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Molecular and Cellular Endocrinology 169 (2000) 133–136

MCE
Molecular and Cellular Endocrinology

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# Storing reproduction for oncological patients: some points for discussion

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**Abstract**

Since the introduction of sophisticated techniques of assisted reproduction such as IVF and ICSI, all male patients that undergo a cancer treatment jeopardizing their future fertility status should be offered the opportunity to bank their semen. Only azoospermic semen samples are to be rejected for pre-treatment banking. Patients who became severely oligospermic or azoospermic after chemotherapy but did not bank their semen, are often not allowed to have assisted reproduction because of the concerns about the mutagenic aspects of their treatment. In a small case series ($n = 10$), we recovered testicular sperm for ICSI in 40% of patients who became azoospermic after chemotherapy. Since, so far, the few clinical data available do no not suggest an increased risk for congenital anomalies in children born from patients obtaining a pregnancy during chemotherapy, the question remains whether the concerns raised about treating patients who became oligozoospermic or azoospermic or even about semen banking during chemotherapy are incontestable. 

*Keywords:* Azoospermia; Cancer; Cryopreservation; ICSI; Semen; TESE

## 1. Cryopreserving semen in oncological patients: is it worth the effort? The oncologists' view

For many years, semen cryobanking for male cancer patients was considered inefficient. Early reports on semen banking focused on the fact that only few cancer patients had semen samples compatible with the current standards for successful cryopreservation (Sanger et al., 1980; Bracken and Smith, 1980; Waxman, 1985). Many oncologists were thus indoctrinated that when the post-thaw semen analysis showed $< 40\%$ motility and when the sperm density was $< 20$ million spermatozoa per ml., cancer patients should not store their semen because the chances of conception after the treatment would be unacceptably low. Furthermore, most series reported showed that even though the pre-freeze sperm quality was in line with the above criteria, the results in terms of pregnancies after artificial insemination were very poor (Hendry et al., 1983; Skammell et al., 1985). As a result, even today, many oncologists consider semen storage for cancer patients to be pointless. However, with the introduction of more sophisticated techniques of assisted reproduction, such as IVF and ICSI, their view has become completely erroneous. Even with in-vitro fertilisation, many patients with poor semen characteristics can father their own genetical children (Davis et al., 1990; Tournaye et al., 1991, 1993). These early results from the conventional techniques of assisted reproduction showed already that the criteria had to change. However, it took a long time before semen banks, especially in the USA, accepted the idea of banking poor-quality semen in view of the new techniques of assisted reproduction (Sanger et al., 1980). Authors who were indirectly responsible for the fact that for years only few oncological patients had been encouraged or allowed to bank their semen, now suddenly changed their ideas and agreed that 'semen banking should be offered as a viable option for any male cancer patient who has any motile sperm and considering the possibility of having future children' Finally they also accepted the concept that for many patients more advanced methods of assisted reproduction than artificial insemination should be used (Sanger et al., 1993a,b). Thanks to ICSI, cured cancer patients can father children who are genetically their own even with the poorest semen samples (Hakim et al., 1995; Chen et al., 1996; Ahuja et al., 1997; Rosenlund et al., 1998;

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0303-7207/00/$ - see front matter 
PII: S0303-7207(00)00366-X

Naysmith et al., 1998). Table 1 shows our results in the period 1994–1996 for ICSI using frozen–thawed semen from cured cancer patients. These results and those published by others show that all efforts to convince our oncologist colleagues of these important advance should be continued. They must get used to the idea that only azoospermic semen samples are to be rejected for pre-treatment cryopreservation.

## 2. Cryopreserving semen in oncological patients: is it worth the effort? The patients' view

While fertility specialists especially put a lot of effort into trying to convince their oncologist colleagues as well as patients undergoing cancer treatment to bank semen as a precaution against lifelong sterility, the question may be asked whether cured patients will bank semen and will ultimately use their banked semen. One study reported that only 42% of patients counselled did bank their semen to counter sterility (Kliesch et al. 1997) while another recent study reported a figure of 54% (Rousillon et al., 1999).

Although in recent years there has been an increase in referrals for cryopreservation, it seems that the existing semen-depots are hardly used. A survey in the UK on the use of semen samples stored from 1977 to 1987 showed that only 133 out of 2219 men eventually used their cryopreserved semen (6%) (Milligan et al., 1989). This figure compares well to the one reported by Kliesch et al. where over an 8-year period, only 8% of patients used their semen for assisted reproduction (Kliesch et al., 1997). There are different reasons for not using the stored semen or even for discontinuing its storage. A recent questionnaire in the USA showed that 41% of patients discontinued storage because of recovery of fertility potential with paternity, 37% because of death, 14% because good sperm quality was regained and 7% because they did not want children (Hallak et al., 1998). A recent French questionnaire reports that only one out of eight men who want children used the banked semen for assisted procreation (Rousillon et al., 1999). More extensive counselling after treatment may increase these figures because some patients may not use their banked semen because they may be concerned about the adverse effects of cryostorage or the genetic impact of their cancer on their offspring.

