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Discordance between self-reported contraceptive use and detection of exogenous hormones among Malawian women enrolling in a randomized clinical trial☆

Anuli N. Nwaohiri[a], **Jennifer H. Tang**[b], **Frank Stanczyk**[c], **Lameck Chinula**[b], **Stacey Hurst**[a], **Nicole L. Davis**[a], **Gerald Tegha**[b], **Lisa Haddad**[d], and **Athena P. Kourtis**[a,*]

[a]Division of Reproductive Health, Centers for Disease Control and Prevention, Atlanta, GA, USA

[b]University of North Carolina Project, Lilongwe, Malawi

[c]Department of Obstetrics and Gynecology, University of Southern California Keck School of Medicine

[d]Emory University, Department of Obstetrics & Gynecology, Atlanta, GA, USA

Abstract

Objective—The objective was to assess the extent of concordance between self-reported contraceptive use and the presence of contraceptive progestins in serum.

Study design—We evaluated self-reported contraceptive use by using radioimmunoassay to examine baseline serum levels of medroxyprogesterone acetate (MPA) and levonorgestrel (LNG) among 97 Malawian women enrolling in a contraceptive trial.

Results—Twelve percent (12/97) of study participants who reported no hormonal contraceptive use in the previous 6 months had either MPA or LNG detected in their serum.

Conclusions—The observed discordance between self-report and detection of exogenous hormones in serum indicates that caution is warranted when drawing conclusions based on self-reported contraceptive use.

Keywords

Contraceptive use; Medroxyprogesterone acetate (MPA); Levonorgestrel (LNG); Misreporting; Discordance

1. Introduction

Research studies often measure contraceptive use by self-report [1,2], including studies assessing the relationship between hormonal contraceptives and acquisition or transmission of human immunodeficiency virus (HIV) and other sexually transmitted infections [3]. However, the accuracy of self-report can be affected by participant recall, study participation

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*Corresponding author. Tel.: +1 770 488 5216; fax: +1 770 488 6391. apk3@cdc.gov (A.P. Kourtis).

motivation or social desirability bias [4]. If self-report is inaccurate, then observed relationships between self-reported contraceptive use and outcomes in research studies can be invalid.

We sought to evaluate the accuracy of self-reported contraceptive use among Malawian women reporting no hormonal contraceptive use in the last 6 months by comparing self-report with laboratory detection of exogenous progestins in serum. In Malawi, only four synthetic progestins are used in the available contraceptives: levonorgestrel (LNG: 0.03 mg progestin-only pill, 0.15 mg combined oral contraceptive and 150 mg two-rod contraceptive implant), etonorgestrel (ENG, 68 mg one-rod implant), norgestrel (0.30 mg combined oral contraceptive) and medroxyprogesterone acetate (MPA, 150 mg depot medroxyprogesterone acetate injectable) [5]. Contraceptives that use other progestins are not locally available.

2. Methods

In a randomized clinical trial in Lilongwe, Malawi, we investigated the effects of progestin-only contraception on HIV viral shedding and immune markers in the genital tract of HIV-infected and uninfected women [6]. Specifically, 97 women (73 HIV infected, 24 HIV uninfected) were randomized to receive either the 3-monthly depot medroxyprogesterone acetate (DMPA) injectable or the 5-year LNG implant [6]. Study enrollment was limited to women who reported no modern contraceptive use in the previous 6 months. Modern contraceptive use was defined as use of oral contraceptives (OC), DMPA injectable, the LNG or ENG implant, or the copper intrauterine device, as these were the hormonal and intrauterine contraceptives available in Malawi at the time. Ever use of modern contraceptives was defined as using contraceptives at any time, including the 6 months prior to study enrollment. Institutional review board approval was obtained from the Malawi National Health Science Research Committee, Malawi Pharmacy, Medicines & Poisons Board, the University of North Carolina at Chapel Hill and the U.S. Centers for Disease Control and Prevention.

Serum samples from the enrollment visit were assessed for MPA and LNG by measuring hormone concentrations using radioimmunoassay (RIA) methods [7]. Blood samples were obtained prior to randomization and subsequent initiation of the study-assigned hormonal contraceptive. The lower limit of quantification was 0.02 ng/ml for LNG and 0.07 ng/ml for MPA. The interassay coefficients of variation were 9.3%, 7.2% and 10.3% at 0.41, 2.80 and 8.0 ng/ml for LNG, and 8.7%, 5.1% and 9.8% at 0.37, 0.87 and 1.85 ng/ml for MPA. p values were calculated using the Fisher’s Exact Test and Wilcoxon rank sum test for the categorical and continuous variables, respectively.

3. Results

Ninety-seven women who reported not using modern contraceptives in the past 6 months had their serum samples tested. Twelve (12.4%) of the 97 women had detectable serum levels for MPA or LNG (Table 1). All women with detectable serum levels were married, with median age 33 years (IQR: 26–37); 50% were HIV positive, and 75% had more than a primary school education. The majority of HIV-infected women were on antiretroviral

regimens, most of them containing efavirenz. Women with and without detectable serum levels had similar baseline characteristics (Table 1).

