High-dose anabolic androgenic steroid (AAS) administration results in hypogonadotropic hypogonadism (HH). Physical manifestations can include one or more of the following: depression, decreased sexual desire, impotence, feelings of apathy, testicular atrophy, and loss of muscle mass and strength. Due to feedback inhibition, laboratory values drop well below established physiologic norms: luteinizing hormone (LH) >3.6 IU/L, follicle stimulating hormone (FSH) >2.25 IU/L, and testosterone (T) >300 ng/dL. A search of the literature reveals an absence of studies dealing specifically with AAS induced HH, and restoration of normal endocrine function. We report on two interesting cases of AAS using bodybuilders who were brought out of the hypogonadal state. Blood samples were taken in the morning for both subjects and analyzed using chemiluminescence (Quest Diagnostics, Irvine, TX). Post-therapy samples were taken 15 days after the last hCG injection. Case 1: 6'0" 206 lbs. 33 yr old Caucasian male with a 10+ year history of steroid self-administration for bodybuilding and powerlifting. By his own admission he was a "heavy" user, taking from 500 mg/wk to 2+ grams/wk. Pre-treatment values: LH < 1.0 IU/L, T 191 ng/dL. One course of therapy (32 days) was given: 2,500 IU of hCG every 4 days (8 injections total), 50 mg clomiphene bid and 10 mg tamoxifen qd. Despite massive drug use patient was an exceptionally good responder. Post-treatment values: LH 5.2 IU/L, T 1072 ng/dL. Case 2: 5'10" 184 lbs 36 yr old Caucasian male with a 2 yr history of continuous nandrolone use (200-400 mg/wk). Pre-values: LH < 1.0 IU/L, T 45 ng/dL. Treat 1 (32 days): 2,500 IU hCG every 4 d (8 total), clomiphene (50 mg bid) and arimidex (1 mg qd). Post-values: LH < 1.0 IU/L, T 38 ng/dL. Treat 2 (60 days): 5,000 IU hCG every 4 days (4 inj total) followed by 2,500 IU hCG every 4 d (4 inj total), clomiphene (50 mg bid) and tamoxifen (10 mg qd). Post-values: LH > 1.4 IU/L, T 63 ng/dL. Treat 3 (32 days): 5,000 IU hCG qod (6 inj total) followed by 2,500 IU hCG qod (6 inj total) given simultaneously with menotropins 150 IU qod (6 inj total), clomiphene (50 mg bid) and tamoxifen (10 mg bid). Post-values: LH 9.8 IU/L, T 507 ng/dL. Restoration of the HPG axis, even in severe cases of hypogonadism, is possible with combined therapies and careful monitoring of the patient. With continued popularity of these drugs, long-term androgen deficiency is a health concern for former AAS users. Further research is needed in this area.

ANDROGEN INDUCED HYPOGONADOTROPHIC HYPOGONADISM:
TREATMENT PROTOCOL INVOLVING COMBINED DRUG THERAPY

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The clinical application of androgens in the treatment of various medical conditions has increased in the last five years. Because of the novelty of applying these agents, especially in wasting syndrome, investigations have focused largely on the anabolic actions and side effects during the course of therapy itself. To date, no consideration has been given to the endocrine status of patients post-treatment, particularly development of iatrogenic hypogonadotrophic hypogonadism. The negative impact of hypogonadism on physical and mental well-being should be of major concern for HIV/AIDS patients upon cessation of androgen therapy. Hypogonadism is characterized by: a negative alteration in protein kinetics, decreased fat oxidation, malaise, depression, compromised immune system integrity, and loss of lean body mass. Thirty-two adult males who had self- administered androgens presented with acquired hypogonadotrophic hypogonadism (total testosterone (TT) <240 ng/dl, luteinizing hormone (LH) <1.5 IU/ml). Upon diagnosis, patients were administered the following agents: (a) human chorionic gonadotropin, (2000-2500 IU/QODx16d); (b) clomiphene citrate (50mg POBIDx30d); and (c) tamoxifen (20mg POQDx45d). All medications were started simultaneously with HCG stopped after 16 days, followed by discontinuation of clomiphene at day 30, then tamoxifen stopped on day 45. HCG, a glycopeptide whose alpha subunit is identical to the alpha subunit of LH and FSH, mimics LH action in the leydig cells. The other compounds rounding out the pharmacotherapeutic compliment are two long acting derivatives of triphenylethylene, clomiphene and tamoxifen, both of which act as mixed agonists-antagonists of the estrogen receptor complex, and stimulate the pituitary gonadal axis (HPGA). Two weeks after last dose of tamoxifen, blood work revealed an average LH increase from 1.15 to 5.0 mIU/ml with a concomitant average increase in TT from 140 to 476 ng/dl. In our sample, combined pharmacotherapy was extremely effective in restoring normal function of the HPGA during this brief evaluation period. Further investigation in the form of long-term controlled clinical studies is warranted.

