BRIEF REPORT



Association Between Vaginal Douching and Genital Human Papillomavirus Infection Among Women in the United States

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The very few studies that have examined the association between vaginal douching and genital human papillomavirus (HPV) infection have found contrary results. We investigated the associations between douching and numbers of HPV genotypes infecting 1271 participants aged 20–49 years in the 2003– 2004 US National Health and Nutrition Examination Survey. After controlling for relevant covariates, douching in the past 6 months was significantly associated with infection by higher numbers of all genital HPV types (relative risk ratio, 1.26; 95% confidence interval, 1.03–1.54) and HPV high-risk types (1.40; 1.09–1.80).

Keywords. vaginal douching; human papillomavirus; cervical cancer; United States.

About one-third of women in the United States practice vaginal douching, with the practice more common among black women [1, 2]. Douching has been suggested to be associated with adverse health outcomes, including sexually transmitted bacterial infections and cervical cancer [1, 2]. Few studies have examined the association between douching and cervicovaginal human papillomavirus (HPV) infection, and those that have investigated this association have found contrary results. Some studies revealed that douching increased the risk of HPV of any type [3, 4]; others, however, suggested that douching reduced the likelihood of genital warts [5], type 6 or 11 HPV infection [6], or HPV positivity of any type [7]. Hypothetically, douching may cause physical epithelium abrasions or disrupt the normal protective vaginal microenvironment, thus facilitating HPV acquisition. Nevertheless, douching, particularly after intercourse,

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may help clear transmitted HPV. Therefore, further evidence regarding the association between douching and HPV infection is needed. In the current study, we investigated the association between douching and a number of HPV genotypes infecting a representative sample in the United States.

METHODS

This analysis comprised 1271 women aged 20-49 years who had participated in the 2003-2004 US National Health and Nutrition Examination Survey (NHANES) [8] and for whom data on douching, sexual behaviors, and genital HPV infection were available. We could not use more recent data sets because douching variables were not collected in later cohorts. Douching was defined to participants as "putting a substance into the vagina either for routine cleansing or for vaginal irritation or signs of infection." Douching practices were measured by 2 questions, "During the past 6 months, did you douche?" and "During the past 6 months, how often did you douche?" Responses for frequency of douching consisted of 4 categories: less than once a month, once a month, 2-4 times a month, and ≥ 5 times a month. Some other sociodemographic and behavioral variables included in our analyses were age, race/ethnicity, education, income-to-poverty ratio, marital status, cigarette use, alcohol use, cocaine or other street drug use, sexual orientation, numbers of sexual partners (in the participant's lifetime and in the past years), birth control pill or hormone use, and feminine hygiene product use.

Cervicovaginal swab samples were tested for HPV DNA using Roche Linear Array HPV Genotyping [9]. This test could detect 16 low-risk HPV genotypes (types 6, 11, 40, 42, 54, 55, 61, 62, 64, 71, 72, 81, 82 subtype IS39, 83, 84, and 89) and 21 high-risk genotypes (types 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 67, 69, 70, 68, 73, and 82). One limitation of previous studies on this topic has been the inclusion of symptomatic HPV-6 and HPV-11 genotypes in the outcome; these 2 genotypes cause symptoms (genital warts), possibly resulting in more douching and masking the association between douching and HPV infection with other asymptomatic HPV types. Thus, we excluded HPV types 6 and 11 (total prevalence, 0.8%) in our analyses. The number of all genital HPV DNA types was the sum of positive results with all 35 genital HPV DNA types, excluding types 6 and 11. The number of all genital HPV DNA high-risk types was the sum of positive results with all 21 high-risk genital HPV DNA types.

Statistical analyses were conducted using Stata software, version 12.0 with survey analysis. The NHANES 2-year interview weight was used in bivariate analyses when douching within the past 6 months was a dependent variable (ie, for analyses of

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variables collected through interviews only). The 2-year medical-examination weight was used in all other bivariate and multivariable analyses (ie, for analyses of variables collected through interviews and medical examinations including HPV testing). To examine associations, logistic regression with the adjusted F test was used when the dependent variables were binary (eg, douching in the past 6 months). Generalized linear models with Poisson log-linear regression for count data (eg, the number of all genital infecting HPV DNA types) were used to assess the effect of douching on HPV infection while controlling for putative confounding variables. Covariates that met priori criteria of confounders [10] and changed the point estimate of douching effect by \geq 10.0% were included in the final models.

