South Africa - The injectable contraceptives depot medroxyprogesterone acetate and norethisterone enanthate substantially and differentially decrease testosterone and sex hormone binding globulin levels: a secondary study from the WHICH randomized clinical trial.

C Avenant, M Singata-Madlik, A Bick, D Africander, Y Balakrishna, K Storbeck, J Moliki, S Dlamini, S Skosana, J Smit, M Beksinska, I Beesham, I Seocharan, J Batting, G Hofmeyr, J Hapgood

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Overview

Identification

ID NUMBER
Theinjectablecontraceptivesdepotmedroxyprogesteroneacetate

Overview

ABSTRACT
HIV acquisition risk with norethisterone (NET) enanthate (NET-EN) is reportedly less than for depo-medroxyprogesterone acetate intramuscular (DMPA-IM). We investigated the effects of these progestin-only injectable contraceptives on serum testosterone and sex hormone binding globulin (SHBG) levels, since these may play a role in sexual behavior and HIV acquisition.

The open-label WHICH clinical trial, conducted at two sites in South Africa from 2018-2019, randomized HIV-negative women aged 18-40 years to 150 mg DMPA-IM 12-weekly (n = 262) or 200 mg NET-EN 8-weekly (n = 259). We measured testosterone by UHPLC-MS/MS and SHBG by immunoassay in matched pairs of serum samples collected at baseline (D0) and at peak serum progestin levels at 25 weeks post initiation (25W) (n = 214-218 pairs).

We report for DMPA-IM and NET-EN users, respectively, a substantial decrease from D0 to 25W in total testosterone (-24.3%, D0 0.560, 25W 0.423 nmol/L, $p < 0.0001$ and -54.1%, D0 0.551, 25W 0.253 nmol/L, $p < 0.0001$), SHBG (-29.8%, D0 45.0, 25W 32.7 nmol/L, $p < 0.0001$ and -65.1%, D0 50.2, 25W 17.6 nmol/L, $p < 0.0001$), and calculated free testosterone levels (-17.2%, $p = 0.0371$ and -40.0%, $p < 0.0001$). The mean percentage difference in change for total testosterone, SHBG and calculated free testosterone levels was significantly more for NET-EN than DMPA-IM (64.9%, $p < 0.0001$; 101.2%, $p < 0.0001$; and 38.0%, $p = 0.0120$, respectively.

The substantial and differential decrease in testosterone and SHBG levels does not explain our previous finding of no detected decrease in risky sexual behavior or sexual function for DMPA-IM or NET-EN users from D0 to 25W. Medroxyprogesterone (MPA) and NET are androgenic and are both present in molar excess over testosterone and SHBG concentrations at 25W. Any within or between contraceptive group androgenic effects on behavior in the brain are likely dominated by the androgenic activities of MPA and NET and not by the decreased endogenous testosterone levels.

The clinical trial was registered with the Pan African Clinical Trials Registry (PACTR 202009758229976).

Producers and Sponsors

PRIMARY INVESTIGATOR(S)

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Sampling

No content available

Questionnaires

No content available

Data Collection

Data Processing

No content available

Data Appraisal

No content available

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File Description

Variable List

Testosterone

Content	
Cases	436
Variable(s)	20
Structure	Type: Keys: ()
Version	
Producer	
Missing Data	

Variables

ID	NAME	LABEL	TYPE	FORMAT	QUESTION
V1	ID	ï»¿ID	contin	numeric	
V2	Site	Site	discrete	character	
V3	ITT_arm	ITT_arm	discrete	character	
V4	PPD025W_arm	PPD0&25W_arm	discrete	character	
V5	Age	Age	contin	numeric	
V6	Ethnicity	Ethnicity	discrete	character	
V7	marital_D0	marital_D0	discrete	character	
V8	education_D0	education_D0	discrete	character	
V9	income_D0	income_D0	discrete	character	
V10	marital_25W	marital_25W	discrete	character	
V11	education_25W	education_25W	discrete	character	
V12	income_25W	income_25W	discrete	character	
V13	DMPA	DMPA	discrete	character	
V14	NETEN	NETEN	discrete	character	
V15	D0_SHBG	D0_SHBG	contin	numeric	
V16	W_SHBG	25W_SHBG	contin	numeric	
V17	T_D0_Sbimp	T_D0_Sbimp	discrete	character	
V18	T_25W_Sbimp	T_25W_Sbimp	discrete	character	
V19	FreeT_D0_Sbimp	Free T_D0_Sbimp	discrete	character	
V20	FreeT_25W_Sbimp	Free T_25W_Sbimp	discrete	character	

