Fertility Preservation in Pediatric Subspecialties: A Pilot Needs Assessment Beyond Oncology

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Physicians from 6 non-oncology pediatric subspecialties were surveyed about fertility preservation (FP) to assess education/service needs. Almost all (96%; 25 of 26) reported having patients at risk of infertility; however, only 58% (15 of 26) had discussed FP with patients' families. Most subspecialists (92%; 23 of 25) would like access to an FP program. Our data support exploring the expansion of FP programs beyond oncology. *(J Pediatr 2017;■■:■■-■■).*

Cancer treatments, including chemotherapy and radiotherapy, can be gonadotoxic in both males and females. As survival from pediatric cancer has improved, focus has shifted toward the consequences of therapy among survivors, one of the most important being fertility.[1] Cytotoxic chemotherapy, particularly alkylating agents such as cyclophosphamide, affects fertility by damaging cell division and DNA function within the gametocytes, resulting in either impaired spermatogenesis or accelerated oocyte loss.[1] By the same mechanism, irradiation, especially to the pelvis, also can decrease fertility.[2] The impact of cancer therapy on fertility depends on treatment factors, including the cumulative dosage and dose intensity of alkylating agents or radiation treatment, and also on patient factors, including sex, age, baseline fertility, and other comorbidities.[1,3]

Fertility preservation (FP) is the process of harvesting and storing gametes with the intent of offering an opportunity for biologically related offspring in the future.[4] Well-established guidelines exist within oncology for approaching FP options as early as possible with all patients of reproductive age, as well as parents of children and adolescents.[5] It is now the standard of care to discuss the risk of infertility and FP options with all patients undergoing cancer treatment, and to refer patients to reproductive specialists when indicated.[5]

Current methods for FP include cryopreservation of sperm of pubertal males, which can be used later via intrauterine insemination or in vitro fertilization and result in successful pregnancies.[1,6] Techniques for prepubertal males remain experimental and rely on surgical extraction of testicular tissue with subsequent cryopreservation for future use. Despite the lack of technology for maturing this tissue in vitro or in vivo, the procedure is being increasingly offered by pediatric cancer programs.[1,4,5] Oocyte and embryo cryopreservation by hormonal stimulation with gonadotropins is an established procedure for pubertal females.[4] For prepubertal females, cryopreservation of ovarian tissue (cortical strips or the whole ovary) obtained by surgical procedure is the sole FP option, and remains experimental.[1,4,5,7] Restoration of ovarian activity and successful pregnancy have been reported after reimplantation of ovarian tissue in the pelvic cavity.[7] Access to accurate information about fertility risk and FP is highly important to patients and/or their parents, regardless of whether or not they elect to pursue FP.

Outside of cancer treatment, many other situations have the potential to affect fertility in a young patient. Various endocrine, genetic, neurologic, rheumatologic, and metabolic diseases put fertility at risk by the nature of the disease process.[8-10] Examples include some genotypes of galactosemia associated with premature ovarian failure,[8,11] Klinefelter syndrome rendering all males azoospermic,[9] and Turner syndrome associated with premature ovarian follicle depletion.[12] In other diseases, treatment has the potential to cause subfertility. Gastrointestinal illnesses, such as inflammatory bowel disease and ulcerative colitis may require surgical intervention, which can be associated with decreased fertility postoperatively.[13] Many nononcologic diseases, such as Hurler syndrome, thalassemia, and chronic granulomatous disease, may be treated with bone marrow transplantation, which requires conditioning that may put the patient's fertility at risk. Cyclophosphamide remains a mainstay of treatment for patients with nephrotic syndrome and rheumatic disease.[13,14] Azoospermia and amenorrhea have been documented in males and females, respectively, undergoing cyclophosphamide-based treatment for renal disease.[15,16]

Transgender youths are another important population to consider for FP, as they are at risk of infertility as a consequence of transition. A recent study showed that only 12.4% of transgender adolescents were seen formally by a fertility specialist for FP, and only 5% underwent gamete cryopreservation.[17] Barriers for this patient population include cost, invasiveness of the procedure, and desire to not delay transition.[17]

FP	Fertility preservation
SKFPP	SickKids Fertility Preservation Program

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Table I. Number of physicians by specialty who responded "yes" to the 5 "yes/no" survey questions, out of the total number of physicians who responded in each specialty

