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JSM Sexual Medicine

Original Research

Testicular Cancer in Chile: Seminal Quality in Explicit Health Assurance Law Patients Compared with Couple Infertility Patients

Diaz Fontdevila M[1,2]*, Inostroza Ballesteros P[2] and Gallardo Polanco P[1,3]

[1]*Hospital San Borja Arriarán, Santiago de Chile, Chile*
[2]*Andrology Laboratory and Reproduction, University of Chile, Chile*
[3]*HCSBA Clinical Laboratory, Santiago de Chile, Chile*

***Corresponding author**
Marina Diaz Fontdevila, Maternal and Child Research Institute (IDIMI), University of Chile, Hospital San Borja Arriarán, Santa Rosa 1234 Second Floor, Santiago Centro, Santiago de Chile, Chile, Tel: 56-9-74316081; Email: diazontdevila@gmail.com

Submitted: 08 February 2022

Accepted: 28 February 2022

Published: 28 February 2022

ISSN: 2578-3718

Keywords
- Seminal parameters
- Semen quality
- Testicular cancer
- Male infertility
- Chile

Abstract

The aim of the study was to evaluate semen quality of Chilean patients with testicular cancer and compared with patients consulted for other cancers and couple infertility.

Seminal samples from 308 patients consulting semen cryopreservation for testicular cancer (TC), 27 patients consulting for sperm banking for other cancers (OC) and 9,655 men that consulted for couple infertility (CI) to the Chile University, were evaluated for seminal parameters.

Patients with TC and OC were younger than CI patients (27±0.2, 25±1, and 35±0.07 years old); they presented a lower sperm/ml and Total Motile Sperm. A higher percent of Oncologic patients presented oligozoospermia versus CI patients (48, 52, 21%) but OC shows higher percentage of azoospermia versus TC and CI patients (15%, 6.7%, 7%). TC and OC men showed higher Asthenozoospermia and total inmotility than IC patients (28, 39, 16.8% and 7%, 18% and 1.2%). In all patients the motility was directly proportional to volume and sperm/ml. A 49% of right, 40% of left and a 6% of both testicles were affected, in the last lower seminal parameters were observed. The age and patients' number were higher in patients with seminoma vs non seminoma and mixed (25%, 18% and 19%). A high percentage of men (37%) did not know the histologic type of their cancer.

Testicular cancer patients presented lower seminal quality in relation to couple infertility patients. This, added to the potential gonadotoxic effect of oncologic treatment, justifies the use of semen banks to preserve their future fertility.

ABBREVIATIONS

TC: Testicular Cancer; OC: Other Cancer; CI: Couple Infertility; GES: Explicit Health Guarantees; MINSAL: Ministry of Health of Chile; IDIMI: Institute of Maternal and Child Research; TSC: Total Sperm Concentration; TMS: Total Motile Sperm; Normo: Normozoospermia; Oligo: Oligozoospermia; Azo: Azoospermia; IVF: In vitro Fertilization; ICSI: Intracytoplasmic Sperm Injection

INTRODUCTION

The magnitude of cancer incidence in Chile has required the development of public policies that promote earlier screening and effective treatments of various types of cancers. Chilean public health system cared for over 2000 patients with "Testicular Cancer" between march1988 to March 2007 (15-40 years old) [1]. This pathology has increased in the world with high incidence in Caucasian, North European, Oceanic and South American populations, mainly affecting young men [2-9]. The use of better therapy promotes a decrease in the mortality index and an increase in the survivors, with more concern about side effects on patients' quality of life [10]. The loss of fertility is one of the most important secondary effects, because fertility after testicular cancer treatment is variable and depends on semen characteristics and on the consequences of treatment on spermatogenesis [11,12].

