Elevated semen platelet-activating factor-acetylhydrolase content is correlated with low sperm motility in men with spinal cord injury. J. Zhu, N. L. Brackett, T. Aballa, D. B. Shapiro, M. W. Witt, W. E. Rodde- bush, Reproductive Biology Associates, Atlanta, GA; University of Miami School of Medicine, Miami, FL.

OBJECTIVE: Platelet-activating factor [1-O-alkyl-2-acetyl-sn-glycero-3- phosphocholine; PAF] is present in human sperm and its content has a significant and positive relationship with motility. PAF-acetylhydrolase (PAFah), the enzyme that removes the acetyl group (responsible for PAF’s activity), is present in semen and serves as a decapping factor. Semen from men with spinal cord injury (SCI) contains sperm with poor motility and this condition may be a result of abnormal PAFah activity in the semen. The study objective was to determine the relationship between PAFah content in semen and sperm motility in men with SCI compared to non-SCI men.

DESIGN: Using a between-subjects design, semen PAF-AH activity was compared in semen specimens from control versus SCI subjects. PAFah activity levels were correlated with sperm motility in each group.

MATERIALS AND METHODS: Semen was obtained from 10 men with SCI and 10 age-matched healthy fertile men as control subjects. Sperm motility was determined (WHO, 1999) prior to measurement of PAFah activity (analyzed by Enclomiphene, Inc., Japan). Data were analyzed by Student’s t-test and linear regression.

RESULTS: Mean (± SEM) seminal PAFah content was significantly higher in SCI subjects (1,068.4 ± 163.78 IU/L; range 589.0–1,881 IU/L) compared to controls (413.5 ± 40.99 IU/L; range 192.0–691.0 IU/L, p < 0.001). Mean sperm motility was significantly lower in SCI subjects (27.9 ± 4.56%, range 4–52%) compared to controls (63.9 ± 3.13%; range 54–80%, p < 0.001). Linear regression analysis revealed a significant negative correlation between PAFah content in semen and sperm motility (R² = 0.212, p < 0.05). Regression analysis demonstrated a biological correlation between PAFah and sperm motility in SCI subjects (R² = 0.45, p = 0.058) and control subjects (R² = 0.38; p = 0.056).

CONCLUSION: PAFah activity levels were elevated in semen of men with SCI compared to age-matched healthy control subjects. PAFah was negatively correlated with sperm motility in SCI and control subjects. Additional studies will elucidate the role of PAFah in semen on sperm motility and determine if high PAFah activity contributes to low sperm motility in men with SCI.

Supported by: Supported in part by an unrestricted grant from Sero- noUSA, Inc (to W.E.R.), the State of Florida Specific Appropriations and the Miami Project to Cure Paralysis (grants to N.L.B.).

Tuesday, October 19, 2004
4:45 P.M.

Androfax™ (oral enclomiphene citrate) raises free and total serum testosterone in hypogonadal men: Comparison with Androgel® 1%. R. D. Wiehle, W. D. Garcia, M. S. Willett, J. S. Podolski. Zonagen, Inc., The Woodlands, TX; Advanced Biomedical Research, Pennington, NJ.

OBJECTIVE: Clomiphene citrate is used to induce ovulation in women. However, clomiphene given to men fails to produce consistently increases in sperm count. This drug is a mixture of two geometric isomers with different properties. Enclomiphene citrate (the trans- or (E)-isomer) has effects consistent with estrogen antagonism whereas zuclomiphene (the cis- or (Z)-isomer) often acts as an agonist. Most preparations of clomiphene contain an unequal mixture of the isomers with a predominance of enclomiphene (~60%). The clearance of each isomer from the blood differs with enclomiphene (D) being cleared more slowly and with a longer plasma half-life (23.5 hours) compared to zuclomiphene (E) with a half-life of 0.77 hours. The difference in half-life, and the divergent biological end points could contribute to the dichotomous effects in men and women.

DESIGN: An randomized, double-blind, placebo- and active-controlled study in hypogonadal men.

