Posthumous sperm retrieval: analysis of time interval to harvest sperm

Shai Shefi1,2,4*, Gil Raviv1, Michael L.Eisenberg2, Ruth Weissenberg1, Liza Jalalian2, Jacob Levron3, Gili Band1, Paul J.Turek2 and Igael Madgar1

1Department of Urology, Chaim Sheba Medical Center, Tel-Hashomer, Israel, 2Department of Urology, University of California San Francisco, San Francisco, CA, USA and 3Department of Obstetrics and Gynecology, Chaim Sheba Medical Center, Tel-Hashomer, Israel 4To whom correspondence should be addressed at: Department of Urology, University of California San Francisco, 1600 Divisidero Street, Rm A722, San Francisco, CA 94143-1695, USA. E-mail: sshefi@yahoo.com

*Recipient of fellowship from The American Physicians Fellowship for Medicine in Israel.

BACKGROUND: Current recommendations regarding posthumous sperm retrieval (PSR) are based on a small number of cases. Our purpose was to determine the time interval from death to a successful procedure. METHODS: Seventeen consecutive PSR procedures in 14 deceased and 3 neurologically brain-dead patients at two male infertility centres [Sheba Medical Center (SMC), Tel-Hashomer, Israel and University of California San Francisco (UCSF), San Francisco, CA, USA] were analysed. Main outcome measures were retrieval of vital sperm, pregnancies and births. RESULTS: PSR methods included resection of testis and epididymis (n = 8), en-block excision of testis, epididymis and proximal vas deferens with vasal irrigation (n = 6), electroejaculation (EEJ) (n = 2) and epididymectomy (n = 1). PSR was performed 7.5–36 h after death. Sperm was retrieved in all cases and was motile in 14 cases. In two cases, testicular and epididymal tissues were cryopreserved without sperm evaluation, and in one case, no motility was detected. IVF and ICSI were performed in two cases in which sperm had been retrieved 30 h after death, and both resulted in pregnancies and live births. CONCLUSIONS: Viable sperm is obtainable with PSR well after the currently recommended 24-h time interval. PSR should be considered up to 36 h after death, following appropriate evaluation. No correlation was found between cause of death and chance for successful sperm retrieval.

Key words: assisted reproduction/male infertility/posthumous/sperm retrieval

Introduction

Cryopreservation of human sperm for a future use was originally employed for men who needed medical or surgical treatments that impair fertility. Posthumous sperm retrieval (PSR) is a relatively new and unconventional use of this technology. Sperm obtained in the post-mortem state was first reported in 1980 (Rothman, 1980; Batzer et al., 2003); since then, only a few pregnancies and births attributed to PSR-derived sperm have been reported (Check et al., 1999, 2002; Belker et al., 2001; Batzer et al., 2003). The sociopolitical implications of this technology and the case law surrounding its use have increased dramatically in the last several years. Modern assisted reproductive technologies (ARTs) have reinforced the feasibility of PSR but have also brought to light many moral, ethical, legal and social issues (Bahadur, 2002; Land and Ross, 2002; Orr and Siegler, 2002; Batzer et al., 2003). Providers who become involved in PSR must take into account an array of existing governmental regulations and institutional and published guidelines (Land and Ross, 2002; Tash et al., 2003).

Guidelines for PSR in the medical literature suggest that the procedure should be performed within 24 h after death to acquire motile or vital sperm (Land and Ross, 2002; Tash et al., 2003). We evaluated a two-institution experience in men in whom PSR was performed to determine whether there is a post-mortem time point after which usable or viable sperm might not be retrieved. The rationale for this study is that requests for this procedure from involved families are not necessarily informed by current guidelines. We hypothesized that the opportunity window for PSR may actually extend beyond the currently recommended 24-h limit.

Materials and methods

We reviewed all PSR procedures performed at the Sheba Medical Center, Israel (SMC; n = 14) and at the University of California San Francisco, San Francisco (UCSF; n = 3), between May 2001 and September 2004. None of the men had left written instructions, a will stating their wishes, nor an explicit consent about their desire for PSR. All applications were processed according to Israeli Attorney General’s guidelines and Israeli Ministry of Health regulations at SMC.
and according to institutional guidelines both at SMC and at UCSF (Rubinstein, 2003). Accordingly, Israeli inclusion criteria for the procedure were (i) application made by the deceased’s partner, (ii) applications made by a partner who was not the legal wife, proof of cohabitation and intention to conceive were necessary, along with a court order, (iii) application by the deceased’s parents authorized by a court order, (iv) an institutional consent form signed by the applicant, stating that future use of the sperm will occur only after court approval and (v) agreement to a 6-month quarantine period in which no use of the procured sperm is allowed. UCSF inclusion criteria were (i) proof of explicit or inferred consent of the deceased, (ii) application made by a spouse or partner of the deceased, (iii) an institutional consent form signed by the applicant, (iv) unanimous support from the applicant’s extended family and (v) agreement to a 6-month quarantine period in which no use of the procured sperm is allowed. In both institutions, the approved PSR applicant had to fill out a special questionnaire before the procedure to exclude genetic or medical conditions of the deceased that would affect future fertilization or offspring health.

