Patient-friendly IVF: how should it be defined?

Eric Flisser, M.D.,[a] *Richard T. Scott, Jr., M.D.,*[b] *and Alan B. Copperman, M.D.*[a]

[a] Reproductive Medicine Associates of New York, New York, New York; and [b] Reproductive Medicine Associates of New Jersey, Morristown, New Jersey

Abstract: "Patient-friendly" IVF must be associated with a healthy newborn achieved in a safe, cost-effective, and timely manner. Patients are best served when physicians provide honest appraisal of treatment techniques and outcomes using the evidence available from scientific study. (Fertil Steril® 2007;88:547–9. ©2007 by American Society for Reproductive Medicine.)

Traditionally, physicians have defined "patient-friendly" care as the best possible outcome with greatest efficiency, using the most cost-effective and least invasive regimens. Rather than using traditional claims of compassionate care, high success rates, and increased patient safety, a growing minimalist front is promoting a new standard for "patient-friendly" practice. However, in this case it refers not to the health of the mother or the birth of a healthy child, but to limiting medical evaluation and degree of treatment. In the U.S. and abroad, an increasing number of fertility centers have recently reverted to minimal stimulation protocols of decades past despite a dearth of evidence-based, peer-reviewed data to support their re-emergence. The premise and promise of less invasive treatments have enticed the media to consider such minimalist strategies as the equivalent of tried and true remedies and protocols. This has further led to difficulties in properly educating patients while web sites, marketing materials, and even international congresses lend a false aura of legitimacy to this technique.

Exponential growth in IVF cycles is flattening and gonadotropin usage is no longer increasing. Although many believe that changing demographics, such as the departure of Baby Boomers from the reproductive age group, and rising success rates, which decrease the need for repeat IVF cycles, may be the causes, others report that infertile couples stop before completing treatment because therapy is too arduous, clinic visits too frequent, and injections too numerous. Practitioners have responded to patient needs with sensitivity by trying to make infertility treatments more palatable. Therapists are now routinely available for patients with emotional needs, computerization has increased scheduling efficiency, and satellite offices of central laboratories have made fertility treatment more accessible.

Received December 24, 2006; revised and accepted March 19, 2007.
Reprint requests: Alan B. Copperman, M.D., Reproductive Medicine Associates of New York, 635 Madison Avenue, 10th Floor, New York, NY 10021 (FAX: 212-756-5770; E-mail: acopperman@rmany.com).

Unfortunately, these advances have not been identified as making IVF more patient friendly. Instead, practitioners of minimalist IVF treatment have co-opted the term "patient-friendly IVF." This spin-doctoring inherently prejudices patients against other forms of treatment and, by implication, suggests that all alternatives are "unfriendly," if not outright "patient-hostile." Ironically, crowning minimalist techniques as "patient-friendly" may produce a lasting, negative effect on patient care.

A search of the internet for "patient-friendly IVF" yields fascinating results. "Regimented" programs that follow protocols are denounced and complaints abound about physicians who require of the patient a long list of "useless tests." One clinic claims that "most of these tests are of no use whatsoever, because they do not affect the treatment or its outcome" (1). Still other programs would do away with the hysterosalpingogram and sonohysterography, despite their well demonstrated efficacy in identifying pelvic pathology that can significantly alter the likelihood of treatment success. Reasoned evaluation of the facts reveals how much of a misnomer "patient-friendly" medicine can be and what magnitude of disservice it does to patient education.

The number of IVF cycles being performed using minimalist techniques is impossible to quantify, but these protocols are garnering much attention. The media have taken up this cause using scare tactics (2), compounding the difficulty of properly educating patients. Celebrity endorsements and international congresses (3) add an air of legitimacy to unsubstantiated technique.

Although performing tests that are only strictly necessary to complete a basic infertility work-up may superficially appear to be "patient-friendly," the associated laboratory work before starting an IVF cycle is performed *for the patient's health*. Although it does not have a direct outcome on the success of fertility treatment, knowing that a patient is free of HIV and *Chlamydia* has significant implications for the patient's health and the health of her baby. Requiring a patient

0015-0282/07/$32.00
doi:10.1016/j.fertnstert.2007.03.055

to have a routine annual Pap smear may seem onerous to some, but delaying treatment of cancer for 9 months would hardly be considered "patient-friendly." Failing to offer testing for genetic disorders that are common and easily detected, such as cystic fibrosis, appears less "patient-friendly" when a child is born with an otherwise preventable disease. These tests may be inconvenient, and some may be costly, but they are examples of good medical practice. Preconception counseling and testing presents a rare moment to intervene and improve the health of our patients and their future offspring, not an opportunity to eschew our responsibility to them. Eliminating appropriate genetic and medical screening would set us back decades, and avoiding follicle and hormone monitoring could increase morbidity significantly.

Although a simplistic, unified, "patient-friendly" approach to IVF treatment sounds attractive, treatment is rarely so straightforward that a single approach or protocol is universally successful. The various protocols now available in the armamentarium of the practitioner permits personalization to the patient to a degree not available in the early days of this emerging technology. As the technology has evolved, so has success.

Making IVF more patient-friendly is a noble goal. Fewer injections, fewer visits, and fewer tests have the potential to decrease patient dropout from stress, cost, emotional duress, and hopelessness. We can think of no outcome of infertility therapy more patient friendly than a healthy newborn. Although effortless and carefree treatment is an ideal to be sought, rarely has the treatment of disease ever been without some small measure of discomfort. As physicians, we wish that this were not true, but the reality of bad medicine and unanticipated outcomes gives us pause about pretending otherwise. The published medical literature has clear examples of how infertility therapies, when improperly managed, can result in severe disability or death.