Survey question	Nephrology	Endocrinology	Rheumatology	Clinical and metabolic genetics	Respiratory medicine	Allergy/ immunology	Total
Do you think preserving fertility is relevant to your patients?	2/2 (100)	5/5 (100)	3/5 (60)	8/8 (100)	2/4 (50)	2/2 (100)	22/26 (85)
Are there particular patient populations that you deal with who are at risk for future fertility problems?	2/2 (100)	5/5 (100)	4/5 (80)	8/8 (100)	4/4 (100)	2/2 (100)	25/26 (96)
Is fertility preservation something you have ever discussed with your patients?	2/2 (100)	3/5 (60)	3/5 (60)	5/8 (63)	1/4 (25)	1/2 (50)	15/26 (58)
Do you know of other centers that discuss fertility with their patients?	0/2 (0)	2/5 (40)	1/5 (20)	0/8 (0)	1/4 (25)	0/2 (0)	4/26 (15)
Is the SKFPP a service that you would want access to for your patients?	2/2 (100)	5/5 (100)	4/5 (80)	8/8 (100)	2/3* (67)	2/2 (100)	23/25 (92)*

SKFPP, SickKids Fertility Preservation Program.
Data are reported as n/N (%).
*One physician left this question blank.

Health care providers across this diversity of disorders might not be able to fully address patient needs or have access to fertility specialists, particularly in pediatrics. For example, barriers to FP for pediatric nephrologists have been described previously and include not knowing where to refer patients, cost concerns, and concerns over delays in treatment.[18]

The role of FP outside of oncology has not been thoroughly reviewed, and there are no related practice standards. The purpose of this single-center pilot needs assessment study was to explore the current FP practices in nononcology pediatric subspecialties and to assess the need for education and service regarding FP.

Methods

This survey study was conducted over an 8-month period at The Hospital for Sick Children, a tertiary care academic institution with substantively staffed pediatric subspecialty departments. Approval was obtained from the Quality Improvement Projects Review Board. Physicians from nephrology, endocrinology, rheumatology, clinical and metabolic genetics, respiratory medicine, and allergy/immunology were educated about FP and then surveyed. Two additional subspecialty departments were approached to participate. Gastroenterology declined, and neurology could not participate due to scheduling conflicts. All physicians in each department were invited to participate, and those who were able to attend the information session were included.

Physicians and other health care professionals were educated by a 15-minute information session which was targeted specifically to each department and given by a pediatric oncologist and a nurse practitioner specializing in FP. Information delivered included patient populations at risk of subfertility, FP procedures available, the importance of disclosure, and the current services available at the hospital.

Following the presentation, an online SurveyMonkey (Palo Alto, CA) questionnaire was administered to attendees on the same day. It was sent to each of the department heads, who then distributed the link to their respective departments. The survey, developed for the purpose of this study, included 7 questions: 5 "yes/no" questions (Table I), 1 question about perceived barriers ("What are some of the barriers you feel you encounter when addressing fertility concerns raised by your patients/families?"), and 1 question asking the physician to estimate the number of annual referrals he or she would make to a FP program if it were available. There was also an open-ended comments section.

Results

Twenty-six physicians were surveyed (Table II) from divisions of nephrology, endocrinology, rheumatology, clinical and metabolic genetics, respiratory medicine, and allergy/immunology. The majority of physicians believed that preserving fertility is relevant for their patients (85%; 22 of 26). The number of estimated annual referrals to a FP program ranged from 0 to 15 (median, 5) for the whole group, but varied among specialties (Table II). Table I presents the data by department for the 5 "yes/no" survey questions. Of physicians surveyed, 96% (25 of 26) reported dealing with patient populations at risk of future fertility problems; however, only 58% (15 of 26) had discussed FP with their patients. By department, 100% of physicians in nephrology, endocrinology, clinical and metabolic genetics, and allergy/immunology believed

Table II. Number of physician participants from each department and the estimated number of referrals per year to an FP program

Department	Number of participants out of the total number of full-time physicians in that specialty	Estimated number of referrals/y, range (median)
Nephrology	2/23	9-10 (9.5)
Endocrinology	5/16	10-15 (12.5)
Rheumatology	5/15	1-10 (8.5)
Clinical and metabolic genetics	8/25	3-6 (5)
Respiratory medicine	4/26	0-3 (2)
Allergy/immunology	2/13	3-4 (3.5)

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