SERA GONADOTROPINS, TESTOSTERONE, AND PROLACTIN LEVELS IN MEN WITH OLIGOZOOSPERMIA OR ASTHENOZOOSPERMIA

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Many previous studies evaluating various hormone levels in males with subnormal semen analyses were performed when the normal semen parameters were considerably higher than now. This study evaluated sera levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), total testosterone (TET), free TET, and prolactin (PRL) in 60 males with oligospermia and decreased motility according to recent World Health Organization standards. Three separate groups were evaluated: group 1, motile density (MD) $< 5 \times 10^6$/mL (but not azoospermia); group 2, $5 \leq MD < 10 \times 10^6$/mL; group 3, $MD > 10 \times 10^6$/mL, but % motility < 30%. There were no significant differences in mean FSH levels between groups. Overall FSH was increased in 47.1% of the cases. In contrast, mean LH levels were normal in all three groups. Only 17.3% of the entire group had elevated LH levels. The TET level was below normal in 32.3% of the entire group, with a fairly equal distribution between the three groups. Overall, only 7.8% had elevated PRL levels, with the highest percentage found in group 3 (22.2%). Only a small minority of patients with increased FSH had low TET levels compared to 48.0% of those with normal FSH. These data demonstrate that when using the lower semen parameters, the most common serum hormone abnormality is increased FSH; men with $MD < 5 \times 10^6$/mL do not have a higher incidence of elevated FSH than those with higher MDs. Serum TET (but not free TET) was the only other hormone measured that was abnormal (i.e., low) in a sizable minority of patients. Hyperprolactinemia is not common in men with subnormal semen parameters.

Keywords oligoasthenozoospermia, testosterone, prolactin, luteinizing hormone, follicle stimulating hormone

Many early studies concerning the concentrations of luteinizing hormone (LH), follicle stimulating hormone (FSH), testosterone (TET), free TET, and prolactin (PRL) in oligoasthenozoospermic males were published at times when the definition of oligoasthenozoospermia was based on World Health Organization (WHO) normals that were significantly higher than the

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present levels (20 × 10^6/mL with 50% progressive motility) [3]. There is even some concern that the present established levels do not truly identify the subfertile men [1, 2].

The study presented herein evaluated in couples with more than 18 months of infertility the aforementioned hormone levels in three separate groups of males with subnormal semen parameters: group 1, motile density (MD) < 5 × 10^6/mL (but not azoospermia); group 2, 5 × 10^6/mL; ≤ MD < 10 × 10^6/mL; group 3, MD > 10 × 10^6/mL but progressive motility < 30%.

MATERIALS AND METHODS

Sera hormone concentrations were obtained on the same days as the two semen analyses and were then averaged. The normal ranges, manufacturer, and type of methodology are shown in Table 1. All men enlisted had either primary or secondary infertility of at least 18 months and were required to have semen parameters equal to or less than the parameters set to establish the three groups (as described in the Introduction).

Statistical analyses included one-way analysis of variance to compare the mean sera levels between male factor groups. Chi-square analysis was used to compare the distribution of abnormal levels (i.e., outside the normal range) between the male factor groups. Two-way analysis of variance was used to compare the mean LH levels by FSH classification (i.e., normal or elevated) and TET classification (i.e., normal or low). All tests were done at the .05 level to determine statistical significance.

RESULTS

Comparison of mean sera gonadotropin and TET and PRL levels by MD and percent motility is shown in Table 2. There were no significant differences in the mean FSH level among groups 1–3. The only group whose mean FSH level was not above the normal range was group 3 (normal MD but asthenospermic). Mean sera FSH was not higher in group 1 (the group with worst MD) as compared to group 2 (less severe oligospermia) or group 3 (asthenozoospermia only). Mean sera LH was normal in all three groups with no statistical differences. The mean LH averaged slightly higher than mid-normal.

The total TET levels were similar in the three groups and were in the low normal ranges. The mean sera-free TET levels were normal and about equal among the three groups and averaged in the low-normal ranges. Sera PRL levels were equal among the three groups, and averaged mid-normal.

The distribution of abnormal sera endocrine parameters by MD and percent motility is shown in Table 3. Sera FSH was the hormone most likely to be elevated (47.1% of all cases).

TABLE 1 Normal Range, Manufacturer, and Methodology of Hormones Measured in the Study

Hormone	Normal Range	Manufacturer[a]	Method
FSH	0.8–9.0 mIU/mL	BMC	ELISA
LH	0.5–10.0 mIU/mL	BMC	ELISA
PRL	0–25 ng/mL	BMC	ELISA
TET	300–1000 ng/mL	ICN	RIA-coated tube
Free TET	9–47 pg/mL	DPC	RIA-coated tube

[a]BMC, Boehringer Mannheim Corp., Indianapolis, IN, USA; ICN, ICN Biomedicals Inc., Costa Mesa, CA, USA; DPC, Diagnostics Products Corp., Los Angeles, CA, USA.