Five (5.2%) women had detectable levels of LNG, and eight (8.2%) women had detectable levels of MPA; one woman had detectable levels of both LNG and MPA (Table 2). The detectable serum levels ranged from 0.02 to 1.83 (ng/ml) for LNG and 0.12 to 0.98 (ng/ml) for MPA. Ten of the 12 women reported ever using contraceptive injections, one reported ever using contraceptive implants, and four reported ever using OCs. One of the 12 women reported no previous modern contraceptive use. Detectable levels of LNG were found in two of eight participants reporting never using implants or OC, and MPA was detected in serum from one of two women reporting never using injections (Table 2).

4. Discussion

Discordance between self-reported contraceptive use and detection of either MPA or LNG occurred among 12.4% of study participants. All oral contraceptives locally available in Malawi contain either LNG or norgestrel as their progestin, both of which can be detected using our LNG assay. The LNG implant is the only other LNG-based contraceptive available in Malawi. Given that LNG is usually undetectable in serum within 120 h of oral contraceptive discontinuation [8] and 5 days to 2 weeks after LNG implant discontinuation [9,10], it is likely that all 5 women who had LNG detectable at enrollment had more recently used LNG-containing contraceptives for prevention of pregnancy, treatment of abnormal uterine bleeding or both.

In contrast, MPA can be detected in the serum for up to 9 months after DMPA injection, although that finding is uncommon [11]. However, it is possible that some of the eight women with detectable MPA concentrations, particularly those with concentrations in the lower range, had received their last DMPA injection more than 6 months prior. MPA concentrations usually range between 1.0 and 1.5 ng/ml during the first 3 months after injection and slowly decline to about 0.2 ng/ml during the fifth month postinjection. Given that the eight participants had MPA concentrations ranging from 0.12 to 0.98 ng/ml, it is likely that most had their last DMPA injection 3–6 months prior to enrollment.

Of note, highly specific and sensitive LNG and MPA RIAs were used in the present study [7]. Assays to measure multiple progestins in the same serum sample using mass spectrometry are in development and will be available in the near future.

In most cases, the women with detectable hormones reported using modern contraceptives prior to the last 6 months, although two women with detectable LNG concentrations denied prior use of both oral contraceptives and implants and one woman with a detectable MPA concentration denied prior use of injectables. There was no further investigation on the source of discordance between self-report and the detection of progestins. However, it could be unintentional due to recall bias or misunderstanding of the question, or intentional due to desire to enroll in the study.

There could be additional women in our study who had used a modern contraceptive within the past 6 months but had MPA or LNG concentrations below our level of detection. The

majority of HIV-infected women in our study were on efavirenz-containing regimens, which are known to decrease serum LNG concentrations [12]; thus, the possibility that undetectable LNG concentrations could be due to pharmacokinetic interactions with efavirenz cannot be excluded. Another potential limitation of this analysis was our inability to test for ENG concentrations at enrollment, so misreporting of ENG implant use could not be estimated.

In conclusion, we found that 12.4% of the women in our study had detectable MPA or LNG concentrations at the time of enrollment in contrast to self-report of no such contraceptive use in the previous 6 months. Confirmation of this finding from larger studies and other study populations is needed for generalizability. However, these findings highlight the importance of assessing serum concentrations of exogenous hormones rather than relying on self-report, as self-report may not accurately reflect actual contraceptive exposure.

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Table 1

Characteristics of study participants by detectable exogenous hormones in the serum at enrollment in a randomized study (*n*=97), Lilongwe, Malawi

	Undetectable *n*=85	**Detectable *n*=12**
Married	56 (66%)	12 (100%)
HIV-positive status	67 (79%)	6 (50%)
Completed more than a primary education	49 (58%)	9 (75%)
Reported history of contraceptive injectable use	58 (68%)	10 (83%)
Reported history of contraceptive implant use	5 (6%)	1 (8%)
Reported history of oral contraceptive use	15 (18%)	4 (33%)
Reported history of intrauterine device use	0%	0%
ART use at study enrollment (HIV-positive only)	63 (94%)	5 (83%)
Use of efavirenz-based regimens	55 (87%)	3 (60%)
	Median (IQR)	Median (IQR)
Age (years)	33 (28–37)	33 (26–37)
Parity	3 (2–3)	3 (2–5)

All p values were N.05.

All detectable hormones occurred in women self-reporting no contraceptive use.

Comparisons were made between women with detectable and nondetectable exogenous hormones.

Table 2

Levels of detectable exogenous hormones and self-reported ever use of modern contraceptives in women reporting no modern contraceptive use in the last 6 months, Lilongwe, Malawi

	LNG (ng/ml)	MPA (ng/ml)	Ever use of modern contraceptive			
			Injection	Implant	Pills (oral)	IUD
1	0.22	–	Y	N	N	N
2	–	0.52	Y	N	N	N
3	–	0.12	Y	N	N	N
4	0.02	–	Y	Y	Y	N
5	–	0.21	N	N	N	N
6	–	0.84	Y	N	N	N
7	0.41	–	N	N	Y	N
8	0.49	–	Y	N	N	N
9	–	0.12	Y	N	N	N
10	–	0.98	Y	N	N	N
11	–	0.90	Y	N	Y	N
12	1.83	0.42	Y	N	Y	N