RESULTS

Distributions of the participants' characteristics are displayed in the second and third columns of Table 1. In this NHANES study sample for our analyses, the weighted prevalence of douching in the past 6 months was 23.0% (95% confidence interval [CI], 19.6%–26.8%). The weighted prevalence of being infected with any type of genital HPV DNA was 48.6% (95% CI, 45.5%-51.7%) when types 6 and 11 were included and 47.8% (44.5%-51.1%) when they were excluded. Among participants who had any-type genital HPV DNA detected except types 6 and 11, 47.5% (95% CI, 41.2%-53.8%) harbored 1 type, 24.9% (20.8%-29.6%) harbored 2 types, and 27.6% (23.2%-32.4%) harbored 3-9 types. Also among those who had anytype genital HPV DNA detected except types 6 and 11, 40.5% (95% CI, 35.0%-46.3%) harbored 1 high-risk type, 16.2% (12.4%-20.9%) harbored 2 high-risk types, and 9.1% (6.9%-11.8%) harbored 3-6 high-risk types.

In bivariate analyses, douching in the past 6 months was associated with most sociodemographic and some behavioral characteristics, including cigarette smoking, having more sexual partners (both in lifetime and in the past year), using other feminine hygiene products, and having vaginal problems (itching, odor, discharge) in the past month (Table 1). Age, race/ethnicity, education, income-to-poverty ratio, marital status, cigarette smoking, numbers of sexual partners, douching in the past 6 months, frequencies of douching, using other feminine hygiene products, and having vaginal problems in the past month were significantly associated with infection by a higher number of all genital HPV DNA types.

When we screened for the potential confounding effect of each sociodemographic and behavioral factor, education, income-to-poverty ratio, current use of birth control pills/hormones, and the use of feminine spray, powder, or wipes/toilettes individually in the past months did not change the point estimates of associations between douching and HPV outcomes by $\geq 10\%$. Thus, these variables were not included in the final models. After controlling for relevant variables (Table 2), douching in the past 6 months was still significantly associated with infection by higher numbers of all genital HPV DNA types (relative risk ratio, 1.26; 95% CI, 1.03–1.54) and all genital HPV DNA high-risk types (1.40; 1.09–1.80). In multivariable models similar to those in Table 2, when douching in the past 6 months was replaced in turn by frequencies of douching and the use of feminine hygiene products in the past month, these variables were not associated with HPV outcomes (data not shown).

DISCUSSION

Our study found that douching was associated with infection by more HPV types, including all types and high-risk types only. These associations were independent from other risk factors for HPV infection such as younger ages or having multiple sexual partners. Moreover, the exclusion of symptomatic HPV types (ie, types 6 and 11) in our analyses and the control for having vaginal problems in the multivariable models suggest that the association between douching and HPV infection was not confounded by vaginal problems, which might be signs of other possible vaginal infections (eg, bacterial vaginosis, genital warts, or another symptomatic sexually transmitted infection). There was no evidence for associations between the use of other feminine hygiene products and HPV infection.

Our results suggest that douching may increase the risk of cervical cancer for 2 reasons. First, douching was directly associated with high-risk HPV infection in our results. Another longitudinal study of 1543 young women with documented or suspected HPV-16 infection in the United States also found that douching was associated with HPV-16 DNA redetection at follow-up [11]. Second, douching was associated with infection by more HPV types, and multiple-type HPV infections have been linked to an increased risk of high-grade precancerous lesions in previous studies [12, 13].

