A qualitative systematic review of coasting, a procedure to avoid ovarian hyperstimulation syndrome in IVF patients

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‘Coasting’, a method which consists of stopping exogenous gonadotrophins and postponing HCG administration until the patient’s serum estradiol (E2) level decreases, is often used to prevent ovarian hyperstimulation syndrome (OHSS). We conducted a systematic review to analyse whether there is sufficient evidence to justify the general acceptance of coasting. The studies, which involved 493 patients in 12 studies, are very heterogeneous in the characteristics and number of patients in the ovulation stimulation schemes. The study designs, control groups, selection criteria for coasting and the OHSS classifications were variable. In most studies a threshold value of E2 was used (often 3000 pg/ml) and/or the number of follicles were considered. The fertilization rates (36.7–71%) and the pregnancy rates (20–57%) were acceptable in terms of IVF results in comparison with those of other large IVF databanks. In 16% of the cycles, ascites was described and 2.5% of the patients required hospitalization. In conclusion, while coasting does not avoid totally the risk of OHSS, it decreases its incidence in high-risk patients. Many questions remain unanswered about how coasting should be managed, and we suggest that a randomized prospective multicentre study is required.

Key words: coasting/IVF/OHSS/prevention

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Introduction

Ovarian hyperstimulation syndrome (OHSS) is a potentially fatal iatrogenic complication of gonadotrophin administration used in IVF procedures (Mozes et al., 1965). IVF is not a vital treatment and there is currently no specific treatment for OHSS. Therefore, it is imperative to avoid OHSS by using efficient prevention measures. In a survey conducted among gynaecologists specializing in fertility treatment, ‘coasting’ appeared to be the most popular method used to prevent OHSS (Delvigne and Rozenberg, 2000). This technique was first described in overstimulated cycles by Rabinovici et al. and also used by Urman et al. (Rabinovici et al., 1987; Urman et al., 1992); it was first applied in IVF cycles by Sher et al. in 1993 (Sher et al., 1993). The method is based on the assumption that estradiol (E2) levels achieved at the time of HCG administration are predictive of the risk of developing OHSS. When a patient considered to be at risk has a high E2 level, exogenous gonadotrophins are stopped while GnRH agonists are maintained. The HCG administration is postponed until the patient’s serum E2 level decreases to a ‘safer zone’, attesting to atresia of granulosa cells.

There are many advantages to using this technique. First, the cycle is not abandoned. Second, this technique allows the transfer of fresh embryos, in contrast to cryopreservation, another method that is used to avoid OHSS. Finally, no supplementary procedure or medical therapy is involved in coasting. It is therefore not surprising that about two-thirds of the physicians who choose to apply a preventive method advocated the use of coasting in our previous survey (Delvigne and Rozenberg, 2000).

The aim of the study was to review, systematically, whether there is sufficient evidence to justify the general acceptance of coasting.

Methods

A Medline search was carried out with the keywords ‘IVF’ and ‘coasting’ for the years 1980–2001. Fifteen articles were found (Sher et al., 1993, 1995; Benadiva et al., 1997; Dhont et al., 1998; Feichtinger, 1998; Lee et al., 1998; Tortoriello et al., 1998; Egbase et al., 1999; Fluker et al., 1999; Waldenström et al., 1999;
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Table I. Population characteristics of the study, design and selection criteria used for coasting

