

Pituitary-Testis Relationships in Paraplegic Men

VICENTE CORTÉS-GALLEGOS, GRACIELA CASTAÑEDA, ROCÍO ALONSO,
HORTENSIA ARELLANO, CARLOS CERVANTES AND ADALBERTO PARRA

Ten men aged 12 to 48 years with a complete neurophysiologic transection of the spinal cord (seven paraplegic, two quadriplegic, and one hemiplegic) were endocrinologically investigated to determine the relationships between the plasma concentrations of gonadotropins, prolactin, and androgens and to search for possible correlations with the time elapsed after the trauma (one-79 months). Peripheral blood samples were obtained from each subject every other day to measure follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin (PRL), androstenedione (A), testosterone (T), and dihydrotestosterone (DHT), and the results were compared with the values obtained from age-matched healthy individuals. On a group basis (without including two prepubertal patients), a significant linear correlation was observed between the time elapsed after the trauma and the plasma levels of T ($r = 0.683$, $P = 0.05$) and DHT ($r = 0.832$, $P < 0.025$), but not A. Both FSH and LH plasma concentrations were elevated in all instances, and 70% of the patients also had higher PRL values when compared with healthy male subjects. The present study emphasizes the need for a careful re-examination of the current clinical management of these patients within the first months after trauma.

Key words: paraplegia, androgens, gonadotropins, prolactin.

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Reprint requests: Dr. V. Cortés-Gallegos, Sección de Fisiología Gonadal, CMN, IMSS, Apartado Postal 73-032 México 73, D.F., Mexico.

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From the División de Endocrinología y Reproducción, Subjefatura de Investigación Científica and Hospital de Convalecencia, C.M.N., I.M.S.S., Mexico City

Studies dating back to 1950 reported the metabolic consequences of paraplegia (Cooper et al, 1950), as well as the atrophy of the germ cells and the presence of normal or hyperplastic Leydig cells in the testes of paraplegic (PPG) males (Stemmerman et al, 1950). Subsequent hormonal studies have shown elevated plasma concentrations of follicle stimulating hormone (FSH) and luteinizing hormone (LH) in 30 to 50% of PPG males (Morley et al, 1979; Hayes et al, 1979), in association with normal plasma prolactin (PRL) (Hayes et al, 1979) and testosterone (T) levels (Mizuntani et al, 1972; Morley et al, 1979). Nevertheless, no information is available on the levels of other important androgens in plasma, such as dihydrotestosterone (DHT) and androstenedione (A), measured alone or simultaneously with T, FSH, LH, and PRL in PPG men. Consequently, this work was undertaken to study the relationship between such adenohipophyseal and testicular hormones in PPG men, as well as to determine whether there is a correlation between plasma concentrations of these hormones and the time elapsed after trauma.

Materials and Methods

Subjects

Group I (Patients) A group of ten men (aged 12-48 years) with complete neurophysiologic transection of the spinal cord agreed to participate in the study. The general clinical data are shown in Table 1. Patients aged 12 and 16 years had genital development at stages II and IV, respectively (Tanner 1962). At the time of the study none of the subjects had any associated endocrine

TABLE 1. General Clinical Data in Paraplegic Men

Patient No. (Age)	Level of Damage	Neurophysiologic Inference*	Libido (Ejaculation)	Time After Trauma at Time of the Study (months)	Total No. of Blood Samples
I (16)	T6-T7	PPG	+† (Present)	1	6
II (12)	T12-L1	PPG	+ (Absent)‡	1.5	6
III (28)	T4-T5	PPG	+ (Absent)	3	4
IV (25)	C5-C6	QPG	+ (Variable)	3	5
V (22)	T7-T8	PPG	+ (Absent)	4	5
VI (48)	C5	HPG	+ (Absent)	12	2
VII (31)	C5	QPG	+ (Present)	24	1
VIII (27)	T2-T3	PPG	+ (Present)	39	7
IX (20)	T11-T12	PPG	+ (Present)	60	6
X (26)	T3-T4	PPG	+ (Present)	79	5

* PPG = paraplegic; QPG = quadriplegic; HPG = hemiplegic.

† + = present.

‡ Due to his chronologic age.

disease, and their kidney function, as evaluated by blood chemistry, urine analysis, and urine culture, was normal. Size and consistency of the testes and the prostate gland were within the normal range for the subjects' stage of sexual development (patients I and II) and for their chronologic age (patients III-X). Because of the difficulties in obtaining semen from these patients, sperm counts were not available.

Groups II (Control). Due to age differences among the patients, the control group consisted of: a) ten clinically healthy children aged 12 to 13 years at stage II of genital development; b) ten clinically healthy adolescents aged 15 to 16 years at stage IV of genital development; and c) 27 clinically healthy males aged 20 to 50 years.

Procedures

Group I. Peripheral venous blood samples were obtained from each patient at 8:00 A.M. for duplicate determinations of plasma FSH, LH, and PRL (Parra et al, 1980) and of A, T, and DHT (Cortés-Gallegos et al, 1980). Multiple samples were collected every other day, but the total number of blood samples taken from each patient (Table 1) varied according to the authorization granted by each individual.

