

Pharmacoeconomic aspects of gonadotrophins choice

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Introduction. Since a few years, recombinant FSH (r-FSH) has been progressively replacing urinary products (u-FSH) that were withdrawn from the market in many countries by the pharmaceutical companies. This policy resulted in a dramatic increase in ovarian stimulation cost, multiplied by 3 to 4, whereas the r-FSH advantages remain controversial in terms of efficacy and safety. In the same time, HMG continued to be prescribed and a new highly purified u-FSH became available on the market, and it may be useful to analyze the influence of these two categories of products on the IVF cost, from the experience of 3 large countries data and from the results of a new controlled study. German data. A new law was recently implemented in Germany, that stated that patients have to carry 50% of all treatment costs associated with assisted reproduction techniques (ART), including drugs. This has led to a dramatic decrease in treatment numbers, with less than 50% of therapies performed in 2004 compared to previous years and resulting in the fact that many patients cannot afford for ART anymore. Thus, decreasing all the costs, including stimulation becomes a key point in Germany and statistical studies were made between r-FSH and HMG (the only available urinary product for now) to determine if the later could be used without decreasing the success, which would allow more people to get ART. When comparing cycles treated by r-FSH (70%) or HMG (30%), drug-costs for stimulation treatment amounted to a total of 700 Euros when urinary HMG was used, compared with total costs of 1000 Euros for recombinant gonadotrophins). In IVF cycles, the per transfer pregnancy rates was 29% with HMG and 28% for r-FSH (NS). The results were comparable for ICSI. Finally, for the year 2003, the total gonadotrophins costs amounted to 22 and 73.5 millions Euros respectively.

French data. The ART costs were calculated in a Public Health setting, including all the cycle costs and using 2 hypotheses of pregnancy rate differences, according published results in the literature, either a 3.5% difference in favour of r-FSH (Daya's metaanalysis) or an absence of difference (as in the only published double blind study by Frydman et al.). Even though r-FSH was associated with a lower mean number of administered units per cycle (2369 vs. 2602), the stimulation with u-FSH resulted in a mean lower cost of 500 Euros per oocyte pick-up (OPU) cycle (1121 vs. 1658 Euros for FSH administration only, and 2422 Euros Vs. 2959 Euros for a whole OPU cycle, respectively for u-FSH and for r-FSH). After including the cancellation rate (12 %), the unsuccessful OPU (1.8%), the failed fertilization cycles (13.9% of OPU), the cost was calculated per initiated cycle, at 2247 Euros for u-FSH and 2784 Euros for r-FSH. For the complete year 2002, in France, where 53,000 cycles were initiated, the potential over-cost of recombinant products reaches 28.4 millions Euros (128,4 Vs. 104,0 millions Euros for r-FSH and u-FSH, respectively). The per baby IVF cost could be estimated at 12,337 Euros for r-FSH and between 11,681 Euros (in case of a difference of 3.7% pregnancy rate per oocyte recovery) and 9,991 Euros (in case of equivalence between the 2 drugs) for u-FSH.

UK data. Observational studies in UK have revealed that women undergoing ART with highly purified urinary gonadotrophins have comparable results with respect to clinical outcome measures including low cancellation rates. Thus, the National Institute of Clinical Excellence (NICE) has advised that cost as well as effectiveness should be considered when choosing gonadotrophins for ART.

New study data. A randomized comparative study was recently conducted in 2 countries (Hungary and France) on 151 patients aged 18-39 with normal basal FSH (< 10 IU) and body mass index <30 kg/m². The results were very similar in the r-FSH and u-FSH groups, in term of collected oocytes (12.1 ± 5.6 and 11.2 ± 4.6, respectively, p=0.31), mature oocytes (9.8 ± 4.7 vs. 9.4 ± 1.7, p=0.66), embryos (6.6 ± 3.7 vs. 6.8 ± 3.3, p=0.75), frozen embryos (1.7 ± 2.7 vs. 2.3 ± 3.3, p=0.21), pregnancy rate per initiated cycle (32.9% vs. 34.7%, p=0.82).

Moreover, Cortvrindt et al. demonstrated on mice, that equal doses of HP u-FSH (Fostimon®) and r-FSH (Gonal F®) induced similar responses in the follicle bioassay, and that folliculogenesis, oogenesis and steroidogenesis characteristics were comparable.

Conclusion. All these data suggest that, in the current state of ART, there is not a real advantage in either type of molecule used for ovarian hyperstimulation. They also show the economic impact related to the medical choice and clearly that, in term of public health, this impact can influence the countries policy.