<table>
<thead>
<tr>
<th>First author (n)</th>
<th>Mean age (years) ± SD (range)</th>
<th>Selection criteria E2 (pg/ml), additional criteria</th>
<th>Design/ control group(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sher et al., 1995 (51)</td>
<td>37.3 (28–42)</td>
<td>E2 &gt;3000, follicle number &gt;29 and 30% follicles ≥15 mm</td>
<td>Descriptive/NA</td>
</tr>
<tr>
<td>Benadiva et al., 1997 (22)</td>
<td>34.5 ± 3.6</td>
<td>E2 ≥3000</td>
<td>Retrospective/cryopreserved patients</td>
</tr>
<tr>
<td>Tortoriello et al., 1998 (44)</td>
<td>32.6 ± 0.7</td>
<td>E2 &gt;3000 and five or more follicles ≥16 mm and two follicles ≥19 mm</td>
<td>Retrospective/subgroup of coasted patients versus two control groups</td>
</tr>
<tr>
<td>Dinh et al., 1998 (120)</td>
<td>NA</td>
<td>E2 &gt;2500 and follicle number ≥20</td>
<td>Retrospective/historical cohort</td>
</tr>
<tr>
<td>Lee et al., 1998 (20)</td>
<td>NA</td>
<td>E2 ≥2777 and many immature follicles of which less than three follicles &gt;18 mm</td>
<td>Retrospective/IVF patients</td>
</tr>
<tr>
<td>Fluker et al., 1999 (63)</td>
<td>32.2 ± NA</td>
<td>E2 rose rapidly and generally ≥3000 'Very high E2' and ≥25 'large follicles' of which the three largest ≥17 mm</td>
<td>Descriptive/NA</td>
</tr>
<tr>
<td>Waldenström et al., 1999 (65)</td>
<td>31.5 (23–39)</td>
<td>E2 &gt;6000 and &gt;15 follicles/ovary and two or more &gt;18 mm</td>
<td>Descriptive/NA</td>
</tr>
<tr>
<td>Egbase et al., 1999 (15)</td>
<td>33.5 ± 2.8</td>
<td>E2 ≥5000 and/or &gt;20 follicles of which three or more follicles ≥18 mm without abdominal pain</td>
<td>Prospective randomized early follicular aspiration</td>
</tr>
<tr>
<td>Dechau et al., 2000 (14)</td>
<td>NA</td>
<td>≥30% follicles ≥16 mm and severe OHSS in previous cycle</td>
<td>Descriptive/NA</td>
</tr>
<tr>
<td>Ohata et al., 2000 (5)</td>
<td>32 (25–37)</td>
<td>E2 &gt;3000 and &gt;20 follicles with a dominant follicle ≥16 mm</td>
<td>Descriptive/NA</td>
</tr>
<tr>
<td>Aboulghar et al., 2000 (24)</td>
<td>29.9 ± 4.6</td>
<td>&gt;20 follicles and 25% ≥15 mm, E2 ≥3596</td>
<td>Retrospective/historical group</td>
</tr>
<tr>
<td>Al-Shawaf et al., 2001 (50)</td>
<td>32.5 ± 4.5 (23–41)</td>
<td>Prospective/observational normal cycle</td>
<td></td>
</tr>
</tbody>
</table>

NA = not available.

Aboulghar et al., 2000; Dechau et al., 2000; Egbase, 2000; Ohata et al., 2000; Al-Shawaf et al., 2001), of which 14 presented results of series of patients. Three articles were eliminated, either because they were not really related to the topic (Feichtinger et al., 1998) or because they were repeated reports of the same patient population (Sher et al., 1993; Egbase, 2000) and we included therefore only the largest series of those patients in our analysis. We had first decided to include only articles from randomized studies, but only one study (with a rather low number of subjects) appeared to be prospective and randomized (Egbase et al., 1999). Therefore, we conducted a qualitative, critical review of the data of 12 articles. For this analysis we considered only as coasted patients those for whom gonadotrophins had been totally and definitely stopped.

We paid attention to the methodology that was used, the study design, the type of control groups and possible sources of bias. The following sources of heterogeneity were studied: the number of patients included and their selection criteria, and the ‘coasting action’ that was undertaken.

Finally, we evaluated whether the conclusions that were drawn from these studies were supported by the data.

Patient selection criteria and design of the studies

In total, 493 patients were followed in 12 studies which evaluated coasting, but some studies involved as few as five patients and the largest involved 120 patients (Table I). Data about the patients’ age were only available for 10 studies. The mean age varied between 29.9 and 37.3 years within the studies and the extremes were 23–42 years. Eight studies provided information about the aetiology of their patients’ sterility. Out of 242 patients, 78 couples suffered from a male fertility problem, 82 from tubal damage, 40 from anovulation and polycystic ovarian syndrome (PCOS), 31 from idiopathic sterility and 23 from endometriosis. Thus, within the group of patients with a known aetiology, ~13% presented PCOS, a well known risk factor of OHSS.

