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Semen production in adolescent cancer patients

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BACKGROUND: The influence of an accompanying person (parent, guardian or nurse) on the ability of an adolescent (post-pubescent, <20 years of age) to produce a semen sample for cryopreservation, is undetermined, as is the potential for use of urine samples to retrieve sperm in those adolescents that are unable to produce a semen sample. METHODS: The records from 1991–2000 inclusive were reviewed to derive those adolescent patients who were unable to produce semen for cryopreservation prior to undergoing treatment for a malignant condition. RESULTS: During the study period 238 adolescents attended our unit of whom 205 (86.1%) banked semen ('producers'). The remaining 33 adolescents (13.9%) were initially unable to produce a sample ('non-producers'), four of these provided a urine specimen for analysis (12.1%) and of these one had sufficient sperm for cryopreservation. Of the 'accompanied' patients 29.7% (19/64) were non-producers while in the 'unaccompanied' patients only 8.0% (14/174) were non-producers ($\chi^2 = 16.58$, $P < 0.001$). The relative risk (RR) of not producing a semen sample for the accompanied group of patients was greater than that for the unaccompanied group (RR = 3.689, 95% confidence interval: 2.0–6.9). One patient returning alone successfully provided a semen sample for storage. CONCLUSION: Units should consider the effect of the presence of an accompanying person when an adolescent is unable to produce a semen sample and should consider requesting urine to retrieve sperm.

Key words: adolescent/cancer/cryopreservation/sperm/spermaturia

Introduction

Survival rates for cancer patients have improved over the years and quality of life for these patients inevitably forms an important consideration in their treatment strategy. On the unique and important consideration of forming a family, the gonadotoxic effect of cancer treatment can become a sensitive and disturbing realization for patients and those closely associated with them. Cryopreservation of semen is an accepted preventative therapeutic strategy followed to circumvent the side-effects of treatment in men with cancer (Aslam *et al.*, 2000; Bahadur, 2000). Unique also to fertility preservation, adolescent cancer patients are likely to be accompanied by persons in a platonic, guardian or nurturing relationship when attending a sperm banking facility.

When a patient fails to produce semen there could be rescheduling or delay in the cancer treatment. For adolescents it is natural to ask questions with regard to the settings, their maturity and what may be done to improve their chances to successfully preserve their fertility prior to the gonadotoxic treatment. These events have not previously been reported in the literature. Through our unique experience of adolescent cancer patients, their relatives and specialists, we report on this patient cohort who were unable to produce semen. This may help patients, their relatives and the numerous specialists involved in the planning of their treatment.

Materials and methods

We retrospectively analysed the sperm banking data from 1991–2000 for adolescent cancer patients who were post-pubescent but <20 years of age. These patients ($n = 238$) were referred to us before chemo- and radiotherapy to determine the feasibility of preserving their fertility by the technique of cyropreservation. Patients who were accompanied by a person in a platonic, nurturing or guardian relationship to the unit were classified as accompanied ($n = 64$), and those attending our clinic on their own were classified as unaccompanied ($n = 174$). The patients were further classified into non-producer ($n = 33$) and producer ($n = 205$) groups for their ability to provide semen by masturbation. Each patient's pubertal status was assessed by the referring physician. After counselling from both the adolescent cancer unit and the fertility laboratories the patient was asked to produce semen. Accompanying persons would only be included in the discussion with the patient's permission. Where no semen was produced a urine sample was requested to check for the presence of sperm. An aliquot of urine (15 µl) was visualized under light microscopy at 400× magnification. Following

Table I. Number of non-producers and producers among accompanied and unaccompanied cancer patients

	Accompanied	Unaccompanied	Total
Non-producers	19	14	33
Producers	45	160	205

examination using a Makler counter, the urine was immediately processed as follows; 50 ml of the urine (full sample) was aliquoted into 10 sterile centrifuge tubes, spun down at 400× *g* for 20 min and the pellet taken up in 0.5 ml of IVF Medicult wash buffer. The re-suspended concentrated solution was checked and the sperm count was recorded. A glycerol-based cryoprotectant was added to the concentrated sample before freezing.

The laboratory records included other information about the accompanying person and their level of participation.

Statistical analyses were performed using the Statistical Package for Social Science (version 6.1). Data are expressed as mean (SD) unless otherwise stated. Association of categorical variables was compared using the χ^2-test with continuity correction. The probabilities of failing to produce a semen sample by patients (non-producers) while attending the unit for fertility preservation in the accompanied and unaccompanied group were estimated and compared, as described previously (Morris and Gardner, 1988). A P-value of < 0.05 was accepted as being statistically significant.

Results

A total of 238 cancer patients was referred to our clinic for fertility preservation. The number of patients who were unable to produce a semen sample for cryopreservation was 33 (non-producers), their diagnoses were; Hodgkin's lymphoma ($n = 9$), non-Hodgkin's lymphoma ($n = 2$), osteosarcoma ($n = 8$), Ewings sarcoma ($n = 3$), leukaemia ($n = 5$), lymphoma ($n = 1$) and other cancers ($n = 5$). The remaining 205 patients were successful in producing a semen sample for cryopreservation (producers). The mean age of the non-producers group was 15.50 years (SD ± 2.28) and that of the producers group was 16.67 years (SD ± 1.78).

