

VARICOCELE IN PREPUBERTAL BOYS

EVALUATION OF CLINICAL, DOPPLER AND HORMONAL FINDINGS

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Summary Hormonal, clinical and scrotal Doppler findings were assessed in 16 prepubertal patients having unilateral varicocele. As already described in pubertal patients, Doppler studies made it possible to detect patterns of prolonged, intermittent or permanent reflux. An LH-RH test and an hCG test measuring LH, FSH and testosterone (T) were performed in all cases. Patients with varicocele showed (median and range): LH B (mIU/ml): 0.40 (0.40-2.1); LH Mx.: 3.7 (1.1-15); FSH B (mIU/ml): 1.95 (0.40-4.5); FSH Mx.: 4.9 (3.1-10); T B (ng/ml): 0.2 (0.1-1.5); T Post.: 2.25 (0.82-11.5). The control group showed: LH B (mIU/ml): 0.40 (0.4-0.85); LH Mx.: 2.15 (0.63-12); FSH B (mIU/ml): 1.45 (0.4-3); FSH Mx.: 4.25 (2.6-5.9); T B (ng/ml): 0.1 (0.1-0.3); T Post.: 3.26 (1.0-5.6). No significant differences were found between the hormonal results of the different groups classified according to the scrotal findings. Basal LH and FSH in grade 3 varicoceles were found to be significantly higher ($p < 0.05$) than those of the control group. Basal T, as well as the maximal response of both gonadotropins to LH-RH, and T response to hCG showed no significant differences with reference to the control group. Our findings provide indirect support to the notion that the gonadal damage would become detectable from puberty onwards.

Key words: prepubertal varicocele, scrotal Doppler, prepubertal gonadal evaluation

Varicocele in the prepubertal stage is an unusual finding; some authors have been unable to detect this condition below the age of ten^{1,2}. We have previously described³ the clinical and biochemical findings, as well as those corresponding to scrotal Doppler in pubertal patients, reporting some alterations in the dynamic responses of luteinizing hormone (LH) and testosterone (T). Similar findings have been reported by other authors^{2,4,5}. Study of varicocele in earlier stages could provide additional information about the natural history of this condition. To this end, we have evaluated a group of prepubertal patients with a diagnosis of varicocele

confirmed by scrotal Doppler, in an attempt to correlate the clinical, biochemical and circulatory findings, analyzing possible differences between this group and that of the previously described pubertal patients. We have also tried to confirm in prepuberty the different circulatory alterations observed in the pubertal stage.

Materials and Methods

Sixteen prepubertal patients (testicular volume < 4 ml) with unilateral left varicocele with a chronological age (CA) range between 8 years 8 months and 13 years 10 months (mean: 11 years 1 month) were studied. All patients were clinically classified according to the classification of Dubin-Amelar⁶, in which grade 1 corresponds to the small varicocele (detected by Valsalva maneuver), grade 2 to the moderate varicocele (detected by simple palpation), and grade 3 to the large varicocele (palpable and visible).

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Doppler study was carried out in both testes, both in the standing and supine positions, using Ultrasonic Monitor Vascular Doppler (M V-1, Tecny Med. SRL, Buenos Aires) with 5-MHz transducer. Sonographic findings were characterized as 1) negative reflux, 2) intermittent reflux, 3) prolonged reflux (it stops after some seconds, without reappearing), and 4) permanent reflux. A luteinizing hormone-releasing hormone (LH-RH) test was performed on all patients (100 µg IV, in bolus) with basal measurement of LH, FSH and T. Both gonadotropins were also determined at 30, 60 and 90 minutes after the LH-RH injection. The administration of human chorionic gonadotropin (hCG) was started 48 hours later (1000 IU/d IM, for 5 days), and a blood sample was taken on the 6th day for T determination. Eight normal prepubertal children (CA 5 years 3 months to 12 years 2 months; mean 9 years 9 months, regularly followed up to evaluate their growth) were included as control group. Consent was obtained in all cases from one or both parents, as appropriate, to perform the different studies. LH and FSH were determined by immunoradiometric assay (IRMA), using commercial kits (Serono Maia-Clone, Milan, Italy). LH standards were calibrated against 1st International Reference Preparation (IRP) 68/40 and FSH against 2nd IRP 78/549. T was measured by RIA double-antibody technique, using commercial kits (CIS Bioindustries, Gif-sur-Yvette, Cedex, France). The intra-assay and interassay coefficients of variations were as follows: LH: 12,9% and 16,2% (mean: 3,4 mIU/ml), 5,0% and 7,5% (mean: 16,6 mIU/ml) and 3,6% and 7,9% (mean: 29,1 mIU/ml), FSH: 9,7% and 15,2% (mean: 4 mIU/ml), 5,8% and 5,9% (mean: 13,7 mIU/ml) and 6,7% and 6,8% (mean 42,8 mIU/ml), and T: 11% and 16,2% (mean: 0,80 ng/ml), 4,8% and 3,2% (mean: 4,39 ng/ml). Kruskal-Wallis test was performed to evaluate the clinical-hormonal and Doppler-hor-

monal correlations; and Dunn test was used for comparison among the different groups.

