size calculations were based on 80% power and 5% significance level. Calculations were based on the following assumptions for number of oocytes: expected means difference 2.00 (Dal Prato et al., 2001). Under these conditions, ≥90 patients were required in each group of the study.

Assignment

Randomization was performed on an individual basis using sealed envelopes containing the name of one of the two medications (triptorelin 1.87 or triptorelin 3.75). Assignment to the different dosage groups occurred when eligible patients agreed to participate, ~2 weeks before triptorelin administration. Dark envelopes were used so that their content could not be seen against bright light. Each envelope and allocation was sequentially numbered to avoid patients being randomized out of sequence. Envelopes were not allowed to be opened in advance and were opened only by a nurse not involved in the trial, but expressly charged with the drug injections. Both patients and physicians involved were blinded to the dosing.

Statistical analysis

Analysis was performed using an SPSS program on an intention-to-treat basis (all patients included in the study) and per protocol (available patients). The results of the two analyses are similar; therefore only the results of the analysis per protocol are presented in detail.

Comparisons of clinical outcomes with half-dose (1.87 mg i.m.) and full-dose (3.75 mg i.m.) depot triptorelin and quality of the embryos between groups were analysed by χ²-test for dichotomous variables (Fisher’s exact test when appropriate). Student’s t-test (Mann–Whitney U-test when appropriate) and Z-test for proportions were used for continuous variables of ovarian stimulation and quality of the embryos. Mean ± SEM and Kolmogorov–Smirnov test to describe distributions and to verify normality were also used. P < 0.05 was considered statistically significant.

Results

Participant flow and follow-up

From September 2000 to September 2002, we randomized a total of 180 women: 90 into the half-dose group (group 1) and 90 into the full-dose group (group 2). Age was comparable in the two groups: 33.2 ± 0.29 in group 1 and 33.7 ± 0.33 in group 2. In all, 172 patients received hCG and underwent oocyte retrieval and 164 completed the study up to embryo transfer. A total of eight cycles were cancelled before oocyte retrieval for poor response to stimulation (one in group 1, seven in group 2; P = 0.07). Figure 1 shows the participant flow and follow-up.

IVF was performed in 52 patients in group 1 and in 51 patients in group 2, while ICSI was carried out in 37 patients in group 1 and in 32 patients in group 2. One patient in both groups did not undergo embryo transfer because of failed fertilization. Three patients in both groups deferred transfer and had all embryos frozen due to risk of OHSS. Nevertheless, since they had their embryos transferred after thawing, they were considered in the analysis.

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LH and progesterone assays performed in each patient on the day of hCG administration showed no evidence of premature LH surge or luteinization in either group. Table I shows the hormonal pattern of the two groups of patients during ovarian stimulation. LH levels were lower in the full-dose group (group 2): on day 7 of stimulation the difference was barely significant ($1.08 \pm 0.06$ IU/l in group 1 versus $0.9 \pm 0.06$ in group 2: $P = 0.035$), but became highly significant on the day of hCG administration ($1.04 \pm 0.05$ IU/l versus $0.75 \pm 0.03$: $P = 0.0007$).

Table I. Hormonal pattern of ovarian stimulation with half-dose (1.87 mg i.m.) and full-dose (3.75 mg i.m.) depot triptorelin

<table>
<thead>
<tr>
<th></th>
<th>Triptorelin 1.87 mg</th>
<th>Triptorelin 3.75 mg</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized patients</td>
<td>90</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>Completed trial</td>
<td>88</td>
<td>82</td>
<td></td>
</tr>
<tr>
<td>LH on day 7 (IU/l)</td>
<td>$1.08 \pm 0.06$</td>
<td>$0.9 \pm 0.06$</td>
<td>0.035</td>
</tr>
<tr>
<td>LH on hCG day (IU/l)</td>
<td>$1.04 \pm 0.05$</td>
<td>$0.75 \pm 0.06$</td>
<td>0.0007</td>
</tr>
<tr>
<td>Progesterone on hCG day (ng/ml)</td>
<td>$0.67 \pm 0.12$</td>
<td>$0.62 \pm 0.08$</td>
<td>0.665</td>
</tr>
<tr>
<td>Estradiol on hCG day (pg/ml)</td>
<td>$1655 \pm 110$</td>
<td>$1298 \pm 80$</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Values are means ± SEM.