Group II. A single peripheral venous blood sample was obtained from each subject at 8:00 A.M. to measure the pituitary and testicular hormones listed above.

Statistical analysis was performed using the two-tailed Student's *t* test for independent samples. The coefficient of correlation was calculated to examine the relationship between the time elapsed after the trauma and the plasma concentrations of the different hormones. The two youngest subjects (patients I and II)

were not included in calculating correlations since they had not attained full sexual maturation. Values expressed in the text and tables represent the means \pm one standard deviation (SD).

Results

A. Testicular Hormones

Androstenedione. In the two youngest patients (I and II) and in three of the eight adult patients (III, V, and VI), the mean plasma concentration was at least one SD below the corresponding mean control value. In the remaining five adult patients mean plasma levels were within the normal range. In adult patients, no correlation was found between the time after trauma and plasma androstenedione concentrations (Table 2).

Testosterone. In patient I as well as in six of the eight adult patients (III-VIII), mean plasma testosterone levels were one SD below the corresponding mean concentrations in control subjects. In the remaining three patients, mean plasma values were within the normal range. There was a linear correlation between the time elapsed after the trauma and the mean plasma T concentrations in adult patients ($r = 0.683$, $P = 0.05$) (see Table 2).

Dihydrotestosterone. In the two youngest patients (I and II), as well as in four of the eight adult males (III, IV, VI, and VII), mean plasma DHT con-

TABLE 2. Individual Plasma Androgens (ng/ml) in Ten Spinal-cord-injured Men in Comparison with Healthy Male Volunteers (Mean ± SD)

Patient No.	Chronologic Age	Spinal-cord-injured			Normal Controls		
		A	T	DHT	A	T	DHT
I	16 yr	0.5 ± 0.1	2.4 ± 0.5	0.2 ± 0.03	1.1 ± 0.3*	3.8 ± 1.0*	0.5 ± 0.1*
II	12 yr	0.4 ± 0.06	2.3 ± 0.5	0.2 ± 0.04	0.9 ± 0.3†	1.1 ± 0.7†	0.6 ± 0.2†
III	28 yr	0.8 ± 0.2	4.8 ± 1.5	0.3 ± 0.1	1.4 ± 0.4‡	6.7 ± 1.7‡	0.7 ± 0.2‡
IV	25 yr	1.1 ± 0.3	3.5 ± 0.6	0.4 ± 0.06			
V	22 yr	0.7 ± 0.3	3.3 ± 0.7	0.6 ± 0.2			
VI	48 yr	0.5, 0.4	4.3, 4.8	0.3, 0.4			
VII	31 yr	1.8	3.2	0.4			
VIII	27 yr	1.1 ± 0.3	4.8 ± 1.0	0.5 ± 0.08			
IX	20 yr	1.6 ± 0.1	6.8 ± 1.5	0.9 ± 0.09			
X	26 yr	1.2 ± 0.4	5.3 ± 0.7	0.8 ± 0.1			

* Normal values from ten healthy adolescents age 15 to 16 years at stage IV of genital development.

† Normal values from ten healthy children aged 12 to 13 years at stage II of genital development.

‡ Normal values from 27 healthy adults aged 20 to 50 years.

centrations were at least one SD below the corresponding mean values in the controls. In the remaining four patients, mean plasma DHT levels were within the normal range. In the adult patients, a significant linear correlation was observed between the time after the trauma and the mean plasma DHT levels ($r = 0.832$, $P < 0.025$) (see Table 2).

B. Pituitary Hormones.

FSH and LH (LER 907). In all ten patients, the plasma concentrations of both gonadotropins were more than two SD above the corresponding mean values for controls. No significant correlation was detected between the time elapsed after the trauma and the plasma concentration of either gonadotropin (Table 3).

Prolactin (VLS-3). In six of the eight adult patients (III, V, and VII–X), plasma PRL levels were moderately elevated in comparison with control values. The mean plasma concentrations in the two youngest subjects could not be correctly evaluated since we do not have normal values for that age or stage of genital development; however, in one of them (II) plasma PRL was within the normal adult range, while in the other (I) it was higher than the normal adult concentrations. No correlation was found between the time after trauma and plasma PRL concentrations (see Table 3).