Cryopreservation of gametes (sperm banking) may be offered before cytotoxic cancer treatment to give the chance to preserve their fertility and allow them the subsequent use of semen for Medically Assisted Reproduction Techniques (*In vitro* Fertilization or Intracytoplasmic Sperm Injection) to achieve pregnancy when infertility problems appear. Despite that, it is reported that only 5 to 15% of males use their cryopreserved samples after cancer treatment [13]. In 2005 (Decree N° 170), as a result of the Health Reform process, the Explicit Health Guarantees (GES) regime was installed for a group of prioritized and highly prevalent diseases; it seeks, among others, to ensure

access, opportunity and financial coverage, reducing the impact on the family budget as a result of the costs associated with major health problems. Among the prioritized diseases, there are some adult cancers such as breast, cervix, stomach, prostate and testicle. One of the initial assurances was seminal cryopreservation (sperm bank) to preserve male fertility prior to their oncologic therapy, to safeguard mature spermatozoa, for future use in assisted reproductive procedures [14]. In 2010 Decree N° 1 and in 2013 Decree N° 4 that included other new guarantees.

Since 1992 our center (IDIMI)) has a state assisted reproductive program that cares for patients of the public health system, but since 2001 it has incorporated seminal cryopreservation for patients of IVF and ICSI cycles including some patients with different cancers. In 2006 we incorporated the sperm bank as a benefit of GES from different regions of Chile.

The main objective of the study was to evaluate the semen quality of Chilean patients with testicular cancer, beneficiaries of GES prior to semen cryopreservation and oncologic treatments between 2006 and 2020. The second objective was to compare these results with seminal parameters of patients that cryopreserved semen for other cancers, and patients that consulted our laboratory for couple infertility during 2003 to 2018.

MATERIALS AND METHODS

Participants

Semen parameters from three different groups of patients were retrospectively analyzed: Group 1: 308 patients, beneficiaries of GES for testicular cancer, referred for seminal cryopreservation (from 20 different Hospitals and 14 regions of Chile, from 2006 to 2020); Group 2: 27 patients who cryopreserved seminal samples before treatment for other cancers: Bladder (2), Pancreas (1) Bone (1), Prostate(1), Colon (2), Thyroid (1), Leukemia (13), No Hodgkin´s lymphoma (3) and Hodgkin´s lymphoma(2), (2003 to 2019); Group 3: seminal samples from 9,655 patients that consulted for couple infertility and were examined by seminal analysis (2003-2018).

Ethical approval

A written informed consent, approved by the Central Ethics Committee of Chile was signed by all men participants to cryopreserved seminal samples, according to Helsinki Declaration for medical research (2019). As approved by the same Committee, informed consent was not required for couple infertility patients because of this retrospective design.

Sperm samples

A total of 10,445 seminal samples were evaluated retrospectively: 740 from group 1, 67 from group 2 and 9,665 from group 3. All the samples were evaluated in the IDIMI clinical andrological laboratory, between 2003 to March 2020. All samples were obtained by masturbation, usually after orchiectomy and prior to other cytotoxic oncologic treatments. In most cases the report of the testicular biopsy indicating the histological type of the tumors was provided by the patients (seminoma, non-seminoma or mixed). Only 83 % of patients from group 1 provided the abstinence days.

Semen Analysis

Seminal parameters were determined and interpreted according to WHO Laboratory manual for the examination and processing of human semen recommendations [15]. Semen volume, abstinence, sperm /ml account, progressive motility, total sperm and total motile sperm were registered according to Björndahl [16] with the following exception: sperm concentration was determined in Makler chamber, because in our laboratory it was compared with the results of the same samples when they were counted in Neubauer or Makler chamber or automated system (Nerthus) and we didn't find differences ($p>0.05$) (manuscript in preparation, unpublished data). Hypospermia was considered when volume < 1.5 ml, oligozoospermia when sperm/ml < 15 million/ml, azoospermia was considered after centrifuging the semen for 30 minutes at 3000 g and no sperm was recovered, asthenozoospermia when <32% spermatozoa with progressive motility. In the case of group 3, strict morphology of spermatozoa was done in all the samples to determine the percentage of normally shaped sperm, but for TC patients we only determined strict morphology in 20 samples and 9 patients, to privilege the sperm available for cryopreservation.