For four other studies, the causes of infertility were not provided per se, but Tortoriello et al. mentioned that they had twice as many PCOS cases in the group of coasted patients than in their control group (Tortoriello et al., 1998), while in the study of Dhont et al. there was no difference in aetiology between control groups and the coasted patients (Dhont et al., 1998). Finally, for two other studies, no information about aetiology was provided at all (Fluker et al., 1999; Aboulghar et al., 2000).

Another source of heterogeneity between the studies is the type of stimulation scheme that was used. In most studies, a long-term scheme with GnRH analogue was used (Sher et al., 1995; Benadiva et al., 1997; Lee et al., 1998; Tortoriello et al., 1998; Egbase et al., 1999; Fluker et al., 1999; Waldenström et al., 1999; Aboulghar et al., 2000; Dechau et al., 2000; Ohata et al., 2000; Al-Shawaf et al., 2001). Only Dhont et al. used a short-term scheme with GnRH analogue (Dhont et al., 1998). Ovarian stimulation occurred using either HMG only (Benadiva et al., 1997; Dhont et al., 1998; Tortoriello et al., 1998; Egbase et al., 1999; Fluker et al., 1999; Aboulghar et al., 2000; Dechau et al., 2000; Ohata et al., 2000), HMG in association with FSH (Sher et al., 1995) or FSH only (Lee et al., 1998; Waldenström et al., 1999; Al-Shawaf et al., 2001).
Information about the daily dose was generally missing, except for in the studies of Lee (161 IU), Dhont (225 IU), Egbasse (150 IU), Aboulghar (150–300 IU in relation to the patient’s age) and Al-Shawaf (varying doses of 112.5–450 IU) (Dhont et al., 1998; Lee et al., 1998; Egbasse et al., 1999; Aboulghar et al., 2000; Al-Shawaf et al., 2001). Ovulation was induced in three studies by administering 5000 units of HCG (Waldenström et al., 1999; Dechaud et al., 2000; Ohata et al., 2000), but more often, with 10,000 units (Sher et al., 1995; Dhont et al., 1998; Tortoriello et al., 1998; Egbasse et al., 1999; Fluker et al., 1999; Aboulghar et al., 2000; Al-Shawaf et al., 2001). In all studies published so far, progesterone supplementation was provided during the luteal phase, either i.m., vaginally or anally.

The selection criteria which determined the decision to use coasting were variable. Either a threshold value of E2 was used, or the E2 slope and/or the number of follicles seen by ultrasound were considered (Table I). The threshold value of E2 varied between 2500 pg/ml (pmol/l conversion factor 3671) and 6000 pg/ml with a majority of studies selecting 3000 pg/ml (Sher et al., 1997; Dhont et al., 1998; Egbasse et al., 1999; Fluker et al., 1999; Aboulghar et al., 2000; Al-Shawaf et al., 2001). In two studies, this value was not described. In addition to the E2 level, some investigators also considered the number of follicles when deciding whether to coast. Seven authors chose to coast when 20–30 follicles were visualized, while eight authors also considered the proportion of the follicles having reached a mature size (15–19 mm) (Table I). The heterogeneity is even more exemplified by the fact that some authors used inverse criteria to decide to begin coasting [fewer than three follicles >18 mm for Lee et al. (Lee et al., 1998)].

Benadiva et al. cancelled the cycle when the decrease of E2 was >20% of the E2 maximum, and Aboulghar et al. when the serum levels of E2 became <1500 pg/ml (Benadiva et al., 1997; Aboulghar et al., 2000). Dechaud et al. cancelled the cycle when the coasting period lasted >4 days and in cases of spontaneous abdominal pain (Dechaud et al., 2000).

Seven authors compared their results with control groups (Benadiva et al., 1997; Dhont et al., 1998; Lee et al., 1998; Tortoriello et al., 1998; Aboulghar et al., 2000; Ohata et al., 2000; Al-Shawaf et al., 2001) while four described only their coated patients (Sher et al., 1995; Fluker et al., 1999; Waldenström et al., 1999; Dechaud et al., 2000). Only Egbasse conducted a prospective study and randomized patients at risk between two interventions: either coating (n = 15) or early follicular aspiration (n = 15) (Egbasse et al., 1999).