$^a$Student’s $t$-test (Mann–Whitney $U$-test when appropriate).

Estradiol levels at hCG administration were significantly higher in the half-dose group ($P = 0.009$).

The characteristics of ovarian stimulation are summarized in Table II. The number of FSH ampoules used ($42 \pm 2$ versus $59 \pm 3$: $P = 0.0001$) and length of stimulation ($11.8 \pm 0.13$ versus $12.4 \pm 0.12$: $P = 0.0143$) were lower in group 1 which also presented significantly more follicles (total and with mean diameter > 17 mm) at hCG administration. The number of collected oocytes and of mature embryos, the fertilization rate and the number of cleaved embryos were higher in group 1. There was no difference in the number of embryos transferred, but there were more embryos suitable for cryopreservation in group 1. Evaluation of the quality of embryos according to ‘embryo grading’ (Hu et al., 1998) showed a significantly higher rate of G1 embryos in the group treated with half-dose triptorelin (Table III).

Table IV shows the clinical outcome. A total of 33 patients conceived in group 1, 20 in group 2. There was a trend toward a higher pregnancy rate per transfer in group 1, but the difference was not statistically significant. No significant differences were found between groups in miscarriage rate. Embryo implantation was slightly, but not significantly, higher in group 1, owing to the greater incidence of twins (eight in group 1 versus three in group 2).
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Table II. Results of ovarian stimulation with half-dose (1.87 mg i.m.) and full-dose (3.75 mg i.m.) depot triptorelin

<table>
<thead>
<tr>
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<th>Triptorelin 1.87 mg</th>
<th>Triptorelin 3.75 mg</th>
<th>P*</th>
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<tbody>
<tr>
<td>Randomized patients</td>
<td>90</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>Completed trial</td>
<td>88</td>
<td>82</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>33.2 ± 0.29</td>
<td>33.7 ± 0.33</td>
<td>0.304</td>
</tr>
<tr>
<td>No of FSH ampoules</td>
<td>42 ± 2</td>
<td>59 ± 3</td>
<td>0.0001</td>
</tr>
<tr>
<td>No. of days of stimulation</td>
<td>11.8 ± 0.13</td>
<td>12.4 ± 0.17</td>
<td>0.0143</td>
</tr>
<tr>
<td>No. of follicles</td>
<td>16.8 ± 0.72</td>
<td>14.0 ± 0.69</td>
<td>0.0044</td>
</tr>
<tr>
<td>No. of oocytes</td>
<td>14.7 ± 0.69</td>
<td>12.9 ± 0.74</td>
<td>0.0453</td>
</tr>
<tr>
<td>No. of mature oocytes</td>
<td>10.1 ± 0.54</td>
<td>7.4 ± 0.55</td>
<td>0.0007</td>
</tr>
<tr>
<td>No. of fertilized oocytes</td>
<td>8.24 ± 0.35</td>
<td>6.34 ± 0.37</td>
<td>0.0003</td>
</tr>
<tr>
<td>No. of embryos</td>
<td>7.8 ± 0.36</td>
<td>5.9 ± 0.37</td>
<td>0.0002</td>
</tr>
<tr>
<td>No. of transferred embryos</td>
<td>2.1 ± 0.05</td>
<td>2.1 ± 0.06</td>
<td>0.7039</td>
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<tr>
<td>No. of frozen embryos</td>
<td>4.02 ± 0.36</td>
<td>2.7 ± 0.32</td>
<td>0.0066</td>
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</tbody>
</table>

Values are means ± SEM.
*Student’s t-test (Mann–Whitney U-test when appropriate).