Table 1
Retrospective case-series of ICSI cycles with frozen–thawed sperm from cured cancer patients

| | *n* | % of A | % of B | % of C |
|---|---|---|---|---|
| Patients | 4 | | | |
| Cycles (A) | 6 | | | |
| M-II oocytes injected (B) | 40 | | | |
| 2-PN oocytes | 24 | | 60 | |
| Good-quality embryos | 17 | | | |
| Transfers (C) | 6 | | | |
| Embryos transferred (C) | 17 | | | |
| Positive hCG | 3 | 50 | | |
| Sacs on US | 5 | | | 29 |
| Children born | 5 | | | |

## 3. When should we bank semen?

Cryopreservation before any cancer treatment is common practice. However, many cancer patients are being referred only when the final diagnosis of their disease is made. Often there remains little time to bank semen samples. For this reason, some authors even suggest banking their semen during chemotherapy (Carson et al., 1991). However, cytogenetic studies have indicated that chemotherapy may induce chromosomal anomalies (Genesca et al., 1990; Rousseaux et al., 1993). Some authors have been expressing their fears about this policy of semen collection during chemotherapy (Meistrich, 1993). Yet the few clinical data available do not suggest an increased risk of congenital anomalies in the children born from patients where pregnancy occurred during the father's chemotherapy (Holmes and Holmes, 1978; Hawkins, 1991; Dodds et al., 1993; Nicholson and Byrne, 1993).

In the near future, new developments in assisted reproduction may be of help: improvements in pre-implantation genetic diagnosis may ensure that embryos obtained with spermatozoa collected during chemotherapy do not carry structural chromosomal anomalies. It is therefore our policy to accept semen cryopreservation during chemotherapy, however, only when patients are fully informed about the possible, although unproven, risks.

Another important aspect is the age at which semen can be cryopreserved. While in adult male patients with cancer undergoing gonadotoxic chemotherapy semen banking is well accepted as a preventive strategy, the same is not true for adolescents. A study by Kliesch et al. (1996) demonstrated that adolescent patients, aged 14–17 years, are good candidates for semen banking, although they are still going through their puberty. From their results it appears that the role of semen cryopreservation should be emphasised even in adolescents.

## 4. What about cancer patients who did not store their semen before cancer treatment?

Many patients will not have had their semen stored before starting cancer treatment. Many will may become severely oligozoospermic after their treatment.

Table 2
Retrospective case-series of ICSI cycles with fresh sperm from cured cancer patients

| | *n* | % of A | % of B |
|---|---|---|---|
| Patients | 3 | | |
| Cycles | 5 | | |
| M-II oocytes injected (A) | 36 | | |
| 2-PN oocytes (B) | 21 | 58 | |
| Good-quality embryos | 16 | | 76 |
| Transfers | 4 | | |
| Embryos transferred | 16 | | |
| Positive hCG | 0 | | |

Table 3
Retrospective case-series of ICSI cycles with testicular sperm from cured cancer patients

| | *n* | % of A | % of B | % of C |
|---|---|---|---|---|
| Testicular retrievals (A) | 10 | | | |
| Sperm found | 4 | 40 | | |
| Patients undergoing ICSI | 4 | | | |
| Cycles | 7 | | | |
| M-II oocytes injected (B) | 59 | | | |
| 2-PN oocytes (C) | 35 | | 59 | |
| Good-quality embryos | 19 | | | 54 |
| Transfers | 6 | | | |
| Embryos transferred | 17 | | | |
| Positive hCG | 0 | | | |

Although these patients may benefit from ICSI, they must be informed about the possible mutagenic effects of their treatment. Table 2 shows a limited series of post-chemotherapy patients undergoing ICSI with their freshly ejaculated spermatozoa in the period 1994–1996. Although fertilization and cleavage were acceptable, no implantation was recorded. Any conclusion from this finding is, however, premature because of the limited number of patients included.

If patients were azoospermic they were offered testicular biopsy in an attempt to recover testicular spermatozoa for ICSI. The results show that even in azoospermic patients there is hope of recovering spermatozoa after chemotherapy. As can be seen from Table 3, none of the embryos transferred implanted, but again, it is too premature to draw any valid conclusion from this small series (1994–1996).

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