Benadiva et al. used as a control group 26 patients in whom oocytes were retrieved when the patient reached an E2 level of at least 4000 pg/ml, after which all embryos were cryopreserved and transferred during a later cycle (Benadiva et al., 1997). Tortoriello et al. proposed to 62 patients who reached a threshold level of E2 of 3000 pg/ml, to choose between either coating (n = 44) or immediate HCG administration (n = 18). Since the E2 level in the coated group was much higher than in the control group (4044 ± 102 versus 3466 ± 475 pg/ml), he subdivided the coated patients into two groups: those who had reached E2 levels of 3000–3999 pg/ml (n = 22), which were compared with the control non-coated groups, and those who had reached E2 levels >4000 pg/ml, who were excluded from this comparison. He also used an additional control group of 22 women who had a normal response curve (Tortoriello et al., 1998).

Dhont et al. compared their coated patients with a historical cohort of patients who had been stimulated before 1993, when coasting wasn’t used, but who had comparable E2 levels. The authors also acknowledged that a long GnRH agonist scheme had been used for the control group, while a short scheme had been used in the coated patients (Dhont et al., 1998).

Lee et al. compared 20 coated patients with 262 consecutive IVF patients who had no particular risk factors for OHSS (Lee et al., 1998).

Ohata et al. compared five coated cycles with five previous cycles of the same patients who had suffered severe OHSS (Ohata et al., 2000).

Aboulghar et al. studied two different schemes of coasting: either they withdrew HMG (classical coasting, n = 24) or they decreased the HMG before stopping it (modified coasting, n = 25) and compared these two groups with a third ‘historical’ group of 32 patients at risk (Aboulghar et al., 2000). More recently, Al-Shawaf et al. conducted a prospective observational study. They compared coated patients (follicles >20 and E2 ≥3596 pg/ml) with a group of ‘modified’ coated patients (>20 follicles and E2 of 817–3596 pg/ml), a ‘maintenance group’ (>20 follicles and E2 <817 pg/ml) and a low-risk group of patients (Al-Shawaf et al., 2001).

For the purpose of the further analysis we have considered only the ‘classical’ coasting groups of patients in the two latter studies.

Results of coasting and IVF

The results of these different stimulation schemes in terms of E2 level on the coasting day and on HCG administration day, the collected oocytes, fertilization and pregnancy rates are provided in Table II. The mean levels of peak serum E2 that were reached varied between 4882 pg/ml (± 183) for the study of Tortoriello et al. and 7650 (range 6270–12780) for Sher et al. (Sher et al., 1995; Tortoriello et al., 1998). This disparity probably reflects the variation in the selected value of E2 to start the coating and different assay methods. Similarly, the number of oocytes collected also varies between studies, ranging from 9.2 to 21.

The fertilization rate varied between 36.7 and 71% and the implantation rate between 9.5 and 31%. Finally, the pregnancy rate varied between 20 and 63.6% and the abortion rate between 3.9 and 28% with a mean of 17.9%.

The mean duration of the coasting period was 3.6 days (range 1.6–5.3). The shortest coasting period was predictably seen in the study of Dhont et al. who also tolerated the lowest maximal E2, considering that Dechaud et al. cancelled cycles when the coasting period lasted for >4 days (Dhont et al., 1998; Dechaud et al., 2000).

In five studies, E2 increased immediately after the coasting period was initiated (Sher et al., 1995; Lee et al., 1998; Egbasse et al., 1999; Fluker et al., 1999; Waldenström et al., 1999). This rise in E2 lasted for 1–3 days after which a decrease in E2 occurred. However, other investigators observed an immediate decrease of E2 when gonadotrophins were withdrawn (Benadiva et al., 1997; Tortoriello et al., 1998). Egbasse, who studied the dynamics of E2, observed an increase in E2 during the first 24 h, which was followed by a daily decrease of 40% thereafter (Egbasse, 2000). Those who studied the evolution of the follicular dynamics of E2, observed an increase in E2 during the first 24 h, which was followed by a daily decrease of 40% thereafter (Egbasse, 2000).
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Table II. IVF data for the coasted cycle. The E2 data are in pg/ml. Means (ranges) or ± SD are given