Table III. Quality of the embryos on day +2 after oocyte retrieval according to ‘embryo grading’ (Hu et al., 1998) (modified)

<table>
<thead>
<tr>
<th></th>
<th>Triptorelin 1.87 mg</th>
<th>Triptorelin 3.75 mg</th>
<th>P*</th>
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<td>Randomized patients</td>
<td>90</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>Completed trial</td>
<td>88</td>
<td>82</td>
<td></td>
</tr>
<tr>
<td>Total no. of embryos</td>
<td>7.8 ± 0.36</td>
<td>5.9 ± 0.37</td>
<td>0.0002</td>
</tr>
<tr>
<td>No of G1 embryos</td>
<td>4.7 ± 0.34</td>
<td>2.97 ± 0.27</td>
<td>0.0002</td>
</tr>
<tr>
<td>No of G2 embryos</td>
<td>2.75 ± 0.22</td>
<td>2.96 ± 0.26</td>
<td>0.716</td>
</tr>
</tbody>
</table>

Values are means ± SEM.
*Student’s t-test (Mann–Whitney U-test when appropriate).

Table IV. Comparison of clinical outcomes with half-dose (1.87 mg i.m.) and full-dose (3.75 mg i.m.) depot triptorelin

<table>
<thead>
<tr>
<th></th>
<th>Triptorelin 1.87 mg</th>
<th>Triptorelin 3.75 mg</th>
<th>P*</th>
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<tr>
<td>Randomized patients</td>
<td>90</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>Completed trial</td>
<td>88</td>
<td>82</td>
<td></td>
</tr>
<tr>
<td>No. of cancelled cycles (%)</td>
<td>1/90 (1.1)</td>
<td>120 (7.8)</td>
<td>0.07</td>
</tr>
<tr>
<td>No. of retrievals</td>
<td>89</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>No. of transfers</td>
<td>85</td>
<td>79</td>
<td></td>
</tr>
<tr>
<td>Pregnancies (%/pregnancy)</td>
<td>33/85 (38.82)</td>
<td>20/79 (25.32)</td>
<td>0.093</td>
</tr>
<tr>
<td>Miscarriages (%/transfer)</td>
<td>2/33 (6.06)</td>
<td>2/20 (10.0)</td>
<td>0.627</td>
</tr>
<tr>
<td>No. of gestational sacs</td>
<td>41</td>
<td>23</td>
<td>0.503</td>
</tr>
<tr>
<td>Implantation rate (%)</td>
<td>41/183 (22.4)</td>
<td>23/167 (13.8)</td>
<td>0.22</td>
</tr>
</tbody>
</table>

Values are means ± SEM.
*Student’s t-test (Mann–Whitney U-test when appropriate).
*Values are means ± SEM.
*Student’s t-test (Mann–Whitney U-test when appropriate).

Table V. Effects of pituitary desensitization on ovarian follicular development

To date, almost all patients who agreed to have embryos frozen, and who did not conceive in their first transfer cycle, have undergone embryo thawing. Seventeen pregnancies arose in group 1 and nine in group 2 (Table V). The cumulative pregnancy rate (fresh plus frozen embryos) was significantly higher in group 1 (56.8 versus 35.4%; P = 0.008).

Discussion

Assisted reproduction treatments are very stressful and tiring procedures for infertile couples. Any simplification in phar- macological treatment is therefore a welcome development. Single administration of depot GnRH agonist instead of daily repeated doses of short-acting GnRH agonist is particularly appreciated by patients, but presents the inconvenience of excessively strong suppression.

Janssens et al. (2000) was the first to demonstrate a direct correlation between the reduction of the daily dosage of short-acting triptorelin and the decrease in the degree of pituitary suppression. Balasch et al. (1992) reported that half-dose depot triptorelin is enough for preventing an LH surge. More recently Hsieh et al. (2000) showed that a single half-dose of leuprolide acetate depot gives pituitary suppression and clinical results comparable with those of 0.5 mg daily leuprolide acetate.