Antiviral Therapy

An official publication of the
International Society for Antiviral Research
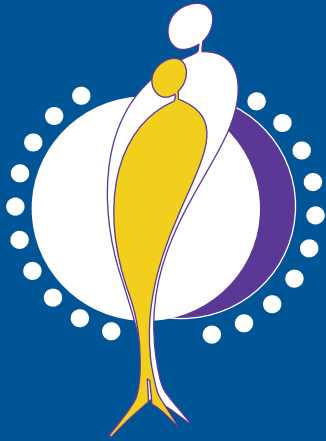
4th International Workshop on
Adverse Drug Reactions and Lipodystrophy in HIV

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raphy, and CT were similar for abdominal fat, but correlations were higher for the subcutaneous (r^2 0.7–0.8) than for the intra-abominal (r^2 0.3–0.6) compartment.

CONCLUSIONS: In antiretroviral-naive asymptomatic HIV-infected adults without clinical evidence of body fat abnormalities, fat measurements are highly dispersed. This dispersion may be due in part to BMI but not to sex. DEXA, abdominal CT scan and sonography may be indistinctly used to measure regional fat in HIV-infected adults.

ABSTRACT 80

The effect of centralized body composition data analysis on an objective case definition of HIV lipodystrophy

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BACKGROUND: An objective case definition (CD) of HIV lipodystrophy (LD) permits reliable LD diagnosis (79% sensitivity, 80% specificity) and rating of LD severity. Its 10 parameters (measured locally) comprise age, gender, HIV duration, CDC stage, waist:hip ratio, anion gap, HDL cholesterol, trunk:peripheral fat ratio and leg fat% on DEXA, and visceral:subcutaneous abdominal fat (VAT:SAT) ratio by CT (L4 level). Centralised DEXA and CT analysis is common in multicentre studies with the aim of reducing imprecision caused by multiple technicians and technologies. We investigated whether centralized DEXA and CT analysis would change or simplify the existing LDCD model or improve its sensitivity and specificity.

METHODS: Of 788 clinical cases and controls, 766 DEXAs and 741 CTs were performed locally. Of local scans, 439 (57%) DEXAs and 434 (59%) CTs were reanalysed centrally by a single technician. The LDCD model was reassessed, and new models constructed, using central data by logistic regression. Analyses were performed using only central data, or with missing central data replaced by local values.

RESULTS: For local and centrally-read scans, respectively, mean (SD) VAT was 111 (76) and 106 (72) cm^2, SAT 111 (95) and 113 (86) cm^2, trunk fat 7.6 (4.0) and 7.5 (3.9) kg, limb fat 5.1 (3.4) and 5.1 (3.4) kg, and leg fat% 16.1 (9.4) and 16.1 (9.1) (all P>0.05). Using central scan data preferentially, the original model retained all 10 parameters (although parameter estimates for VAT:SAT and trunk:peripheral fat increased somewhat) with similar sensitivity (77%) and specificity (80%). Using only central data, the original model was simpler (all parameters remained except VAT:SAT ratio), with 79% sensitivity and 81% specificity. A rebuilt model derived from central in preference to local data did not include age or waist:hip ratio, but included waist circumference and lactate dehydrogenase (78% sensitivity and 79% specificity).

CONCLUSIONS: Centralized DEXA and CT soft tissue data did not differ significantly from data derived from local analysis, but were up to 9% less variable. Central analysis did not substantially simplify the original LD CD model, nor significantly alter its sensitivity or specificity.

ABSTRACT 81

Hypothalamic pituitary gonadal axis normalization protocol after androgen treatment

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OBJECTIVE: To develop an approach to cycle androgens that would result in significant changes in body composition and accelerate the normalization of the hypothalamic pituitary gonadal axis (HPGA) after cessation of androgens.

METHODS: An uncontrolled study of 19 HIV-negative eugonadal men, ages 23–57 years, administered testosterone cypionate and nandrolone decanoate for 12 weeks, and then were treated simultaneously with a combined regimen of human chorionic gonadotropin (hCG) (2500 IU/four times daily ×16 days), clomiphene citrate (50 mg PO twice daily ×30 days) and tamoxifen (20 mg PO once daily ×45 days), to

restore the HPGA.

RESULTS: Mean FFM by DEXA increased from 64.1 to 69.8 kg ($P<0.001$); percent body fat decreased from 23.6 to 20.9 ($P<0.01$); strength increased significantly from 357.4 lb to 406.4 lb ($P=0.02$). No significant changes in serum chemistries and liver function tests were found. HDL-C decreased from a mean value of 44.3 to 38.0 ($P=0.02$). Mean values for luteinizing hormone (LH) and total testosterone were 4.5 and 460, respectively, prior to androgen treatment. At the conclusion of the 12-week treatment with androgens the mean LH <0.7 ($P<0.001$) and total testosterone was 1568 ($P<0.001$). The mean values after treatment with the combined regimen were LH=6.2 and testosterone=458.

DISCUSSION: The use of androgens has been reported to improve lean body mass, strength, sexual function, and mood, accompanied by side-effects caused by continuous uninterrupted use of these compounds (polycythemia, testicular atrophy, hypertension, liver dysfunction [oral androgens] and alopecia). Androgen-induced HPGA suppression causes a severe hypogonadal state in most patients that often require an extensive period of considerable duration for normalization. This prevents most if not all individuals from cycling off these medications due to the adverse impact of this state on their previously gained LBM and quality of life. The protocol of hCG-clomiphene-tamoxifen was successful in restoring the HPGA within 45 days after androgen cessation. Further controlled studies are needed to determine if these results can be duplicated in HIV-positive subjects.

