Commentary

One million and counting

Keith Gordon1,3, Marjanne Prins2, Klaus Schuller1, Joy Lewin1
1Organon International, Roseland, New Jersey, USA; 2NV Organon, Oss, The Netherlands.
3Correspondence: e-mail: keith.gordon@organon.com

Abstract

Ten years have passed since follitropin-beta first became commercially available. It is estimated that more than one million children have been born after ovarian stimulation and/or ovulation induction with this recombinant FSH in assisted reproduction.

Keywords: follitropin-beta, ovarian stimulation, ovulation induction, recombinant FSH

Organon International is currently celebrating 10 years since the launch of the recombinant follicle-stimulating hormone (r-FSH) product follitropin beta (Puregon®/Follistim®; Organon, Oss, The Netherlands). Such a milestone raises the question of just how many children had been born as a result of the use of follitropin beta. As there is no universal registry of children born as a result of assisted reproductive technology (ART) procedures, a certain amount of uncertainty is inherent when it comes to making such an estimate. At the recent 2006 ESHRE meeting in Prague, Jacques de Mouzon estimated that more than three million babies have been born as a result of ART methods since the first birth 28 years ago. As the manufacturer of one of the products used to stimulate follicular growth, we can make a fairly accurate estimate if certain assumptions and approximations are accepted.

In order to allow such an estimate to be made, the number of treatment cycles that have been performed with follitropin beta and the average success rate of those treatment cycles must be estimated in terms of the number of babies anticipated to have been born as a result of those treatments.

Some things are known with a high degree of certainty, such as the number of international units (IU) of follitropin beta sold. In order to back-calculate how many cycles this equates to, we need to estimate the average number of IU used per cycle. Gonadotrophin products are used to stimulate follicular development. Different amounts are needed to achieve different degrees of ovarian stimulation suitable for the desired treatment outcomes.

For ovulation induction in anovulatory women, the desired ovarian response is unifollicular development, which requires much less FSH than full ovarian stimulation as a prelude to in-vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI). Surveying the recent literature, we found that approximately 450–1000 IU is commonly needed to achieve ovulation induction (Garcia et al., 2004; Kettel et al., 2004; Platteau et al., 2006). Ovarian stimulation is also done as a prelude to intrauterine insemination (IUI) when the underlying cause of infertility is unexplained or mild male factor. Under those circumstances, slightly higher quantities of gonadotrophin are used. Recent figures quoted in the literature range from 500 to 1500 IU (Checa et al. 2006; Lambalk et al., 2006; Ragni et al., 2006). Last, but not least, when ovarian stimulation is employed prior to IVF or ICSI, the amounts of gonadotrophin used vary considerably depending on the patient population being treated, with anywhere from 1800 IU for relatively good prognosis patients (Kolibianakis et al., 2005) to upwards of 3000 IU for poor responders (Arslan et al., 2005; Dragisic et al., 2005).

For ovulation induction and IUI, the numbers of IU reported in a recent survey of practice patterns in France (646 and 763 IU, respectively) (Sedbon et al., 2006) were used. Justification for using these numbers lies in the fact that they fall within the boundaries of those reported in the literature and more accurately reflect general practice patterns rather than the controlled situation more often reflected in the published clinical trial literature. For similar reasons, the number of IU cited in this survey for IVF/ICSI (2106 IU) was used as representative of practice in the rest of the world. However, within the ovarian stimulation segment, a different (higher) value (2500 IU) was used for the USA, to reflect the different treatment patterns.

The average success rates for each treatment have to be estimated, and the proportion of each type of stimulation estimated. As mentioned above, gonadotrophins are used for the treatment of anovulatory and oligo-ovulatory women, but usually only after repeated failure of clomiphene citrate. Hence, ovulation induction with gonadotrophins is rarely performed without the additional step of IUI. For the purpose of the estimation, a 17% success rate for gonadotrophin-stimulated ovulation induction was used, with an associated 28% incidence of multiple births (Messinis, 2005). For gonadotrophin-stimulated IUI in non-anovulatory women, a success rate of 14% (Lambalk et al., 2006), with an associated 11% incidence of multiple births, was used. For IVF and ICSI, different rates for the USA and the rest of the world were used: for the USA, a success rate of 30% with a multiple rate of 35% (Centers for Disease Control and Prevention, 2005); and for the rest of the world, a success rate of 25% with a multiple rate of 25% (Andersen et al., 2005).

Of all gonadotrophin-stimulated treatment cycles, an estimated 70% are ovarian stimulation prior to IVF or ICSI (Table 1) and 30% are milder ovarian stimulation prior to IUI and for correction of ovulatory disorders. All of these factors can then
be used to calculate the total number of babies delivered as a result of these treatments.

Allowing for a certain degree of uncertainty concerning the above calculations, a significant demographic milestone appears to have been passed. There have now probably been more than one million children born worldwide as a result of the skilled application of ART techniques following ovarian stimulation with follitropin beta.

References


Centers for Disease Control and Prevention 2005 Assisted Reproductive Technology Success Rates: National Summary and Fertility Clinic Reports. Atlanta, Georgia: Centers for Disease Control and Prevention.

Checa MA, Prat M, Robles A, Carreras R 2006 Use of gonadotropin-releasing hormone antagonists to overcome the drawbacks of intrauterine insemination on weekends. Fertility and Sterility 85, 573–577.


Platteau P, Andersen AN, Balen A et al. JC 2006 Similar ovulation rates, but different follicular development with highly purified menotrophin compared with recombinant FSH in WHO Group II anovulatory infertility: a randomized controlled study. Human Reproduction 21, 1798–1804.


Received 19 April 2006; refereed 15 May 2006; accepted 7 July 2006.

Table 1. Statistics for use of recombinant FSH in treatment for assisted reproduction.

| Table 1. Statistics for use of recombinant FSH in treatment for assisted reproduction. |
|---|---|---|---|---|---|
| Percentage | No. of cycles performed with Puregon®/Follistim®* | Success rate (%) | Multiple rate (%) | Births (n) | Babies (n) |
| COS cycles (% of total cycles) | 70 | 1,846,329 | – | – | – |
| Cycles in USA (% of cycles worldwide) | 20 | 321,194 | 30 | 35 | 96,358 | 130,083 |
| Cycles outside USA (% of cycles worldwide) | 80 | 1,525,136 | 25 | 25 | 381,284 | 476,605 |
| Non-COS cycles (% of total cycles) | 30 | – | – | – | – | – |
| OI (% of non-COS cycles) | 30 | 799,077 | 17 | 28 | 135,843 | 173,879 |
| IUI (% of non-COS cycles) | 70 | 1,578,605 | 14 | 11 | 221,005 | 245,315 |
| Total | – | – | – | – | 834,490 | 1,025,883 |

*Estimated from internal sales data (data on file).