<table>
<thead>
<tr>
<th>Study</th>
<th>E2 day of coating</th>
<th>E2 day of HCG retrieved</th>
<th>ΔE2</th>
<th>Coasting duration</th>
<th>Oocytes</th>
<th>Fertilization rate (%)</th>
<th>Pregnancy rate (%)</th>
<th>Patients with ascites</th>
<th>Patients with haemoconc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sher et al., 1995</td>
<td>2083 ± 3</td>
<td>1053 ± 24</td>
<td>0.9</td>
<td>15±6</td>
<td>69</td>
<td>41±8</td>
<td>12</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Benadiva et al., 1997</td>
<td>3803 ± 731</td>
<td>2260 ± 932</td>
<td>1.9</td>
<td>6.1 (3–11)</td>
<td>21</td>
<td>62.2</td>
<td>63.6±6</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Tortoriello et al., 1998</td>
<td>4015 ± 112</td>
<td>2407 ± 130</td>
<td>2.6</td>
<td>9.1±0.9</td>
<td>15±6.5</td>
<td>58.9</td>
<td>44.4±5</td>
<td>1 at ultrasound</td>
<td>6 (5 clinically and 1 / ultrasound)</td>
</tr>
<tr>
<td>Dhont et al., 1998</td>
<td>3834 ± 96</td>
<td>2348 ± 472</td>
<td>1.9</td>
<td>1.94±0.8</td>
<td>19.7±0.6</td>
<td>NA</td>
<td>37.4±9</td>
<td>4 (2 paracentesis)</td>
<td>NA</td>
</tr>
<tr>
<td>Lee et al., 1998</td>
<td>NA</td>
<td>2832 ± 129</td>
<td>2.8</td>
<td>1.3±0.3</td>
<td>NA</td>
<td>63</td>
<td>40±6</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Fluker et al., 1999</td>
<td>NA</td>
<td>2245 ± 53</td>
<td>10.8</td>
<td>0.5±0.5</td>
<td>71</td>
<td>36.5±9</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

*Pregnancy rate/cycle; b pregnancy rate/retrieval; c pregnancy rate/embryo transfer.
NA = not available.

Diameter observed a follicular growth during the first 36 h of the coasting period (Sher et al., 1995).

It is impossible quantitatively to summarize the risk of developing mild, moderate or severe OHSS associated with coasting, because of the different classifications of OHSS that were used by the investigators: three studies used a classification described by Schenker and Weinstein (Schenker and Weinstein, 1978), four used Navot’s (Navot et al., 1992) classification, two Golan’s (Golan et al., 1989) classification, two used their own classification and one study did not state precisely which classification was used.

Thus, only a descriptive analysis can be provided. About 2% of patients for which the data were accessible (n=3) required hospitalization. Ascites was either diagnosed by ultrasound or clinically defined as necessitating paracentesis, and it was found in 16.3% of cases (46/283). Haemoconcentration occurred in 2.8% of the patients (7/378) for which this information was available (Table III).

Some studies compared the incidence of OHSS with that of a control group: Benadiva et al. found an incidence of 4.6% moderate OHSS in his population of coasted patients and 7.6% in a group of women for whom the embryos were cryopreserved (not statistically different) (Benadiva et al., 1997). Tortoriello et al. compared the group of coasted women with a group of women who reached similar E2 levels at the time of HCG administration without coasting and also with a third group of women who responded ‘normally’ to stimulation (Tortoriello et al., 1998). In their experience there was no difference in the incidence of moderate and severe OHSS between the three groups of women.

In a subgroup of 22 coasted women who reached E2 levels >4000 pg/ml, three patients (13, 6%) developed a severe form of OHSS while none of the coasted women who reached lower E2 levels did so. Furthermore, the only ‘critical’ OHSS that occurred happened among the non-coasted women who had reached rather high E2 levels.

