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Serum Immunoglobulins in Infertile Males with Seminal Tract Infection: Effect of an Indigenous Drug (Septilin)

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SUMMARY

Chronic non-specific seminal tract infections are commonly encountered in infertile males and are often not satisfactorily managed by the usual antibiotics; many of these antibiotics may also depress spermatogenesis in the long run. As an alternative, 20 patients were administered an indigenous drug, Septilin (Himalaya Drug Co.), for one month while 10 healthy adults were kept as control. There was some clinical improvement in 27.3% of the patients and a significant rise in sperm count in 30.8% oligospermics. No pregnancy, however, occurred during this period. Serum IgG was higher in the infertile group as compared to the control and the level increased further with Septilin. There was no significant change in serum IgA or IgM in both the Septilin and no-drug groups. Although Septilin had no *in vitro* antibacterial activity, it shows considerable potential as an 'adaptogen of plant origin'.

Key words: Male infertility Immunoglobulins Seminal infection Septilin Indigenous drugs

INTRODUCTION

A large number of infertile males with azoo-or oligospermia have chronic seminal tract infection (1) which, in our experience, is often not satisfactorily resolved to the point of normal fertility by antibiotics and anti-inflammatory agents. Some of these drugs may also directly depress the sperm count on long use (2,3). As a possible alternative for these patients, we tried Septilin (Himalaya Drug Co.), an indigenous formulation advocated primarily for chronic upper respiratory infections.

A number of reports over the last thirty years endorse the usefulness and safety of Septilin (4—6), although its mechanism of action remains obscure. It has shown no *in vitro* antibacterial activity, but there are indications that Septilin enhances the phagocytosis of microorganisms by leucocytes (7,8). Is Septilin stimulating the immunological defence of the body and indirectly checking chronic bacterial infections? This appeared to be an interesting question, and a study on the use of Septilin in infertile males was planned accordingly. Besides the usual clinical evaluation and semen examination, we have focussed our attention on changes in the serum immunoglobulin profile which reflects an important aspect of the body's defence mechanism.

MATERIAL AND METHODS

The study is based on 30 adult males. Twenty of these were patients presenting themselves in the Human Reproduction Laboratory, Department of Physiology, S.M.S. Medical College for the investigation of an infertile marriage. Another 10 formed a healthy control group. These were fair-

ly matched for age and were free from any signs of urinary or seminal infection.

The infertile patients had been married for more than 18 months and their wives had never conceived although their tubal patency and ovulatory status was normal. The criteria for selection were essentially two:

(a) Oligospermia (count less than 20 million/ml), or azoospermia; and

(b) some evidence of chronic seminal tract infection:

—localised epididymal tenderness
—pus cells in seminal plasma
(more than 5 per high power field)
—poor or delayed liquification.
(one or more of these three)

Septilin was administered in the dose of 2 tablets thrice daily for 30 days to the experimental group. Complete semen examination was carried out before and after treatment. To ensure uniformity, this was done by the same person (M.J.) every time, using the same equipment. Clinical evaluation was similarly carried out by one person only, experienced in andrological practice (L.K.K.). During the period of study the patients were advised not to take any other drug and report at once if there was any illness requiring attention. To ensure proper compliance the patients were called for weekly check-up, and the purpose as well as clinical utility of the programme was fully explained to them.

Immunoglobulin estimation

Immunoglobulins IgG, IgA, and IgM were estimated quantitatively by immunodiffusion assay on agar gel plates (Behring-Hoechst Tri-Partigen Plates). This was done before starting Septilin and repeated one month later, as soon as the treatment was over. Control serum was always used as a standard reference to give ± 15% confidence range with each plate. Blood samples were coded and the person performing the Ig assay was totally blind to their identity to avoid any bias. For the control group also IgG, IgA and IgM were similarly estimated initially and after a lapse of one month, but without any drug.

Statistical analysis was done by the Student's (t-Test) for paired data.

RESULTS

In vitro bacteriological study

Preliminary experiments were carried out to test for any direct anti-bacterial activity of Septilin. Pure Septilin powder in dry form or dissolved/extracted in the common solvents (water, alcohol) was incubated against E. Coli and Staph. aureus cultures on agar plates.