Results

Clinical findings

Of 16 patients, 10 (63%) were grade 1 according to our adapted Dubin-Amelar classification; 2 (12%) corresponded to grade 2, and 4 (25%) to grade 3. The chronological age ranged between 8y 8m and 13y 1m for grade 1 varicoceles, between 9y 8m and 11y 3m for grade 2 varicoceles, and between 10y and 13y 10m grade 3 varicoceles.

Doppler findings

Prolonged reflux was observed in 6 patients (38%). Intermittent reflux was detected in 2 patients (12%), and permanent reflux in the remaining 8 (50%). The correlation between clinical and scrotal Doppler findings is shown in Figure 1.

Biochemical findings

Patients with varicocele as a whole showed (Median and range): LH B (mIU/ml) 0.40 (0.40-2.10); LH Mx.: 3.7 (1.1-15); FSH B (mIU/ml) 1.95 (0.40-4.5); FSH Mx.: 4.9 (3.1-10); T B (ng/ml): 0.2 (0.1-1.5); T post.hCG: 2.25 (0.82-11.5). The control group showed: LH B (mIU/ml): 0.4 (0.4-0.85); LH Mx.: 2.15 (0.63-12) FSH B (mIU/ml): 1.45 (0.4-3.0);

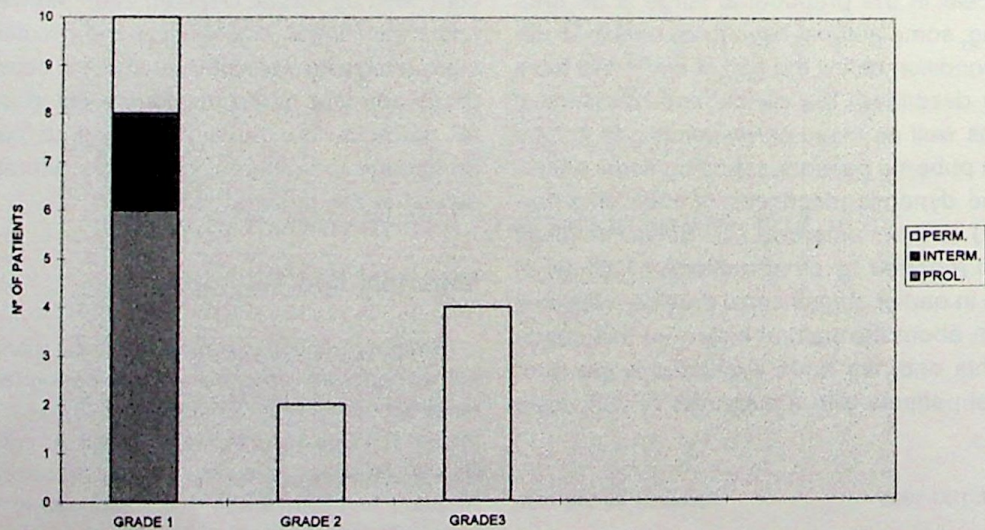


Fig. 1.— Correlation between clinical and Doppler findings

FSH Mx.: 4.25 (2.6-5.9); T B (ng/ml): 0.1 (0.1-0.3); T post hCG: 3.26 (1.0-5.6).

Basal levels of LH, FSH and T, and their maximal response to LH-RH and hCG, for each group, are shown in Table 1. Grade 2 varicoceles (clinical classification) and intermittent reflux varicoceles (according to sonographic patterns) were not included in the statistical analysis because of the low number of cases found in the study. No significant differences were found among the hormonal results of the different groups classified according to the scrotal Doppler findings. Basal LH and FSH in grade 3 varicoceles were found to be significantly higher ($p < 0.05$) than those of the control group. Basal T, as well as the maximal response of both gonadotropins to LH-RH, and T response to hCG showed no significant differences between the control group and grades 1 and 3 varicoceles. The maximal response for LH and FSH was observed between the 30 and 60 minutes determinations, both in patients with varicoceles and in the control group. No differences were found, either, when comparing among the different evaluated groups the

response to LH-RH of gonadotropins determined at each time.

Discussion

The harmful effect of varicocele on the reproductive function is well known, as well as the progressive worsening of this function as the patient grows older^{7, 8, 9}. Data available on adolescent patients provide no information about the time at which this deterioration starts. Therefore, early endocrinological evaluation could contribute to solve this question. We have undertaken the dynamic evaluation of the hypothalamic-hypophyseal-gonadal axis in prepubertal patients with varicocele, in order to determine possible alterations at this stage. No pathological responses were found in this study to LH-RH, nor T modifications to stimulus with hCG. In a previous report on adolescents we had described an increase of the LH response to LH-RH in patients having bilateral varicocele, as well as an increase of T to hCG in some patients with unilateral varicocele³.

