Is a prolonged bed rest following embryo transfer useful?

Giuseppe Botta1,3 and Gedis Grudzinskas2

1Ecocenter and Fertility Center, Clinica ‘C.G. Ruesch’, 39 via Maria Cristina di Savoia, 80122, Naples, Italy and 2Academic Department of Obstetrics and Gynaecology, St Bartholomew and Royal London Hospital, School of Medicine and Dentistry, London E1 IBB, UK
3To whom correspondence should be addressed

A total of 182 infertile patients undergoing in-vitro fertilization (IVF)-embryo transfer were randomly assigned into two groups. Eighty-seven patients (group A) underwent 97 treatment cycles and had 87 embryo transfer procedures followed by a 24 h period of bed rest. Ninety-five patients (group B) underwent 102 treatment cycles and had 93 embryo transfer followed by a 20 min period of bed rest. There were no statistically significant differences seen between the groups with respect to age, duration and causes of infertility and number of previous fertility treatments. The clinical and biological procedures were identical in both groups, the only difference being the length of bed rest. There were 21 pregnancies in group A (pregnancy rate per embryo transfer: 24.1%) while in group B there were 22 (pregnancy rate per embryo transfer: 23.6%). There were four spontaneous miscarriages (19%) and three twin pregnancies (14.2%) in group A, while in group B there were four spontaneous miscarriages (18.1%) and three twin pregnancies (13.6%). None of these values was statistically significant (P > 0.05). This study shows that a 24 h period of bed rest following embryo transfer is not associated with a better outcome of the IVF-embryo transfer when compared with a 20 min rest period. Prolonged bed rest does not appear to influence the implantation rate after IVF-embryo transfer.

Key words: bed rest/embryo transfer/IVF

Introduction

Embryo transfer is an important stage of the in-vitro fertilization (IVF) procedure, and may substantially influence the outcome of treatment. Many variations in the embryo transfer protocol have been evaluated, including: position of the patient (Jones et al., 1983; Englert et al., 1986; Rienhard et al., 1986), quantity of culture medium (Martinez and Trounson, 1986), number of embryos transferred, administration of drugs before and after embryo transfer (Hazout and Menezo, 1996), type of catheter (Gonen et al., 1991), position of the catheter in the uterine cavity (Yovich et al., 1985), timing of embryo transfer (Sholtes and Zeilmaker, 1996), and the use of fibrin sealant (Feichtinger et al., 1992; Ben Rafael et al., 1995).

Historically bed rest following embryo transfer has been generally advised, ranging in duration from 15 min to 24 h or more (Sharif et al., 1995). A long period of bed rest is a common precautionary measure used to try to improve the implantation rate. However, this has never been shown to be related to a higher success rate and its relevance in IVF is still controversial. In this study we compare a 20 min period of bed rest with a period of 24 h bed rest following embryo transfer.

Materials and Methods

Patients

Between January 1993 and December 1994, 182 infertile patients underwent a complete IVF-embryo transfer procedure at ‘C.G. Ruesch’ Clinic. The patients were randomly assigned into two groups, which were homogeneous with respect to age, duration and causes of infertility or number of previous treatments (Tables I and II). A total of 87 patients (group A) underwent 97 treatment cycles and had 87 embryo transfer procedures followed by a 24 h period of bed rest. In contrast, 95 patients (group B) underwent 102 treatment cycles and had 93 embryo transfer procedures followed by a 20 min period of bed rest.

The clinical, surgical and biological procedures were identical in the two groups, and were carried out in the same operating theatre and in the same laboratory by the staff including the authors. The only difference was therefore the duration of bed rest.

Ovarian stimulation and oocyte retrieval

The protocols for ovarian stimulation included the administration of a single i.m. injection of o-Trp-6-LH RH (Decapeptyl; Ipsen, Milan, Italy) or Leuprolerin (Enantone; Takeda Italia Farmaceutici, Italy) and the administration of human menopausal gonadotrophin [HMG, Pergonal 500; Serono, Rome, Italy] or leutinizing hormone (FSH) 75 IU plus luteinizing hormone (LH) 75 IU per ampoule or FSH (75 IU per ampoule, Metrodin 75; Serono) and has been described in detail elsewhere (Botta et al., 1995). Typically the gonadotrophin dosage was three or four ampoules from day 1 to day 4, the HMG dosage from day 5 being adjusted according to the oestradiol concentrations and the ultrasound findings of follicular growth. A total of 10 000 IU of HCG (Profasi HP 5000; two ampoules; Serono), were administered when two or more follicles >17 mm in diameter were seen and the oestradiol concentration was >800 pg/ml. The luteal phase was supported by the administration of 100 mg of progesterone (Gestone 100; AMSA, Milan, Italy), every other day. The oocytes were retrieved by transvaginal ultrasound-guided puncture 34 h after HCG administration.

Embryo transfer

In both groups embryo transfer was performed 46–50 h after oocyte retrieval. The patients were placed in a modified lithotomy position on a gynaecological bed, without any reference to fullness of the bladder. A sterile disposable Cusco’s speculum was inserted and the
The results are summarized in Tables III and IV, only clinical pregnancies being considered. The mean number of ampoules of HMG or FSH/cycle was 50 in group A and 54 in group B. The mean number of follicles >14 mm on diameter on the day of HCG administration was 7.6 in group A and 7.2 in group B. The mean number of oocytes collected was 5.2 in group A and 5.4 in group B. The mean number of embryos obtained was 3.5 in group A and 3.8 in group B and the mean number of embryos transferred was 2.1 in group A and 2.3 in group B (Table III).