Cryopreservation and seminal maintenance

Cryopreservation of sperm was performed using Test Yolk Buffer (1:1 dilutions) according to the manufacturer´s instructions (Irvine Inc. USA). The gametes were stored in liquid nitrogen for at least two years according to the signed consent and the period that the state recognizes and pays for group 1. Once the cryopreservation consent expired, only 17 patients (5.5%) signed a new consent to continue with the samples cryopreserved. A 2 % of samples were discarded as part of procedure, after patients' deaths, and 1 % of samples by themselves. Only four men used their cryopreserved gametes for in vitro treatment (1.3%) but no further follow up of patients undergoing fertility treatments could be performed. Three patients (1%) for testicular cancer could not obtain seminal samples and 17 patients (5.5%) were not capable of cryopreserved seminal samples because they did not have gametes or did not have motile sperms.

Statistical Analysis

The results were expressed as Mean ± Standard Error. All statistical analyses were performed using SPSS® version 21, intergroup comparisons were analyzed using two-tailed single-factor ANOVA for group comparison or unpaired Student t-test.

A statistically significant level of $p<0.05$ was considered for all tests.

RESULTS

A total of 308 patients and 740 samples of patients with testicular cancer were evaluated, the number of patients/years that consulted for banking sperm shows an increase from 3 to 40 patients/ year (2006-2019). Twenty-seven patients with other cancers including Bladder (2 cases; 7.7%), Pancreas (1 case; 3.8%), Bone (1 case; 3.8%), Prostate (1 case; 3.8%), Colon (2

cases; 7.7%) and Thyroid malignancy (1 case, 3.8%), Leukemia (13 cases; 50%), Non Hodgkin Lymphoma (3 cases; 11.5%) and Hodgkin Lymphoma (2 cases; 7.7%) with a total of 67 samples were evaluated. We also analyzed 9,655 samples of patients that consulted for couple infertility. The GES program only considers patients >14 years old, so pre pubertal patients will not be included in this study.

During the study, twelve patients died: six for group one (2 % from 308 patients) and six for group two (22 % of 27 patients): from Bladder cancer (2), Pancreatic cancer (1), Bone cancer (1) and Leukemia (2). Most of the patients delivered 2 or 3 samples for cryopreservation (86 and 46 %, respectively) but 3 patient couldn´t provide a sample (0.96 %). The patients were also evaluated according to the geographic region of origin, considering that in Chile there are 15. The majority of them were from the Metropolitan, Antofagasta, Coquimbo and Valparaiso regions.

Seminal Parameters

The seminal parameters of each group were shown in Table 1. In TC group we analyzed the data of one (the first) or all samples. A higher abstinence was seen if we considered only the first sample of TC patients versus all TC, or CI or OC samples ($p < 0,05$). A lower age, lower sperm concentration/ml, lower Total Sperm Concentration (TSC), lower progressive motility and lower Total Motile Sperm (TMS) were seen in oncologic patients (TC and OC) (one or all samples evaluated) versus couple infertility patients ($p< 0.05$).

Age and seminal parameters

The tendency shows a high number of TC and OC patients younger (15 to 31 years) than CI patients (26 to 45 years).

Semen parameters of TC patients between 41- 45 years of age presented the smallest seminal volume ($p< 0.05$), they also had a lower TSC, progressive motility and TMS than TC patients of other ages but still inside the reference values [15].

Seminal volume and semen parameters

Patients from group 1 with seminal volume <1.5 ml presented lower TSC, progressive motility and TMS ($p< 0.05$), (Table 2). The same was observed for CI and OC patients, but the abstinence was lower while sperm concentration/ml, TSC and TMS were higher than in the TC group. A 51 percent of patients from TC, presented hypospermia (seminal volume <1.5 ml) versus a 44 % in OC patients and only 23% of CI patients. Logically to lower volume, lower TSC, progressive motility and TMS.

Relation between sperm concentration/ml and other semen parameters

Patients from group 1 with testicular cancer presented the following seminal characteristics: 45.7% normozoospermia (Normo), 47.6% oligozoospermia (Oligo), 6.7 % azoospermia (Azo), comparing with 32.8% (Normo), 52.2% (Oligo) and 15 % (Azo) for the second group and 79 %, 16 % and 5 % respectively for the group 3 (Table 3). A lower percentage of normozoospermic patients (sperm concentration ≥15 mill/ml) were seen in oncologic patients (Groups 1 and 2) and also a higher percentage of oligozoospermia (< 15 mill/ml but >0 mill/ml) compared with the non-oncological patients group, but the percentage of patients azoospermic was similar in groups 1 and 3 (6.7 and 5%), lower than group 2 (15%) (Table 3).

Oncologic normozoospermic patients (group 1 and 2) presented sperm concentration/ml, TSC and TMS statistically lower than normospermic CI patients (p<0.05), but progressive motility is statistically lower for oligospermic patients than normozoospermic patients from the three groups, but within reference values (15).

Relation between progressive motility and semen parameters

The percentage of patients with different asthenozoospermia rate was determined. A 28% of TC patients presented progressive motility lower than 32% : 7% were totally immotile (progressive motility = 0%) and 21% presented motility between 1-31%, 39%

Table 1: Seminal parameters per and all samples for TC, OC and CI.

SEMINAL PARAMETERS	TC ONE SAMPLE	TC ALL SAMPLES	OC ALL SAMPLES	CI ALL SAMPLES
(n)	308	740	67	9655
Age	26±0.3	27±0.2	25±1	35±0.07[a]
Abstinence	12±2	5.0±0.6[b]	4.7±1.33[b]	4.5±0.05[b]
Volume	2.2±0.1	1.7±0.05c	1.8±0.16	2.6±0.01 [c]
Concentration/ml	25±1.7	23±1.0	20±3.7	68±0.6 [d]
Total Sperm Concentration	54±4.4	39±2.3	47±12	172±2.0[e]
Progressive Motility	47±1.4	47±0.9	37±3	53±0.2 [f]
Total Motile Sperm	31±3.1	22±1.6	24±6	110±1.4[g]

Age is expressed in years, Abstinence in days, Volume in ml, Concentration/ml in sperm millions/ml, Total Sperm Concentration in sperm millions, Progressive Motility in percentage (%) and Total Motile Sperm in sperm millions.
The n for abstinence data in TC one sample is 253 because only 83% of patients provided the abstinence days.
[a]*p<0.05,* when compared CI vs. TC one or all samples and OC all samples.
[b]*p<0.05,* when compared TC one sample vs. TC, OC and CI all samples.
[c,d,e,f,g] *p<0.05*, when comparing CI vs. TC one or all samples and OC.

Table 2: Influence of seminal volume in TC patients, seminal parameters.

Seminal Parameters	Seminal Volume <1,5 ml (51%)	Seminal Volume ≥1,5 ml (49%)
Age	27 ± 0.3	26 ± 0.3
Abstinence	4.0 ± 0.8	6.3 ± 0.9
Volume	0.76 ± 0.02	2.7 ± 0.07[a]
Concentration/ml	21 ± 1.4	24 ± 1.6
Total Sperm concentration	17 ± 1.3	61 ± 4.2[b]
Progressive motility	46 ± 1.3	49 ± 1.3[c]
Total motile sperm	9 ± 0.8	36 ± 2.9[d]
Progressive motility	46 ± 1.3	49 ± 1.3[c]
Total motile sperm	9 ± 0.8	36 ± 2.9[d]

[a,b,d] *p=0.00*
[c] *p=0.051*

Table 3: Sperm concentration for TC, OC and CI patients.

SEMINAL PARAMETERS	NORMO TC	NORMO OC	NORMO CI	OLIGO TC	OLIGO OC	OLIGO CI	AZ0 TC	AZ0 OC	AZO CI
(/%)	45.7%	32.8%	79%	47.6%	52.2	16%	6.7%	15%	5%
Age (years)	27±0.3	30±2	35±0.08 [a]	26±0.3	22±0.8	36±0.2 [a]	26±0.9	23±3	35±0.3 [a]
Abstinence (days)	4.0±0.6	5±2	4.5±0.03	6.0±1.0	3±1.0	4.4±0,1	11±4	10±8	4.4±0.09
Volume (ml)	1.7±0.06	2.6±0.3	2.6±0.02 [b]	1.8±0.04	1.4±0.2	2.6±0.04[b]	1.3±0.2	1.3±0.4	2.2±0.07
Concentration (mill/ml)	44±1.6[c]	54±7 [c]	85±0.7[c]	4.9±0.25	3.6±0.7	5.3±0.11	0	0	0
Total Sperm Concentration (mill)	74±4[d]	135±27 [d]	215±2[d]	9.5±1.0	5.7±1.7	14±0.4	0	0	0
Progressive motility (%)	55±1.1[e]	47±5[e]	57±0.2[e]	45±1.3	41±3	37±0.6			
Total Motile Sperm (mill)	44±3 [f]	70±14[f]	132±1.5[f]	3.8±0.3	2.8±0.9	6±0.2	0	0	0

[a-f] *p=0.00* when compared different seminal parameters between normospermic vs. oligospermic and azoospermic patients with TC, OC versus CI
n: number of samples
%: percentage of samples

Table 4: Comparison of different rates of sperm progressive motility for TC, OC and CI.

SEMINAL PARAMETERS	PM ≥ 32%			PM 1-31%			PM 0%		
Patient Group	TC	OC	CI	TC	OC	CI	TC	OC	CI
Percent of patients	72%	61%	33%	21%	21%	15.8%	7%	18%	1.2%
Age (years)	27±0.3	26±1.3	35±0.1[a]	26±0.6	20±1.4	37±0.2	26±0.8	25±0.3	39±0.9
Abstinence (days)	4.1±0.6	4.4±1.2	4.5±0.03	7.2±2	1.7±0.6	4.6±0.1	10±3.7	9.8±7	5.6±1.2
Volume (ml)	1.8±0.106	2±0.22	2.7±0.02	1.6±0.1	1.3±0.25	2.4±0.04	1.2±0.17	1.5±0.4	1.8±0.16
Concentration (mill/ml)	27±1.4	26±5	79±0.7[b]	15±1.4	15±8	36±1.2	0.008±0.003	3±2	12±2
Total Sperm Concentration (mill)	47±3	72±18	202±2[c]	23±3	8.6±5	81±3.4	0.011±0.006	7.2±7	20±4.4
Progressive motility (%)	59±0.7	54±2	61±0.2[d]	19±0.7	18±3	18±0.2	0	0	0
Total Motile Sperm (mill)	29±2	39±9	130±1.6[e]	5.3±0.98	1.8±1	16±0.7	0	0	0

PM: progressive motility
[a-e] *p<0.05* comparing different parameters for patients with different progressive motility rates, and between TC, OC and CI groups.
n: number of samples; %: percentage of samples

of patients with OC presented progressive motility lower than 32%, 18% of immotile sperm and 21% with motility between 1-31%, while CI patients presented 17% of asthenozoospermia, 1.2% without motility and 15. % with motility between 1-31% (Table 4).

A significant difference in age, sperm concentration/ml, TSC and TMS was detected ($p<0.05$) for different progressive motility values. These differences were directly proportional to motility: for lower progressive motility, lower sperm concentration/ml, TSC and TMS for the entire group studied (Table 4). The sperm concentration/ml was lower for oncologic than CI patients, but immotile sperm presented oligozoospermia in the three studied groups. Total sperm concentration was lower for oncologic than CI patients. Only patients without motility had parameters lower than the reference values. Comparing seminal parameters of TC versus CI patients for each different degree of motility, we observed that in immotile samples only sperm concentration/ml and TSC were statistically different, but when we compared samples with progressive motility 1-31% with samples with progressive motility ≥ of 32%, there were differences in sperm concentration/ml, TSC and TMS.

Sperm morphology and semen parameters

No significant difference was detected between sperm morphology from TC and CI patients: 5.1±0.8 % of normal forms for TC versus 6.3 ± 0.05 of normal forms for CI group ($p<0.05$) were seen, but in the first group, a significantly low number of samples were analyzed compared with CI group (20 vs. 7,167).

Table 5: Sperm morphology versus sperm/ml and progressive motility in CI patients.

Sperm Morphology (%)	Concentration/ml (Millions/ml)	Progressive motility (%)	Patient %
0	16±1.4[a]	30±1.2[b]	5
1-4	45±1.0[a]	45±0.5[b]	26
5-7	67±1.1[a]	55±0.4[b]	26
8-13	87±1.2[a]	62±0.4[b]	35
≥14	96±2.4[a]	66±0.7[b]	8

a: significant differences between concentration/ml and morphology (p<0.05)
b: significant differences between progressive motility and morphology (p<0.05)
n: number of samples samples
%: percentage of samples

Table 6: Testicle affected and seminal parameters for TC patients.

SEMINAL PARAMETERS	RIGHT	LEFT	BOTH
Patient Percent	49%	40%	6%
Age	27±0.4	26±0.3	27±0.8
Abstinence	5.4±1.0	5.4±1.0	5.3±1.0
Volume	1.7±0.12	1.8±0.08	1.2±0.16[a]
Concentration/ml	24±1.6	24±1.6	7±1.8[b]
Total sperm concentration	41±3.6	42±3.4	7±2.3[c]
Progressive motility	48±1.3	49±1.4	40±5[d]
Total motile sperm	24±2.4	24±2.4	4±1.7[e]

[a,b,c,e] p<0.02 and [d] p=0.059 when compared seminal parameters for all samples collected from patients with one or both testicles affected by cancer.
np: number of patients
%: percentage of patients
n: number of samples

These preliminary results suggested that testicular cancer did not affect the spermatic morphology, but a higher number of TC samples should be evaluated for sperm morphology to elucidate this point.

We also observed in a group of 7,719 couple infertile patients a positive correlation (Pearson´s coefficient) between concentration/ml versus strict morphology, ρ = 0.314 and strict morphology versus progressive motility ρ = 0.354. It was also analyzed if there were a relationship between the three variables. For this, a trivariate (multiple) regression analysis was performed, which indicates that the variables are associated (morphology is dependent and concentration/ml and progressive motility are independent, R^2 = 0.170).

The higher percentage of infertile couples studied between 2003-2015 in our Laboratory (Clinical Andrological Lab., IDIMI) had spermatic morphology between 8-13 % (Table 5) and a statistically significant difference (p<0.05) between sperm concentration/ml and progressive motility with sperm morphology were seen [17].

Testicle affected by cancer and semen parameters

Cancer affected the right testicle of 151 patients (49%), the left testicle of 123 (40%), both testicles of 18 (6%) and in 16 patients (5%) the affected testicle was not registered.

No differences between seminal parameters were seen, depending on the testicle affected (right or left). In the patients with both testicles affected, a decrease in volume, sperm concentration/ml, TSC and TMS was seen (p<0.05). Progressive motility was lower but not statistically significant (p=0.059) as shows Table 6.

The group without record of testicle affected, a decrease in abstinence, sperm concentration/ml, TSC, progressive motility and TMS was seen (data not shown).

Testicular histology and semen parameters

Histological subtypes of our testicular cancer patients included seminoma (25%), non-seminoma (18%), mixed (19%), and unregistered patients with unknown testicular histology (38%), these subtypes were evaluated for seminal parameters (Table 7). A statistical difference was seen in patients' age: higher for those who presented seminoma (p<0.05), like Fraietta (3) lower sperm concentration/ml and TSC for patients with seminoma versus no seminoma and mixed testicular cancer patients (p=0.005 and p=0.032) but within reference values. Clarifying that 36% of patients did not have the result of testicular biopsy at the time of cryopreservation and the histologic data could not be rescued. The remaining 2% of patients cryopreserved sperm before orchiectomy, testicular biopsy, and histological type determination.

DISCUSSION

The second cause of death in Chile by non-infectious diseases are malignant tumors, however, testicular cancer ranks seventh among the different types of cancer in the country. Although its causes are not well specified, family history, cryptorchidism, testicular trauma, inguinal hernia, hormonal, nutritional factors, and exposure to toxins are described as the most frequent causes for this pathology [18]. The worldwide incidence and mortality rates for testicular cancer correspond to 1.5 and 0.3%. In the USA,

Table 7: Testicular histology and seminal parameters for TC patients.

SEMINAL PARAMETERS	SEMINOMA	NON SEMINOMA	MIXED
Patient Percent	25%	18%	59 19%
(n)	184	127	143
Age	29±0.4[a]	24±0.5	24±0.4
Abstinence	4±1	7±2	4±1
Volume	1.7±0.1	1.5±0.1	1.7±0.1
Concentration/ml	21±2[b]	26±2	27±3
Total sperm concentration	37±5[c]	43±5	49±6
Progressive motility	45±2	52±2	47±2
Total motile sperm	22±3	25±3	26±4

[a,b,c] p<0.05 when comparing seminal parameters from patients with seminoma vs. non seminoma and mixed
np: number of patients
%: percentage of patients
N: number of samples

5.1 and 0.2%, in Europe 4.8 and 0.4%, in South America 2.4 and 0.4%, in Chile, the highest 5.9 % and 1%, respectively [14,19].

As far as we know, this is the first report of seminal parameters of patients with testicular cancer, beneficiaries from GES, who banked semen in our laboratory (IDIMI). We also compared these results with seminal parameters of patients with other cancers that also banked with us, and with patients that consulted our center for couple infertility.

The majority of seminal reports of patients suffering from different types of cancer, or systematic review of online database, indicate a decreased seminal quality [3,9, 20,21] agreeing with the results of our study.

Hypospermia

We detected a decrease in seminal volume in 36 % of 308 patients with testicular cancer in the first sample provided, but in 51 % of the total 740 samples analyzed. The lower volume was observed in patients with bilateral orchiectomy at the cryopreservation time, different to a recent report from Mackenna (28.7 % in 543 patients with 540 samples) who did not report the testicle affected, nor testicular histology [21]. Our couple infertility patients (9,655) presented only 23 % of hypospermia and from 27 patients that consulted for other cancers a 44%. Only three patients could not be sampled (0.96%) unlike Auger's reports (3-4 %) (8).

Normozoospermia

the percentage of patients with normal sperm concentration/ml was 44,9% as reported by Mackenna (44%), lower than Auger, Salinas (51%) and Hotaling (59%), but higher than Williams (37%, using the OMS 1999 criteria). While our CI patients presented a 79% of normozoospermic men and patients with OC, the lowest, only 32.8%. However, the mean concentration/ml of group 1 was within the reference values (15): a volume of 1.7 ml, 22 million/ml and 47% of progressive motility, similar to Caponecchia who reported 18 mill/ml and 35% progressive motility [7,8 ,9,15,21-23].

Oligozoospermia

A decrease in concentration/ml was observed in 48% of patients as Lass (49.8 %) but higher than Mackenna (35%) and Howel (24%). Patients evaluated for CI and OC presented 16% and 52% of oligospermia. In our oncologic group, the lowest concentration/ml and TSC was seen in patients with bilateral orchiectomy before cryopreservation time [2,21,24].

Azoospermia

Absence of gametes was recorded in 6.7% of evaluated patients, and it was the same result if the first or all samples/patients were analyzed. Other authors reported lower azoospermic rates: 3.3; 3.9; 4.1; 5; 6.1% (3,6,8,9,14,24).–while others show a higher azoospermic group 9.7, 17.3,15.3 and 24% (2,11,21,24), Our CI men presented a 5% of azoospermia but patients who cryopreserved for OC had a higher percentage of azoospermia (15%).