Discussion

The present study describes the existence of a direct relationship between the time elapsed after spinal cord injury and plasma levels of testoster-

TABLE 3. Individual Plasma Pituitary Hormones (ng/ml) in Ten Spinal-cord-injured Men in Comparison with Healthy Male Volunteers (Mean ± SD)

Patient No.	Chronologic Age	Spinal-cord-injured			Normal controls		
		FSH	LH	PRL	FSH	LH	PRL
I	16 yr	384 ± 87	173 ± 105	13 ± 2	80 ± 15*	42 ± 10*	—
II	12 yr	311 ± 78	418 ± 143	6 ± 3	31 ± 7†	10 ± 4†	—
III	28 yr	470 ± 92	391 ± 144	8 ± 1	121 ± 41‡	88 ± 28‡	4 ± 2‡
IV	25 yr	445 ± 71	263 ± 136	5 ± 1			
V	22 yr	593 ± 198	269 ± 223	14 ± 3			
VI	48 yr	281, 280	403, 387	6, 4			
VII	31 yr	282	347	16			
VIII	27 yr	335 ± 48	144 ± 72	8 ± 1			
IX	20 yr	248 ± 98	322 ± 147	8 ± 1			
X	26 yr	334	251	10			

* Normal values from ten healthy adolescents age 15 to 16 years at stage IV of genital development.

† Normal values from ten healthy children aged 12 to 13 years at stage II of genital development.

‡ Normal values from 27 healthy adults aged 20 to 50 years.

one and dihydrotestosterone, but not androstenedione. This relationship was evident regardless of the level of neurophysiologic damage and/or its clinical consequences. These findings are in agreement with the earlier observations of similar changes in plasma testosterone in traumatic quadriplegic (QPG) patients under stable clinical conditions (Claus-Walker et al, 1977). However, our results are at variance with the reports of other authors who observed no correlation between the duration or level of the neural cord lesion and the plasma levels of testosterone (Mizutani et al, 1972; Morley et al, 1979; Hayes et al, 1979). These discrepancies could be at least partially explained by the fact that the latter three studies based their observations on determinations of plasma hormone levels in a single blood specimen. Furthermore, no hormonal determinations were performed within the first four to six months after the trauma, a time when a decline in plasma testosterone and dihydrotestosterone was demonstrated in the present study. It is unlikely that differences in methodology could explain these discrepancies, since plasma concentrations of both androgens and gonadotropins in the normal controls in the present study closely agree with those previously obtained in our laboratory in studies of other populations (Barberia et al, 1973; Cortés-Gallegos et al, 1980) as well as with those reported by others (Purvis et al, 1975).

Normal androstenedione levels observed in these patients may be a reflection of adrenal production rather than being of testicular origin (Hudson et al, 1967).

The hormonal changes described in this study appear to mimic those found after major surgery, particularly the significant fall in plasma testosterone and the rise in plasma LH observed within one month after such procedures (Monden et al, 1972). However, in our study the low levels of T and DHT, as well as the increased levels of gonadotropins, were observed as late as three months post trauma. Thus, it seems unlikely to ascribe these low levels of androgens to the cord-injury-induced stress alone.

The observed elevation of plasma gonadotropin levels is in good agreement with previous reports (Morley et al, 1979) as well as with the demonstration that the function of the hypothalamic-pituitary-testis axis is disturbed for at least four months after spinal cord injury (Naftchi et al, 1980). It remains unclear whether this abnormality in plasma

gonadotropin levels is a direct consequence of a disturbance in the hypothalamic-pituitary-testis axis, a response secondary to primary testicular damage, or a combination of both. Seventy percent of the patients studied had a modest rise in plasma concentrations of PRL, which indirectly suggests that this hormone may be related to testicular dysfunction (Bartke, 1974). Apparently, in these patients the damage to the Leydig cells is transient, and the LH-PRL-mediated chronic overstimulation of those cells is necessary to maintain androgen synthesis as close to normal as possible. Several authors have described primary damage to the seminiferous tubules in some PPG men (Stemmerman et al, 1950). This is consistent with the elevated plasma levels of FSH in our patients.

These findings indicate the need for careful re-examination of the current clinical management of patients with paralysis resulting from spinal cord injury, particularly within the first four to six months after trauma.

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International Symposium on Recent Advances in Male Reproduction: Molecular Bases and Clinical Implications

The International Symposium on Recent Advances in Male Reproduction: Molecular Bases and Clinical Implications will take place in Catania-Taormina, Italy, June 27-30, 1982. The Symposium is sponsored by the Italian Society of Endocrinology and the Italian Society of Andrology. The Program Organizing Committee members are C. W. Bardin (United States), R. D'Agata (Italy), M. B. Lipsett (U.S.), L. Martini (Italy), M. Serio (Italy), R. J. Sherins (U.S.), E. Steinberger (U.S.), and H. J. van der Molen (Netherlands).

Topics of the Symposium will include: ABP in the testis, Sertoli and Leydig cell function, LH-RH effect on pituitary and testis, desensitization by hCG and clinical implications, hypothalamic-pituitary-testicular function in prepubertal stages and old age, regulation of gonadotropin release, inhibin and other gonadal peptides, and epididymal and spermatozoal function.

Some 30 speakers have been invited. The official language is English. A limited number of free communications and poster presentations will be selected. Abstracts must be sent to the scientific secretaries (address below) before March 15, 1982.

Scientific Secretary:

R. D'Agata

Unità Endocrina—Istituto di Patologia Medica I

Ospedale Garibaldi

95124 Catania (Italy)

(095) 317983-310899