

The Interest of Testicular Biopsy Indices in the Analysis of Testicular Biopsies in Infertile Men with Bilateral Varicocele

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Abstract

The aim of our study was the evaluation the indices of testicular biopsy obtained starting from the quantitative analyses of bioptic samples, taken according to the odd-couple procedure. The selection of odd quadrants for each testis permits to analyze the relative difference of spermatogenetic process perturbed by the hemodynamic effect of the varicocele. The introduction of bilateral testicular biopsies during the microsurgical correction of bilateral varicocele permits to obtain specific indices representative of the spermatogenetic status in patients with infertility problems. The Mean Number of Spermatids per tubule is obtained during the quantitative analysis of the bioptic sample for each biopsy (MNS); then the global mean number of spermatids per tubule in the odd-couple for each testis (MNST) is calculated; the represents the relative potential of the pool of spermatids available for the passage into the epididymis. The quantitative differences between the percentage of spermatids per tubule (MNS) in each odd-couple is calculated (DMNS). The relative difference in each testis (DMNS) is evaluated and compared to the degree of bilateral varicocele. A Global Index (GI) that describes the relative status of both testes in a whole is introduced as a parameter specific for each patient. The analyses of the variations of the Testicular Indices (TI) for each couple of varicocele describe to patterns of clinical classes: Pattern A which a high degree of varicoceles corresponds two a low index and a low degree of varicocele to a high TI; Pattern B in which there is a correspondence between the degree of varicocele and the level of the TI.

Keywords: *testicular biopsy, varicocele, microsurgery, spermatogenesis, male infertility*

Introduction

The incidence of varicocele generally varies from 15% to 20 % in the male population [1,3]. In the case of varicocele the testicular biopsy may be abnormal and demonstrate spermatogenesis derangements in the form of maturation arrest or hypospermatogenesis accompanied by various degrees of tubular and peritubular sclerosis [2,3].

Today New diagnostic, non-invasive, tools permit to detect infraclinical bilateral varicoceles and to confirm the degree of clinical bilateral varicoceles for staging and classification. Echo-Color Doppler and Duplex scan detect small to moderate refluxes and measure the arterial inflow [1,5]. Microsurgical techniques in the correction of varicocele permits to select specifically the venous compartment sustaining the venous impairment (selective microdissection and ligature), sparing the autonomic nervous contingent of the cord and the lymphatic drainage of the testis .On theses bases the

scrotal exploration with bilateral testicular biopsy is sistematically coupled to the microsurgical correction of bilateral varicoceles, in order to study the correlation between the pattern and the fonctionnal degree of varicocele and the quantitative analysis of testicular biopsy [2,3,4]. The predictives parameters of recovery from oligo-astheno-theratospermia in patients with bilateral varicocele are obtained on a quantitative base, as global indices of spermatogenesis in relation to the degree of clinical varicoceles [5].

Material and Methods

Between 1990 and 2003, 745 varicocele patients, of whom 238 had bilateral varicocele, were consulted for infertility in the Urology and Andrology department of the SAINT ANTOINE and TENON hospitals. The varicocele cases have been classified into four different grades. The basics of our classification are presented in *Tab.1*.

The testicular biopsy is realized using a microsurgical protocol, the SINB procedure, in which 4 parameters are evaluated: 1.the sector of the biopsy, that is the quadrant in which the sample will be taken (quadrants super-lateral, infero-lateral, medial-medial, medial-medial); 2.the incision of the albuginea of the testis (transversal, oblique); 3.the Number of samples taken from the specific zone. 4. Bleeding under the albuginea incision. For each incision 3 micro-samples are obtained for histo-pathological, cytological and computer-assisted analyses. The Mean Number of Spermatids per tubule is obtained during the quantitative analysis of the bioptic sample for each biopsy (MNS); then the global mean number of spermatids per tubule in the odd-couple for each testis (MNST) is calculated; the represents the relative potential of the pool of spermatids available for the passage into the epididymis. The quantitative differences between the percentage of spermatids per tubule (MNS) in each odd-couple is calculated (DMNS); this represents the degree of perturbation of spermatogenesis between the quadrants and it is correlated to the degree of varicocele: at low-degrees varicoceles the distribution and the variability of the differences are large, where as at high-degrees varicoceles the distribution is narrow and the differences values are low.

