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EFFECT OF ARGININE ON OLIGOSPERMIA*

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Several amino acids have been detected in human semen. They have been implied to play a role in spermatozoal motility.[2] Among invertebrates the addition of any one of a number of amino acids and peptides to spermatozoa extends their duration of motility.[11] Several amino acids have been used to treat cases of oligospermia and asthenospermia with varying degrees of success. Of the amino acids utilized for this purpose, arginine has received enthusiastic acceptance.[7] Out of 21 patients reported by Ishigami,[5] 19 showed a favorable response and 5 pregnancies ensued. Similarly, Bernard,[1] Tanimura,[10] and Giarola and Agostini[3] reported encouraging results. However, the dosages were variable and the clinical response was unpredictable.

This study was designed to evaluate the effect of arginine in oligospermia and to correlate any improvement in spermatogenesis with a specific histologic appearance in the testis.

MATERIALS AND METHODS

Twenty-eight men were selected for the study from a large group with the problem of infertility. A complete history as well as a specific history relating to their infertility was obtained. A physical examination with special attention to the examination of the genitals and prostate was performed. They were otherwise normal, healthy males who showed no evidence of any gross endocrine disturbance. Their ages ranged from 24–44 years. The diagnosis of oligospermia was established after at least two sperm counts performed by the same experienced technician. Semen specimens were obtained by masturbation after abstinence of at least 3 days. The analysis included observation on volume of ejaculate number of spermatozoa, motility, and morphology. Twenty-four patients underwent open testicular biopsy and the tissue was fixed in Bouin's solution.

Patients were given 2 gm. of arginine hydrochloride daily for 10 weeks. The treatment was started generally around 2 months after the biopsy to rule out any local injurious effects of the biopsy. At the end of the treatment period semen count was obtained and again 1 month after that.

RESULTS

The treatment was well tolerated in all subjects. There was no change in patient's libido.

Testicular Biopsies. Arrest of spermatogenesis at the primary and secondary spermatocytes was seen in 7 cases, decreased spermatogenesis-hypoplasia was encountered in 6, and atrophy and fibrosis in 4; the remaining 7 patients had a normal testicular morphology.

Volume of Ejaculate. There was no significant change in the volume of the ejaculate. The mean volume prior to treatment was 3.14 cc and after treatment was 3.30 cc.

Spermiocytogram. An improvement of 100% in sperm count, when the count after treatment is 20 million/cc. or over, or significant improvement in the motility morphology without a corresponding increase in the number of spermatozoa was considered to be a good response to treatment.

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TABLE 1. *Results of Treatment of Oligospermia with Arginine*

Initials	Age	Semen analysis before treatment				Semen analysis after treatment				Testicular biopsy
		Volume	No./cc.	Motility	Normal	Volume	No./cc.	Motility	Normal	
	yr.	*cc.*	*millions*	%	%	*cc.*	*millions*	%	%	
T. A.	27	3.1	—	0	0	2	—*	0	0	Arrest of maturation at spermatogonial level
H. H.	32	1.5	1	70	70	2.5	0.2	0	70	Reduced cellularity, some tubules are fibrosed
A. S.	30	4	10	60	70	4	13	65	70	Hypoplasia of tubules
H. O.	31	1.5	20	50	70	2.5	34	50	70	
D. K.	28	2	15	50	60	2	30	50	90	Normal spermatogenesis
M. M.	34	1.5	10	0	50	3	6	5	50	Normal spermatogenesis
M. Y.	25	5	5.9	5	95	3	10	40	90	Atrophic testes—left, normal spermatogenesis—right
F. B.	44	2	—*	0	0	3.0	—*	0	0	Arrest of spermatogenesis, peritubular fibrosis
M. N.	38	3	—*	0	0	3.0	—*	0	0	Spermatogonia only—pus cells in intertubular area
A. K.	35	3.2	—*	0	0	3.0	15	20	60	Right testis—normal spermatogenesis, left testis—atrophic tubules
A. I.	30	25	18.6	30	60	3.4	16	30	60	Normal spermatogenesis
M. B.	29	3	5	20	75	3	2.5	17	68	Reduced cellularity, partial fibrosis
K. S.	24	5	15	60	80	6	22.5	60	90	
H. S.	26	6.2	8	30	60	7.0	12	35	70	Maturation arrest, thickened basement membranes
A. S.	37	2	—*	0	0	2	—*	0	0	Partial atrophy, arrest at spermatid's level
M. S.	32	2	—*	0	0	2	0.5	0	0	Mild fibrosis, arrest at spermatogenesis
E. S.	25	2	—*	0	0	3	—*	0	0	Most tubules are atrophic, few have arrest of spermatogenesis
A. D.	30	45	7.4	15	70	5.2	10.2	20	70	
M. S.	40	4.0	3.6	5	80	4.8	6.0	10	75	
A. S.	28	3	1	0	0	2	—*	0	0	Hypoplasia—most tubules have low spermatogenic activity
A. A.	36	2.6	—*	0	0	4	—*	0	0	Few tubules are normal, majority have only Sertoli cells
F. A.	40	2	—*	0	0	2	20	50	80	Normal spermatogenesis
H. T.	29	4	6.8	30	45	3.8	8	35	40	Maturation arrest, thickening of basement membranes
C. H.	30	3.6	3.4	20	80	34	5	28	80	Normal spermatogenesis
M. A.	27	2	3	60	70	2.6	2	60	50	Hypoplasia
N. M.	30	2	5	70	70	2	10	75	70	Decreased spermatogenesis

*, rare for valid count.

Table 1 shows that only 1 patient (D. K.) showed a response in the number of spermatozoa. Another patient (S. K.) had a modest improvement to 22.5 million/cc. and his wife became pregnant.

DISCUSSION

The relationship of arginine to spermatogenesis is suggested from the work of Holt et al.[4] They found that upon the administration of an arginine-free diet to nor-

mal persons the spermatozoal count fell to one-tenth of normal, but recovered upon the restoration of arginine to the diet. Similarly, in the albino rat, testicular disturbances have been produced by arginine-free diets.[8] However, Marden et al.[6] found no decrease in the size or histology of the testes and no detectable changes in the prostate or seminal vesicles upon the administration of an arginine deficient diet.

In the human semen Tanimura[8, 9] found free and bound arginine in fairly good amounts. Positive correlation could be observed between spermatozoal count and bound arginine content and between spermatozoal motility and free arginine content.

Although arginine is a nonessential amino acid because it is readily synthesized in the body, this substance is indispensable as a material for the synthesis of cellular and tissue protein. Thus during active stages of growth, as in infancy, the amount of arginine synthesized fails to meet the demand. Arginine takes part in sperm formation; it has been found to be the basic component of the nucleo protein of spermatozoa of various species.

Despite the varied histologic picture exhibited by the oligospermic males included in this study, no response to arginine was noted in any category. These results are at variance with other reports of favorable reaction to this drug. In fact, in some of the patients studied, further sperm count depressions were experienced following medication. The depression in spermatogenesis sometimes observed after a testicular biopsy could not have contributed to the results since treatment was started 2 months after the biopsy. The duration of therapy was adequate to cover a whole spermatogenic cycle.

SUMMARY

Arginine hydrochloride was administered to 28 oligospermic infertile males with varying testicular histologic derangements. Regardless of the pathology no definite improvement in spermatozoal counts was noted.

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