The total number of accompanied and unaccompanied patients attending their treatment session was 64 and 174 respectively (Table I); 29.7% (19/64) of the accompanied patients were non-producers while 8.0% (14/174) of the unaccompanied patients failed to produce a semen sample before their treatment ($\chi^2 = 16.58$, $P < 0.001$). The relative risk (RR) of not producing a semen sample was higher in the accompanied group of patients than in the unaccompanied group (RR = 3.7, 95% confidence interval: 2.0–6.9).

One 15 year old patient diagnosed with Hodgkin's lymphoma, produced a urine sample containing $<1\times10^6$ ml of twitching, motile and non-progressive sperm, which were retrieved, processed and cryopreserved. Only four out of 33 patients (12.1%) volunteered to produce urine.

An accompanied patient (aged 18 years) suffering from leukaemia failed to produce a semen sample on his first visit but was successful in his attempt on a subsequent unaccompanied visit to our clinic [sperm count = 3×10^6 ml, motility = 50%, progression = 1/4 (4 = highest, 1 = lowest), semen volume = 2.5 ml].

The youngest patients ($n = 3$) who were unable to produce semen were diagnosed as: Ewings sarcoma (11 year old); lymphoma (11 year old) and osteosarcoma (12 year old), and each patient was accompanied by one or both parents. Significantly, each patient could accurately describe masturbation, ejaculation and semen consistency, and acknowledged the reason for sperm storage, during a one-to-one counselling.

Discussion

This retrospective study of post-pubescent adults of <20 years of age who were unable to provide a semen sample for cryopreservation demonstrated a negative influence on their ability to produce a semen sample, if the patients were accompanied when attending a sperm banking unit. Furthermore, it would be prudent to request a urine sample to analyse for sperm cells, following unsuccessful attempts to produce semen. An offer was always made to the patient to produce the semen from home if he were unable to do so in a clinical environment. Collectively, these two features deserve careful attention in order to understand the difficulties adolescent males face, and to help optimize their chances for sperm banking.

Understandably it is a sensitive topic to ask adolescent patients to provide semen (Bahadur *et al.*, 2001). Reasons for the inability to produce semen may include the lethargy of their illness, but particularly with adolescents, shyness and immaturity may be important features. They may be too embarrassed to admit to or be known to be masturbating or have nocturnal emissions in the presence of parents or an accompanying guardian. Against this backdrop, there is unavoidable involvement of parents with regards to the recovery and welfare of the adolescent cancer patients (Bahadur *et al.*, 2000; Dockerty *et al.*, 2000). One welfare aspect concerns a common thread for both the patient and parents, and this is the fertility potential which holds promise for continuity of the family line. Failure to bank semen can therefore have much wider concerns and it is important to question further when a patient fails to produce semen.

The subject of 'non-production of semen' has not previously been reported. In one report, 53.3% (24/45) of adolescent cancer patients appeared not to bank semen, although a detailed account of these non-producers was lacking (Muller *et al.*, 2000). This figure contrasts with 13.9% (33/238) in our cohort who did not bank semen. From the aspect of the welfare of patients and relatives, however, such a negative event can become profoundly distressing and disturbing especially at a time of being given news of a potentially life-threatening disease. An element of failure for the patient can be lessened by analysing the urine (spermaturia analyses) (Schaefer *et al.*, 1990), following on from an unsuccessful or attempted masturbation. A post-masturbation urine sample is easily produced and may give the patient some sense of hope and alleviate the failure factor, whilst the demands on most laboratories are insignificant. This is also by far the least invasive of techniques when considering other options such as surgical extraction of gonadal tissue and penile vibratory

stimulation and rectal electroejaculation (Schmiegelow *et al.*, 1998; Hovav *et al.*, 2001). The presence of sperm in the urine of adolescents seems to be an interesting observation since this group of patients are not expected to have weakness in their bladder neck and urethral structures, as found in those adults suffering from retrograde ejaculation. The analyses of urine after unsuccessful attempts to produce semen led to a successful attempt at sperm cryopreservation in one patient in our cohort, although the uptake of this technique was low (12.1%).

Adult patients storing sperm are more likely to be accompanied by a partner, who has a direct reproductive and sexual involvement. In contrast, and unique to fertility preservation, adolescent cancer patients are likely to be accompanied by persons of a platonic or nurturing relationship when attending a sperm banking facility. Whilst noting the negative association of sperm banking success with the accompanied group, the presence of an accompanying person should not be seen to be a bar since 22% in the successful group were accompanied. The presence and participation of the accompanying person can be helpful, but a balance needs to be struck in relation to their continued presence just before and when the patient attempts to produce a semen sample by masturbation.

In conclusion, adolescent cancer patients who fail to produce semen should be encouraged to provide a urine sample for analysis. Importantly, practitioners should give careful attention to the presence of an accompanying adult, a factor that has not previously been commented upon, to enable a balanced and successful outcome for the adolescent patient.

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