Sperm Banking in the United Kingdom is Feasible in Patients 13 Years Old or Older with Cancer

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Abbreviations and Acronyms

ACU = Assisted Conception Unit

AL = acute leukemia

MBT = malignant bone tumor

TC = testicular cancer

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Study followed principles of the Helsinki Declaration.

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Purpose: Assisted reproductive technologies are increasingly being used to treat infertility. Male adolescents with cancer are particularly encouraged to bank semen to preserve fertility before beginning chemotherapy or radiotherapy. We evaluated the feasibility of semen preservation in 12 to 17-year-old patients with cancer.

Materials and Methods: We retrospectively collected data from the sperm banking database at our institution for the years 1995 to 2009. Outcomes measured were histological diagnosis, success rate, sperm concentration and sample volume.

Results: A total of 180 patients with a mean age of 16.1 years (range 13.2 to 17.9) were referred for cryopreservation during the study period. Underlying diagnoses included lymphoma (64 patients), leukemia (50), bone tumors (18), testicular tumors (13), soft tissue sarcoma (13), brain tumor (6), germ cell tumors (6) and other cancers (10). Of the patients 119 (66%) successfully banked sperm. A total of 26 patients did not attend their appointment. Of those who attended 15 (10%) were unable to provide a sample and 20 (13%) had azoospermia. A total of 20 patients died after banking sperm and their specimens were subsequently destroyed.

Conclusions: Cryopreservation of semen of acceptable quality for future use in assisted conception is feasible for most adolescents from age 13 years onward.

Key Words: adolescent, fertility, neoplasms, sperm banks

THE improvements in cancer survival in children and adolescents during the last 40 years have been dramatic. As a result, a significant portion of the adult population are survivors of childhood cancer, and managing the long-term consequences of their cancer treatment has become more important.[1] A number of cytotoxic drugs, including procarbazine and alkylating agents such as cyclophosphamide and chlorambucil, are capable of causing damage to the germinal epithelium of the testis, and radiotherapy is similarly damaging.[2] Therefore, significant numbers of male cancer survivors will have reduced sperm counts as a consequence of their treatment.[3,4]

Assisted reproductive technologies are increasingly used to treat infertility.[5] Facilities are widely available for semen cryopreservation in the United Kingdom, and male adolescents with cancer are encouraged to bank sperm to preserve fertility before beginning chemotherapy or radiotherapy.[6] In single center studies semen cryopreserva-

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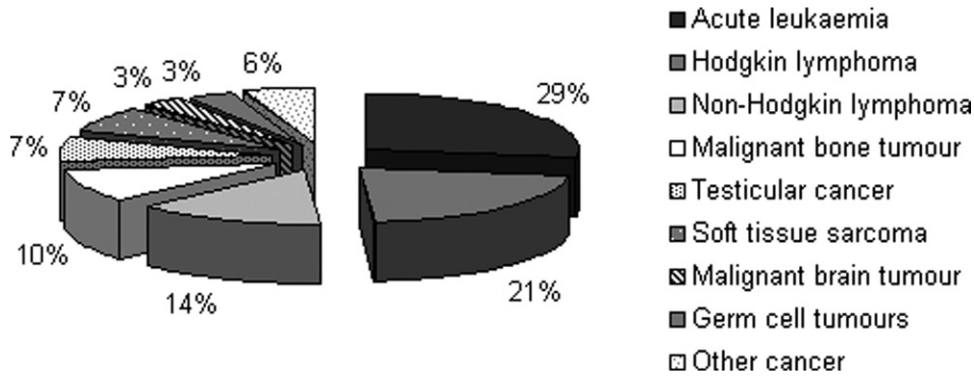

Distribution of malignant disease type in patients referred for semen cryopreservation

tion is possible in as many as 88.5% of patients 13 to 20 years old.[7] In the United Kingdom 85% of pediatric oncology centers refer adolescents for gamete collection from ejaculation before initiating treatment.[8,9] However, our previous study of a relatively small number of 13 to 21-year-old patients suggested that only 67% had been able to store semen.[10] A United Kingdom Fertility Working Group suggests that any child with testicular volume greater than 4 ml should be considered as potentially harboring mature gametes.[11] We retrospectively studied adolescents referred to our ACU for semen cryopreservation to evaluate the feasibility of semen preservation in this group of patients and the variability of sperm parameters with age.

