REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY

Turner's syndrome and other forms of congenital hypogonadism impair quality of life and sexual function

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OBJECTIVE: We sought to assess the burden of Turner's syndrome (TS) and other congenital hypogonadisms (OCH) on quality of life (QOL) and sexual function.

STUDY DESIGN: An observational study was undertaken in a gynecological endocrinology unit of a teaching hospital. Three cohorts of women aged 20-50 years were compared: 26 TS patients, 21 women with OCH and wild-type karyotype, and 41 healthy age-matched women who were included as controls. All subjects filled out the Medical Outcome Study Short Form (SF-36) and the Female Sexual Function Index.

RESULTS: TS subjects had significantly worse QOL scores in physical functioning ($P = .026$) and role physical functioning ($P = .032$) whereas OCH showed significantly worse scores in physical functioning ($P = .027$) and bodily pain ($P = .025$) compared to controls. In all, 80% of OCH and 50% of TS patients declared sexual activity. Sexually active TS patients had poorer arousal outcomes ($P = .009$) and OCH women showed significantly worse scores in arousal ($P = .002$), orgasm ($P = .007$), pain ($P = .001$), and Female Sexual Function Index total score ($P = .004$) compared with healthy controls. No differences between sexually active and inactive TS women were found in SF-36 scores, clinical characteristics, or anthropomorphic characteristics.

CONCLUSION: TS and OCH subjects presented impaired physical domains in QOL. Women with TS are less likely to be involved in sexual activity, arousal dysfunctions being their main symptom. Conversely, arousal, orgasm, pain, and total score were significantly affected in OCH subjects.

Key words: hypogonadisms, quality of life, sexuality, Turner's syndrome

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Turner's syndrome (TS) is a genetic disorder that affects 1 in 2500 females, characterized by the total or partial absence of one of the X chromosomes. The main characteristics of TS are short stature and gonadal dysfunction, as well as dysmorphic features varying in severity that may affect quality of life (QOL). In addition, increased morbidity is caused by the association of TS with some medical conditions such as cardiac and renal malformations, hypothyroidism, osteoporosis, diabetes mellitus, and hearing disturbances.[1-4]

Although intelligence quotient and verbal abilities are usually normal, some subjects with TS show impaired spatial-numerical processing or disabilities affecting recognition or executive functions.[5,6] Depression is the most prevalent psychiatric diagnosis in TS adults compared with the general population; however, TS subjects demonstrate more shyness, social anxiety, and low self-esteem than those without TS.[7] This profile leads to weaker social relationships and poorer school performance.[8] Despite this psychosocial profile and medical complaints, young women with TS reported normal health related to QOL when they had an age-appropriate induced puberty and had reached normal height.[9,10] A few reports have suggested that sexual function is impaired in women with TS.[11,12]

Similar psychosocial difficulties have been reported in women with other forms of congenital hypogonadisms (OCH) and 46,XX karyotype, without either physical dysmorphology or neurocognitive dysfunctions.[13,14] Therefore, whether these difficulties are caused by the effects of X chromosome deletion or early ovarian failure is a question pending resolution.

Remarkably, to our knowledge, no previous studies exist where TS women were compared with OCH in terms of QOL and sexual function. Based on this understanding, the current investigation was undertaken to address this subject using TS patients, in addition to 2 appropriate comparator groups: OCH and a control group taking exogenous hormones. The aim of this study was to assess the burden of TS on QOL and sexual function in adult women using generic (Medical Outcome Study Short Form-36) and specific (Female

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TABLE 1
Clinical characteristics of study population

Characteristic	Controls (n = 41)	TS (n = 26)	OCH (n = 21)
Patients completing SF-36	41 (100)	26 (100)	21 (100)
Patients completing FSFI	41 (100)	13 (50)	17 (81)
Age, y	34.6 ± 7.2	36.7 ± 8.4	34.3 ± 8.9
Weight, kg	60.8 ± 11.0	56.6 ± 11.6	63.3 ± 13.3
Height, cm	163.3 ± 5.3	149.1 ± 21.8	162.0 ± 25.2
Age at diagnosis, y	—	11.1 ± 10.1	18.4 ± 10.2
Age of menarche, y	12.3 ± 1.3	18.2 ± 5.4	17.8 ± 3.2
Patients with spontaneous menarche	41 (100)	13 (50)	11 (52)
Patients with comorbidities[a]	7 (17)	18 (69)	9 (43)
Patients with stable partner	35 (85)	10 (38)	6 (38)

Results are expressed as total numbers (percentages) and as mean ± SD.
FSFI, Female Sexual Function Index; *OCH*, other congenital hypogonadisms; *SF-36*, Medical Outcome Study Short Form; *TS*, Turner's syndrome.

[a] Including high blood pressure, hypothyroidism, dyslipemia, hypertransaminasemia, osteoporosis, diabetes mellitus, renal or cardiac malformations.

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Sexual Function Index [FSFI]) QOL questionnaires, compared to OCH and control groups.

Materials and Methods

Patients

A total of 47 women aged 20-50 years presenting primary amenorrhea were included in this prospective cohort study from June 2010 through July 2011. According to the American Society for Reproductive Medicine criteria,[15] patients had TS or OCH.

TS women (n = 26) were included as the first cohort. TS diagnosis was done by blood sample karyotype showing total or partial absence of X chromosome in, at least, >10% of leukocytes. All women were receiving hormone replacement therapy (HRT) for the development of secondary sexual characteristics and to maintain feminization. Sequential preparations of estradiol hemihydrate 2 mg/1 mg and 1 mg of norethisterone acetate were used.

Women with OCH (n = 21) were selected as the second cohort. Seven women had pure gonadal dysgenesia 46XX (hypergonadotropic hypogonadism), and 14 had idiopathic hypogonadotropic hypogonadism, including Kallmann syndrome. These patients were similarly receiving the same HRT due to their congenital hypoestrogenism.

Nonexposed age-matched women were included as the control group (n = 41). All of them were being treated with estrogen and progestin for contraception, menstrual cycle regulation, or mild primary dysmenorrhea. To build the age-matched group, TS patients were sorted in 5-year groups, and the control women were recruited to meet the percentage of patients of these 5-year groups. They were recruited at our gynecological outpatient area, and none were taking any other drug or had any disorder that could have altered the study results. Inclusion criteria in the control group were people taking hormonal contraception in order to avoid possible bias related to exogenous hormones.

All patients were monitored using follicle stimulating hormone, lutenizing hormone, and estradiol blood determination to make sure they were being supplemented with an adequate dose of estrogen, and only subjects with >1 year of HRT or contraception were included.

Study design

An analytical study of 3 independent cohorts was designed: TS, OCH, and controls. All subjects were asked to fill out validated questionnaires on health-related QOL and sexual function during a routine visit in the outpatient area. They received diagnosis and follow-up at the Endocrinological Gynecology Unit of Hospital Clinic of Barcelona. Subjects were informed of the study's characteristics, and the data obtained from questionnaires would be entered into a database with an identifier code, ensuring the patients' anonymity. Women who agreed to participate signed informed consent, and completed the questionnaires alone without assistance.

QOL questionnaires

The Medical Outcome Study Short Form-36 (SF-36) is a generic QOL questionnaire that has been adapted for the Spanish-speaking general population with good reproducibility and validity.[16,17] The questionnaire SF-36 contains 36 self-administered questions developed to measure health status in 8 domains, covering both physical and mental health. The physical component summary includes 4 domains: physical functioning (10 questions), role physical functioning (4 questions), bodily pain (2 questions), and general health (5 questions). The mental component summary includes 4 domains: vitality (4 questions), role emotional functioning (3 questions), social functioning (2 questions), and mental health (5 questions). Domain scores range from 0–100, with higher scores showing a better health status. SF-36 was scored according to the equivalence of SF-36 summary health scores estimated using standard and country-specific algorithms in Spain, following the results from the International QOL Assessment Project.[18,19] The results for each domain were calculated to give an average score for each. Afterward the result of the domain was normalized by subtracting the average of the Spanish population and dividing by its SD.

The FSFI is a multidimensional self-reporting instrument for the assessment of the key dimensions of female sexual function in clinical and nonclinical samples. This questionnaire contains 19 items assigned to 6 sexual domains: de-