

**TRIBULUS TERRESTRIS AND HUMAN MALE FERTILITY:
I. IMMUNOLOGICAL ASPECTS**

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Infertility affects about 15% of the married couples in the country [6]. Sperm antibodies have been established as the sole cause of infertility in a low but significant percentage or as additional causative factor. "Unexplained sterility" has been found in 9% of the males and 15% of the females studied by us [8] with positive results of antibodies in their serum, cervical mucus and seminal fluid proved by several methods. Other researchers in this field reported results similar to our findings [1-5,7]. Both comparative review of the diagnostic methods and clinical links can be found in other papers [7,8].

Once the sperm antibody activity is diagnosed, the following step is the attempt for treatment. The earliest communications refer to the administration of methylprednisolone in immunologically-conditioned infertility [2-5,7]. We carried out a clinical trial with Tribestan (total extract of *Tribulus terrestris*) [6]. The drug administered to males with disturbed spermatogenesis increases the ejaculate volume and the percentage of the motile spermatozoa. With consideration given to the pharmacodynamics of furostonol compounds present in this plant and the absence of adverse reactions we decided to use this drug for treatment of immunologically-conditioned infertility.

Material and methods. The material for this study covers the examination and treatment of patients within the period from January 1993 to December 31, 1998. The married couples were followed up throughout the examination in terms of routine study of sterility including also the withdrawal of blood samples and seminal fluid from the males and blood serum and cervical mucus from the females. Sperm analysis was carried out in compliance with WHO criteria, third edition, 1992 [9]. These biological fluids were tested for the presence of antibodies by the method of Kibrick et al. and by mixed antiglobulin reaction, described in details in other publications [7,8].

The main group of patients covered sperm antibody positive males. These patients were thoroughly informed about the results from the testing and naturally, about the forthcoming treatment. The recommended course of treatment consists of oral administration of one Tribestan tablet, three times daily for 60 days (1 treatment course), which was repeated or prolonged when necessary till conceiving of the wife. The wife was given 1 tablet orally, 3 times daily for 7 days, initiating from the 21st day of the beginning of her cycle on.

All data were filed and statistically processed and covered 100 Tribestan-treated patients who were presented in tables. The following information was collected for each patient:

GENERAL INFORMATION: out-patient department number, age, duration of infertility, primary or secondary infertility.

HISTORY OF THE MALE COVERED: previous findings from examinations preceding our diagnostic studies, with particular attention paid to seminal analysis and the presence of sperm agglutinations in ejaculate. Some other factors that can cause infertility

were also written down: varicocele, herniotomy, parotitis, inflammatory diseases and their treatment.

The sperm quality was determined prior to and after Tribestan treatment. This quality was determined as: poor: with less than 20×10^6 /ml spermatozoa and motility lower than 50% and more than 3 agglutinations per microscopic field, low magnification; good: 20 to 80×10^6 /ml spermatozoa, motility more than 50% and less than 3 agglutinations per field, low magnification; excellent: over 80×10^6 /ml spermatozoa, motility over 70% and less than 3 agglutinations per microscopic field, low magnification.

METHOD OF KIBRICK ET AL. The results were classified as follows: negative—with titre less than 1:4; low titre—1:4 and 1:8; moderate titre—1:16 up to 1:128; high titre—over 1:128.

THE MIXED ANTIGLOBULIN REACTION (MAR) WAS CLASSIFIED as: negative—erythrocytes adhered to less than 10% of spermatozoa; low—erythrocytes adhered from 10% to 20% of spermatozoa; high—erythrocytes adhered from 21% to 100% of spermatozoa.

The months after the initiation of Tribestan treatment versus the data of the presumable ovulation were recorded in case of conceptions. The outcome of each pregnancy was also recorded.

Results. Conception was observed as early as the first course of treatment among the group of patients (100 males with spermagglutinating antibodies). The females were subjected to post-coital test which was abnormal (poor or negative) prior to the treatment in 74 females and positive in 26 (good). Adverse reactions were observed in two patients after a longer treatment (over 6 months) as gastrointestinal complaints which were eliminated with antacid administration; pain in the knees which abated spontaneously after the discontinuation of the treatment and the realization of conception. These complaints were coped with after consultation with rheumatologist about the schedule of prednisolone treatment during the following 6 months.

The time from the initiation of the treatment till the conception was recorded for each couple separately (Table 1). The average time was 5.2 months (between 2 weeks up to 12 months). Table 1 illustrates also the number of treatment courses (months) of the patients till conception.

Two groups of patients were compared in Tables 2 and 4: patients who conceived and patients that failed to conceive. Table 2 shows the changes in the sperm quality in the treated patients comparing those with conception and without conception.

Table 3 reveals the change in antibody titre according to the method of Kibrick et al. comparing those conceived and those that failed to conceive.