Sperm retrieval procedures

Methods used for sperm procurement included en-bloc orchiectomy with epididymectomy and vasal sperm aspiration, orchiectomy plus epididymectomy and epididymectomy alone. Electroejaculation (EEJ) was used in neurologically unresponsive men on ventilatory support.

Definitions

Sperm retrieval was performed on two types of patients in this study. Post-mortem sperm retrieval, often performed outside a conventional medical facility, was performed on men who were deceased. In contrast, perimortem sperm retrieval was performed on mechanically ventilated, neurologically unresponsive patients, with presumed normal circulation and oxygenation. Importantly, the time of death and brain death was determined medico-legally by physicians and other healthcare providers participating in the care of these patients. As they were uniformly recorded in all cases, we used these time points to calculate the relevant sperm retrieval intervals.

Sperm processing and analysis

Owing to significant technical variability among PSR procedures and the involved andrology laboratories, no single sperm processing protocol was adopted or prescribed in this study. Except for two cases in which data were not available, all cases included an evaluation of sperm motility, and one included an assessment of sperm viability with eosin Y (Bjornsdahl et al., 2003).

Subsequent ART procedures

When possible, we recorded the subsequent activity of partners who followed PSR guidelines and elected to conceive with retrieved sperm.

Results

All subjects were previously healthy men who suffered sudden death. The time interval from death to surgical sperm retrieval is shown in Figure 1.

Post-mortem patients

Fourteen procedures were performed on deceased men, including en-block excision of testis, epididymis and vas deferens with vasal irrigation (six), orchiectomy and epididymectomy (seven) and epididymectomy alone (one). Mean patient age was 30 years (range 19–50). Causes of death were gunshot wound (n = 6), motor vehicle accident (n = 4), fall from height (n = 1), sudden cardiac death (n = 1), anaphylactic reaction (n = 1) and plane crash (n = 1). Patient characteristics and andrological findings from these procedures are outlined in Table I. Sperm and/or tissue were cryopreserved in all cases. Andrological sperm assessment detected motile sperm in 12 of 14 cases. In one case, motile sperm was not detected, and in another case, laboratory analysis of sperm quality was not performed and the epididymis and testis were cryopreserved. Mean time to retrieval was 20.4 h after death (range 10–36). In the case with the longest post-mortem time interval (36 h), epididymal sperm with 5% motility and 7% viability by vital stain was obtained.

In two cases, the deceased patient’s partners elected to use retrieved sperm to conceive. In both cases, the time interval from death to harvest was 30 h. IVF and ICSI were used in both cases. To each of the two partners, a healthy female child was born. The details of the quality of the thawed sperm used for IVF and ICSI were not available for this study. No additional applications for the use of banked sperm have been made to date for other specimens obtained in this study.

Perimortem patients

Two EEJ procedures and one orchidoepididymectomy were performed on three mechanically ventilated neurologically unresponsive men. Patient ages were 29, 43 and 26. Causes of brain death included motor vehicle accident, intracranial haemorrhage and gunshot wounds. Patient characteristics and andrological findings from surgical procedures are outlined in Table I. In these perimortem cases, we recorded the time from the declaration of brain death to sperm harvest in two cases: 7.5 and 24 h. Motile ejaculated sperm was cryopreserved in two EEJ cases. Testicular tissue was also cryopreserved in one of these cases by testicular aspiration. Tissue was cryopreserved after orchidoepididymectomy in one case who did not undergo formal andrological evaluation.

Discussion

Over the last 25 years, increased public awareness of the feasibility of PSR has led to more frequent requests for the procedure. However, the limited reported worldwide experience which
clinical characteristics and results of post-mortem and perimortem sperm retrieval procedures