Despite the inconsistent association between douching and HPV infection in the literature, this analysis in the US general population revealed that douching was associated with infection by an increased number of HPV types. Compared with previous studies, the strengths of our study include a relatively large sample size and the ability to examine the number of infecting HPV types instead of HPV positivity with any type. However, because only 2 douching variables were collected in the NHANES, we could not investigate the practice more thoroughly with regard to behavioral initiation (eg, age at first douching), types of practices (eg, using a douching device), timing (eg, before vaginal sex, during menstruation), or solutions used. Douching or intravaginal cleansing practices vary considerably across populations and countries [1, 14]. These differences may explain the inconsistent findings about the association between douching and HPV infection. Further studies, particularly longitudinal ones, are needed to determine whether specific types of douching or specific solutions actually increase the risk of HPV infection and persistence. Also needed is a trial that

Table 1. Unadjusted Associations Between Participants' Characteristics, Douching Practice, and HPV Infection

	Unweighted Counts ^a (Weighted % in Total Cohorts ^b) (n = 1271)	Douched in Past 6 mo ^b		No. of All Infecting HPV DNA Types (Except 6 and 11) ^c	
Characteristic		OR (95% CI)	P Value (or P Trend)	RRR (95% CI)	P Value (or P Trend)
Age group, y			(.02)		(<.001)
20–29	463 (30.8)	1		1	
30–39	425 (32.9)	1.12 (.76–1.65)	.55	0.74 (.60–.90)	.003
40–49	383 (36.4)	1.72 (1.14–2.59)	.01	0.59 (.48–.72)	<.001
Race/ethnicity					
Non-Hispanic white	609 (67.3)	1		1	
Non-Hispanic black	296 (13.9)	4.01 (2.98-5.39)	<.001	1.46 (1.16–1.83)	.001
Mexican American	265 (9.6)	0.97 (.51–1.88)	.93	1.10 (.82–1.49)	.52
Other Hispanic	47 (4.2)	1.10 (.60-2.02)	.74	1.43 (.97–2.10)	.07
Other race	54 (5.0)	0.76 (.29–2.02)	.56	1.34 (.90–1.97)	.15
Educational level			(<.001)		(.004)
Less than high school	283 (15.2)	1		1	
High school or equivalent	305 (24.2)	0.95 (.64–1.39)	.76	0.74 (.57–.97)	.03
Some college or higher	683 (60.6)	0.47 (.35–.63)	<.001	0.69 (.55–.86)	.001
Income-to-poverty ratio ^d			(<.001)		(<.001)
<1.0	299 (18.7)	1		1	
≥1.0 to <2.0	310 (21.4)	0.65 (.43–.99)	.04	0.84 (.65–1.09)	.19
≥2.0 to <3.0	167 (15.4)	0.66 (.43-1.00)	.052	0.89 (.67–1.17)	.39
≥3.0	433 (44.5)	0.29 (.19–.43)	<.001	0.60 (.48–.76)	<.001
Marital status					
Never married	309 (23.0)	1		1	
Married or living with partner	770 (61.9)	0.87 (.59–1.30)	.48	0.57 (.47-0.69)	<.001
Widowed, divorced, or separated	192 (15.2)	1.43 (.78–2.60)	.22	1.06 (.84–1.34)	.62
Cigarette smoking ^e					
Never or former	779 (66.6)	1		1	
Current	311 (33.4)	2.61 (1.78–3.82)	<.001	1.41 (1.17–1.70)	<.001
Alcohol use in past year, average drinks/ wk			(.08)		(.12)
0	381 (28.1)	1		1	
<1	427 (39.4)	0.62 (.37–1.03)	.06	1.02 (.80–1.30)	.87
1 to <7	244 (25.1)	0.88 (.52-1.49)	.60	1.17 (.91–1.52)	.22
7 to <14	45 (4.8)	1.29 (.76–2.17)	.32	1.41 (.95–2.11)	.09
≥14	20 (2.6)	1.35 (.52–3.49)	.52	1.63 (1.01–2.63)	.046
Ever used cocaine or other street drug					
No	921 (81.4)	1		1	
Yes	180 (18.6)	1.49 (.88–2.52)	.13	1.25 (1.00–1.56)	.047
Ever had sexual intercourse					
No	34 (3.7)	1		1	
Yes	1067 (96.3)	7.34 (.88–61.34)	.06	5.26 (1.56–17.72)	.007
Sexual orientation					
Heterosexual	1002 (96.2)	1		1	
Homosexual or bisexual	40 (3.8)	0.58 (.23–1.43)	.22	1.34 (.85–2.11)	.21
No. of lifetime sexual partners ^f			(.004)		(<.001)
0	42 (4.7)	1		1	
1	195 (15.5)	4.21 (.53–33.12)	.16	0.82 (.39–1.74)	.61
2–5	437 (38.6)	9.22 (.99–85.78)	.051	2.08 (1.07-4.07)	.03
6–10	218 (21.1)	10.88 (1.43-82.59)	.02	2.52 (1.28–4.97)	.007
11–20	130 (11.6)	13.99 (1.49– 131.43)	.02	3.52 (1.78–6.96)	<.001
≥21	79 (8.4)	16.25 (2.33– 113.40)	.008	2.52 (1.24–5.11)	.01
No. of sexual partners in past year ^f			(800.)		(<.001)
0	111 (12.0)	1		1	
1	821 (73.1)	2.34 (1.04-5.23)	.04	1.21 (.86-1.70)	.27