In our study, the effect of the differently dosed drugs on the pituitary was quite different in the two groups, as can be seen from the levels of LH in mid- and late follicular phases, that confirm the reduced pituitary desensitization induced by half-dose triptorelin. Despite this difference between the mean LH levels of the two groups, 1.87 mg triptorelin administration proved sufficient to prevent an LH surge. LH and progesterone assay performed at hCG administration provided no evidence of an LH surge or premature luteinization in any of our patients. Moreover, oocytes were found at each retrieval and the number of post-mature or degenerative oocytes was very low.

Recently a randomized trial in which patients were stimulated with hMG (Yim et al., 2001) reported similar findings. Pituitary suppression was significantly lower with half than with the conventional dose, but this did not affect IVF outcome. There was no difference in the gonadotrophin doses used, the number of oocytes and embryos, or pregnancy rates.

In contrast, the difference in LH levels in our study seems to have affected the clinical outcome. In the patients treated with half-dose, quicker stimulation, requiring a smaller amount of gonadotrophins, led to a larger number of oocytes collected and, what is more, a larger number of oocytes being classified as ‘mature’ via cumulus–oocyte complex examination. The higher number of fertilized oocytes obtained in this group is probably due to the better quality of oocytes collected.

These findings contrast with the work by Janssens et al. (2000). They found a direct correlation between the GnRH agonist dose and the number of follicles and oocytes. On the contrary, in the present study, the lowest depot GnRH agonist dose gives rise to a higher number of follicles and oocytes. The difference between the two studies might result from the different drug formulation administered: depot in the present study, daily in Janssens et al.’s work. Moreover the levels of LH reported by Janssens et al. with very low daily GnRH agonist doses seem to be higher than those achieved in our trial. Tesarik and Mendoza (2002) investigated the effect of exogenous LH in oocyte donors stimulated with rFSH and suggested the concept of a window for LH requirement in ovarian follicular development. In donors with profound pituitary suppression (LH levels < 0.1 IU/l), the addition of exogenous LH increased the number of mature oocytes.
and good quality embryos. In contrast, when LH levels at the beginning of stimulation were >1 IU/l, exogenous LH administration impaired oocyte and embryo quality and decreased the implantation rate in recipients.

The actual quality of the embryos is an interesting issue. In Group 1 there were not only more embryos available for cryopreservation, there was also a higher rate of grade 1 embryos. A larger number of best morphology embryos available for transfer or cryopreservation resulted in a higher implantation rate after both fresh and thawed transfer. Combining the results of the fresh and frozen–thawed embryo transfers, the final outcome of the treatment cycle was therefore significantly better in the group treated with half-dose triptorelin.

The difference between the results of our study and those reported by Yim et al. (2001) lies probably in the kind of gonadotrophin used: hpFSH (virtually devoid of LH activity) in the present study, hMG (with LH activity) in that of Yim et al. The administration of exogenous LH in the latter may have partially balanced the effects of the different degrees of pituitary suppression on the quality of ovarian stimulation.

According to the two-cell two-gonadotrophin theory, both FSH and LH are required for a normal follicular (and oocyte) growth and maturation. However, the actual role of LH in ovarian stimulation is a matter of debate. Overly high LH levels during the follicular phase may induce excess follicular androgen secretion, thus increasing follicular atresia and producing low quality embryos (Loumaye et al., 1989). On the other hand, Fleming et al. (1996) showed that follicular fluid E2 levels, oocyte yield and fertilization are decreased and the follicular phase is longer when LH concentrations are <1 IU/l, indicating a reduction in normal follicular steroid metabolism. These findings were confirmed in a subsequent report (Fleming et al., 1998) in women with more profoundly suppressed mid-follicular phase LH (<0.5 IU/l), who had significantly fewer embryos available for cryopreservation. The rate of blastocyst formation, however, was normal, indicating that embryo development potential is not impaired by the degree of LH suppression.

Moreover, it has been recently suggested that a direct action of LH on uterine LH receptors is required to support endometrial growth and uterine receptivity (Tesarik, 2003), and that the expression of endometrial estrogens and progesterone receptors is altered in COS when GnRH agonist is used and in which LH levels are low (Bourgain et al., 2002).

