Reasons for discontinuation of IVF treatment: a questionnaire study

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BACKGROUND: IVF and embryo transfer has become an established and increasingly successful form of treatment for infertility, yet significant numbers of couples discontinue treatment without achieving a live birth. This study aims to identify major factors that influence the decision to discontinue IVF treatment. METHODS: Questionnaires were sent to 1510 couples who had undergone IVF treatment at Ninewells Hospital and Medical School, Dundee, Scotland, between January 1995 and December 2001. The main outcome measure was the number of couples who discontinue treatment and the reasons for discontinuation including live birth, lack of success, lack of funding, psychological stress, medical advice, physical discomfort, personal and other reasons. RESULTS: The response rate was 55% (732/1327) with 183 questionnaires returned as address unknown. A total of 515 couples had discontinued treatment at time of response, with 266 (52%) having achieved a live birth. Achieving a live birth was the reason for discontinuation where a single reason was given. Those who did not conceive gave a combination of reasons. Lack of personal and/or National Health Service funding was cited by 23% of couples as a reason. Lack of success and psychological stress were reported as factors by 23 and 36% of couples respectively. These two factors are very strongly associated (P < 0.001), both being reported by 18% of couples with a reciprocal increase in those quoting lack of success and psychological stress as reasons for discontinuation with increasing number of attempts (P < 0.0005). Changes in personal circumstances were reported by 30% and <10% gave general discomfort or advice from medical staff as reasons. CONCLUSIONS: Though funding is an important issue, factors including lack of success and psychological stress play a greater role in influencing the decision to discontinue treatment. Better information and support are needed to improve the continuation rates.

Key words: discontinuation/funding/IVF/psychological stress

Introduction

IVF and embryo transfer has become an established and increasingly successful form of treatment for infertility. The last two decades have seen major advances in reproductive technologies, which along with improved data collection and documentation have increased public awareness of the availability and efficiency of assisted conception. The Human Fertilisation and Embryology Authority (HFEA) 9th Annual Report (2000) shows an improvement of live birth rate from ∼14% in 1991–1992 to ∼22% in 2000–2001 for IVF treatment in the UK.

Increasing awareness, combined with better knowledge of availability of services, has led to an increased demand for assisted conception treatment over the last decade. In 1998–1999, 35363 IVF treatment cycles were undertaken in the UK compared to 17031 treatment cycles in 1992–1993. The American Society for Reproductive Medicine/Society for Assisted Reproductive Technology Registry has reported a 13.5% increase in the number of treatment cycles from 1999 to 2001. The first cycle of treatment is statistically the most successful attempt, but multiple attempts improve the probability of achieving a pregnancy (Templeton et al., 1996). The estimated cumulative conception rate after four attempts has ranged from 54% (Tan et al., 1992) to 75% (Sharma et al., 2002).

Despite the improvements in assisted reproduction technologies and their increasing availability and success, <30% of women have more than one attempt at IVF in the UK (Templeton et al., 1996). Many factors have been proposed to explain why so few couples have only one IVF treatment cycle, and in the UK this has been mainly attributed to the lack of National Health Service (NHS) funding. High drop-out rates in assisted conception treatment are a common feature reported in several studies (Croucher et al., 1998; Roest et al., 1998; Sharma et al., 2002; Schroder et al., 2004; Smeenk et al., 2004). The high drop-out rate following the first treatment cycle often coincides with the end of funding by health authorities, though it is argued that poor prognosis and psychological reasons also contribute to discontinuation of further treatment. Goldfarb et al. (1997) reported that lack of finance was the major reason for
discontinuation of treatment after a failed IVF cycle. On the other hand, Emery et al. (1997) documented that one in five couples withdrew from the programme before completion of the available number of treatment cycles while a further one in three significantly delay their treatment cycles. Olivius et al. (2004) have recently reported a drop-out rate of 54% with 26% of couples discontinuing their treatment for psychological reasons, despite state funding being available. Similarly in Australia, Hammerberg et al. (2001) reported that the mean number of cycles started in their population was 3.0 even though funding was available for up to six cycles, indicating that lack of funding is not the sole reason for discontinuation of IVF treatment.

This study aims to determine the number of couples who discontinue assisted conception treatment over a 6 year period, to identify major factors that influence this decision. This is based on questionnaire data collected from a large cohort of patients attending a single tertiary centre in the UK.