MATERIALS AND METHODS: Oral enclomiphene citrate in doses of 12.5 mg (n=10), 25 mg (n=11), and 50 mg (n=11) compared to placebo (n=10) and AndroGel® 1% (5.0 G) (n=10) were administered for 14 days. Subjects at screening had low or borderline low (99–343 ng/dL) total serum testosterone levels with normal LH and FSH levels. On the first day of treatment, men in the study had total serum testosterone (TT) levels of 275 ± 88 ng/dL (mean ± SD).

RESULTS: After 14 days of treatment, there was a dose-dependent rise in TT levels with enclomiphene: 12.5 mg per day was associated with a level of 412 ± 194 ng/dL; 25 mg per day with 520 ± 160 ng/dL, and 50 mg per day with 589 ± 172 ng/dL, values in the normal range (298 to 1034 ng/dL). AndroGel® 1% (5.0 G), the active control, resulted in a level 473 ± 289 ng/dL, which is consistent with levels reported in the medical literature. All four treatments demonstrated statistically significant increases compared to day 1. The placebo group showed no increase in serum testosterone (mean change -1.2 ng/dL). AndroGel® 1% was also associated with a disproportionate rise in DHT relative to TT. The ratio of DHT to TT in men on AndroGel® 1% increased between day 1 and day 15 by a factor of 1.59. In comparison, men receiving placebo showed almost no change (1.07) and men on the highest dose of enclomiphene had a lower ratio by a factor of 0.83. Apparent free serum testosterone levels measured byRIA demonstrated a dose-dependent rise in serum testosterone with enclomiphene whereas the placebo group did not increase.

CONCLUSION: Enclomiphene citrate (designated as Androxal™) significantly increased total and apparent free serum testosterone without increasing DHT proportionally. This new agent may represent a new oral modality for elevating testosterone in men with secondary hypogonadism.

Supported by: None.

Tuesday, October 19, 2004
5:00 P.M.

Microdissection testicular sperm extraction (TESE) outcomes in patients with azoospermia and cryptozoospermia for intracytoplasmic sperm injection. M. E. Bakircioglu, S. Kahraman, S. Sertyel, N. Findikli, H. Yelke, S. Unal. German Hospital, Istanbul, Turkey; Istanbul Memorial Hospital, Istanbul, Turkey.

OBJECTIVE: To evaluate the results of microdissection TESE in patients with non-obstructive azoospermia and cryptozoospermia for intracytoplasmic sperm injection (ICSI).

DESIGN: Two hundred seven azoospermic and 33 cryptozoospermic patients were attempted 245 cycles for ICSI treatment and underwent microdissection TESE for sperm recovery in between June 2002 – December 2003.

MATERIALS AND METHODS: All patients completed an evaluation including volume estimation by orchidometer, karyotype analysis, Y chromosome microdeletions and serum levels determination of FSH and Total Testosterone.

RESULTS: Testicular sperm was successfully retrieved 136 out of 245 (55.5%) ICSI cycles with microdissection TESE. Within the cryptozoospermic subgroup, 28 out of 33 (85%) TESE attempts were successful for sperm recovery while in the azoospermic group 108 out of 212 (51%) TESE attempts were successful. Karyotype analysis was showed 36 non-mosaic and 3 mosaic Klinefelter’s syndrome. Six azf microdeletion was diagnosed for Y microdeletion. At the time of the operation, testicular biopsies were taken for histological evaluation in 148 cases (Table 1). Statistical analysis did not find age, testicular volume, FSH and Total Testosterone levels to have predictive value for the presence of sperm.

CONCLUSION: For non-obstructive azoospermic patients microdissection TESE is an effective sperm retrieval procedure. Although testicular sperm retrieval rate is high in cryptozoospermic patients, repeated semen analyses and sperm collection for cryopreservation should considered before ICSI treatment. Non-obstructive azoospermic patients should recommend both karyotype analysis and Y chromosome microdeletions.

Supported by: None

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<th>Table 1. Distribution of the histologic patterns in azoospermic and cryptozoospermic patients.</th>
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