HOT TOPICS

Multiple pregnancies: a plea for informed caution

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At present, assisted reproduction techniques form part of the health care routine in our hospitals. With >1 x 10^6 IVF babies already born in the world, the efficacy of these techniques is beyond question. However, we must now fight for the safety of these procedures, since safety and efficacy are closely connected aspects.

Figures from the Spanish National Institute of Statistics for the period 1982–2002 show that the rate of twin births has doubled, while there has been a 7-fold increase in triplets. From the obstetric point of view we know that multiple pregnancies are associated with a considerable increase in the risks for these patients. As for fetal risks, it is accepted that each additional fetus means a 3 week reduction in the duration of the pregnancy, with the result that levels of prematurity and cerebral palsy increase exponentially in a clear association with the number of fetuses. Nor can we overlook the significant increase in health care costs that arise in these procedures, since safety and efficacy are closely connected aspects.

Although the majority of high-order multiple pregnancies come from ovulation induction or enhancement treatment (Tur et al., 2005), the large majority of twin or triple pregnancies have their origin in IVF (Jain et al., 2004; Nyboe Andersen et al., 2004). This is the very technique in which prevention can be practised clearly and directly by limiting the number of embryos to be transferred, thus optimizing efficiency without increasing risks. Talk of crude pregnancy rates is now obsolete and we must incorporate new parameters such as the BEST score (birth emphasizing a successful singleton at term), which shows the percentage of live term birth of singleton baby per assisted reproduction treatment cycle begun (Min et al., 2004). However, the good results of modern obstetrics mean that twin pregnancies are medically acceptable and so, as with single pregnancies, they can be considered as successes for assisted reproduction treatment (Dickey et al., 2004).

In recent years and thanks to the pioneering work of the Scandinavian teams (Vilska et al., 1999) policies of limiting the number of embryos to transfer have proliferated. In young patients it is possible to perform selectively one elective single embryo transfer (ESET) or double embryo transfer (DET) without the pregnancy rates being noticeably affected (Heijnen et al., 2004). Nevertheless, it is obvious that for widespread application of these strategies an IVF team has to have an outstanding performance accompanied by an excellent embryo-freezing programme, and must not suffer legal restrictions to embryo freezing as currently happens in some European countries. If these conditions exist, I feel that this is the time for evaluation of the quality of a programme not only in terms of implantation rates but of the percentage of cycles in which ESET is applied (Land and Evers, 2004; Ombelet et al., 2005).

With a view to having objective criteria as to the advisability of transferring one, two or three embryos, we have designed a multiple pregnancy score (MPS) based on the retrospective analysis of our own material. After the application of the appropriate statistical methodology by means of receiver operating curves (ROC) we were able to identify that the parameters most closely connected with the establishment of a multiple pregnancy were the age of the patient (<34 years) and the total number of high quality embryos that were available for replacement; high MPS values make it advisable to transfer fewer embryos (Table I) (Barri et al., 2004). The utility of this lies in the fact that it makes it possible to base the decision as to the number of embryos to be transferred on objective criteria, thus avoiding subjective bias on the part of the doctor or of the patient. I am convinced that if a programme has implantation rates of >25% and pregnancy rates by cryoreplacement >35% then there is an obligation to apply restrictive policies on the number of embryos to transfer.

In our programme we have never transferred more than three embryos in the last 3 years. We have ESET rates of 30%, and 45% for DET, and three embryos are transferred in 25% of the IVF cycles. According to the experience acquired when applying the MPS based on these criteria of patient’s age and total number of top quality embryos, we have been able to design a more restrictive policy of embryo replacement. This procedure has
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Table I. Multiple pregnancy score

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>No. High quality embryos</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>30–34</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>35–39</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>≥40</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table II. Embryo replacement policy

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>No. of top quality embryos available</th>
<th>No. of embryos to replace</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>30–32</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>33–34</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>35–37</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>38–39</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>≥40</td>
<td>0</td>
<td>0</td>
</tr>
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References


been very useful to us from a practical point of view (Table II). This strategy makes it possible to individualize each case depending on the different age groups and the number of good quality embryos available. Following these criteria, in the last year we have succeeded in reducing the twin pregnancy rate to 18% and the triplet rate to 1.5%.

As has been suggested by the French groups (Antoine et al., 2004), when dealing with the problem of the multiple pregnancies that arise from the application of assisted reproduction techniques, the assessment and the strategic decision lie with a trio made up of three elements: the medical team, the patient or the couple, and society itself. The gynaecologists are treating efficiently but not always safely (Lambert, 2002) and sometimes they risk too much as a result of the pressure that they are put under by infertile couples with their strong desire to have offspring, which leads them to undervalue the risks of multiple pregnancies. Similarly, infertile couples should ask for specific information from each centre (ongoing clinical pregnancy rates, multiple pregnancy rates, etc.), while at the same time they should be aware of the independent national recommendations. Finally, independently of the source of finance of the assisted reproduction techniques, society at large should make a multi-parameter assessment, which should take into account both the efficacy that we have to offer to the patients and the safety that they deserve, thus making it possible to set objective guidelines.

We must foster an atmosphere of shared trust between doctors and patients that is based on transparent information, on the internal quality controls of each centre and on external audits.

Personally, I think that we doctors will not lose our freedom if we accept more restrictive policies that may be proposed by the health authorities or by the scientific societies. I believe that the self-discipline that we must impose on ourselves, together with the regulation that society should demand from the politicians, will help us to achieve acceptable multiple pregnancy rates. In this way we can be sure of avoiding as far as possible the drawbacks arising from unfortunate situations such as embryo reduction or from the serious maternal-fetal complications that are common in multiple pregnancies.