The number of cycles with embryo transfer of at least one embryo were 87 (89.7%) in group A and 93 (90.3%) in group B. In group A there were 21 pregnancies (pregnancy rate per embryo transfer: 24.1%), while in group B they were 22 (pregnancy rate per embryo transfer: 23.6%). In group A there were 4 spontaneous miscarriages (19%) and 3 twin pregnancies (14.2%), while in group B there were 4 spontaneous miscarriages (18.1%) and 3 twin pregnancies (13.6%). The results of the two groups were similar and the statistical analyses did not show any statistical significance in the observed differences.

Discussion

To our knowledge, this is the first study analysing the effects of 24 h bed rest on implantation rate following IVF-embryo transfer. As low implantation rates and a high incidence of early pregnancy loss in patients after IVF have been observed, the clinical miscarriage rate in these patients has been considered to be higher than in women who conceive spontaneously (Liu et al., 1988; Hamori et al., 1989; Glatstein et al., 1995). Failure of implantation is the most common cause of failure of IVF treatment (Sharif et al., 1995). Therefore, embryo transfer has been approached with caution and care from the early days of IVF programmes, since this is the single most critical step and a mistake in this procedure could influence the rate of implantation.
In recent years, several investigations have examined various aspects of embryo transfer techniques, including position of the women, medications, catheter characteristics and rest after embryo transfer. It has been suggested that women with a retroverted uterus should assume the knee-chest position while a modified lithotomy position is preferred for women with an anteverted uterus (Jones et al., 1983). Others have suggested the modified lithotomy position for both these situations (Englert et al., 1986; Rienthaller et al., 1986).

The administration of drugs such as diazepam and tetracyclines (Jones et al., 1983), antiprogestaglandins (Poindecker et al., 1986) or anaesthetics (Fishel et al., 1985) has also been suggested before embryo transfer. In addition, progesterone or HCG are commonly prescribed for luteal phase support (Ron El et al., 1993; Hazout and Ménéo, 1996). Different types of catheter have been evaluated (Gonen et al., 1991) as well as the depth of catheter insertion, the midcavity position being considered preferable (Yovich et al., 1985).

Investigations on the optimal timing to perform embryo transfer after oocyte collection have been carried out (Scholtes and Zeilmaker, 1996). The amount of medium (from <30 up to 100 µl) needed for the transfer has also been reviewed (Martinez and Trounson, 1986). Some authors have evaluated the use of a fibrin sealant after embryo transfer (Feichtinger et al., 1992; Ben Rafael et al., 1995), but did not observe any increase in the implantation or pregnancy rate.

Finally, many fertility centres have advised bed rest of 24 h or more following embryo transfer, together with some restrictions in the patient's daily life (Ron El et al., 1993; Sharif et al., 1995). A long period of bed rest is generally thought to be prudent, but experimental or clinical data are not available to validate this view. Furthermore, Sharif et al. recently reported a study on 103 IVF procedures with no bed rest following embryo transfer, the pregnancy rate for embryo transfer in that study being 40%. These authors concluded that their positive results strongly supported the hypothesis that bed rest is unnecessary to improve the reproductive outcome.

The nature and number of critical factors necessary to result in successful implantation following IVF–embryo transfer are not clear (Landgreen et al., 1996).

In natural conceptions, early pregnancy wastage is attributed to (i) embryo abnormality or (ii) poor receptivity of the endometrium (Liu et al., 1988; Coulam et al., 1994). In IVF procedures many other factors may be involved, including ovarian hyperstimulation and extracorporeal manipulation of gametes and embryos (Liu et al., 1988; Hamori et al., 1989). Implantation begins 4–7 days after fertilization (Edwards, 1994). Since embryo transfer is generally performed 2 days after the oocyte collection, implantation may begin 2 days following this. Furthermore, delayed nidation of the embryos following embryo transfer, in comparison to natural pregnancies, is well recognized (Englert et al., 1984). The delay may be as long as 4 days or more (Englert et al., 1984; Hamori et al., 1989). This has also been observed after gamete intra-Fallopian transfer, suggesting that it may be related to the extracorporeal manipulation (Remorgida et al., 1988).

Thus, mechanisms of nidation following embryo transfer are probably different from those following spontaneous pregnancy, and the biological events affecting embryos in the period between transfer and implantation, or their relationships with the endometrium, are largely unknown. Embryo implantation is a very complex event influenced by hormonal and biological factors. To date, no evidence has been presented to show that mechanical factors such as mobilization of the patient or the upright position may negatively influence the implantation rate following IVF–embryo transfer.

Our study shows that a bed rest of 24 h following embryo transfer is not associated with a better outcome of the IVF procedure when compared to a bed rest of 20 min. We have concluded that a long period of bed rest is unnecessary. The women, a few minutes after embryo transfer, can stand, empty their bladder and return home with no apparent risk to the process of implantation. No restriction of the routine activity of the patients need be advised after the transfer. This observation has some important economic implications: a short bed rest following embryo transfer avoids an extra day of recovery in the clinic and its related costs. Moreover, the early return of the patient to her daily activities allows an immediate return to work with no loss in productivity.

Acknowledgements

We are grateful to the members of Fertility Center’s staff for their clinical support in this study.

References


G. Botta and G. Grudzinskas


Received on February 13, 1997; accepted on August 1, 1997