Septilin did not show any *in vitro* bactericidal or bacteriostatic activity. Its very sparing solubility was certainly restricting its diffusion into the bacterial colonies, so that even if any of its constituents possess some antibacterial activity this could not be demonstrated by the usual *in vitro* methods.

Clinical evaluation

The age of the 20 patients ranged between 23 and 46 years (mean 31 years). They had all been married for 2 to 14 years at the time of the study. The average age of the 10 control subjects was 33 years (20-51 years).

The salient clinical features and the response to one month treatment with Septilin is shown in Table 1.

Table 2 indicates the influence of Septilin on the sperm count of these 20 patients. Since the sperm count is known to fluctuate considerably even under physiological conditions, any change less than ± 20% of the initial value was overlooked as insignificant. Septilin raised the sperm count in approximately onethird of the patients with seminal tract infection.

No pregnancy was, however, achieved during the period of follow up which was around two months.

Immunoglobulin profile

Serum Ig values of the 10 healthy adult males were all well within the normal range for the Behr-

Table 1: *Clinical response of 20 patients to one month of Septilin administration.*

	No. of cases	Patients showing improvement* Number	Percentage
(A) Infertility	20	0	0.0**
(B) Seminal Infection			
Epid. tenderness	11	3	27.3
Pus cells	13	4	30.8
Incomplete liquification	3	1	33.3

* Resolution to within normal limits.

** No conception during period of follow up.

Table 2: *Sperm count before and after one month of Septilin.*

	No. of cases	Patients showing improvement* Number	Percentage
(A) Azoospermia	7	1	7.1**
(B) Oligospermia (<20 million/ml)	13	14	30.8

* Increase by 20% or more of the initial count.

** Occasional non-motile sperms per high power field found in one patient.

ing Hoechst immunodiffusion assay system, as indicated below:

	Normal range (mg/dl) given	Observed values in control group (mean ± S.D.)
IgG	800-1800	1126 ± 247
IgA	90-450	225 ± 66
IgM	60-250	185 ± 36

When repeated after 1 month, without any drug, no significant change was observed in any of the Ig (Table 4).

In the experimental group, Ig assay could be completed before and after one month of Septilin treatment in 19 of the 20 patients (Table 3). In case of IgA and IgM the values were essentially within the normal range and not significantly different from the healthy adults. Septilin administration also did not produce any change.

In the case of IgG, however, there were two salient findings:

(i) the initial IgG levels in these infertile males with seminal infection were higher than in the control ($P < 0.05$), the mean values being 1462 ± 342 and 1126 ± 247 mg/dl, respectively (Table 4).

(ii) Septilin administration produced a further rise in the IgG ($P < 0.05$). It increased in 13 out of the 19 patients, i.e. in nearly 70%. In one case (No. 2, VKJ, Table 3), the rise was from 1552 to as high as 2447 mg/dl).

Table 3: *Immunoglobulin profile of 19 patients before and after one month of Septilin.*

No.	Name	Immunoglobulins (mg/dl)					
		IgG		IgA		IgM	
		before	after	before	after	before	after
1.	D.P.	725	1507	131	218	51	94
2.	V.K.J.	1552	2447	356	196	237	247
3.	V.N.S.	1735	2137	218	279	200	216
4.	A.A.	1507	1737	295	271	116	133
5.	I.	1833	1290	296	203	199	100
6.	V.M.	1618	1442	338	224	249	329
7.	M.M.G.	1802	1802	218	109	200	147
8.	H.S.	1982	1500	196	218	200	200
9.	B.K.D.	1329	1618	338	203	241	154
10.	G.S.	1500	1618	218	182	126	177
11.	R.D.	1802	1993	296	183	241	224
12.	S.R.B.	958	1500	176	296	200	241
13.	P.M.	1865	1802	225	296	140	200
14.	M.G.	1500	1500	149	162	285	210
15.	S.L.	1219	2125	218	279	107	200
16.	O.P.L.	1273	1618	169	256	24	208
17.	R.C.	909	1385	143	203	65	116
18.	G.R.S.	1500	1802	256	248	241	162
19.	V.C.	1165	1802	225	155	161	123
	Mean	1462	1717	235	220	173	183
	± S.D.	±342	±287	±67	±50	±72	±57

Table 4: *Analysis of Ig values estimated initially (before) and after one month on Septilin or no-drug (after).*

	IgG		IgA		IgM	
	before	after	before	after	before	after
Control (no drug)	1126 ±247	1216 ±246	225 ±66	217 ±76	185 ±36	185 ±40
Experimental (Septilin)	1462* ±342	1717* ±287	235 ±67	220 ±50	173 ±72	183 ±57

* $p < 0.05$

Side effects

No side effects of any consequence were observed with Septilin. One patient complained of excessive dryness of nose and felt that there was an increased frequency of micturition. But there was nothing which warranted discontinuing the drug.