Limiting the number of injections is truly a "patient-friendly" goal. Use of GnRH antagonists has decreased the number of injections for some patients (4). Long-acting or nasally active gonadotropins and in vitro maturation may soon be available. Instead of patiently looking to the future, however, some would mistakenly return to the past by reinventing clomiphene citrate–only and clomiphene citrate–hMG combination IVF. These stimulation protocols were largely abandoned after recombinant FSH and purified hMG products became available, because the improvement in quantity of retrieved oocytes improved IVF success, even if only by attrition of lesser-quality embryos. Despite historically low success with clomiphene IVF cycles, some have chosen marketing over science and have touted the "advantages" of minimal stimulation protocols.

Improvements in laboratory technology and technique have yielded higher implantation rates, renewing interest in minimal stimulation protocols, but optimal laboratory conditions are not a panacea to poor protocol selection, and there are little new data to support the use of clomiphene in IVF. In fact, clomiphene citrate may be no better than natural cycle IVF, which has repeatedly been shown to be inefficient (<10% clinical pregnancy per cycle) (5–8). Repeating one procedure that has a 10% chance of success four times is not mathematically equivalent to performing a procedure with a 40% chance of success once. Cumulative pregnancy rates after three cycles of minimal stimulation have been disappointingly low, yielding per-cycle success rates of only 8% (9), similar to the expected rate of clomiphene citrate–intrauterine insemination rates, limiting its utility.

Practice development in a competitive medical field is challenging, because medicine and advertising are not comfortable partners. Consequently, marketing to patients is a complicated venture. Advertising in all disciplines of medicine, and in particular reproductive medicine, has been scrutinized and criticized, opening a debate about what is acceptable and ethical behavior. Because the doctor-patient relationship is based on mutual trust and respect, physicians are expected to be above personal material interests in the pursuit of the best medical care for patients. Promoting procedures known to have poor results undermines this trust. Patients may prefer lower-yielding IVF procedures because lower implantation rates may offer lower risks of multiple gestation, but they must be carefully counseled about their choices. To do less is unconscionable. Past violations of ethical standards have undermined the public's image of physicians. Unsubstantiated claims and opinions, opportunistic reporting and fictionalizations, and the absence of tort reform have contributed to the calls for increased oversight and regulation. Questionable medical practices have given the public reason to call for increased scrutiny.

The "less is better" thesis has tremendous emotional appeal, because patients inherently dislike taking medications for any reason, viewing it as unnatural. Minimal stimulation techniques thrive on this appeal. However, promoters of minimal stimulation protocols largely use theoretic arguments to support their methods, rather than scientific proof, pointing to effects that *might* occur. It is a challenge to counter arguments that lack significant proof or data. What is *possible* illogically trumps what is *known*. A recent review of abstracts presented at the First World Congress on Natural Cycle/Minimal Stimulation reports "doubts," theory that "requires confirmation," claims that "stressed … uncertainties," and procedures that "might be superior" (10). The lack of definitive statements is telling. We do not claim that concerns regarding safety and attempts to create more efficacious treatment are not valid, just that without proof they do not justify serving our patients poorly.

Making minimal stimulation IVF synonymous with patient-friendly stimulation is an example of a marketing neologism overcoming science. George Orwell warned against this kind of "newspeak," by which words are, "deliberately constructed … intended to impose a desirable mental attitude upon the person using them." The opposite of minimal stimulation is not maximal stimulation, but optimal stimulation,

a goal toward which we should all strive, and because the intent of medicine is always to achieve the best outcomes this adjective rarely needs to be explicitly stated.

We live in an era of evidence-based medicine and professionalism. Having evolved from mystical thinking to scientific process, we must not exchange honest goals for marketing taglines and glamour. The information age has given patients ready access to the world but no filter to distinguish reputable and responsible practitioners from those who would prey on their hopes, fears, and insecurities. "Patient-friendly" IVF must be associated with a healthy newborn achieved in a safe, cost-effective, and timely manner.

REFERENCES

1. Malpani Infertility Clinic. Patient friendly IVF—IVF in 2 weeks. Available at: http://www.drmalpani.com/patient-friendly-ivf.htm. Accessed April 14, 2007.
2. Fertility at risk from IVF drugs. Sydney Morning Herald December 4, 2006.
3. First World Congress on Natural Cycle/Minimal Stimulation IVF. December 15–16, 2006. London, England.
4. Copperman AB. Antagonists in poor-responder patients. Fertil Steril 2003;80:S16–24.
5. Fahy UM, Cahill DJ, Wardle PG, Hull MGR. In-vitro fertilization in completely natural cycles. Hum Reprod 1995;10:572–5.
6. Paulson RJ, Sauer MV, Francis MM, Macaso TM, Lobo RA. In vitro fertilization in unstimulated cycles: the University of Southern California experience. Fertil Steril 1992;57:290–3.
7. Claman P, Domingo M, Garner P, Leader A, Spence JEH. Natural cycle in vitro fertilization–embryo transfer at the University of Ottawa: an inefficient therapy for tubal infertility. Fertil Steril 1993;60:298–302.
8. Pelnick MJ, Hoek A, Simons AHM, Heineman MJ. Efficacy of natural cycle IVF: a review of the literature. Hum Reprod Update 2002;8:129–39.
9. Pelinck MJ, Vogel NEA, Hoek A, Simons AHM, Arts EGJM, Mochtar MH, Beemsterboer S, et al. Cumulative pregnancy rates after three cycles of minimal stimulation IVF and results according to subfertility diagnosis: a multicentre cohort study. Hum Reprod 2006;21:2375–83.
10. Edwards RG. Are minimal stimulation IVF and IVM set to replace routine IVF? Reprod Biomed Online 2007;14:267–70.