Materials and methods
A cohort of 1510 couples who underwent their first IVF/ICSI treatment cycle in the Assisted Conception Unit, Ninewells Hospital, Dundee, UK, over a 6 year period between January 1995 and December 2001 were identified. An average of 500 cycles is undertaken in the Unit each year providing both NHS and self-funded assisted conception treatment to five health boards. Up to three attempts are offered on NHS funding, and the waiting time to start the first and any subsequent attempts varies from 6 weeks to 2 years. A 6 year period was therefore selected to give a more complete reflection of discontinuation rates, as couples would have completed two or three NHS funded cycles in this time.

Questionnaire
The data for this study were obtained from a questionnaire, which was posted to all couples whose current address was available from the unit database. As the responses were anonymous, couples’ medical records could not be examined.

The questionnaire had three parts, the first part was for demographic data, the second for details of their assisted conception treatment to date, and the third to determine if treatment had been discontinued and any reasons for this.

The first mailing of 1510 questionnaires was in January 2003 to couples who had completed at least two full cycles of treatment prior to the survey. Those who had first treatment cycle in 2001 would have completed their second attempt at the time of survey. In total, 183 (183/1510, 12.1%) questionnaires were returned as address unknown or moved away, so up to 1327 questionnaires were received by couples. After an initial period of 4 months a total of 532 responses had been received. The questionnaire was therefore sent a second time, to the same couples, 6 months after the first. On this occasion it was again sent to all couples as it was not possible to tell who had responded the first time. Couples were instructed not to reply if they had already done so and it is assumed they complied with this. In all, 732 (732/1327, 55.2%) responses were received, an additional 200 returned from the second mailing.

Statistical methods
Most data handling and analysis was performed with the Minitab (v13) package. In general, the questionnaire was designed so that results could be recorded as frequency or percentage in each category of response. Approximate 95% confidence intervals (CI) were used to express the precision of estimates of population percentages.

The complete frequency distribution was obtained for discrete quantitative variables such as number of completed IVF treatment cycles. Some grouping of extreme values was made in cases where there were a large number of low frequency values in a long upper tail. Quartiles and extremes were used to summarize frequency distributions. Pearson’s χ²-statistic, with appropriate degrees of freedom, was used to test for independence between categorical variables. Odds ratios with 95% CI were used to compare probabilities of events in different subgroups of patients. For the results of test procedures and CI to be meaningfully interpreted and applied to a general population of couples who had experienced assisted conception, the sampling procedure used must be assumed to introduce no biases.

Ethics
All aspects of the study were given approval by the Local Medical Research Ethics Committee. All data were stored under the terms of the Data Protection Act 1998.

Results
A comparison was made between the responses received from the two mailings of the questionnaire, in particular for the variables: ages of female and male partner at start of treatment; number of IVF cycles started; number of frozen embryo transfers; and discontinuation of treatment. There was no appreciable difference between the responses of those who replied to the first mailing and of those who replied to the second mailing for any of these variables. The results from the two mailings were therefore pooled and analysed together for all 732 respondents.

As was to be expected, a large percentage (94%) of first treatment cycles was undertaken at Ninewells Hospital with similarly high percentages for the second (94%) and third (93%) attempts, which can be attributed to the stability of the local population. The percentage had dropped by the fourth and fifth and further attempts to 91 and 84% respectively.

Demographics
The mean age of the female partner of couples treated in the Unit during the study period was 36 (range 23–44) years, with the mean number of attempts being 3 (range 1–6) and a clinical pregnancy rate of 20.5%. The indication for IVF treatment included tubal factor (29%), unexplained infertility (36%), endometriosis (14%), anovulation (7%), and male factor (14%).

The median age of the female partner at time of response was 37 years and the age ranged from 24 to 48 years; for the male partners, the corresponding median age was 39 years, with ages ranging from 25 to 65 years. Overall, 9.6% of female partners and 15.3% of male partners already had one or more children, while in 5.6% of couples both partners already had children. A total of 575 (78.6%) couples reported primary subfertility. The median duration of subfertility was 4 years, the lower and upper quartiles were 3 and 6 years respectively, and it was ≥10 years in 8.7% of couples. Ninety-two per cent of female partners were between 26 and 40 years at first treatment. The mean live birth rate per attempt reported by the respondents was 16.8%.