Dhont et al. obtained a significantly lower number of OHSS cases (moderate and severe) in coasted patients than in their control group (P < 0.01). Similarly, more patients were hospitalized within the group of women who were not coasted than within the group who were (Dhont et al., 1998).

On the other hand, Lee et al. observed more severe OHSS cases (20%) within the coasted women than in the general reference population (1%), but these women presented no risk factors for OHSS (Lee et al., 1998).

In the randomized study of Egbase et al. no significant difference was observed among severe OHSS cases (20 versus 26.6%) between coasted patients (n=15) and those who underwent a unilateral follicular aspiration (n=15) (Egbase et al., 1999).

Ohata et al. observed that no OHSS developed in five women during a coasted cycle, while all had developed severe OHSS when they were not coasted during a previous cycle (Ohata et al., 2000).

Aboulghar et al. observed an incidence of severe OHSS of 25% (eight cases out of 32) in a ‘historical’ cohort of women with rather high E2 levels (mean 7200 ± 2150 pg/ml) as compared with 17% (four cases out of 24) in the coasted group (Aboulghar et al., 2000).

Discussion

All investigators defined coasting as a preventive method that was performed by withdrawing the administration of gonadotrophins in patients who had reached a certain threshold value of serum E2 and/or a critical number of follicles. Globally, a majority of the authors selected an E2 value >2500–3000 pg/ml as the threshold limit with the presence of at least three mature follicles. It is possible that the number of mature follicles has no prognostic value since Lee et al. paradoxically only started to coast with fewer than three mature follicles and obtained comparable results.
with others (Lee et al., 1998). In our previous survey, a majority of clinicians had also selected the value of 3000 pg/ml E2 as the critical threshold value (Delvigne and Rozenberg, 2000).

The IVF results that were reported by the different coasting studies were comparable or even superior in terms of success rates than those reported by many large databanks for IVF such as the Society for Assisted Reproductive Technology (SART) and the French National Register on In vitro Fertilization and Pregnancy Rates (FIVNAT, 1996). Likewise, the pregnancy rate of 20–36.3% and the miscarriage rate of 17.9% are acceptable in comparison with those of SART (respectively 26.2 and 16.6%) (Society for Assisted Reproductive Technology, 1999).

It is impossible to draw conclusions about the optimal decrease in E2 during the coasting period, and about its optimal duration. One can only observe that Benadiva et al. who cancelled the cycle when E2 decreased by >20% (in five patients out of 22) did not achieve superior results in terms of oocyte retrieval, fertilization and pregnancy rates (Benadiva et al., 1997). Likewise, Aboulghar et al. who cancelled the cycle when E2 decreased to a level <1500 pg/ml did not achieve superior results either (four patients out of 24) (Aboulghar et al., 2000). Tortoriello et al. found a significant relationship between the duration of coasting and the E2 level that was reached (Tortoriello et al., 1998). The number of retrieved oocytes decreased in relation to the duration of the coasting period. Similarly, the pregnancy rate tended to be lower when the coasting period was long. To be complete, one should also mention that two other authors (out of 12) cancelled some cycles: Waldenström et al. cancelled four cycles out of 65 either for logistic reasons or vaginal bleeding (Waldenström et al., 1999); Dechaud et al. cancelled the cycle when the coasting period lasted >4 days and in cases of spontaneous abdominal pain (in four patients out of 14) (Dechaud et al., 2000).

It is also impossible to synthesize the data of the different studies as a global and single result in terms of the risk of developing OHSS because of the wide heterogeneity of the study protocols, their diversity of control groups and even their varied definitions of OHSS classes. In order to quantify the true benefit of coasting, a large randomized controlled study where protocols are standardized would be needed.