Table 4 presents the changes in the levels of the antibodies according to the method

T a b l e 1

Results from the treatment carried out for conception of patients treated with Tribestan: duration of treatment and therapeutic regimen of treatment

Number of months after initiation of treatment	Number of pregnancies	Number of treatment courses	Number of pregnancies
0-2	7	1	12
3-4	10	2	9
5-6	3	3	6
7-9	4	4	1
10-12	6	5	2
12	1	6	1
Total	31	Total	31

Table 2

Changes in sperm quality in the treated patients comparing the conceived with not conceived

Status prior to treatment	Number	%	Change after treatment			
			Increased	Not increased	Decreased	Unknown
Group with conception						
Excellent	4	14	—	2	2	—
Good	15	54	4	8	2	1
Poor	9	32	5	4	—	—
Total	28	100	9/27=33%	14/27=52%	4/27=15%	
Unknown	3	—				
Group with no conception						
Excellent	2	5	—	2	—	—
Good	21	57	2	14	1	4
Poor	14	38	2	8	1	3
Total	27	100	4/30=13%	24/30=80%	2/20=7%	
Unknown	3	—				

Table 3

Change in antibody titre (Kibrick's method) comparing conceived with not conceived

Status prior to treatment	Number	%	Change after treatment			
			Increased	Not increased	Decreased	Unknown
Group with conception						
High	9	29	7	—	—	2
Moderate	9	29	6	3	—	—
Low	9	29	4	4	1	—
Negative	4	13	—	3	—	1
Total	31	100	17/28=61%	10/28=36%	1/28=4%	
Group with no conception						
High	—	—	—	—	—	—
Moderate	12	31	5	5	—	2
Low	18	46	10	7	—	1
Negative	9	23	—	6	—	0
Total	39	100	15/33=45%	18/33=55%		

of mixed antiglobulin reaction, comparing those that conceived with those that failed to conceive.

Discussion. It has properly been documented by many researchers [2-5,7,8] during the last 25 years that the immunological factors, the antibodies in particular, reacting to spermatozoa either in males and in females play important role if not essential, causing infertility in some cases [8]. A great number of methods has been elaborated for detection and diagnosis of immunologically-conditioned sterility [2,3,7,8]. The diagnosis is of great importance so as to answer the problem affecting many married childless couples. But as the ancient Romans have said: "Qui bene diagnoscit, bene curat" (who makes a proper diagnosis, cures well). Corticosteroids have been used as immunosuppressors by many authors [2-5]. Tribestan treatment of patients with sperm antibodies have been used by us for the first time for this kind of sterility. It is well known that the steroid saponins of furostanol type are biologically active substances with a very broad spectrum of action: sex stimulating action, manifested as effect on the serum level of the hormones of the hypophysial-gonadotropic axis, but without disturbing the hormonal balance in the body; anti-inflammatory action, due to their similarity with corticosteroids; hypocholesterolemic action—normalizes blood cholesterol; anti-tumour action.

Table 4

Change in antibody levels of MAR test comparing conceived and not conceived

Status prior to treatment	Number	%	Change after treatment			
			Increased	Not increased	Decreased	Unknown
Group of conceived females						
High	5	21	4	1	—	—
Low	6	25	4	2	—	—
Negative	13	54	—	13	—	—
Total	24	100	8/24=33%	16/24=67%		
Group with no conception						
High	7	23	4	2	—	1
Low	6	19	5	—	—	1
Negative	18	58	—	18	—	—
Total	31	100	9/29=31%	20/29=69%		

Data on antibacterial, antiviral (mostly flu and herpes viruses) and fungicide action have been described by various authors.

To give an answer to the results obtained by Tribestan, the hypothesis put forward and by other authors should be admitted, namely manifested orchitis to a certain extent, often undistinguished, can be observed in males with oligozoospermia and that this inflammation can be improved by the above mentioned properties of *Tribulus terrestris*, eliminating the blockage of sperm antibody flow. With a view of the results obtained, the testing for sperm antibodies should be an integral part of the diagnostic study of all males with oligozoospermia.

Conclusion. Since the incidence of success, i.e. conception obtained, is good, we are in the opinion that this treatment should be used in many cases in the practice. We used it for males with sperm antibodies regardless of antibody titre. Our studies indicate that males with a higher titre of sperm antibodies have a better chance with this type of treatment than the males with lower titres of sperm antibodies. Cases with high titre should be selected as the main indication of Tribestan treatment. This treatment, however, can be used also for males with low sperm antibody titre depending on the individual conditions (e.g. long-term sterility after marriage). The patients should be informed that though the chances for success are not high, it is still a good chance for them. As far as the adverse reactions are concerned, they were observed only in two cases without serious sequelae, very likely being exacerbation of preexisting diseases.

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