Characteristic	Unweighted Counts ^a (Weighted % in Total Cohorts ^b) (n = 1271)	Douched in Past 6 mo ^b		No. of All Infecting HPV DNA Types (Except 6 and 11) ^c	
		OR (95% CI)	P Value (or P Trend)	RRR (95% CI)	P Value (or P Trend)
≥2	169 (14.9)	3.56 (1.61–7.86)	.004	2.42 (1.68–3.49)	<.001
History of genital herpes or genital warts					
No	956 (89.1)	1		1	
Yes	111 (10.9)	0.98 (.50–1.90)	.94	1.26 (.97–1.65)	.08
Current use of birth control pills or hormones					
No	954 (81.8)	1		1	
Yes	163 (18.2)	0.78 (.46–1.33)	.34	1.08 (.86–1.35)	.53
Douched in past 6 mo					
No	851 (77.0)			1	
Yes	265 (23.0)			1.56 (1.28–1.90)	<.001
Frequency of douching in past 6 mo					(.001)
None	851 (77.0)			1	
>1 time/mo	82 (7.7)			1.49 (1.09–2.05)	.013
1 time/mo	91 (7.4)			1.54 (1.14–2.09)	.005
2–4 times/mo	85 (7.2)			1.63 (1.21–2.21)	.002
≥5 times/mo	7 (0.7)			1.77 (.71–4.42)	.22
Used any feminine hygiene product in past month					
No	262 (15.3)	1		1	
Tampons	395 (35.3)	2.47 (1.16–5.26)	.02	1.08 (.82–1.44)	.58
Sanitary napkins	612 (60.5)	2.35 (1.10–5.02)	.03	1.02 (.77–1.35)	.91
Feminine spray	70 (5.3)	11.66 (4.15–32.79)	<.001	1.40 (.99–1.99)	.056
Feminine powder	45 (3.3)	10.79 (3.75–31.00)	<.001	1.75 (1.23–2.49)	.002
Feminine wipes or toilettes	126 (10.6)	5.56 (2.60–11.88)	.001	1.31 (.98–1.76)	.07
Any of the above	854 (84.7)	3.04 (1.47-6.28)	.005	1.11 (.85–1.46)	.44
Vaginal problems (itching, odor, discharge) in past month					
No	935 (85.6)	1		1	
Yes	181 (14.4)	2.66 (1.57–4.49)	.001	1.36 (1.08–1.72)	.01
HIV status					
Negative	1218 (99.7)	1		1	
Positive	5 (0.3)	4.96 (.50–49.76)	.16	2.31 (.88–6.09)	.09

Abbreviations: CI, confidence interval; HPV, human papillomavirus; OR, odds ratio; RRR, relative risk ratio

^a Analyses were restricted to individuals aged 20–49 years, for whom data on douching practice (aged 14–49 years), sexual behavior (aged 20–59 years), and genital HPV DNA results (age 18–59 years) were available (unweighted n = 1271).

^b Using 2-year interview weight.