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**Distribution of couples (number and percentage) with each attempt at which they discontinued treatment**

Figure 1 gives the distribution of the number of IVF treatment cycles started. Of 732 respondents who made at least one attempt, 486 (67%) made two or more attempts, 303 (42%) made three or more attempts, 119 couples (16%) made four or more attempts and 48 (7%) made five or more attempts. NHS funding was available to 55–60% of couples in their first, second, third and fourth attempt, with the remaining couples funding themselves. Thirty-five per cent of those who had a fourth attempt and were funded by the NHS gave a history of a previous abandoned cycle.

**Chances of successful IVF treatment**

More than 95% of couples had discussed the chances of successful IVF treatment, i.e. of pregnancy. Their awareness of the success rate with one attempt, which was given as 10–30%, and only 26% of couples quoting a more realistic value of ≥30%. The proportion of couples who did not venture a response to success rate with three attempts was somewhat higher than for success with a single attempt at 17%.

**Counselling**

Sixty-seven per cent of the respondents recalled being offered counselling; however, only 20% of couples saw an independent counsellor at the Assisted Conception Unit. Of those who stated that counselling had not been offered, 153 of the 187 respondents (82%) felt it should have been.

**Discontinuation of treatment**

Of the 732 responding couples, 513 (70%) had discontinued IVF treatment while the remaining 217 were considering further treatment. Of these, only 71 (71/217, 32.7%) were on an NHS waiting list for further treatment cycles. A total of 247 patients of the 732 respondents (34%) had discontinued treatment without achieving a pregnancy.

Table I shows the number of couples who undertook exactly 1, 2, 3 or ≥4 cycles along with the total number who dropped out, the number who achieved a live birth, and those who did not become pregnant but discontinued treatment in each of these groups. The drop-out rate was 70% overall and per attempt it was lowest at 66% for those who had undergone two treatment cycles to date and highest at 79% for couples who had undergone three cycles.

**Reasons for discontinuation of treatment**

Fifty-two per cent (266/513) of those discontinuing treatment had achieved a pregnancy, with the remaining 48% couples discontinuing treatment without doing so. Percentages for each of the reasons suggested for discontinuing treatment in the questionnaire are shown in Figure 2. Most couples gave more than one of these reasons.

Lack of personal or NHS funding was cited by 23% of couples as a reason. Lack of success and psychological stress were reported as factors by 23 and 36% of couples respectively. These two factors are very strongly associated (P < 0.001), both being reported by 18% of couples. Other reasons, which include change in personal circumstances, were reported by 30% of couples. Less than 10% of couples gave general discomfort or advice from medical staff and others as reasons.

**Reasons for discontinuation by number of treatment cycles**

Table II gives the percentage of couples discontinuing treatment after each started attempt from first to fourth or later attempt for each of the suggested reasons. For each reason, the χ²-test with 3 degrees of freedom was used to investigate whether it would be reasonable to suppose that the drop-out rate was the same at every treatment cycle. The P-values for these tests are also given in Table II.

There was a reduction in the percentage of couples discontinuing treatment because of pregnancy with increasing number of treatment cycles (P < 0.0005). This reflects that the success rate decreases with each further attempt. There was a reciprocal increase in the percentage of couples quoting lack of success (P < 0.0005) and in those reporting psychological stress (P < 0.0005) as reasons for discontinuing treatment with increasing number of attempts.

**Table I.** Distribution of couples (number and percentage) with each attempt at which they discontinued treatment

<table>
<thead>
<tr>
<th>No. of cycles started</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>≥4</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of couples (%)</td>
<td>246(34)</td>
<td>183(25)</td>
<td>184(25)</td>
<td>119(16)</td>
<td>732(100)</td>
</tr>
<tr>
<td>No. of couples</td>
<td>175(74)</td>
<td>118(66)</td>
<td>140(79)</td>
<td>80(67)</td>
<td>513(70)</td>
</tr>
<tr>
<td>with live birth</td>
<td>113(46)</td>
<td>57(31)</td>
<td>66(36)</td>
<td>30(25)</td>
<td>266(52)</td>
</tr>
<tr>
<td>discontinued treatment (%)</td>
<td>62(25)</td>
<td>61(33)</td>
<td>74(40)</td>
<td>50(42)</td>
<td>247(48)</td>
</tr>
</tbody>
</table>