TABLE 2 Distribution of Sera Gonadotropin and Androgen Levels in Males with Low Motile Density and/or Motility

	MD < 5 Million/mL (n = 34)	5 ≤ MD < 10 Million/mL (n = 16)	MD > 10 Million/mL (n = 10)	Total Sample (n = 60)
FSH (mIU/mL)				
n	28	15	8	51
Mean (SD)	10.3 (8.1)	12.3 (6.9)	7.7 (6.5)	10.5 (7.4)
No. (%) > 9	11 (32.3%)	10 (66.7%)	3 (37.5%)	24 (47.1%)
No. (%) < 0.8	0	0	0	0
LH (mIU/mL)				
n	29	15	8	52
Mean (SD)	7.17 (5.4)	7.8 (5.1)	5.2 (6.7)	7.3 (5.5)
No. (%) > 10	5 (17.2%)	3 (20.0%)	1 (12.5%)	9 (17.3%)
No. (%) < 0.5	0	0	0	0
Free TET (pg/mL)				
n	29	14	10	53
Mean (SD)	0	0	0	0
No. (%) > 47	1 (3.4%)	2 (14.3%)	1 (10.0%)	4 (7.5%)
No. (%) < 9				
TET (ng/mL)				
n	33	16	10	59
Mean (SD)	384 (157)	401 (206)	384 (122)	389 (165)
No. (%) > 1000	0	0	0	0
No. (%) < 300	10 (30.3%)	5 (31.2%)	4 (40.0%)	19 (32.3%)
PRL (ng/mL)				
n	27	15	9	53
Mean (SD)	11.6 (5.8)	12.8 (5.2)	14.5 (8.0)	12.5 (6.1)
No. (%) > 25	1 (3.7%)	1 (6.7%)	2 (22.2%)	4 (7.5%)
No. (%) < 9	0	0	0	0

Note. No significant differences were found between the groups, $p > .05$, ANOVA.

TABLE 3 Distribution of Abnormal Sera Endocrine Parameters by Motile Density and % Motility

	Group 1 MD $<5 \times 10^6$	Group 2 $5 \times 10^6 <$ MD $< 10 \times 10^6$	Group 3 MD $\geq 10 \times 10^6$ Motility <50%
Elevated levels			
FSH (>9 mIU/mL)	11 (39.3%)	10 (66.7%)	3 (37.5%)
LH (>10 mIU/mL)	5 (17.2%)	3 (20.0%)	1 (12.5%)
Free TET (>47 pg/mL)	0	0	0
TET (>1000 ng/mL)	0	0	0
PRL (>25 ng/mL)	1 (3.4%)	1 (14.3%)	2 (10.0%)
Low levels			
FSH (<.8 mIU/mL)	0	0	0
LH (<.5 mIU/mL)	0	0	0
Free TET (<9 pg/mL)	1 (3.7%)	2 (6.7%)	1 (22.2%)
TET (<200 ng/mL)	10 (30.3%)	5 (31.2%)	4 (40.0%)
PRL (<9 ng/mL)	0	0	0

Note. Data presented as number observed (percentage), $p > .05$, chi-square comparing distribution between male factor groups.

TABLE 4 The Relationship of Mean LH, FSH, and TET Levels in Males with Subnormal Sperm Count and Motility

	Normal FSH Normal TET $n^a = 14$	Normal FSH Low TET $n^a = 13$	Elevated FSH Normal TET $n^a = 20$	Elevated FSH Low TET $n^a = 4$
FSH (mIU/mL)				
Mean (SD)	5.1 (1.5)	6.2 (2.3)	15.7 (7.4)	17.2 (7.8)
Range	3–8	3–9	10–38	11–27
LH (mIU/mL)[b]				
Mean (SD)	6.4 (6.7)	4.5 (2.7)	8.8 (5.2)	10.5 (6.2)
Range	1–28	2–11	3–21	4–19
TET (ng/mL)				
Mean (SD)	449 (121.7)	218 (54.7)	486 (169.1)	256 (36.9)
Range	330–814	97–287	325–980	211–289

[a] $p < .05$ chi-square comparing proportion of patients with low TET by FSH levels.
[b] $p < .05$ comparing mean LH levels for nL or elevated FSH levels.

Only 17.3% had elevated sera LH levels. Only 7.8% had elevated sera PRL levels. The serum TET level was below normal in 32.3% of the entire group; the incidence of low levels was fairly equal but was the highest in group 3 (asthenozoospermia). The serum free TET level was low in only 7.5% of cases and was fairly equally distributed; interestingly, the group with the most severe oligoasthenozoospermia had the least cases with low serum-free TET of 3.4%.

The relationship of mean sera LH, FSH, and TET levels in males with subnormal sperm count and percent motility is summarized in Table 4. About half of the patients with normal FSH (13/27) had low sera TET levels as compared to only 16.6% (4/24) with low sera TET when sera FSH was elevated ($p = .017$, chi-square). The mean LH was the highest (10.5 mIU/mL) when the FSH was elevated and the TET was low, and the mean LH was the lowest (4.5) when FSH was normal and TET was low. Only four patients had increased PRL levels; the TET levels were 266, 287, 506, and 980 with a mean of 509.7 ng/mL (SD 331). Thus, 2/4 had low TET when the serum PRL was increased.

DISCUSSION

The fact that the lowest and highest mean LH levels were noted in groups with the lowest sera TET levels suggests that when FSH is high the pathological process responsible for damaging germinal epithelium frequently also damages Leydig cells. But the subsequent higher LH levels help to compensate, so the TET levels return mostly to normal. When FSH is low or normal a hypothalamic–pituitary disorder seems likely, leading to a higher incidence of low sera TET levels.

Since only a small percentage of males with high FSH levels have low sera TET levels, the increase in LH seems to compensate and keep TET levels in the low normal range. About 50% of males with subnormal semen parameters may have testicular germinal epithelium damage, as evidenced by increased FSH.

If only men with normal FSH and low TET are able to respond to medical therapy aimed at increasing intratesticular TET levels, then only a fourth of the men with subnormal sperm

would be expected to respond. Since TET was low in 40% of cases of men with asthenozoospermia exclusively, medical therapy aimed at improving intratesticular TET levels might also be attempted. Serum TET seems to be a better marker than serum free TET, since the latter hormone is far more likely to be within normal limits of the assay. Though numbers are small, since half of patients with increased serum PRL had low TET, a trial of bromocriptine seems reasonable; nevertheless, hyperprolactinemia rarely occurs (only 7%).

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