DISCUSSION

Although Septilin has shown no direct antibacterial activity in culture media, Behl and Pradhan(7) and Bhat(8) have made the interesting observation that phagocytosis of bacteria by polymorphonuclear leucocytes is significantly greater in persons who have taken Septilin for

a month or more. Phagocytic Coefficient I, measuring the percentage of polymorphs with ingested bacteria, rose to a greater extent than Coefficient II measuring the number of bacteria ingested per polymorph. Apparently, long term Septilin administration enhanced the phagocytic potential of polymorphs, not as much as antibiotics like chloremphenicol but more than placebo or multivitamins.

We thought of studying this problem from another angle. Does Septilin influence the immunoglobulins? In other words, we focussed our attention on humoral immunity rather than cell mediated immunity. Immunodiffusion assay has given interesting results. Although IgA and IgM have shown no change after Septilin, IgG has risen significantly (Table 3,4). In 13 out of 19 patients, IgG level was higher after Septilin treatment than before. Simultaneously, the 10 control subjects who were not taking Septilin did not show any significant change in the Ig levels when the estimation was repeated after the lapse of one month.

It may be worth recapitulating here that IgG is the dominant immunoglobulin of the serum and body secretions—a general purpose antibody forming almost 75% of the total Ig. IgG is also the principal antibody involved in antibody dependent cell mediated immunity (ad-CMI) and is known to increase in bacterial infections. It binds to bacteria and increases their phagocytosis. Thus, the earlier reports on enhanced phagocytosis under Septilin treatment and the increase in IgG observed presently corroborate each other.

A major constituent of Septilin is Balsamodendron mukul (guggul) which is attracting considerable attention these days because of its hypolipidemic action. Gujral et al (9) have demonstrated its anti-inflammatory and antiexudative properties. Another constituent, Phyllanthus emblica, is amongst the richest natural sources of vitamin C and directly inhibits the growth of many bacteria. Similar antibacterial principles have been isolated from Moringa pterygosperma present in Septilin. Therefore, it can be surmised that although Septilin shows no *in vitro* antibacterial activity, within the body it perhaps acts by many undefined ways to stimulate the body's defence mechanisms. For example Septilin could:

(i) increase the IgG level;

(ii) increase the activity of phagocytic cells;

(iii) increase the vitamin C level;

(iv) produce effective antimicrobial action by cumulative action of its constituents on prolonged use.

The increase in sperm count in some cases (Table 2) and the rise in IgG level in the majority (Table 3), taken together, uphold the usefulness of Septilin. It could be tried as an adjuvant to antibiotics and anti-inflammatory drugs for the long term treatment of oligospermia associated with seminal tract infection.

Interestingly enough, recent clinical and experimental work has clearly demonstrated that many complex glycoproteins of plant origin, like lectins, have the ability to induce a proliferative response in lymphocytes and emotional stress can also greatly influence the immune system (10,11). Theoretically, therefore, a complex herbal formulation has several possible ways in which to interact with the body's defence mechanism.

The use of herbal drugs is now attracting wide attention because of their relative safety, good tolerance, low cost, and in many cases their all round health promoting effect (12). Brekhman and Dardymov (13) have classified many such drugs as 'adaptogens of plant origin'. The effect of Septilin on the IgG level observed in the present study is, therefore, promising and calls for a more comprehensive study on the use of herbal drugs for strengthening the body's resistence against infections.

APPENDIX

Each Septilin tablet contains : Balsamodendron mukul-0.16 g; Maharasnadi quath-65 mg; Exts. Phyllanthus emblica-16 mg; Tinospora cardifolia-49; Rubia cordifolia-32 mg; Moringa pterygosperma-16 mg; Pristimera indica-6 mg; Shankh bhasm-32 mg.

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