How Do Adolescent Minors Banking Sperm Before Cancer Therapy Subsequently Use The Fertility Service? A Post Banking Re-evaluation.

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BACKGROUND

More and more adolescents are surviving cancer. But treatments may be gonadotoxic. Fertility is a potential reproductive right. Minors deemed sexually mature have been offered the chance to bank sperm before treatment at University College Hospital since 1999. We previously reported our experience in 16 adolescents offered banking at diagnosis.

OBJECTIVES

1. To re-evaluate how many patients banking sperm successfully (GpA) returned for post treatment re-evaluation compared with those who attempted but failed (GpB).
2. To compare longitudinal sperm counts, fertility rates and survival, by group and prior gonadotoxicity risk.

METHODS

Retrospective collection of post treatment survival, semen analysis (sperm count, concentration, motility and volume), and biochemical (LH/FSH/testosterone) parameters in 76 of 117 patients who succeeded in their attempt to bank sperm between 2000-2010 and of whom 38/117 returned for re-evaluation.

GpA) Successful: any viable sperm banked (n=76).
GpB) Unsuccessful: azoospermia or necrospermia (n=17).
GpC) Unable: to produce a sample (n=24).

Gonadotoxicity Risk

The risk of developing subfertility based on the initial treatment regimen was graded:

1) Low < 20% 2) Medium = 20 – 80% 3) High > 80% as per current UK guidance.

"Infertility" was defined as FSH >15IU/l or azoospermia.

Data are shown as median and range; intergroup comparisons were made using non parametric statistics. P values < 0.05 were significant.

RESULTS

Table 1 – Original cohort of those who attempted to bank initially

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (years)</th>
<th>Chronic or Died</th>
<th>Re-evaluated</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Successful</td>
<td>65</td>
<td>09</td>
</tr>
<tr>
<td></td>
<td>n=6</td>
<td></td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>Reproductive</td>
<td></td>
<td>24</td>
</tr>
<tr>
<td></td>
<td>FSH &gt;15 IU/l</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>33</td>
</tr>
<tr>
<td>B</td>
<td>Unsuccessful</td>
<td>15</td>
<td>04</td>
</tr>
<tr>
<td></td>
<td>n=7</td>
<td></td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Reproductive</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>FSH &gt;15 IU/l</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>C</td>
<td>Unable</td>
<td>12</td>
<td>04</td>
</tr>
<tr>
<td></td>
<td>n=24</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Reproductive</td>
<td></td>
<td>5</td>
</tr>
</tbody>
</table>

**Infertile** was defined as FSH >15IU/l or azoospermia.

A significant minority at highest risk 13/38 (34%) died.

There was no significant change in biochemistry in available paired data: FSH (n=7), LH (n=8), testosterone (n=4) (Wilcoxon all p>0.5).

Paired sperm count (n=6), sperm concentration (n=3) and sperm motility (n=12) were also unchanged (Wilcoxon p>0.05), but sperm volume (n=15) increased over time (p=0.001).

**CONCLUSIONS**

- Low gonadotoxicity risk patients at low priority for fertility preservation were correctly identified before treatment.
- High risk patients need prioritising but were least likely to survive and therefore be able to use the banked sperm.
- Patients azoospermic or necrospermic at initial attempt (GpB survivors) showed no signs of recovering fertility up to 11 years later.
- The low survivor re-evaluation rates suggest improved post treatment endocrine/fertility assessments are required to properly assess the cost benefit of fertility preservation to underage patients.

**Fig 1 Flow diagram of Group A (Successful)**

**Fig 2 Flow diagram of Group B (Unsuccessful)**

**Fig 3 Flow diagram of Group C (Unable)**

1. GpC were younger and failed to produce a specimen on initial assessment.
2. n=5 who returned for re-evaluation had no biochemistry; 2 of these are infertile and 1 low risk ALL patient has retained fertility (sperm concentration 6.9 million/ml, count of 28 million and motility of 57%).

Intergroup analysis by gonadotoxicity risk

**Low risk**: 9/15 patients considered at low risk of gonadotoxicity banked initially; 2 died and 4 returned a median 9.7[8.08-10.20] years later, aged 25.50[24.70-26.10] years. One other unable to bank at diagnosis, returned and banked successfully. All successful bankers remain fertile with a median sperm count of 43.45[36.5-50.0] million.

**Medium risk**: 18/29 patients who initially banked at 16.00[13.04-22.08] years were re-evaluated 8.25[3.80-14.00] years later aged 23.80[19.80-29.80] and 4 had died. 14/18 retained fertility, but 4 are now potentially infertile (n=3 sperm count of 0.1 million, FSH 16.5IU/1L).

**High risk**: Of 38 patients who initially banked aged 15.10[13.05-18.01] years, 20 died aged 17.90[14.11-22.01] and 9 were reevaluated 6.80[3.70-8.00] years later aged 23.60[18.20-26.50]. Of these 2/9 have potentially become infertile: n=1 has FSH >15 (normal sperm count) and n=1 is azoospermic.

At reassessment, sperm concentration was higher in patients receiving low gonadotoxicity risk treatment than those receiving medium (p=0.008) or high-risk (p=0.023) therapy.