European Journal of Obstetrics & Gynecology and Reproductive Biology 178 (2014) 95–99

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

The psychological effects and patient acceptability of a test to predict viability in early pregnancy: a prospective randomised study

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ARTICLE INFO

Article history:
Received 16 May 2013
Received in revised form 8 January 2014
Accepted 4 April 2014

Keywords:
Early pregnancy
Anxiety
Ultrasonography
Progesterone
Prediction

ABSTRACT

Objective: To establish if women obtain any measurable short term psychological benefit or perceived benefit from having a test to determine the probability of their pregnancy being on-going when this is uncertain on ultrasound examination.
Study design: This was a prospective randomised controlled study conducted January 2012–June 2012 at the EPU of King's College Hospital. The study population was women who conceived spontaneously and had a single intrauterine gestational sac of <20 mm mean diameter, with no visible embryo on their first ultrasound scan. Eligible women were randomised to have a test to calculate the probability of viability (cases) or not (controls). Depression and anxiety levels were calculated using the Hospital Anxiety and Depression Score (HADS) and were performed prior to randomisation and seven days later. A repeat scan for pregnancy outcome was performed after one to two weeks as clinically indicated. A sample size of 69 in each group was calculated to have 80% power to detect a probability of 0.362 that an observation in the cases was less than an observation in controls using a Wilcoxon Mann–Whitney rank-sum test with a 0.05 two-sided significance.
Results: At recruitment there was no significant difference in anxiety levels between cases and controls. After seven days anxiety levels were significantly lower in cases than controls ($p = 0.04$). Of those who received the probability score, 55/70 (78.6% 95% CI 67.5–86.7%) found it useful and 58/70 (82.9% 95% CI 72.2–90.1) would choose to have the test in a future pregnancy if indicated.
Conclusions: This study has demonstrated that there is evidence of psychological benefit from a simple blood test that gives women the likelihood that their pregnancy will be on-going at the next scan.

Introduction

Women who are found to have a small gestational sac with no visible embryo on their initial assessment in an Early Pregnancy Unit, need to undergo a period of waiting for one to two weeks, until it can be established whether the pregnancy is on-going or destined to miscarry. This finding is common in Early Pregnancy Units (EPUs) and a recent audit at our hospital showed found that 25% of ultrasound scans demonstrate early intrauterine pregnancies of uncertain viability when women first present. The overall risk of miscarriage in these women is estimated to be 12%. This increases to 30% in the presence of vaginal bleeding [1]. As clinicians, we usually give women an educated opinion as to whether their pregnancy is likely to be ongoing, likely to miscarry or we are genuinely uncertain based on their history and ultrasound findings. However, in women with a gestational sac measuring less than 20 mm in diameter and no visible embryo, the probability of the pregnancy being viable can be calculated by taking into account maternal age, size of the sac and serum progesterone levels [2]. This model was developed on a study population and validated in clinical practice in our unit [1,2]. The aim of the current study was to determine whether women's depression and anxiety levels are influenced by having this test performed in addition to standard care in the EPU. The study also set out to establish how useful women perceived the test to be.

Methods

This was a prospective randomised controlled study conducted January 2012–June 2012 at the EPU of King's College Hospital. The study was approved by the NHS Research Ethics Committee London and all the participants gave written informed consent.

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http://dx.doi.org/10.1016/j.ejogrb.2014.04.002
0301-2115/

Women were referred to the EPU by their General Practitioner, the emergency department or they self-referred. Women were not seen in the EPU as part of their routine antenatal care; the unit is for the assessment of women with symptoms such as bleeding, abdominal pain, hyperemesis or for the assessment of asymptomatic women at high risk of an ectopic pregnancy or with previous miscarriages. The patients' demographic details, clinical history and ultrasound measurements and images were documented on a computer database (PIA Foetal Database, Viewpoint Bildverarbeitung GnbH, Munich, Germany). Trans-vaginal ultrasound scans (Voluson E6) were performed by the attending clinicians who were specialist trainees or consultants in Obstetrics and Gynaecology. The gestational sac was measured from the inner edges of the trophoblast in three orthogonal planes and the mean of these three measurements recorded as mean gestational sac diameter (GSD). The presence of a yolk sac, appearance of the uterus, ovaries, pouch of Douglas and ultrasound images were recorded on the same database. All patients attending the department received immediate feedback from the clinicians regarding the implications of the ultrasound findings in the context of their case.

Inclusion criteria for the study included a positive pregnancy test (Clearview HCG 11), spontaneous conception, and a single intrauterine gestational sac of less than 20 mm with no visible embryo. A yolk sac was not considered to be a visible embryo so these women were also eligible.