ABSTRACT 82

A prospective study of body fat redistribution and metabolic abnormalities in patients initiating highly active antiretroviral therapy

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OBJECTIVE: A high prevelance of lipodystrophy is reported in cross-sectional studies in patients on highly active antiretroviral therapy (HAART). Without baseline data, the incidence and rate of development of abnormalities is unclear. This study is designed to prospectively determine abnormalities in body fat redistribution, and glucose and fat metabolism in patients initiating protease inhibitor (PI)-based therapies.

METHODS: Body habitus changes are monitored by standardized circumference measures, and regional DEXA scanning; lipid abnormalities by fasting cholesterol and triglyceride; glucose abnormalities by glucose, C-peptide, insulin and proinsulin measures fasting and during a glucose tolerance test (GTT). Median changes were compared to zero by the signed rank test.

RESULTS: Data [median change, interquartile range (IQR)] are presented on the first 30 patients who have 12-month follow-up and 18 patients who have 24-month follow-up. For the 12-month (24-month) follow-up, significant increases were seen in measurements of waist 1.00 cm (1.00, 6.38), $P<0.01$ [24-month: 7.50 cm (–1.25, 10.75), $P=0.02$] but not in chest 1.25 cm (–1.00, 3.50), $P=0.13$ [24-month: –0.50 cm (–3.25, 4.75), $P=0.86$], left thigh –0.25 cm (–1.88, 2.00), $P=0.80$ [24-month: –1.00 cm (–2.50, 0.75), $P=0.14$], hip 0.75 cm (–1.88, 4.88), $P=0.17$ [24-month: –1.00 cm (–3.00, 3.50), $P=0.98$] or left bicep 0.00 cm (–0.50, 2.00), $P=0.26$ [24-month: 1.00 cm (0.00, 3.25), $P=0.08$] circumferences. Using DEXA scan analysis, the median (IQR) change in total body fat for the 12-month (24-month) follow-up was –918 g (–2276, 1223), $P<0.32$ [24-month: –74 g (–853, 517), $P=0.64$]; trunk fat –420.8 g (–995, 1162), $P=0.82$ [24-month: 57 g (–441, 1284), $P=0.52$]; left leg fat –200 g (–737, 6), $P=0.02$ [24-month: –407 g (–580, –28), $P=0.01$]; left arm fat –50 g (–165, 122), $P=0.31$ [24-month: –3 g (–159, 166), $P=0.89$]. For the 12-month (24-month) follow-up, median change (IQR) in fasting cholesterol was 1.05 mmol/l (0.22, 2.24), $P<0.01$ [24-month: 1.57 mmol/l (0.83, 2.03), $P<0.01$], fasting triglyceride 0.81 mmol/l (0.01, 1.48), $P<0.01$ [24-month: 1.13 mmol/l (0.61, 1.64), $P<0.01$] and fasting glucose –0.04 mmol/l (–0.85, 0.02), $P=0.07$ [24-month: 0.40 mmol/l (–0.15, 0.60), $P=0.19$].

CONCLUSIONS: Mild changes in body fat redistribution primarily in the trunk and waist occur within the first 2 years of initiation of PI-based antiretrovirals. Increases in cholesterol and triglyceride are observed, although usually remain within the normal range. Although insulin resistance is noted, frank diabetes is uncommon.

ABSTRACTS

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Abstract #34

Uncontrolled Case Study of Medical Treatment for Elimination of Hypogonadism After Androgen Cessation in a Man With Human Immunodeficiency Virus Positivity and Secondary Polycythemia Related to Continuous Testosterone Treatment for 2 Years

Michael C. Scally, MD, Julia A. Kovacs, MD, Joseph C. Gathe, MD, and Andrew L. Hodge, MS

Objective: To assess the potential for prevention or minimization of clinically significant hypogonadism after androgen cessation in previously eugonadal human immunodeficiency virus-positive (HIV+) men with secondary polycythemia.

Methods: Medical treatment with human chorionic gonadotropin (2,500 IU subcutaneously every other day for 16 days), clomiphene citrate (50 mg orally twice a day for 30 days), and tamoxifen (20 mg orally daily for 30 days) and therapeutic phlebotomy were used in an HIV+ man with problematic secondary polycythemia due to 2 years of uninterrupted testosterone therapy.

Results: The combination of medical treatment and therapeutic phlebotomy was successful in normalization of the hemoglobin level (from 17.2 to 15.6 g/dL), hematocrit (from 51.2% to 45.5%), luteinizing hormone (from <0.2 to 7.3 mIU/mL), and testosterone (from >1,200 to 626 ng/dL) with no intervening period of hypogonadism after androgen cessation.

Conclusion: Medical treatments that would allow for the interruption of testosterone treatment and eliminate or minimize the period of hypogonadism after androgen cessation need to be explored.