METHODS

Data were collected retrospectively from our ACU sperm banking database from 1995 to 2009. Males 12 to 17 years old with malignant disease were included in the study. Recorded parameters included underlying condition, success of producing a sperm sample, sperm concentration (million per ml), sperm motility (percent rapid plus forward motility) and sample volume measured (ml and ampules stored).

Semen samples were collected by masturbation at the ACU. Semen analysis was performed according to World Health Organization recommendations after liquefaction for 20 minutes at 37C.[12] Sperm freezing was performed after dilution in a cryoprotectant medium.

Statistical analyses were performed using StatsDirect statistical software, version 2.7.1 (Altrincham, Cheshire, United Kingdom) and R, version 2.12.2 (R Foundation for Statistical Computing, Vienna, Austria). Data are expressed as mean ± standard deviation or median (IQR), as appropriate. ANOVA and Kruskal-Wallis tests were used for multiple group comparison. A p value of less than 0.05 was accepted as being statistically significant. Data collected were anonymized, and in lieu of a formal ethics committee, the principles of the Helsinki Declaration were followed.

RESULTS

A total of 180 patients 12 to 17 years old with malignant disease were referred for cryopreservation during the study period. Mean patient age was 16.1 years (range 12.3 to 17.9). Underlying malignant disease types were AL (50 patients), Hodgkin lymphoma (38), non-Hodgkin lymphoma (26), malignant bone tumor (18), testicular cancer (13), soft tissue sarcoma (13), brain tumor (6), teratoma/germ cell tumor (6) and other cancer (10, see figure).

Success in Banking Sperm Samples

A total of 119 patients (66%) successfully banked sperm samples by masturbation (table 1). Of the patients 26 did not attend their appointment, 15 (10%) who attended were unable to provide a sample and 20 (13%) had azoospermia.

Number of Ampules Stored

The number of ampules banked per patient increased significantly with age, from 1 at 13 years (range 1.0 to 3.0) to 4 at 17 years (2.0 to 6.0). No significant difference was observed in the number of ampules stored relating to type of disease.

Semen Parameters

Semen volume increased significantly with age (table 2) from 0.5 ml at 13 years to 1.5 ml at 17 years. Semen volume did not differ significantly between disease types (table 3).

Table 1. *Cryopreservation referral outcomes by age*

Age (yrs)	No. Pts	No. Banked Samples (%)	No. Azoospermia	No. Unable to Produce Sample	No. Not Attending Appointment
12	1	0 (0)	1	0	0
13	8	7 (88)	0	1	0
14	24	14 (58)	3	2	5
15	42	22 (52)	6	6	8
16	63	44 (70)	8	6	5
17	42	32 (76)	2	0	8

Table 2. *Correlation of semen parameters with age*

Age (yrs)	No. Pts	Ml Vol (range)	Million/ml Concentration (range)	% Forward Motility (range)
13	7	0.5 (0.3–0.6)	10.0 (2.0–60.0)	32.0 (16.0–62.0)
14	14	0.5 (0.3–0.7)	38.0 (20.0–59.0)	51.0 (23.3–57.5)
15	22	0.8 (0.5–1.3)	12.5 (5.0–30.8)	43.5 (30.8–55.0)
16	44	0.8 (0.5–1.8)	31.0 (14.0–92.0)	40.5 (20.0–53.5)
17	32	1.5 (0.8–2.9)	19.9 (6.3–42.8)	44.5 (30.5–56.3)
p Value	—	<0.001*	0.654	0.887

* Kendal rank correlation coefficient tau b = 0.316016.

Sperm concentration varied significantly according to disease type (table 3). On further multiple group analysis sperm concentration was significantly lower in patients with TC compared to AL or MBT. Sperm concentration was not correlated with age (table 2). Forward motility was not correlated with age in patients with malignant disease and did not vary significantly between disease types.

Treatment Outcomes

A total of 20 patients with cancer died after banking sperm and their specimens were subsequently destroyed. Only 1 of the 119 patients who successfully stored semen has used the semen and was able to achieve a successful pregnancy following 2 attempts using intrauterine sperm injection.

Comparison of Disease Types

Success rate of cryopreservation varied according to disease type (table 4). Sperm was successfully banked by 85% of patients with soft tissue sarcoma and 50% of those with brain tumor.