Exclusion criteria included assisted conception, multiple pregnancy, use of exogenous progesterone, women who declined to be randomised, women who intended to terminate the pregnancy, women receiving treatment or investigation for a psychiatric disorder or who were non-English speaking.

Women meeting the inclusion criteria were counselled regarding the significance of a small gestational sac, i.e. that they were either too early in a viable pregnancy to see an embryo or that it was a pregnancy where development had arrested at an early stage. Eligible patients who consented to take part in the study completed a baseline Hospital Anxiety and Depression Score (HADS). The HADS has been developed to identify possible and probable anxiety and depression among non-psychiatric patients [3]. It has been used in pregnant populations in longitudinal and cross sectional studies [4] and consists of seven items measuring anxiety and seven measuring depression. Each item has four answer categories giving a score between 0 and 3. The higher the score the greater the anxiety or depression [4]. The HADS has not been validated in non-English speaking patients therefore non-English speaking patients were excluded from the study.

Women were randomly allocated to receive a probability of viability score or to the control group who did not receive any intervention in addition to the routine clinical discussion of the ultrasound findings. Randomisation was carried out by means of computer-generated random numbers performed by an independent researcher. Concealment of allocation was achieved by using opaque sealed envelopes labelled according to study participant number.

Patients who were allocated to receive the score had a blood sample taken for serum progesterone. Progesterone was measured in nmol/l using an auto-mated immunoassay technique (Advia Centaur Immunoassay system, Siemens AG, Germany). The probability of viability was calculated using the following equation:

$$\text{probability of viability} = \frac{1}{1 + e^{-z}}$$

where $z = (6.091 \times \ln \text{progesterone nmol/l}) - (0.159 \times \text{sac diameter mm}) - (0.164 \times \text{maternal age years}) - 17.435$

This was calculated using a an excel spreadsheet on the computer desktop. Patients who were randomised to intervention received the results the same day and could choose to do so either face to face or over the telephone. All patients chose to receive the result by telephone. Both groups had a date for a rescan arranged in one to two weeks as was clinically appropriate. The General Practitioner was informed of the patient's participation in the study. Both groups of patients were contacted by telephone seven days after their initial assessment and a repeat HADS performed. At the rescan appointment the outcome of the pregnancy was documented. A viable pregnancy was defined as the presence of an embryo with visible cardiac activity. Following this scan, women who received the score were then asked two questions regarding their perceived usefulness of the test.

A pseudo-anonymous record of all women that were approached to enter the study was kept in order to compare demographic details to assess if there was any bias in the uptake of the study which may have reflected or influenced initial anxiety levels.

The primary outcome was the difference in HADS at 7 days between cases and controls.

A sample size of 69 in each group was calculated to have 80% power to detect a probability of 0.362 that an observation in the cases was less than an observation in controls using a Wilcoxon Mann–Whitney rank-sum test with a 0.05 two-sided significance level [4]. Allowing for a 20% drop out and a 50% consent acceptance rate, a total number of 346 patients was estimated to be required to obtain a sample size of 69 in each group. For each of the variables analysed, univariate descriptive statistics provided an overall picture of the data. Continuous variables were presented as median and inter-quartile range (IQR), unless otherwise stated. For categorical variables, frequency counts and percentages were presented as summary statistics for the subgroups of interest. To compare study groups, the *t*-test was used for continuous variables, and the Fisher's test for categorical variables. Differences were considered significant at $p < 0.05$.

Results

There were 200 women with early intrauterine pregnancies who met the study inclusion criteria. Of these, 157 consented to participate in the study. The demographic and clinical data of the study group and those who declined to participate are shown in Table 1. Women that attended for dating of the pregnancy were significantly more likely to agree to participate in the study. Other than this there was no significant difference in demographics between the two groups. There was no significant difference in demographic data, indication for ultrasound scan or ultrasound parameters between cases and controls (Tables 1 and 2). Fig. 1 is a flow chart of participants through the study.

There was no significant difference between the baseline HADS of cases and controls at the time of the initial scan and consultation (Table 2). After seven days, anxiety levels fell in both groups, but they were significantly lower in cases than controls ($p = 0.04$). The depression scores for both groups rose over seven days, but there was no significant difference in depression scores between the two groups.

There was no significant difference in the number of viable pregnancies between the two groups at the follow up scan (Table 2). Overall, 55/70 (78.6% 95% CI 67.5–86.7%) women found it useful to receive the probability of viability score. There was no significant difference in acceptability according to pregnancy outcome (Table 3). Women were also asked if they would choose to have the test again should they be in a similar position in a future pregnancy, and 58/70 (82.9% 95% CI 72.2–90.1%) women would do so. Again there was no significant difference in pregnancy outcome between those that would choose the test and those that would not (Table 3).