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ARTICLE

Luteal-phase support in assisted reproduction treatment: real-life practices reported worldwide by an updated website-based survey

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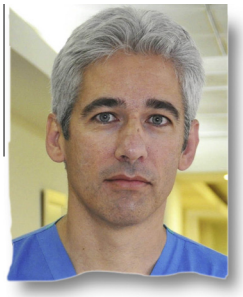

Edi Vaisbuch obtained his medical degree at the Hebrew University and Hadassah School of Medicine in Jerusalem and completed his residency at the Kaplan Medical Centre, Israel. In 2007 he joined the Perinatology Research Branch of NICHD/NIH/DHHS in Detroit as a research associate and in 2008 was appointed as an Assistant Professor at the Wayne State University in Detroit, Michigan. Currently, he is in charge of the high-risk pregnancy unit at Kaplan Medical Centre. His special interest is in complications of pregnancy and pregnancy outcomes and he is an author and co-author of more than 90 peer-reviewed publications.

Abstract An updated worldwide web-based survey assessed the real-life clinical practices regarding luteal-phase supplementation (LPS) in assisted reproduction. This survey looked for changes since a former survey conducted nearly 3 years earlier. The survey questions were: If you support the luteal phase, when do you start the regimen you are using?; Which agent/route is your treatment of choice to support the luteal phase?; If you use vaginal progesterone, which formulation do you use?; and How long you continue progesterone supplementation if the patient conceived? Data were obtained from 408 centres (82 countries) representing 284,600 IVF cycles/year. The findings were: (i) most practitioners (80% of cycles) start LPS on the day of egg collection; (ii) in >90%, a vaginal progesterone product is used (77% as a single agent and 17% in combination with i.m. progesterone), while human chorionic gonadotrophin as a single agent for LPS is not being used at all; and (iii) in 72% of cycles, LPS is administered until 8–10 weeks' gestation or beyond. When compared with the initial survey, the results of this survey are encouraging as there is a clear shift towards a more unified and evidence-based approach to LPS in IVF cycles.

KEYWORDS: ART, human chorionic gonadotrophin, IVF, luteal phase, LPS, progesterone

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Introduction

It is well established that the ovarian stimulation regimens used in virtually all assisted reproduction cycles alter the luteal phase (Edwards et al., 1980; Kolibianakis et al., 2003; Macklon and Fauser, 2000; Ubaldi et al., 1997). Ovarian stimulation ultimately causes an inadequate development of the endometrium and an asynchrony between the endometrium and the transferred embryos, resulting in adverse effects on endometrial receptivity (Abate et al., 1999; Devroey et al., 2004; Kolibianakis et al., 2002; Macklon and Fauser, 2000; Nikas et al., 1999; Smitz et al., 1988). In more than 50% of the cases, ovarian stimulation delays endometrial development by 2 or more days, which hampers the implantation chances (de Ziegler et al., 1994).

The first meta-analysis on luteal-phase supplementation (LPS) nearly 20 years ago concluded that both human chorionic gonadotrophin (HCG) or progesterone supplementation improve pregnancy rates (Soliman et al., 1994). Since then, several other meta-analyses and Cochrane reviews have confirmed and expanded these early results (Daya and Gunby, 2004; Nosarka et al., 2005; Pritts and Atwood, 2002). Recently, Van der Linden et al. (2011) published an updated Cochrane Review of 69 studies totaling 16,327 women, which confirmed the beneficial effects of LPS using exogenous progesterone. In this review, the addition of other agents such as oestrogen or HCG did not seem to improve outcome.

IVF-Worldwide (www.IVF-Worldwide.com) is a comprehensive IVF-focused website for doctors, embryologists, nurses and social workers. The primary aim of IVF-Worldwide is to offer to its members the possibility to locate IVF programmes anywhere in the world and communicate directly with their members. The website, which brings together doctors and assisted reproduction specialists from around the world, promotes dialogue and discussions on all sorts of treatment and management issues. The website is a non-commercial entity supervised by an advisory board of 52 key leaders in the field. It regularly reviews questions of general interest in assisted reproduction treatment, such as those on LPS as reported here.

Studies reporting on LPS and the meta-analyses that sum up their findings rely on data obtained in the women who partook in the published studies. Generally these women have to satisfy sometimes-stringent exclusion and exclusion criteria, *de facto* making them subgroups of the general population. This explains that lingering questions remain as to whether the results of the classic studies are always relevant for the everyday life problems encountered by assisted reproduction specialists around the world. In order to address these issues, IVF-Worldwide conducted a first web-based survey on LPS in assisted reproduction and posted its results on the website of IVF-Worldwide.com in 2009 (Vaisbuch et al., 2012). Strikingly, the survey revealed that doctors generally failed to abide by the rules of evidence-based medicine in their everyday medical practices. Indeed, nearly two-thirds of programmes reported that vaginally administered progesterone was the preferred form of LPS. Yet, in apparent contradiction with the above, oral progesterone, i.m. progesterone and HCG were still routinely used by many practitioners for LPS despite published data highlighting their disadvantages. The present work reports an update of the original web-based survey, posted on www.IVF-Worldwide.com. The new data were mustered for assessing whether LPS practices in assisted reproduction had changed since the initial survey conducted nearly 3 years ago.

Materials and methods

The web-based questionnaire entitled 'An updated survey on the use of progesterone for luteal-phase support in stimulated IVF cycles' was posted on the IVF-Worldwide website on 24 May 2012 and remained open for entering data until 26 June 2012. The survey contained demographic questions including the name of the unit's medical director, the name of the IVF unit, email address, country and number of IVF cycles in the unit in the most recent year.

The specific questions addressed progesterone support in IVF and included: (i) If luteal-phase support is offered, when is your regimen started? The survey offered four possible answers for this question: (a) day of egg collection; (b) day of embryo transfer; (c) day of HCG administration; and (d) a few days after embryo transfer; (ii) Which agent/route is your treatment of choice for luteal-phase support? The offered answers were: (a) vaginal progesterone; (b) i.m. progesterone; (c) oral progesterone; (d) combination of the drugs mentioned above; (e) HCG; and (f) other; (iii) If you use vaginal progesterone, which formulation do you use? The offered answers were: (a) vaginal tablets; (b) vaginal progesterone gel; (c) vaginal suppositories; and (d) combination of the above; and (iv) How long do you continue progesterone supplementation when the patient conceives? The offered answers were: (a) until pregnancy is confirmed in a blood or urine test; (b) until the presence of fetal heart beat; (c) until gestational weeks 8–10; and (d) until gestational week 12 or later.

Quality assurance methods

In order to minimize duplicate reports from a unit and possible false data, quality assurance methods were used as previously described (Vaisbuch et al., 2012). In brief, the consistency of four parameters in the self-reported data of the unit surveyed with existing data of units registered on the IVF-Worldwide website was assessed using a computerize software. These parameters included the name of the unit, the name of the unit director, country and email address. If at least three of these parameters from the survey matched the website archive data, this reporting site's data was included in the statistical analyses.

Statistical analysis

The analysis was based on the number of IVF cycles reported by the unit and not on the number of units in the study. For each question, the survey provided multiple choices from which only a single answer could be chosen ('radio buttons'). For example, for a question with four answers (a, b, c, d), the following results were calculated: