Archives of Sexual Behavior, Vol. 23, No. 2, 1994

Sexual Function in Women with Hypothalamo-Pituitary Disorders

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The extent to which hypothalamo-pituitary disorders in women affect sexual desire and sexual functions was investigated. Sexual functions and sexual appreciation were assessed in a comprehensive interview of 48 women with well-defined hypothalamo-pituitary disorders. Data about sex life were correlated to blood hormone levels and diagnosis. In most of the women (64.8%), the first clinical symptom indicating a hypothalamo-pituitary dysfunction began in the age group 16 to 35. In 43 patients (89.6%), the initial symptom was menstrual irregularities. Altogether 45 (93.8%) of the women declared that they had or had had significant sexual problems. Two of the three women who did not report sexual problems had never had intercourse. Thirty-eight (79.2%) of the women had developed a lack of or a considerable decrease in sexual desire. Problems with lubrication or orgasm were reported by 31 (64.6%) and 33 (68.7%) of the women, respectively. Normal menstrual pattern, young age, and intrasellar tumor growth correlated better with normal sexual desire and sexual functions than did normal prolactin levels and normal testosterone levels. However, at the time of interview, only 7 women had hyperprolactinemia. Serum testosterone values correlated significantly only with masturbation.

KEY WORDS: female sexuality; menstruation; hypothalamo-pituitary disorders; testosterone; prolactin.

INTRODUCTION

Hypothalamo-pituitary disorders often give symptoms of sexual dysfunction. In large series of patients (Bakay, 1950, Younghusband *et al.*,

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0004-0002/94/0400-0171$07.00/0

1952; Heimbach, 1959; Fischer, 1963; Fürst, 1966; Batzdorf and Stern, 1973) reduced sexual desire was reported to occur with a frequency from 35 to 73%. It is believed that changes in sexual desire are at least in part dependent on blood levels of androgens in the male and androgens together with estrogens in the female. Hyperprolactinemia is reported to result in a decrease in libido in males and females. However, the mechanisms of hyperprolactinemia are complex and prolactin has effects on many different levels of the hypothalamo-pituitary-gonadal brain circuit. The department of neurology in Uppsala is a center for treatment of patients with hypothalamo-pituitary disorders in central Sweden. This position has made it feasible to study sexual problems and sexual dysfunction in a large group of patients. It has been possible to correlate data about the sex life of the patients with diagnosis, tumor extension and pathology, endocrine insufficiency, and pituitary hormone hypersecretion in four different study groups comprising more than 250 patients.

Three studies from this center have been published. In one (Lundberg and Wide, 1978), of 63 adult males with pituitary tumors of different types, 48 (76.2%) reported decreased or absent sexual desire. The figure was higher for patients with larger tumors extending into the suprasellar region (88.1%) than for those with intrasellar tumors (52.3%). Twenty (31.7%) patients reported decreased sexual desire as the first symptom of their tumor. However, only 1 of these 20 patients actually did seek medical advice because of this symptom. A significant correlation was found between a decrease in serum testosterone and a decrease in libido. Fourteen patients in this study had hyperprolactinemia. Only 1 had normal sexual desire and potency. However, there was no significant correlation ($p > 0.05$) between hyperprolactinemia and a reduced sexual desire.

In the next group of patients (Muhr *et al.*, 1985; Hulting *et al.*, 1985), only male patients with pituitary tumors resulting in hyperprolactinemia were included. Among 37, decreased sexual desire was the first symptom in 18 (48.6%). Nine of these men had lived with this problem for more than 9 years. In 29 (78.4%) the symptom was reported at the time of diagnosis. Even in this group of patients low serum testosterone prevailed among those with decreased libido. However, some males with normal serum testosterone, but hyperprolactinemia, also reported decreased libido.

In the third study (Lundberg *et al.*, 1986), of 109 females (ages 20–60) with morphologically verified hypothalamo-pituitary disorders, 68 (62.4%) had noticed an absence or a considerable and troublesome decrease in sexual desire. This problem was registered for 53 (84.1%) of the 63 women with hyperprolactinemia but only in 15 (32.6%) of 46 women with normal serum prolactin ($p < 0.001$).

Almost all women had amenorrhea. There was, however, no significant correlation between low serum estradiol levels in the amenorrhoic women or low serum testosterone levels in all women and reduced sexual desire. Loss of sexual desire was noticed in almost all patients with craniopharyngiomas but only in half of those with acromegaly. The frequency of the problem was higher among patients with intrasellar adenomas (76.7%) and invasive adenomas (83.3%) than among those with large expansively growing adenomas (59.3%). Most tumors in the first two groups were prolactin producing.

In previous studies, sexual dysfunctions were looked upon as a global problem of sexual desire and function. However, modern sexual physiology has taught us that it is necessary to separate sexual desire from sexual arousal, and to recognize well-defined sexual reactions in the genital organs such as erection/lubrication, emission and ejaculation/genital experience of orgasm. Therefore, we find it essential to analyze the different parts of the sexual reaction pattern in patients where sexual dysfunction could be expected.

The present study investigated the extent to which hypothalamo-pituitary disorders in female patients had affected their sexual desire and sexual functions and correlated data about the sex life of patients with blood hormone levels and diagnosis.

METHOD

The women were interviewed by the female co-author (B.H.) who is a tutor in nursing and registered nurse with a special education in sexology and neurology. Interviews included social, medical, and detailed sexological case histories.

Interviews had the following content: family background and information on sexual matters during childhood and youth; religious/moral misgivings as regards sexuality; sexual experiences, début; events that could have affected the sexual life; occupation; family situation; alcohol and smoking habits; body image, sex identification; possible homosexual interest and experiences; illnesses, diseases, surgery, medical treatments; menstrual history, pregnancies, children, deliveries, breast-feeding, and abortions. Patients were also asked about sexual habits and sexual functions before the first clinical symptom of the hypothalamo-pituitary disorder as well as at the time of interview. Other questions concerned contentment/discontentment and any wishes for alterations. A final question concerned the interview experience.

Each interview lasted 1–2 hr. To test the questionnaire and the interview situation, two pilot interviews were performed with healthy colleagues of the interviewer. To facilitate cooperation, both written and verbal information was given. The patient and the interviewer were sitting in comfortable chairs, almost opposite each other, with a small table in between. The patient was reminded that she could quit participation in the study at any time and that she could also refuse to answer any particular question that would be embarrassing. None of these occurred during the study. A lot of background information from the forms is left out of the present report. This paper concentrates on sexual and medical matters.

Definitions

We define the "initial symptom" of a hypothalamo-pituitary disorder as any pertinent symptom described by the patient at the first clinical examination for this specific disorder. We asked for symptoms of sexual dysfunction at a point just before any treatment was given, considered to be the period in the life of the patient when the neuroendocrine disturbance reached its maximum. We also investigated the sexual symptomatology at the time of interview for correlation with blood hormone levels on that day. If not stated otherwise, the following description of the patient's sexual problems refers to the situation at the time of interview.

"Lubrication" is an expression for the appearance of extra fluids in the vagina when sexually stimulated.

"Orgasm" is an expression for a sexual peak-experience by most women accompanied by involuntary muscle activity in the pelvis-bottom. The patients are the ones to judge whether they experience orgasm.

The expression "normal" is used when the sexual functions are described by the patient as they should be, with the presumption that it is normal for grown women to experience sexual desire, to have sufficient lubrication to enable pleasurable coitus, and to enjoy orgasms.

"Decreased" sexual desire is defined by the patient as a decrease in comparison to her earlier experiences. "Absence" of sexual desire is defined as a total lack of desire.

"Decreased" lubrication and "difficulty" in achieving orgasms or a total absence of orgasmic responses are defined by the patients in comparison with their earlier experiences. No reference is made to how the orgasms are achieved (e.g., through masturbation or intercourse) unless stated.

Hormone Assays

All patients went through a comprehensive endocrine evaluation. In the present report only data concerning some endocrine parameters are presented. Venous blood samples were taken in the morning. Radioimmunosorbent techniques were used for measuring serum concentrations of prolactin and testosterone (Wide, 1969). The reference range for serum prolactin was less than 20 μg/L. The reference range for serum testosterone in women was 0.8–3.0 nmol/L.

Statistics

For testing differences of proportions, a two-tailed *t* test, ANOVA with Fisher PLSD, and the chi-square test with Yates' correction were applied.

Ethics

This study was ethically approved by the Committee of Ethics at the Medical Faculty of the University in Uppsala.

Subjects

Fifty-three women with hypothalamo-pituitary disorders were asked to participate: 48 agreed (ages 17–57 years, median 42) and 5 declined for various reasons. Patients over 60 were not asked to participate. The age distribution of the women at the time of interview is shown in Fig. 1. One can identify two groups: less than 35 years and more than 35 years of age. For statistical analyses the women were divided into these two groups. On the basis of CT and/or MRI, patients were divided into five groups (Table I). Most patients (38, 79.2%) had tumors of the sellar region. Among 28 with pituitary adenomas, 10 had serum prolactin levels higher than 100 μg/L. They were diagnosed as having prolactinomas. A further 22 had prolactin values between 20 and 100 μg/L. However, at the time of interview only 7 had elevated serum prolactin (>20 μg/L). Six women had acromegaly caused by growth hormone producing adenomas.

In most of the patients (31, 64.6%), the first clinical symptom indicating a hypothalamic or pituitary dysfunction began between the age of 16 and 35. The median age was 23 years (range 10–57). However, a hypothalamo-pituitary disorder may give clinical symptoms and signs at any

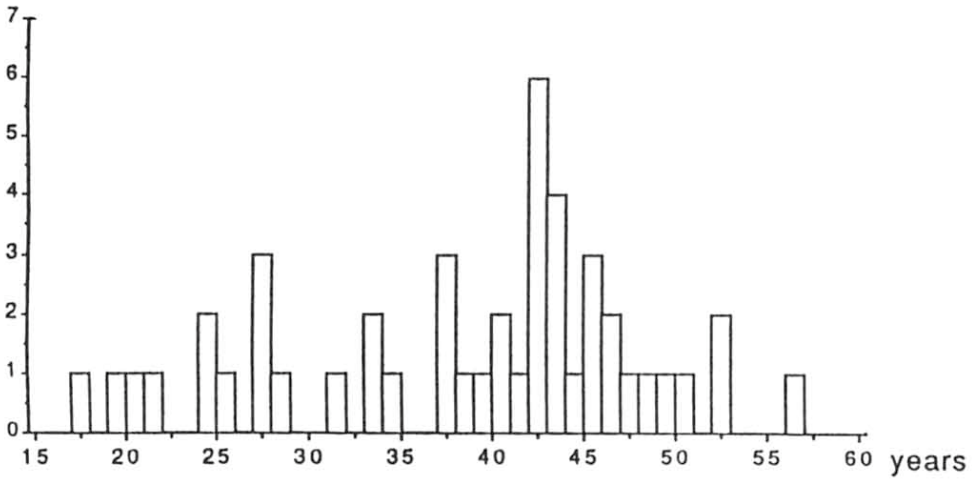

Fig. 1. Age at interview.

Table I. Roentgenological Diagnosis (N = 48)

	n	%
Pituitary atrophy or empty sella	10	20.8
Intrasellar pituitary adenomas	8	16.7
Expansively growing pituitary adenomas with suprasellar extension	14	29.2
Invasively growing pituitary adenomas with parasellar extension	6	12.5
Suprasellar tumors	10	20.8

age. The median duration of the disorder was 10.5 years (range 0–28) at the time of interview.

In 43 patients (89.6%), the initial symptom of the hypothalamo-pituitary disorder was menstrual problems. In 14 a decrease in sexual desire was present at the beginning of the case history (Table II). However, in none of the patients had this particular symptom prompted them to seek medical advice. Viewed over the period of time up to diagnosis, menstrual dysfunction was the predominant symptom. Three women had had irregular menstruations from menarche. Secondary amenorrhea was experienced in 38 cases and primary amenorrhea in 2.

Partly as a result of given therapy (not substitution) 15 of the women were menstruating regularly (ages 24–46 years, median 40) at the time of interview. However, 33 did not menstruate (ages 17–57 years, median 42); 6 of these 33 were above 50 years of age.

Table II. Initial Symptom Reported by the Patient[a]

Symptom	*n*
Amenorrhea or irregular menstruations	43
Galaktorrhea	16
Visual disturbances	15
Decrease in sexual desire	14
Headache	8
Acromegalic growth	6
Tiredness	2
Dizziness	1

[a]Note that the same patient may have had more than one initial symptom.

Table III. Sexual Experiences

Number of sexual partners: mode 1 (x 3.9, range 0–16)

	Normal		Reduced or absent	
	n	%	*n*	%
Sexual desire, ever	42	87.5	6	12.5
	Yes		No	
	n	%	n	%
Masturbation, ever	22	50.0	22	50.0
Intercourse, ever	44	91.7	4	8.3
Cohabiting, now	35	72.9	13	27.1

RESULTS

The women had had very different sexual experiences. The majority (35, 72.9%) were cohabiting with a male sexual partner at the time of the interview (Table III). Six (12.5%) could not recall ever having experienced a feeling of sexual desire. Twenty-two (50%) had never tried masturbation (4 missing answers). Ten (20.8%) had had sexual intercourse with only one partner; 4 (8.3%) (ages 17–27 years) had never had intercourse. The explanations given by the patients for the lack of experience were vaginismus, lack of an attractive partner, fear after attempted rape, and performance anxiety. Altogether 45 (93.8%) of the women declared that they currently had or had had significant sexual problems. Two of the three women who did not report sexual problems had never had intercourse. Thirty-eight

Table IV. Sexual Functions in Relation to Menstruation at Time of Interview

	Normal		Decreased	
	n	%	*n*	%
Sexual desire				
Menstruating	7	46.7	8	53.3
Amenorrhea	9	27.3	24	72.7
		ns		
Lubrication				
Menstruating	8	53.3	7	46.7
Amenorrhea	13	39.4	20	60.6
		ns		
	Normal		Difficult	
Orgasm				
Menstruating	12	80.0	3	20.0
Amenorrhea	7	21.2	26	78.8
		$p < 0.001$		
	Yes		No	
Masturbation				
Menstruating	5	41.7	7	58.3
Amenorrhea	3	9.4	29	90.6
		$p < 0.02$		

(79.2%) had developed a lack of, or a considerable decrease in, sexual desire. Problems with lubrication or orgasms were reported by 31 (64.6%) and 33 (68.7.%) of the women, respectively.

At the time of interview 15 women had a normal menstrual pattern and 33 had amenorrhea. If presence or absence of sexual dysfunction was compared to normal menstrual pattern vis-à-vis amenorrhea a statistically significant correlation was found only for orgasmic capacity and masturbatory activity (Table IV).

No significant correlation was found between elevated serum prolactin levels and sexual dysfunction (Table V) at the time of interview. However, at this point in time, only 7 patients had hyperprolactinemia. When serum testosterone values were correlated, a significance was observed only for masturbation (Table VI).

Younger age correlated positively to normal sexual desire ($p < 0.01$). Intrasellar adenomas correlated positively to normal sexual desire ($p < 0.01$), lubrication and orgasm ($p < 0.05$) in comparison to the expansively growing pituitary adenomas with both intra- and suprasellar extension (Table VII).

Table V. Sexual Functions in Relation to Serum Prolactin Levels at Time of Interview

	Normal		Decreased	
	n	%	*n*	%
Sexual desire				
Prolactin < 20 µg/L	15	36.6	26	63.4
Prolactin > 20 µg/L	1	14.3	6	85.7
		ns		
Lubrication				
Prolactin < 20 µg/L	19	46.3	22	53.7
Prolactin > 20 µg/L	2	28.6	5	71.4
		ns		
	Normal		Difficult	
Orgasm				
Prolactin < 20 µg/L	17	41.5	24	58.5
Prolactin > 20 µg/L	2	28.6	5	71.4
		ns		
	Yes		No	
Masturbation				
Prolactin < 20 µg/L	8	21.6	29	78.4
Prolactin > 20 µg/L	0		7	100
		ns		

Table VI. Sexual Functions in Relation to Serum Testosterone Level at Time of Interview

	Normal		Decreased	
	n	%	*n*	%
Sexual desire				
Normal testosterone	6	28.6	15	71.4
Subnormal testosterone	10	37.0	17	63.0
		ns		
Lubrication				
Normal testosterone	12	57.1	9	42.9
Subnormal testosterone	9	33.3	18	66.7
		ns		
	Normal		Difficult	
Orgasm				
Normal testosterone	10	47.6	11	52.4
Subnormal testosterone	9	33.3	18	66.7
		ns		
	Yes		No	
Masturbation				
Normal testosterone	6	33.3	12	66.7
Subnormal testosterone	2	7.7	24	92.3
		$p < 0.05$		

Table VII. Sexual Functions Correlated to Intrasellar (n = 8) Vis-à-Vis Expansively Growing Pituitary Adenomas (n = 14) with Intra- and Suprasellar Extension

	Normal	Decreased
Sexual desire		
Intrasellar tumors	6	2
Expansively growing tumors	2	12
	$p < 0.01$	
Lubrication		
Intrasellar tumors	6	2
Expansively growing tumors	4	10
	$p < 0.05$	
	Normal	Difficult
Orgasm		
Intrasellar tumors	6	2
Expansively growing tumors	3	11
	$p < 0.05$	

DISCUSSION

Altogether 45 (93.8%) of the women declared that they had or had had significant sexual problems. Thirty-eight (79.2%) had a considerable decrease in sexual desire. Thirty-one (64.6%) had problems with lubrication, and 33 (68.7%) had problems with orgasms.

In male patients hormone levels were proven to be of great importance for the maintenance of normal psychosexual functions. (Carter *et al.*, 1978; Franks *et al.*, 1978; Lundberg and Wide, 1978; Nagulesparen *et al.*, 1978; Davidson *et al.*, 1979; Buckman and Kellner, 1985; Hulting *et al.*, 1985; Muhr *et al.*, 1985; Hipkin *et al.*, 1986; Gooren, 1987). The situation seems somewhat different in women. The frequency of decrease in sexual desire was similar in the two female groups (62.4% in Lundberg *et al.*, 1986 and 79.2% in the present study) as well as in the male groups (76–78% Lundberg and Wide, 1978,; Muhr *et al.*, 1985; Hulting *et al.*, 1985). In the first study of females (Lundberg *et al.*, 1986), there was a significant correlation between hyperprolactinemia and reduced sexual desire as reported by other authors (Buvat, 1982). In the present study the difference was not significant. However, in this study the number of patients with hyperprolactinemia at the time of interview was only 7.

In a majority of the women (n = 31) in the present study, the first clinical symptom indicating a hypothalamo-pituitary dysfunction began in the age group 16 to 35. The most frequent initial symptom was amenorrhea.

Normal menstrual pattern, young age, and intrasellar tumor growth correlated more strongly to normal sexual desire and sexual functions than did normal prolactin levels and normal testosterone levels. Statistical significance was reached as normal menstrual pattern ($p < 0.02$) and normal serum testosterone ($p < 0.05$) correlated to masturbatory activity.

The general problem with the unreliability of retrospective data and one-shot monitoring is pointed out by Sherwin (1985). Better controlled methods when working with populations of consecutive patients with distinct diagnoses would be of great interest, but they confront us with practical and ethical dilemmas.

In a prospective, crossover investigation of 53 surgically menopausal women, Sherwin *et al.* (1985) assessed various parameters of sexual functioning. Patients randomly received either an estrogen-androgen combination, estrogen alone, androgen alone, or placebo. Endogenous androgen enhanced the intensity of sexual desire and arousal and the frequency of sexual fantasies. However, there was no evidence that testosterone affected the physiological response or interpersonal aspects of sexual behavior. The findings suggest that the major impact of androgen in women is on sexual motivation and not on sexual activity per se. Sherwin *et al.* used the term "sexual motivation" to describe the libidinal aspects of sexuality and it was operationally defined as comprising three issues — sexual desire, sexual arousal, and sexual fantasy. The major finding in that study was that all three measures of sexual motivation increased with circulating levels of plasma testosterone. Data provide strong support for the hypothesis that sexual motivation in women is androgen-dependent. Estrogens were not causally related to sexual motivation in the human female.

Results of two studies on young cycling women support this view. Persky *et al.* (1978) found no relationship between plasma estradiol levels and sexual arousal, intercourse frequency, and sexual gratification in healthy women with a mean age of 24 years. Abplanalp *et al.* (1979) likewise did not find any association between estradiol level and enjoyment of heterosexual activities in 23- to 39-year-old regularly cycling women. On the other hand, Cutler *et al.* (1986) found that women who had weekly sex with men had higher luteal phase estradiol values than women with lower heterosexual activity. Sherwin *et al.*'s (1985) findings on generally healthy surgically menopausal women based on 240 days of daily monitoring per patient confirmed reports from numerous estrogen replacement therapy studies of premenopausally oophorectomized women. Although estrogen administration alleviates atrophic vaginitis and associated dyspareunia in postmenopausal women, it seems to be without effect on libidinal aspects of sexuality such as desire and arousal (Campbell and Whitehead, 1977, Coope, 1976).

Masturbation seems to be a better measure of sexual desire than coital activity. Bancroft *et al.* (1983) found that although midcycle testosterone levels correlated positively with masturbation frequency, there was no corresponding increase in frequency of sexual activity with partners at that time. There are different possible explanations for that. Coital frequency tells more about communication and cooperation with the partner than about the actual sexual desire of the women. Sexual initiatives are mainly controlled by sex roles. The traditional female role is passive, adjustive to the more active and demanding male role.

In our series of studies, tumors of a large size, both in male and in female, more often produced sexual problems than did intrasellar tumors. This could be due to the fact that a larger tumor usually results in a more pronounced pituitary insufficiency, that larger tumors are more likely to involve a posited center for sexual desire in the basal hypothalamus (Roeder *et al.*, 1971), or that some larger tumors (invasive adenomas, Lundberg *et al.*, 1977) may be combined with a pronounced hyperprolactinemia. Another factor may have been that certain types of large tumors, the craniopharyngiomas, start to grow at an early age. Thus, in many patients this occurs before psychosexual development was completed.

For many reasons, a normal menstrual pattern is crucial for the sex life of women. However, the weight of the accumulating evidence strongly suggests that the primary behavioral action of androgen on sexual functioning in both male and female is on sexual interest and motivation and not on interpersonal activity or the physiological response. It is possible that hormonal factors do not play an important role in females.

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