TABLE 1.— Basal and maximal response of LH and FSH to LH-RH and of T to hCG in varicocele and control group*#

Group	n	LH B	LH Mx mIU/ml	FSH B	FSH Mx	T B ng/ml	T post
<i>Clinical</i>							
G1	10	0.40+ (0.40-2.10)	3.4+ (1.10-13)	1.70+ (0.40-2.80)	4.90+ (3.1-10)	0.20+ (0.1-1.5)	2.20+ (0.82-9.6)
G2	2	0.4 1.8	3.0 9.2	0.40 1.50	3.9 3.6	0.1 0.1	0.86 2.8
G3	4	1.15 § (0.75-1.5)	10.25+ (1.60-15)	3.90 § (1.95-4.5)	5.7 + (4.0-10)	0.66 + (0.2-1.2)	5.90 + (1.60-11.5)
<i>Doppler</i>							
Prol ∞	6	0.40 + (0.40-0.80)	3.70 + (1.10-9)	1.60 + (0.40-2.60)	4.90 + (3.40-10)	0.20 + (0.10-0.56)	1.73 + (0.82-6.80)
Interm γ 2		2.1 0.4	13 1.1	2.5 0.68	3.8 3.1	1.5 0.1	9.6 1.6
Perm ξ	8	1.10 + (0.40-1.80)	5.85 + (1.10-15)	2.80 + (0.40-4.50)	5.45 + (3.60-10)	0.20 + (0.10-1.20)	2.25 + (0.86-11.5)
Control	8	0.40 (0.40-0.85)	2.15 (0.63-12)	1.45 (0.40-3.0)	4.25 (2.60-5.90)	0.10 (0.10-0.30)	3.26 (1.0-5.6)

* Values are median and range. # Individual data in G2 and intermittent reflux. + p not significant vs. Control § $p < 0.05$ vs control. ∞ prolonged reflux. γ intermittent reflux. ξ permanent reflux

This lack of agreement could be related to the absence of hormonal changes during the prepubertal state, showing —though indirectly— that the damage could start at puberty. It should also be considered that the experimental design used in this study might not be able to detect already existing disorders. We have not found an adequate explanation for the increased gonadotropin basal levels found in grade 3 varicoceles. However, we have not placed emphasis on this, because they showed no correlation with hyper-response to LH-RH. These increased levels could, perhaps, represent auto-crine and paracrine alterations in the regulation of the testicular function in prepubertal patients with varicocele. If this finding were confirmed in a greater number of cases, it could lead to a new approach in the pathophysiological understanding of this clinical situation. Interestingly enough, this study enabled us to demonstrate, by means of Doppler in prepubertal patients, the same pattern of circulatory disorders as that already reported in adolescents³. The permanent reflux pattern was present in prepubertal patients with a frequency similar to that found in pubertal boys (50% prepubertal and 63% pubertal). Our findings would provide indirect support to the notion that the gonadal damage would become detectable from puberty onwards. Further longitudinal studies could perhaps provide valuable information to detect individuals at high risk of testicular alterations.

Resumen

Varicocele prepuberal. Correlación entre hallazgos clínicos, hormonales y del Doppler escrotal

El varicocele en la etapa prepuberal constituye un hallazgo poco frecuente. Por ello hemos evaluado un grupo de 16 pacientes prepúberes con varicocele unilateral confirmado por Doppler escrotal; correlacionando los hallazgos clínicos, bioquímicos y circulatorios.

Al igual que lo previamente descrito en pacientes puberales el estudio mediante el Doppler nos permitió identificar tres patrones de reflujo venoso: prolongado, intermitente y permanente. En todos los casos se efectuó prueba de LH-RH (100 µg IV en bolo, con dosajes de LH y FSH a tiempos 0, 30, 60 y 90 min) y test de hCG (1000 U/día IM durante 5 días con dosaje de testosterona [T]

basal y al 6° día). Los resultados se compararon con los de un grupo control de 8 prepúberes normales. Los pacientes con varicocele mostraron (mediana y rango) LH B (mUI/ml): 0,40 (0,4-2,1); LH Max.: 3,7 (1,1-15); FSH B (mUI/ml): 1,95 (0,4-4,5); FSH Max.: 4,9 (3,1-10); T B (ng/ml): 0,2 (0,1-1,5); T post.: 2,25 (0,82-11,5). El grupo control presentó LH B: 0,4 (0,4-0,85); LH Max.: 2,15 (0,63-12); FSH B: 1,45 (0,4-3,0); FSH Max.: 4,25 (2,6-5,9); T B: 0,1 (0,1-0,3); T post.: 3,26 (1,0-5,6). No se hallaron diferencias significativas (Test de Kruskal Wallis-Dunn) en los resultados hormonales entre los controles y los diferentes grupos de varicoceles clasificados de acuerdo al Doppler. La LH y la FSH basales de los varicoceles grado 3 (de acuerdo a la clasificación clínica) fueron significativamente mayores ($p < 0,05$) que los del grupo control, sin embargo la respuesta de ambas gonadotropinas al LH-RH así como los valores de T B y post. hCG no mostraron diferencias estadísticas con respecto a los controles. El hallazgo de mínimos cambios hormonales sólo en los varicoceles grado 3, así como el predominio de cuadros clínicamente leves (grado 1) observados en nuestro estudio, sugerirían la conveniencia de mantener a estos pacientes bajo control clínico, reservando el tratamiento quirúrgico para los varicoceles grado 3.

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