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ï»¿ID (ID)
File: Testosterone

Overview

Type: Continuous
Format: numeric
Decimals: 0
Range: 1-436

Valid cases: 436
Invalid: 0
Minimum: 1
Maximum: 436
Mean: 218.5
Standard deviation: 126

Site (Site)
File: Testosterone

Overview

Type: Discrete
Format: character
Width: 4

Valid cases: 436
Invalid: 0

ITT_arm (ITT_arm)
File: Testosterone

Overview

Type: Discrete
Format: character
Width: 7

Valid cases: 436
Invalid: 0

PPD0&25W_arm (PPD025W_arm)
File: Testosterone

Overview

Type: Discrete
Format: character
Width: 33

Valid cases: 436
Invalid: 0

Age (Age)
File: Testosterone

Overview

Type: Continuous
Format: numeric
Decimals: 0
Range: 18-39

Valid cases: 436
Invalid: 0
Minimum: 18
Maximum: 39
Mean: 25
Standard deviation: 4.7

Ethnicity (Ethnicity)
File: Testosterone

Overview

Type: Discrete
Format: character
Width: 19

Valid cases: 436
Invalid: 0

marital_D0 (marital_D0)
File: Testosterone

Overview

Type: Discrete
Format: character
Width: 7

Valid cases: 436
Invalid: 0

education_D0 (education_D0)
File: Testosterone

Overview

Type: Discrete
Format: character
Width: 37

Valid cases: 436
Invalid: 0

income_D0 (income_D0)
File: Testosterone

Overview

Type: Discrete
Format: character
Width: 13

Valid cases: 436
Invalid: 0

marital_25W (marital_25W)
File: Testosterone

Overview

Type: Discrete
Format: character
Width: 7

Valid cases: 434
Invalid: 0

education_25W (education_25W)
File: Testosterone

Overview

Type: Discrete
Format: character
Width: 37

Valid cases: 434
Invalid: 0

income_25W (income_25W)
File: Testosterone

Overview

Type: Discrete
Format: character
Width: 13

Valid cases: 434
Invalid: 0

DMPA (DMPA)
File: Testosterone

Overview

Type: Discrete
Format: character
Width: 3

Valid cases: 317
Invalid: 0

NETEN (NETEN)
File: Testosterone

Overview

Type: Discrete
Format: character
Width: 3

Valid cases: 130
Invalid: 0

D0_SHBG (D0_SHBG)
File: Testosterone

Overview

Type: Continuous
Format: numeric
Decimals: 0
Range: 4-234

Valid cases: 436
Invalid: 0
Minimum: 4
Maximum: 234
Mean: 55.6
Standard deviation: 30.9

25W_SHBG (W_SHBG)
File: Testosterone

Overview

Type: Continuous
Format: numeric
Decimals: 0
Range: 1-131

Valid cases: 434
Invalid: 2
Minimum: 1
Maximum: 131
Mean: 28.8
Standard deviation: 18.8

T_D0_Sbimp (T_D0_Sbimp)
File: Testosterone

Overview

Type: Discrete
Format: character
Width: 5

Valid cases: 436
Invalid: 0

T_25W_Sbimp (T_25W_Sbimp)
File: Testosterone

Overview

Type: Discrete
Format: character
Width: 5

Valid cases: 436
Invalid: 0

Free T_D0_Sbimp (FreeT_D0_Sbimp)
File: Testosterone

Overview

Type: Discrete
Format: character
Width: 5

Valid cases: 436
Invalid: 0

Free T_25W_Sbimp (FreeT_25W_Sbimp)
File: Testosterone

Overview

Type: Discrete
Format: character
Width: 7

Valid cases: 436
Invalid: 0

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