Home ovulation testing in a donor insemination service

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The use of home ovulation testing kits in donor insemination (DI) has been proposed to increase patient and clinic convenience while not compromising fecundity rates. Such a system was introduced into our DI service in December 1994, and we here report an audit of experience over 6 months. Patients were offered home or laboratory luteinizing hormone (LH) testing, and those requesting home testing were asked to store an aliquot of tested urine for subsequent assay in the laboratory allowing retrospective analysis of the accuracy of cycle timing. Insemination using cryopreserved semen was performed on the day home testing predicted ovulation, or on the day an LH surge was detected in the laboratory, and on the following day. Pregnancy rates were significantly reduced in home testers: 3.4\% per cycle (174 cycles, 64 women) versus 12.7\% (110 cycles, 53 women) over the same time period ($P < 0.005$, 95\% confidence interval 6.5–18.9). Urine samples from 140 cycles from 51 women using home testing were analysed. There were insufficient data in nine to allocate the cycle. Of home tested cycles, 37 (28\%) were inseminated on a day other than the first day of the LH surge. In 13 of these insemination was performed after the first day of the LH surge. Incorrect treatment was associated with high baseline LH, but those with ‘late’ treatment had low basal LH concentrations, similar to those correctly treated. Analysis of individual urine samples showed that the positive predictive value of home testing was 72\%. These results suggest that home ovulation testing results in reduced chance of pregnancy, with increased frustration for both patients and clinic staff. This may be particularly so in women with high baseline LH concentrations.

Key words: donor insemination/ovulation/timing of insemination

Introduction

Donor insemination (DI) requires accurate timing for success. A variety of techniques has been used to assess the time of ovulation, including temperature charts, cervical mucus scoring, ultrasound scanning and measurement of plasma and urinary luteinizing hormone (LH) (Kenn, 1982; Vermeesch et al., 1987; Odem et al., 1991). While the LH surge is the most accurate way of predicting impending ovulation (Hoff et al., 1983), it requires daily attendance at the clinic, which is time-consuming and inconvenient for patients and staff alike. Recent advances in monoclonal antibody technology have allowed the development of simple and rapid testing kits suitable for home detection of the LH surge (Corsan et al., 1990). Suggestions have been made that the use of such semiquantitative kits results in pregnancy rates similar to traditional symptomatic methods of ovulation detection (Robinson et al., 1992) or plasma LH assay (Cant et al., 1989).

Home testing has also been used to time studies of luteal phase uterine volume and blood flow (Bourne et al., 1996).

Our routine practice has been daily assay of morning urinary LH, with insemination on the day of detection of the LH surge and on the following day. We here report our experience of introducing home ovulation detection.

Materials and methods

From December 1994 all women being treated with DI were freely offered the choice of home or laboratory urinary LH testing; 64 women chose home testing, and 53 women chose laboratory testing in the 6 month period to 31 May 1995. Spontaneous ovulation had been previously demonstrated biochemically in 59 women (160 cycles) in the home testing group, and in 42 women (81 cycles) in the laboratory testing group. Ovulation was induced using clomiphene citrate in the remaining women, and was confirmed by luteal phase urinary pregnanediol assay in all women. Laparoscopy and hysterosalpingography had been performed confirming tubal patency in 56 (88\%) of home testers and 43 (81\%) of laboratory testers. Patients purchased the test kit of their choice, 50\% used ‘Conceive’ (Quidel, San Diego), 43\% ‘Clearplan’ (Upjohn, Bedford, UK) and 7\% ‘ Predictor’ (Schefaro International BP, Rotterdam, Netherlands). All kits used a quantitative colour change which was compared to a reference colour (quoted by the manufacturer of the most widely used kit to be equivalent to a LH concentration of 2.5 IU/l). Patients were given detailed instruction in the use of the kits, and asked to freeze an aliquot of each tested urine sample for subsequent delivery to the laboratory for assay of LH (Maiaclone, Serono, Geneva, Switzerland), with results expressed as IU/mmol creatinine. Patients attended for insemination on the day they assessed the kit to give a positive result, i.e. on the presumed day of the LH surge, and on the subsequent day. Some patients declined to attend for the second insemination.