Results

The mean (M) of the whole set of MNST values is calculated and compared to the Mean Difference (MD) of the whole set of DMNS values for each degree of varicocele. The comparisons between the global mean percentage (M) and the global gradient (MD) shows that there is a strong correlation between both in relation to the degree of varicocele. The introduction of the relative ratio between the mean percentage number of spermatids per tubule of each testis (MNST) and the difference between the percentage numbers of spermatids per tubule in the odd-couple of the testis (DMNS) permits to obtain a special Index (TI) characteristic of each testis with its varicocele.

A low TI indicates a large gradient in each testis, independent of the mean value of percentage of spermatids per tubule. A high TI, on the contrary,

demonstrates a high stability of the percentage of spermatids into the testis. The difference between the bilateral testicular indices (Indices Variation) represents the Global Index (GI) that describes the potential status of spermatogenetic balance of both testes as a whole and identifies the position of the patient in the exponential distribution of the varicoceles population.

Two classes of patients with bilateral varicoceles are identified through the application of Global Index distribution relative to the bioptic analyses. In Class A the Global Index is high: there in an inverse correspondence between the TI on one side and the degree of varicocele and the DMNS on the other side. In Class B the Global Index is low: there is a direct correspondence between the TI and the degree of varicocele and an inverse correspondence between the TI and the DMNS.

Discussions

The introduction of bilateral testicular biopsies during the microsurgical correction of bilateral varicocele permits to obtain specific indices representative of the spermatogenetic status in patients with infertility problems. The indices are obtained starting from the quantitative analyses of bioptic samples, taken according to the odd-couple procedure. The selection of odd quadrants for each testis permits to analyze the relative difference of spermatogenetic process perturbed by the hemodynamic effect of the varicocele.

The relative difference in each testis (DMNS) is evaluated and compared to the degree of bilateral varicocele. A Global Index (GI) that describes the relative status of both testes in a whole is introduced as a parameter specific for each patient. The analyses of the variations of the Testicular Indices (TI) for each couple of varicocele describe to patterns of clinical classes: Pattern A which a high degree of varicoceles corresponds two a low index and a low degree of varicocele to a high TI; Pattern B in which there is a correspondence between the degree of varicocele and the level of the TI.

CATEGORY	CLASS		INSPECTION	PALPATION	VALSALVA		ECHO-DOPPLER	
	Left	Right			Standing	Lying		
I	4	62	Infraclinal	-	-	- +	-	+
II	40	145	Clinical	- +	+	+	- +	+
III	147	31	Clinical	+	+	+	+	+
IV	47	-	Clinical	+	+	+	+	+

Tab.1 Classification of varicocele in adult males.

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Интерес показателей биопсии яичка в анализе биоптата у бесплодных мужчин с двусторонним варикоцеле

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РЕЗЮМЕ

Эксплорация мошонки в протоколе микрохирургической операции варикоцеле сопровождается двусторонней биопсией яичек, что позволяет точно определить зависимость стадии варикоцеле и нарушения сперматогенеза. С 1993 по 2003 гг в отделение урологии и андрологии больницы Тенон у 238 больных с двусторонним варикоцеле проведена двусторонняя микрохирургическая коррекция варикоцеле с одновременной двойной двусторонней биопсией яичек. Биопсия произведена в соответствии с протоколом SINB, согласно которому было введено четыре параметра: 1) участок биопсии яичка (верхний внешний, верхний внутренний, нижний внешний, нижний наружный квадранты); 2) разрез белой оболочки (поперечный или вертикальный); 3) количество биоптатов; 4) уровень кровотечения из разреза. Три биоптата из указанной зоны предназначены для гистологического, цитологического и компьютерно-асистированного исследования. С помощью нижеуказанных показателей (indices) можно анализировать полученные данные: MNST – среднее количество сперматидов в семенном канальце, DMNS – разница между средними количествами сперматидов в двух квадрантах того же яичка, TI -показатель биопсии (Spectral Testicular Index) – соотношение между MNST и DMNS. GI (global index) показывает разницу между TI справа и TI слева. С помощью анализа биопсии и аппликацией глобального индекса было выделено два основных класса больных с двусторонним варикоцеле: класс А (с высоким показателем глобального индекса), где соотношение между TI и стадией варикоцеле того же яичка обратно пропорционально, а соотношение TI и DMNS прямо пропорционально; класс В (с низким глобальным индексом), где соотношение TI прямо пропорционально стадии варикоцеле того же яичка, а соотношение TI и DMNS обратно пропорционально.

Ключевые слова: холестаза, экспрессия генов раннего ответа, регенерация печени, частичная гепатэктомия