^c Using 2-year medical examination weight.

^d Index for the ratio of family income to poverty threshold, specific to family size, year, and state. A value <1 denotes a family income below the poverty threshold.

^e Current smokers included those who had smoked a cigarette in the past 30 days.

^f Including partners of both sexes.

randomizes a group of women who douche into a douching cessation arm versus a control arm to observe whether HPV incidence or redetection rates are reduced.

This study had some other limitations. First, because NHANES is cross-sectional, temporal relationships between douching and HPV outcomes cannot be inferred. Nevertheless, infection with HPV types other than 6 and 11, particularly infection with high-risk types, is often asymptomatic and thus was unlikely to result in douching. Second, douching was not well defined at the time of the survey; therefore, its definition in 2003–2004 does not align with recent definitions and classifications (eg, classification of vaginal practices by the World Health Organization Gender, Sexuality and Vaginal Practices Study Group) [15]. This makes interpretation and comparison of the results somewhat difficult.

Third, douching practice and frequencies might not be accurately reported. Fourth, in adjusted analyses, the effect of douching in the past 6 months was attenuated, and the effect of frequencies of douching became insignificant. Although these results might have been due to small numbers of cases

Table 2. Adjusted Associations Between Participants' Characteristics, Douching Practice, and HPV Infection

	No. of All Infecting HPV DNA Types (Except 6 and 11) ^a (Unweighted n = 801)		No. of Infecting HPV DNA High-Risk Types ^a (Unweighted n = 801)		
Variable	RRR (95% CI)	P Value (or P Trend)	RRR (95% CI)	P Value (or P Trend)	
Douched in past 6 mo					
No	1		1		
Yes	1.26 (1.03–1.54)	.03	1.40 (1.09–1.80)	.01	
Age group, y		(.02)		(.002)	
20–29	1		1		
30–39	0.83 (.64–1.08)	.16	0.76 (.52–1.13)	.16	
40–49	0.60 (.43–.82)	.004	0.47 (.34–.67)	<.001	
Race					
Non-Hispanic white	1		1		
Non-Hispanic black	1.23 (1.06–1.43)	.009	1.16 (.91–1.47)	.22	
Mexican American	1.25 (.87–1.80)	.20	1.20 (.90–1.59)	.20	
Other Hispanic	1.18 (.88–1.57)	.25	1.02 (.69–1.53)	.91	
Other race	1.21 (.55–2.68)	.61	1.27 (.54–3.01)	.56	
Cigarette smoking					
Never or former	1		1		
Current	1.16 (.91–1.47)	.22	1.23 (.92–1.64)	.15	
Lifetime sexual partners, No.		(.002)		(.005)	
0	1		1		
1	1.62 (.68–3.84)	.25	1.74 (.74–4.10)	.19	
2–5	4.13 (1.59–10.67)	.006	4.03 (1.61–10.12)	.006	
6–10	4.81 (1.93–11.95)	.002	3.90 (1.62-9.39)	.005	
11–20	6.21 (2.53–15.20)	.001	6.57 (2.70–16.00)	<.001	
≥21	4.47 (1.80–11.12)	.003	3.99 (1.78-8.95)	.002	
Vaginal problems (itching, odor, discharge) during past month					
No	1		1		
Yes	1.22 (1.01–1.48)	.04	1.25 (.92–1.71)	.14	

Abbreviations: CI, confidence interval; HPV, human papillomavirus; RRR, relative risk ratio.

^a Using generalized linear models with Poisson log-linear regression for count data.

in each category of the variables, they suggest that the associations observed might have been subject to residual confounders (eg, history of sexually transmitted infections, microbiome changes); thus, there may have been no association between douching and HPV infection. Finally, our analyses were restricted to a subgroup of the NHANES owing to the availability of variables of interest. Thus, some of the reported descriptive statistics (eg, weighted HPV prevalence) might not have been representative.

In conclusion, vaginal douching was associated with infection by more HPV types, including oncogenic types. Thus, douching may increase the risk of HPV-related genital cancers. There was no evidence for associations between the use of other feminine hygiene products and HPV infection.

Notes

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