DISCUSSION

Rates of nonproduction of semen in adolescents with cancer vary from 13.9% to 53.3%.[13,14] This study demonstrates that 66% of 180 patients 13 to 17 years old referred for semen cryopreservation successfully banked sperm. This finding is identical to the rate we reported in our previous study, where we interviewed 55 patients 13 to 21 years old who had been diagnosed with cancer between 1997 and 2001.[10] Of the 154 patients who attended their appointment the success rate was 77%. We attribute this success rate to good patient preparation before attending the ACU. Information leaflets and multimedia resources are given to adolescents to reduce their anxiety, which could lead to nonproduction of semen.

WHO reference values for semen characteristics have only been validated for males older than 18 years.[15] Semen characteristics at age 18 years can be affected by cancer and benign conditions such as varicocele.[16,17] Lower semen volume has previously been noted in younger patients compared to older men.[18] However, few data have been published describing the effect of age on the semen characteristics in adolescent males. Our findings confirm that semen volume increases significantly with age, while semen concentration and forward motility are not correlated with age. This study identifies significant differences in semen concentration according to cancer type. A limitation of the study is the lack of a control group, which would identify normal values for adolescents without malignant disease.

During the study period 1 patient used the specimen for reproductive purposes. Other studies have shown that during a longer period 5% used their specimens for reproduction.[19] It is noteworthy that at data collection the youngest patient was 13 years and the oldest was 31 years. Mean age for first maternal conception in the United Kingdom was 29.4 years in 2009.[20] Mean paternal age is unknown but is likely to be similar or higher.

Patients younger than 16 years in Scotland and younger than 18 years in England and Wales must be Fraser competent to undergo this procedure.[11,21] All patients in our study could describe masturbation, ejaculation and semen consistency, and understand the reason for sperm storage, and thus could be considered competent.

Table 3. *Semen parameters by disease type*

	Mean ± SD Yrs Age (range)	Mean ml Vol (range)	Mean Million/ml Concentration (range)	Mean % Forward Motility (range)
AL	16.4 ± 1.0	0.7 (0.5–1.3)	35.5 (17.8–101.0)	27.0 (8.3–47.0)
Hodgkin lymphoma	16.2 ± 1.2	0.5 (0.4–1.1)	15.0 (1.0–56.0)	20.0 (13.0–29.0)
Non-Hodgkin lymphoma	16.2 ± 1.3	1.3 (0.5–2.0)	20.0 (13.0–29.0)	45.0 (31.0–55.0)
MBT	15.7 ± 1.0	0.9 (0.5–2.7)	54.5 (20.3–122.3)	52.0 (43.3–61.3)
TC	16.6 ± 1.0	2.5 (0.9–3.0)	6.5 (4.9–8.8)	32.0 (20.3–54.5)
Soft tissue sarcoma	16.0 ± 1.5	0.9 (0.4–1.3)	30 (5.6–71.0)	55.0 (38.0–62.0)
p Value	0.641 (ANOVA)	0.213 (Kruskal-Wallis)	0.001 (Kruskal-Wallis), TC less than AL or MBT (Kruskal-Wallis multiple intergroup)	0.015 (Kruskal-Wallis)

Groups with fewer than 8 patients were excluded from analysis.

Table 4. *Cryopreservation outcomes by disease type*

Disease	No. Pts	No. Banked Samples (%)	No. Azoospermia	No. Unable to Produce Sample	No. Not Attending Appointment
Acute leukemia	50	32 (64)	4	8	6
Hodgkin lymphoma	38	23 (61)	6	2	7
Non-Hodgkin lymphoma	26	19 (73)	2	3	2
Malignant bone tumor	18	12 (67)	0	1	5
Testicular Ca	13	8 (62)	3	0	2
Soft tissue sarcoma	13	11 (85)	1	1	0
Brain tumor	6	3 (50)	1	0	2
Teratoma/germ cell tumor	6	4 (67)	2	0	0
Other Ca	10	7 (70)	1	0	2

CONCLUSIONS

In previous studies it has been reported that spermatozoa production in prepubertal boys is generally effective at age 13 to 14 years and, therefore, testicular tissue cryopreservation can be performed.[22] In our study the majority of 13 to 17-year-old patients with cancer referred for semen cryopreservation were able to produce a sample. Age must not be the only discriminative parameter, but sensitive discussion is also required to assess emotional and physical maturity, and there will always be a proportion of patients who are unable to produce a suitable sample for cryopreservation. However, semen cryopreservation should be considered in all physically mature adolescent males with cancer before treatment is begun.

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