### Table III. Clinical description of the registered OHSS cases

<table>
<thead>
<tr>
<th>First author (number of coasted patients)</th>
<th>Number of patients with ascites</th>
<th>Haemoconc.</th>
<th>Comment/ OHSS classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shet et al., 1995 (51)</td>
<td>12</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Benadiva et al., 1997 (22)</td>
<td>NA</td>
<td>NA</td>
<td>1 moderate OHSS/classification non precise</td>
</tr>
<tr>
<td>Tortoriello et al., 1998 (44)</td>
<td>6 (5 Clinically and 1 at ultrasound)</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Dhont et al., 1998 (120)</td>
<td>NA</td>
<td>1</td>
<td>5.8% of moderate (involves ascites) and severe OHSS</td>
</tr>
<tr>
<td>Lee et al., 1998 (20)</td>
<td>4 (2 paracentesis)</td>
<td>NA</td>
<td>4 severe OHSS (distress with ovarian enlargement and ascites)</td>
</tr>
<tr>
<td>Fluker et al., 1999 (63)</td>
<td>1</td>
<td>1</td>
<td>Cumulated results of 2 groups (classical and modified coasting n = 93), 9/93 had nausea and vomiting, 2 had ascites</td>
</tr>
<tr>
<td>Waldenström et al., 1999 (65)</td>
<td>&lt;300 ml: 6/61 300–800 ml: 3/61 &gt;800 ml: 2/61</td>
<td>2/61</td>
<td>1 paracentesis</td>
</tr>
<tr>
<td>Egbase et al., 1999 (15)</td>
<td>3</td>
<td>NA</td>
<td>3 additional cases of moderate OHSS when considering the classification of Schenker</td>
</tr>
<tr>
<td>Dechaud et al., 2000 (14)</td>
<td>NA</td>
<td>0/10</td>
<td>Refers only to severe forms of OHSS</td>
</tr>
<tr>
<td>Ohata et al., 2000 (5)</td>
<td>5</td>
<td>0</td>
<td>Ascites at ultrasound</td>
</tr>
<tr>
<td>Aboulghar et al., 2000 (24)</td>
<td>4</td>
<td>0</td>
<td>Ascites at ultrasound (moderate according to the classification of Goland)</td>
</tr>
<tr>
<td>Al-Shawaf et al., 2001 (50)</td>
<td>1^/50</td>
<td>NA</td>
<td>2 moderate OHSS according to the classification of Navot</td>
</tr>
<tr>
<td>Total</td>
<td>46/283</td>
<td>7/378</td>
<td></td>
</tr>
<tr>
<td>%</td>
<td>16.3</td>
<td>2.8</td>
<td></td>
</tr>
</tbody>
</table>

^This patient was excluded concerning a protocol violation
NA = not available.
Still, in 16% of the cycles ascites was described, but this includes both moderate OHSS forms which were occasional ultrasound findings, as well as clinical symptomatic ascites, necessitating paracentesis to relieve patients from respiratory symptoms. In ~2.5% of the patients the OHSS required hospitalization, and 2.8% presented haemoconcentration abnormalities.

The reported incidence of 2.5% of severe forms of OHSS in coated cycles is rather low in relation to their calculated mean E2 level (5785 pg/ml for the 190 patients from which the maximum E2 value was available). It is also low in relation to their calculated mean oocyte number of 15. Indeed, the reported risk of OHSS in ‘regular IVF’ is much higher when elevated E2 levels or high oocytes numbers are reached. According to Ash et al. 38% of patients with E2 levels >6000 pg/ml develop a severe form of OHSS, whereas 23% develop it when >30 oocytes are retrieved and 80% when both conditions are encountered (Ash et al., 1991). Morris et al. also observed that 20% of high-risk patients developed a severe form of OHSS after embryo transfer (Morris et al., 1995). Coasting can thus be used to prevent OHSS, since it considerably decreases the OHSS incidence in these high-risk patients.

Nevertheless, coasting does not totally avoid the risk of OHSS and one should be aware of this. Furthermore, many questions remain unanswered about the way coasting should be managed and many contradictions are found in the published studies. It remains doubtful whether it is useful to obtain mature follicles before starting the coasting, and whether it is necessary to cancel cycles when E2 levels decrease below a certain value or when the coasting period is too long. We think that it would be unethical to randomize women exposed to a very high risk, either to coasting or regular IVF. Nevertheless, it would be feasible to perform a prospective randomized trial where either cycle cancellation or regular IVF. Nevertheless, it would be feasible to perform a prospective randomized trial where either cycle cancellation or regular IVF.

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References


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