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Post-mortem interval (hours)</th>
<th>Retrieval method</th>
<th>Sperm found</th>
<th>Motility</th>
<th>Cryopreservation</th>
<th>Offspring</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>29</td>
<td>24</td>
<td>EEJ</td>
<td>+</td>
<td>+</td>
<td>Sperm</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>41</td>
<td>19</td>
<td>OE</td>
<td>+</td>
<td>+</td>
<td>Sperm, epididymis and testis</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>24</td>
<td>10</td>
<td>OE</td>
<td>+</td>
<td>+</td>
<td>Sperm</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>30</td>
<td>14</td>
<td>OE, VA</td>
<td>+</td>
<td>+</td>
<td>Sperm and testis</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>32</td>
<td>30</td>
<td>OE</td>
<td>+</td>
<td>+</td>
<td>Sperm and testis</td>
<td>+</td>
</tr>
<tr>
<td>6</td>
<td>43</td>
<td>7.5</td>
<td>EEJ, TA</td>
<td>+</td>
<td></td>
<td>Sperm, epididymis and testis</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>19</td>
<td>10</td>
<td>OE, VA</td>
<td>+</td>
<td></td>
<td>Sperm and testis</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>31</td>
<td>20</td>
<td>OE, VA</td>
<td>+</td>
<td></td>
<td>Sperm and testis</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>50</td>
<td>16</td>
<td>OE</td>
<td>+</td>
<td></td>
<td>Sperm and testis</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>30</td>
<td>16</td>
<td>OE</td>
<td>+</td>
<td>–</td>
<td>Sperm and testis</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>27</td>
<td>18</td>
<td>OE</td>
<td>+</td>
<td>+</td>
<td>Sperm and testis</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>35</td>
<td>30</td>
<td>EE</td>
<td>+</td>
<td></td>
<td>N/A Sperm</td>
<td>+</td>
</tr>
<tr>
<td>13</td>
<td>26</td>
<td>N/A</td>
<td>OE</td>
<td>+</td>
<td></td>
<td>Epididymis and testis</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>28</td>
<td>36</td>
<td>OE</td>
<td>+</td>
<td></td>
<td>Sperm, epididymis and testis</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>28</td>
<td>18</td>
<td>OE, VA</td>
<td>+</td>
<td></td>
<td>Sperm and testis</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>20</td>
<td>27</td>
<td>OE, VA</td>
<td>+</td>
<td></td>
<td>Sperm and testis</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>28</td>
<td>21</td>
<td>OE, VA</td>
<td>+</td>
<td></td>
<td>Sperm, epididymis and testis</td>
<td></td>
</tr>
</tbody>
</table>

EE, epididymal extraction; EEJ, electroejaculation; N/A, information not available; OE, orchectomy and epididymectomy; TA, testicular aspiration; VA, vasal aspiration.

*Perimortem procedure.

includes ~100 requests and 35 post-mortem and perimortem sperm retrieval procedures, combined with the wide variations in political and cultural belief systems that exist internationally, has made it impractical to propose uniformly acceptable guidelines regarding PSR procedures (Land and Ross, 2002; Tash et al., 2003). Despite the increased feasibility of using retrieved sperm with modern ART protocols, medico-legal, moral and ethical issues abound and limit the number of PSR procedures performed (Kerr et al., 1997; Kahan et al., 1999; Finnerty et al., 2001; Bahadur, 2002; Land and Ross, 2002; Orr and Siegler, 2002; Batzer et al., 2003; Hill, 2003; Tash et al., 2003). One example of this is a previous, single-centre study in which local guidelines appeared to dramatically limit the number of approved PSR procedures (Tash et al., 2003).

From the recent literature, it is advised that PSR be performed within 24 h of death (Land and Ross, 2002; Tash et al., 2003). To address the validity of this recommendation, we reviewed in this study a two-institution experience in a consecutive cohort of men who underwent PSR. Our experience shows that successful sperm retrieval can be performed 36 h post-mortem. In fact, we find that we have no clinical or other indication to make solid recommendations regarding the maximum time interval to perform sperm retrieval after death. Studies of post-mortem sperm retrieval in other species support this statement. Viable sperm has been found in rams 48 h post-mortem and in deer 40 h post-mortem (Kaaabi et al., 2003; Soler and Garde, 2003). Moreover, this interval can vary considerably, as it is undoubtedly influenced by factors such as the cause of death, accompanying ventilatory support, surgical technique and the location of the procedure.

We noted that diverse surgical techniques are used to retrieve sperm in the post-mortem state. We also noted no correlation between cause of death and chance for successful sperm retrieval. This suggests that unless reproductive organs are damaged in the fatal event, sperm retrieval is possible at least within 36 h of death.

In this study, we drew a relevant distinction between two different types of procedures: post-mortem and perimortem. Post-mortem procedures were more frequently performed and occur after death. Perimortem procedures are performed before termination of life support in a neurologically unresponsive patient, after appropriate declaration of brain death. These procedures are performed in patients with presumably reasonable circulation and oxygenation. In these circumstances, the interval to sperm harvest might vary widely and could easily exceed 36 h. In addition, EEJ can be considered for sperm retrieval in such cases.

There are limitations to this study. Detailed sperm parameters were not formally assessed in most cases, largely because a variety of surgical procedures were employed for sperm retrieval, in a wide variety of medical and non-medical settings. Additionally, the unique and urgent circumstances in which these procedures are performed preclude proper analysis about which surgical technique is the best for retrieving vital sperm. Lastly, there may be wide variability in the criteria used to establish the time of death among clinicians, given the various different mechanisms and locations of death, which could lead to inaccurate estimates of sperm retrieval intervals. However, the impact of this variable would probably uniformly increase the estimated time to sperm harvest after death, as in many cases of traumatic injury patients will have expired a substantial time before the actual clinical declaration of death. Despite these caveats, this data suggest that PSR is not adversely affected by various traumatic and other causes of death and can be performed well after the currently recommended 24-h limit and that viable pregnancies are possible with sperm retrieved after this limit.

References

Submitted on February 20, 2006; resubmitted on April 26, 2006; accepted on May 16, 2006