Figure 1. Total number of couples undergoing IVF attempts (1+ = 1 or more, 2+ = 2 or more etc.) and National Health Service funding for the attempts.
Discontinuation of IVF treatment

Drop-out due to personal financial difficulties showed an increase with number of cycles, particularly after the second attempt ($P < 0.01$), whereas drop-out reported from lack of NHS funding appeared roughly constant across all cycles ($P = 0.48$) averaging out at 19%. There was a noticeable increase with number of attempts in drop-out in those couples obtaining others’ advice ($P = 0.037$) but no real change with number of attempts in drop-out from discomfort ($P = 0.60$). The percentage of couples who gave ‘other’ reasons was effectively constant at 30% with increasing number of attempts ($P = 0.17$).

Age of female partner at discontinuation of treatment

Age at discontinuation of treatment did not appear to have a great impact on the percentage of those giving any of the listed reasons for discontinuing treatment. However, the female partner was significantly younger on average for those couples who stopped treatment after the first attempt than for those who had more than one treatment cycle ($P < 0.0005$). This was still true even when the couples who achieved pregnancy were omitted ($P < 0.001$).

Single versus multiple reasons for discontinuation of treatment

Of the 513 respondents who had discontinued treatment, 250 couples gave only one reason (group 1). This was listed as pregnancy achieved in 71% of this group, while other personal reasons were quoted by a further 17% (Figure 3). None of the other listed reasons was cited by >3% of couples in this group.

Where more than one reason was cited (group 2 comprising 263 couples), the percentages of couples indicating each of the listed reasons is shown in Figure 3. Psychological stress was reported by 69% of these couples. Interestingly 25% of this group had also achieved a pregnancy but did not wish to consider further treatment because of other indicated reasons.

The most commonly cited pair of reasons for discontinuing treatment was psychological stress and lack of success.

Discussion

Several studies have reported rates of discontinuation of IVF treatment. In The Netherlands, where state funding is available for up to three attempts, the drop-out rate after three cycles was reported as 62.4% (Land et al., 1997), while in Sweden, OliviU et al. (2004) reported a drop-out rate of 54% even though funding was still available to these couples. In the UK the drop-out rates are reported to be higher (Templeton et al., 1996) as very little and disparate NHS funding has been available to most couples. However, even in the UK, Emery et al. (1997) reported a high drop-out rate from a clinic where funding was available to couples. Studies have shown that both female and male partners give evidence of stress while undergoing IVF treatment (Boivin and Tafekman, 1995) while others have shown that the aspiration and waiting to become pregnant can be more stressful than the treatment itself (Laffont and Edelmann, 1994b).

This study was carried out in an Assisted Conception Unit in Scotland, where NHS-funded assisted conception treatment has been available for two or three fresh attempts within set eligibility criteria, along with self-funded treatment. The aim of the study was to estimate the actual discontinuation rates in an assisted conception programme over a 6 year period. The response rate to the survey questionnaire was 55%, with 266 (36%) couples discontinuing treatment after achieving a live birth. Thirty-four per cent (247/732 respondents) had discontinued treatment without achieving a pregnancy in the 6 year period.

A couple’s decision to discontinue treatment is probably due to a complex interplay of factors. Several potential factors were included in the study, so those which are relevant could be identified and highlighted. In this cohort ~70% of the respondents had more than one treatment attempt, in

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**Table II.** Drop-out (%) for each listed reason by number of attempts

<table>
<thead>
<tr>
<th>Attempt no.</th>
<th>Reasons</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>65</td>
<td>9</td>
<td>18</td>
<td>15</td>
<td>4</td>
<td>25</td>
<td>6</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>48</td>
<td>22</td>
<td>17</td>
<td>16</td>
<td>5</td>
<td>33</td>
<td>8</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>47</td>
<td>29</td>
<td>18</td>
<td>24</td>
<td>10</td>
<td>41</td>
<td>8</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>≥4</td>
<td>38</td>
<td>44</td>
<td>25</td>
<td>32</td>
<td>13</td>
<td>52</td>
<td>11</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
<td>23</td>
<td>19</td>
<td>21</td>
<td>7</td>
<td>36</td>
<td>8</td>
<td>30</td>
<td></td>
</tr>
</tbody>
</table>