Asthenozoospermia

A decrease in progressive motility of gametes, was observed in 28 % of TC patients as Salinas (25%) but only a 7 % presented total in motility, while patients with OC presented 39% of astenospermia with 18% of immotile gametes, and patients that consulted for CI presented 16.8 % of asthenozoospermia with only a 1.2 % of patients with total in motility (22).

Histological classification

in our Hospital, Martinez Osorio reported for 253 patients with TC orchiectomized but without preserved gametes, a 46% of seminoma and 48% with non-seminoma, compared with our patients who presented 25% seminoma and 18 % no seminoma (25). Meanwhile, 19 % correspond to mixed cancer; unfortunately, we have a large group of patients without identifying their histological type (39 %). Patients with seminoma were older than no seminoma or mixed, as reported by Fraietta and Caponnechia (3,9). The Chilean testicular cancer clinical guides 2010 reported an average age of 36 years for patients with seminoma and 29 years for no seminoma, also the percentage of patients was superior 35.7% for seminoma and 64.3% for no seminoma in 2,184 patients evaluated. All the papers did not report mixed patients, which were probably included as no seminoma.

Regions

Our patients came from different regions of Chile (because not all regions have updated health services) different to Martinez Osorio study, where the patients are only from the Metropolitan region. We did not find differences in seminal quality per regions, but in some of them, the number of patients was very small [1,25].

The percentage of deceased patients (2%) is higher and responded to the cancer stage at the cryopreservation time. Znaor and Trabert reported an increased mortality rate in Latin and Central America and also in East Europe Population (higher in Chile, 1.1 per 100,000) as Mousani who shows a higher incidence of testicular cancer in the first generation of Chilean immigrants in Sweden between 1998 and 2008 (8.8 per 100,000) [1,10,25-27]. Patients with other cancers presented a higher mortality rate than those of testicular cancer evaluated (14.8%) but it corresponds to a small number of patients.

The increase in patients who consulted our center for thirteen years (from 3 in 2006 to 50 in 2019), not only depended on the increase in the incidence of this pathology, but also to greater and better information from treating doctors (clinical derivation) about preservation for future fertility procedures, through gametes cryopreservation, prior to gonadotoxic treatments.

SUMMARY

A major decrease in volume, number of gametes, and progressive motility was recorded in patients with bilateral orchiectomy at cryopreservation time. Patients with seminoma were older ($p<0.05$) than those with no seminoma. The patients with TC and OC compared to CI patients show a higher percentage of hypospermia; almost double oligospermia in all types of cancers including testicular and double azoospermia in patients with OC, while those of TC remain at almost the same level as CI. Asthenozoospermia (<32%) was higher only for patients with OC while the percentage of patients with severe decrease in progressive motility (0%) was higher for TC and OC compared to CI.

CONCLUSION

Our patients with TC presented lower age, greater abstinence, greater volume (due to greater abstinence), lower concentration/ml, total sperm and total motile gametes and progressive motility, similar to those consulted for OC (except abstinence) than in patients who consulted for CI. However, the values were within the WHO reference values, 2010.

Among the clinical considerations for storing sperm, the first is the low number of patients referred to cryopreserve gametes (although they have increased in recent years), the second is that some men can´t emit seminal samples, the third is the poor quality of some seminal samples, in parameters such as volume (hypospermia), concentration/ml (oligo and azoospermia) and progressive motility (asthenozoospermia), a fourth consideration is that not all regions have a laboratory or professionals prepared to cryopreserve gametes.

In patients with altered semen parameters, a non-detected testicular dysfunction prior to testicular cancer was seen. Since infertility is reported as one of the causes of testicular cancer the idea is to prevent it.

For early testicular cancer detection, a routine seminal analysis should be done for boys 15 years onwards, so as to diagnose variations in their parameters and associate this to testicular cancer. Other pending matter is the detection of some genes related to testicular cancer.

ACKNOWLEDGEMENTS

We are grateful to Professor Oscar Oyaneder for the English revision of the manuscript.

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