Data were analysed from a 6 month period. A cycle was regarded as correctly treated if insemination was performed on the first day a LH surge was identifiable. This was defined as LH value 2.5 times baseline, or twice baseline if the subsequent sample showed a further rise confirming the onset of the LH surge.
Home ovulation testing in donor insemination

Figure 1 Pregnancy rates in home-tested and laboratory-tested cycles Mean ± 95% confidence limits.

Table 1 Characteristics of patients using home-testing kits or laboratory testing for detection of ovulation

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Home testing</th>
<th>Laboratory testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-4</td>
<td>32 0 ± 0 3</td>
<td>32 9 ± 0 4</td>
</tr>
<tr>
<td>5-8</td>
<td>39%</td>
<td>38%</td>
</tr>
<tr>
<td>9+</td>
<td>19%</td>
<td>27%</td>
</tr>
<tr>
<td>No. male partners with azoospermia (%)</td>
<td>36 (56)</td>
<td>34 (64)</td>
</tr>
<tr>
<td>No. male partners with oligozoospermia (%)</td>
<td>22 (34)</td>
<td>13 (25)</td>
</tr>
</tbody>
</table>

Women requesting laboratory testing were required to deliver morning urine samples to the clinic by 0900 h, and were inseminated on the day of detection of the LH surge and on the subsequent day. Cryopreserved semen from the same pool of donors was used for both groups of patients.

A brief questionnaire was posted to 63 couples who had used home testing to assess the acceptability of this method.

Statistical analysis

Data are presented as mean ± SEM. Student's t-test was used for comparison of urinary LH concentrations. Pregnancy rates and characteristics of home versus hospital testing groups were compared using the χ² test, and Fisher's exact test was used to compare the distribution of baseline LH concentrations.

Results

Between 1st December 1994 and 31st May 1995, 174 cycles in 64 patients were treated using home testing and 110 cycles in 53 patients using laboratory testing. The pregnancy rate in home-tested cycles was significantly reduced at 3.4% per cycle [95% confidence interval (CI) 0.7-6.1], compared to 12.7% in laboratory-tested cycles (P < 0.005, 95% CI 6.5-18.9, Figure 1). Characteristics of the patients having home and laboratory testing are given in Table 1. Age at treatment was similar in the two groups, as was the distribution of the indication for DI. The home testing group had fewer previous cycles (P < 0.05), being within the patient's first four cycles in 42% compared to 28% in hospital testers. Single insemination was performed in 28% of home-tested cycles compared to 19% of laboratory-tested cycles (not significantly different). There was also no significant difference in the pregnancy rates according to whether the patient was inseminated once or twice (7.3 and 7.0% respectively). While the indication for DI was 'oligozoospermia' in an apparently greater number of home-tested cycles, this did not reach statistical significance.

To investigate possible reasons for this reduced pregnancy rate, data from individual home-tested cycles were analysed retrospectively. A total of 140 home-tested cycles from 51 women was assessed, nine of which there was insufficient data for analysis. No samples were collected from a further 48 cycles, despite the patients being requested to do so. Insemination was found to have been performed at an 'incorrect' time, i.e. other than on the first day of the LH surge, in 37 (28%) of the cycles. In 13 (10%) of the cycles insemination was found to have been performed after the onset of the LH surge ('late' treated cycles). Thus in 72% of cycles insemination was judged to have been performed on the 'correct' day (Figure 2). Analysis of a total of 652 individual urine samples gave a sensitivity for detection of the LH surge of 82%, specificity of 93%, and a positive predictive value of 72%.

Mean baseline LH concentrations in the incorrectly treated group were 1.14 ± 0.14 IU/mmol creatinine, and 0.87 ± 0.05 IU/mmol creatinine in correctly treated cycles. These values were not statistically different, but analysis of the distribution of baseline LH concentrations showed a pronounced skew towards higher values in the incorrectly treated group (Figure 3). Thus 25% had a baseline LH >2.0 IU/mmol creatinine, compared to 5% in correctly treated cycles (P < 0.01). This difference in baseline LH, however, did not apply to late treated cycles: mean baseline LH was 0.71 ± 0.10 IU/mmol creatinine in these cycles (Figure 3). If these cycles were excluded from the incorrectly treated group, mean baseline LH for that group rose to 1.23 ± 0.16 IU/mmol creatinine, which was significantly different from both the correctly treated group and the late treated group (P < 0.01, both comparisons). Anti-oestrogens were not used in any of the incorrectly treated cycles.
Correct

Incorrect

Late

Figure 3. Baseline luteinizing hormone (LH) concentrations in correctly, incorrectly, and late treated cycles. The distribution of LH concentrations (IU/mmol creatinine) is given in 0.2 IU intervals.