$P$ ($\chi^2$-test) = <0.0005 <0.0005 0.5 <0.01 0.037 <0.0005 0.60 0.17

Reasons: 1 = pregnant; 2 = lack of success; 3 = lack of NHS funds; 4 = personal financial; 5 = medical/others’ advice; 6 = psychological stress; 7 = discomfort/disruption; 8 = other reasons (including personal circumstances).
contrast to previously published data (Templeton et al., 1996). NHS funding was available to ∼55–60% of the couples up to the fourth attempt and undoubtedly has contributed to 40% of couples having up to three attempts, unlike previous data suggesting only 30% of couples have more than one attempt. Though NHS funding is usually for up to three attempts, reported funding of a fourth attempt may reflect previous abandoned cycle. Despite funding being available for up to six cycles in a population in Australia, the mean number of cycles started in that study was 3.0 regardless of achieving a live birth (Hammerberg et al., 2001). This study also confirms that lack of funding is not the sole or main reason for discontinuing treatment. Seventy-two per cent of the respondents in this study had discontinued treatment at the time of the response, with 52% of those discontinuing after achieving a live birth. Of those still considering treatment, only one-third were still on a waiting list, implying that the decision to continue treatment was not based solely on funding issues.

Couples had a good awareness of the estimated chances of a live birth with one attempt of IVF treatment, though their awareness or understanding of the cumulative live birth rates with three or more attempts was poor. Counselling is offered to all couples before, during or after treatment, both in a written information pack, and during consultations. Only 67% of couples recalled that counselling had been offered, while 20% saw an independent counsellor in the unit. This is similar to the experience of previous researchers (Boivin, 1997; Hammerberg et al., 2001). Although patients may express an interest in taking up counselling, the actual take-up rate is <25%. However, they are reassured to know that counselling is available (Laffont and Edelmann, 1994a).

An increasing number of attempts was linked to increasing personal financial strain, though lack of NHS funding after the third attempt did not significantly influence the drop-out rate. Physical discomfort or disruption had no apparent impact on the decision to discontinue. The observed increase in the drop-out rate for ‘other reasons’, including changed personal circumstances after the third attempt had failed, was not significant. Medical advice or advice from family and friends played a minor role. In this study, the age of the female partner was lower in those who discontinued treatment after one attempt, indicating that prognosis was not a major factor influencing their decision to stop treatment despite failing to achieve a pregnancy.

The three most significant factors influencing the decision to discontinue treatment appear to be decreasing pregnancy rates, the continuing lack of success, and the psychological stress associated with increasing number of attempts. Similar findings of increasing despair after repeated unsuccessful cycles of IVF have been reported in a recent qualitative study by Peddie et al. (2005). In summarizing the relationship between stress and infertility, Domar (2004) reported that the most common reason for termination of treatment was psychological burden. Other studies have shown that psychological stress was the most common reason for discontinuing treatment (Goldfarb et al., 1997; Olivius et al., 2004) and may have an impact on treatment outcome (Klonof-Cohen, 2001; Smeenk et al., 2001). Emotional stress is inherent to infertility itself, with this study showing the increasing degree of distress following failure to conceive after consecutive attempts of IVF treatment. A previous study has shown that women find a negative pregnancy test, waiting for the result and the wait between attempts to be the most stressful stages of IVF (Laffont and Edelman, 1994b). More support should be considered from providers of IVF treatment at these stages, though whether it will ameliorate anxiety needs evaluation.

This study highlights the fact that couples need clear and individualized information about their treatment to make an informed decision, which should be restated between attempts. The information regarding the cumulative live-birth rates following three or four attempts at IVF treatment was not well understood by this group of patients. A better understanding of this information may help in coping with failures after repeated attempts and help to reduce the psychological stress that this unavoidably causes. Whether better uptake of counselling services will reduce the drop-out rate is not clear, though couples need to know that it is available. While the efficiency of IVF treatment is improving, it does not guarantee a successful outcome. Health care providers involved in assisted conception treatment need to be more aware of the psychological stress associated with repeated attempts at IVF and strategies to improve outcome and support to couples need to be considered.

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References
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