

Special Article - In Vitro Fertilisation

Quo Vadis *In Vitro* Fertilisation (IVF)? The Benefit of Preconception Nutraceutical Food Supplementation

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Introduction

There is no doubt that the invention of *in vitro* fertilization has revolutionized reproductive medicine, and has helped to satisfy the desire for children of millions of infertile couples. Barratt, Anderson and De Jonge [1] have characterized “Assisted reproductive technology (to be), globally, a highly innovative and successful billion-dollar health industry”, in particular since this technology can be applied to many more situations than the original indication of obstruction of the Fallopian tubes. The “industry” has enormously expanded by offering a possible solution for so-called male factor infertility thanks to Intracytoplasmic Sperm Injection (ICSI). However, there are some major problems remaining to be solved. First and foremost relates to the health concerns in the offspring, mainly the increased prevalence of paediatric malignant diseases [2,3], and the metabolic and the cardiovascular pathologies which probably are related to oxidative and epigenetic alterations of DNA [4]. The second problem concerns the elevated cost of the procedure, both regarding the medication for Controlled Ovarian Stimulation (COS) using gonadotropins containing Follicle Stimulating Hormone (FSH), and the expense of laboratory techniques. Thirdly, there are the low pregnancy rate and the increased risk of spontaneous abortion possibly due to alterations of the DNA of the gametes (oocytes and spermatozoa) and of the biochemical composition of follicular fluid [5]. These result in a high cost per successful pregnancy.

The present paper addresses these concerns and summarises possible ways to resolve these.

Materials and Methods

In 1994 the centre for reproductive medicine and fertility of the general hospital Jan Palfijn of Ghent (Belgium) has introduced IVF (WD). The yearly pregnancy rate has been recorded and compared to the average pregnancy rate of all Belgian centres for reproductive medicine. Pregnancies were defined by the presence of a heart beating embryo.

During the time span of 25 years several interventions have taken place and their effects on the pregnancy rate was registered. These interventions included in sequence order: the systematic investigation and treatment of the male partner implementing the WHO guidelines [6] from 2006 onward (FC), the preconception food supplementation with the nutraceuticals Fertility man[®] and Fertility woman[®] (Nutriphyt Ltd, Beernem, Belgium) since 2008

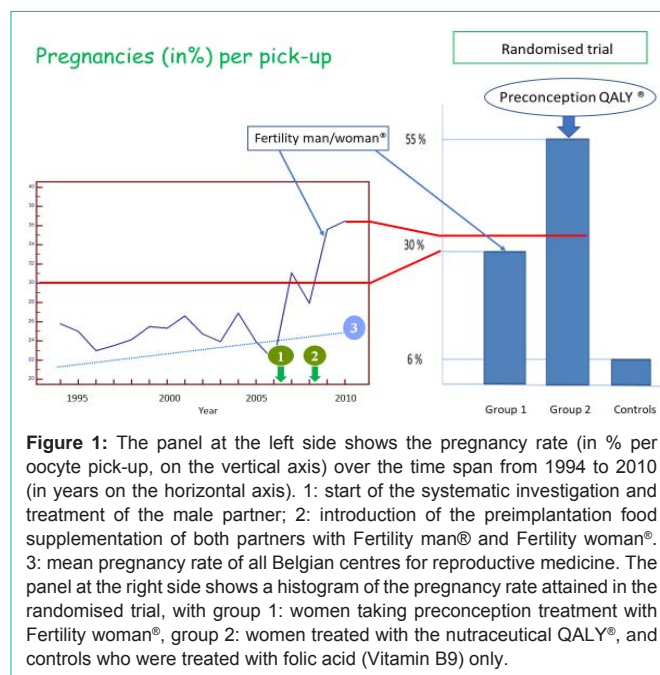


Figure 1: The panel at the left side shows the pregnancy rate (in % per oocyte pick-up, on the vertical axis) over the time span from 1994 to 2010 (in years on the horizontal axis). 1: start of the systematic investigation and treatment of the male partner; 2: introduction of the preimplantation food supplementation of both partners with Fertility man[®] and Fertility woman[®]. 3: mean pregnancy rate of all Belgian centres for reproductive medicine. The panel at the right side shows a histogram of the pregnancy rate attained in the randomised trial, with group 1: women taking preconception treatment with Fertility woman[®], group 2: women treated with the nutraceutical QALY[®], and controls who were treated with folic acid (Vitamin B9) only.

[7], the investigation of an alternative protocol for COS using low-dose Human Chorionic Gonadotrophin (hCG) in 2016, and the comparison of Fertility woman[®] supplementation with the newly formulated nutraceutical QALY[®] (JonaPharma, Elversele, Belgium) in a randomised trial during 2017-2018 [4].

All data were collected in Excel files and statistically analysed with the MedCalc programme (MedCalc Ltd, Ostend, Belgium) [8] using appropriate methods.

Results

Figure 1 represents the longitudinal registration of pregnancies per year and the result of the controlled randomised trial with the two nutraceuticals. Both the introduction of the systematic investigation and treatment of the male partner, and the preconception food supplementation with the Fertility[®] supplements resulted in a significant increased pregnancy rate. This was further enhanced by replacing Fertility woman[®] by the preconception intake of QALY[®] in the controlled randomised trial.

The alternative COS protocol using low-dose of the cheap Human Chorionic Gonadotrophin (HCG) to replace the FSH-containing Human Menopausal Gonadotrophin (HMG) not only increased the pregnancy rate by 38%, but also substantially lowered the cost per pregnancy [9]. As a result, the expense for obtaining 10 pregnancies using the conventional FSH protocol was sufficient to achieve 18 pregnancies when using the low-dose HCG protocol for COS.

In the controlled randomised trial several important findings were recorded in the group treated with QALY[®], namely decreased concentration of oxidised DNA (8-hydroxy 2-deoxyguanosine) in urine, lower concentration of homocysteine in blood, and decreased methylation of the Human Telomerase Reverse Transcriptase (hTERT) promoter region in the cells of the corona radiata obtained at follicular puncture.

The pregnancy rate attained by IVF in the group (group 2, fig 1) treated with QALY[®] exceeded that in both the control group taking folic acid only, and the cases treated with Fertility woman[®] (group 1), the latter being similar to the pregnancy rate recorded in the observation period from 2008 to 2016. It should be underscored that the pregnancy rates recorded in this randomised trial relate to a relatively small number of cases, and need to be confirmed in a larger pragmatic study.

Discussion

Overcoming the major obstacles and resolving the concerns related to the IVF procedure and the health of offspring seems within reach. The mechanisms responsible for oxidative and epigenetic DNA alterations and biochemical deregulation related to controlled ovarian stimulation can be corrected by preconception food supplementation with a judiciously composed nutraceutical. Together with the implementation of an alternative protocol of controlled ovarian stimulation, food supplementation increases the pregnancy rate and reduces the cost per ongoing pregnancy. Complementary development of cheaper laboratory techniques, such as explored by the “Walking egg” project, [10] may further reduce the cost of IVF. It should be stressed that thorough investigation and treatment of both partners is mandatory before assisted reproductive techniques are applied. Thanks to this, up to 40% of infertile couples will achieve spontaneous conception, avoiding drastic and potentially disruptive medical interventions.

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