Filicori et al. (2001) compared highly purified FSH and hMG in normo-ovulatory GnRH agonist-suppressed women, candidates for intrauterine insemination, and found a shorter treatment duration with lower gonadotrophin consumption in the hMG-treated group, underlining a facilitatory role of LH activity in ovulation induction.

Thus, evidence in the literature suggests that there may be a role for LH co-administration in cycles treated with depot GnRH agonist and FSH. However, the good results achieved in our trial suggest that lowering the dose of depot GnRH agonist may reduce the LH requirement in patients undergoing assisted reproduction treatment. This management may be preferable to screening for women that might benefit from the addition of exogenous LH. This approach seems simpler and cheaper. In view of the high costs of assisted reproduction treatment procedures, shorter treatment with smaller amounts of drugs for stimulation might be a financial advantage for patients.

As a final consideration, specific GnRH receptors have been found in murine and human granulosa cells (Bramley et al., 1985; Latouche et al., 1989) and GnRH agonist has been shown to have a direct effect on ovarian steroidogenesis (Casper and Yen, 1979; Tureck et al., 1982; Parinaud et al., 1988). More recently Zanagnolo et al. (1996) observed that pharmacological doses of leuprolide may exert a negative effect on oocyte function in the rabbit by direct action on the oocyte. These findings should furthermore suggest the use of the possibly lower dose of GnRH agonist.

In conclusion, the results of our study show that half-dose (1.87 mg) depot triptorelin can be successfully used in ovarian stimulation for IVF or ICSI. LH levels confirm the lower level of pituitary desensitization elicited by half-dose triptorelin. The better quality oocytes recovered in the half-dose group might explain the higher fertilization rate as well as the higher number of good quality embryos available for transfer or cryopreservation, and subsequently the higher cumulative pregnancy rate.

Acknowledgements
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References
Balasch J, Gomez F, Casamitjana R, Carmona F, Rivera F and Vannell JA (1992) Pituitary-ovarian suppression by the standard and half-doses of

### Table V. Final outcome of the treatment: cumulative results of fresh plus frozen–thawed cycles

<table>
<thead>
<tr>
<th></th>
<th>Triptorelin 1.87 mg</th>
<th>Triptorelin 3.75 mg</th>
<th>P&lt;sup&gt;a&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>Randomized patients</td>
<td>90</td>
<td>90</td>
<td></td>
</tr>
<tr>
<td>Completed trial</td>
<td>88&lt;sup&gt;b&lt;/sup&gt;</td>
<td>82&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Pregnancies in fresh cycle (%/transfer)</td>
<td>33/85&lt;sup&gt;b&lt;/sup&gt; (38.82)</td>
<td>20/79&lt;sup&gt;b&lt;/sup&gt; (25.32)</td>
<td>0.093</td>
</tr>
<tr>
<td>No. of patients undergoing embryo freezing</td>
<td>66</td>
<td>51</td>
<td></td>
</tr>
<tr>
<td>No. of patients undergoing frozen/thawed cycles</td>
<td>38</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Pregnancies after embryo thawing (%/patient)</td>
<td>17/58 (44.7)</td>
<td>9/30 (30.0)</td>
<td>0.322</td>
</tr>
<tr>
<td>Pregnancies in fresh + frozen–thawed cycles (%/retrieval)</td>
<td>49/88&lt;sup&gt;b&lt;/sup&gt; (56.8)</td>
<td>29/82&lt;sup&gt;b&lt;/sup&gt; (35.4)</td>
<td>0.008</td>
</tr>
</tbody>
</table>

<sup>a</sup><sup>x</sup> - Test (Fisher’s exact test when appropriate).
<sup>b</sup> - Three patients in both groups deferred transfer and had all embryos frozen due to risk of ovarian hyperstimulation syndrome.
II. Presumptive LH suppression in the periovulatory phase of stimulated embryo transfer cycles in comparison with natural cycles and relation to clinical pregnancy outcome.