While baseline LH concentrations in late treated cycles were similar to correctly treated cycles, LH values on the first day of the LH surge were lower. Mean LH concentration on day 1 of surge was 4.8 ± 0.3 IU/mmol creatinine in correct group, and 3.0 ± 0.5 in the late group (P < 0.001). Peak LH concentrations in the late treated group were 4.8 ± 0.6.

The questionnaire was returned by 40 (63%) couples. Of these, 73% thought the kits expensive, 86% found the kits easy to use, and 75% found the result easy to interpret; 81% expressed confidence in their use, but 33% would have liked further assistance in using the kits. Furthermore, only 48% would prefer home testing in future cycles. Even with the convenience of home testing, 67% felt that undergoing treatment with DI significantly interfered with their working lives.

Discussion

Home testing has been suggested to offer the increased convenience of reduced clinic attendance without compromising fecundity rates (Robinson et al., 1992). Home testing was offered to all patients attending for DI, and over a 6 month period a small majority (55%) chose this method. There was a significantly lower pregnancy rate in those choosing home testing. This study is an analysis of the use of home ovulation detection kits in practice rather than a randomized study, thus there may be confounding factors accounting for this result. The results in the table demonstrate that the patients in the two groups were comparable in age and indication for treatment. Those using home testing had fewer previous treatment cycles, which would tend to increase the likelihood of conception. A similar proportion in both groups required anti-oestrogen treatment to induce ovulation. The number of cycles inseminated twice was higher in the laboratory testing group, but this did not reach statistical significance. There was also no significant difference in pregnancy rate between singly and doubly inseminated cycles. It is therefore likely that the significantly reduced pregnancy rate in the home testing group is a result of the method of detection of the LH surge rather than a confounding factor. This contrasts with the results of previous studies. Possible reasons for this discrepancy include problems with the kits themselves, or patient factors which resulted in inaccuracies in the use of the kits.

All kits in the present study rely on an increase in intensity of a colour strip with increasing concentration of LH, and comparison with a standard colour strip of known LH concentration. The distinction between a positive and negative result can be difficult to see, and is more difficult in artificial light. The manufacturers of the most widely used kit in this study claim an accuracy (presumably meaning positive prediction rate) of 90%, which compares with the value of 72% found by us. We do not have any direct data on the accuracy of the kits themselves. However, detailed analysis of individual cycles identified two patient factors associated with inaccuracy in the timing of ovulation. Thus insemination was more likely to be performed with incorrect timing in women with higher baseline LH concentrations. In these cycles a positive home test was not temporally related to the LH surge. This did not apply to those cycles in which insemination was performed late, i.e. after the onset of the LH surge: these cycles had low baseline LH levels similar to those correctly treated, but the delay in treatment resulted from low LH concentrations on the first day of the surge although the subsequent peak LH value was similar to that in the correctly treated group. Although anti-oestrogens were used to induce ovulation in a small proportion of women in this study and might have contributed to higher baseline LH concentrations, these drugs were not in fact taken in any of the cycles in the incorrectly treated group. The likelihood of pregnancy resulting from intercourse in relation to time of ovulation has recently been re-examined (Wilcox et al., 1995): no pregnancies occurred when intercourse occurred after ovulation, but the chance of conception was similar for the day of ovulation and the 2 preceding days. It is likely that cryopreservation reduces the duration of viability of spermatozoa, thus increasing the need for accuracy of insemination timing (Wolf, 1995).

There was also evidence from the questionnaire that home testing was not an ideal solution to the problem. The kits were perceived as expensive, and although the great majority
expressed confidence in their use, 33% would have liked further assistance despite receiving clear verbal and written instructions, and slightly less than half would use home testing in the future. This was in a self-selected population who had specifically opted to use home testing.

In conclusion, these results suggest that in routine use, home ovulation kits of this type are associated with a significantly reduced pregnancy rate. We have identified on biochemical grounds two 'patient factors' that may contribute to this, by adversely affecting the accuracy of timing of insemination. Such kits should therefore be used with caution by clinics, as they result in an ineffective service to patients and wastage of scarce resources.

References


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