Health Promotion Journal of Australia, 2013, **24**, 219–223
http://dx.doi.org/10.1071/HE13073

Sitting time, physical activity and cervical intraepithelial neoplasia in Australian women: a preliminary investigation

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Abstract

Issue addressed: Physical activity affects the immune system, which in turn may modify the risk of cervical intraepithelial neoplasia (CIN). The effect of sitting on CIN is unknown. This study investigated the relationship between sitting time, physical activity and the risk of CIN.

Methods: Community-dwelling adult women within metropolitan Perth, Western Australia, who had had a Papanicolaou (Pap) smear test at any of five clinics and medical centres, were approached by their general practitioners. In total, 348 women were recruited and interviewed for information on sitting time, physical activity level and lifetime physical activity exposure using the International Physical Activity Questionnaire (IPAQ) – short form. Associations of exposure variables with CIN risk were assessed by unconditional logistic regression analyses.

Results: The prevalence of abnormal Pap smear status indicating CIN was found to be 15.8%. Women with prolonged sitting duration ($\geq$ 42 h per week) had significantly increased risk of CIN (adjusted OR 3.49, 95% CI 1.12–10.88) than women who sat less than 24.5 h per week. Although the effect of total physical activity level was non-significant ($P = 0.408$), being always involved in physical activity during the entire life appeared to be inversely associated with the CIN risk ($P = 0.036$).

Conclusions: Prolonged sitting time was significantly associated with increased risk of abnormal Pap smear status indicating CIN.

So what? This preliminary investigation highlights a new prospect for health-promotion intervention to reduce the risk of CIN. Health practitioners should encourage women to reduce their sitting time and maintain physically active throughout their life course.

Key words: prolonged sitting, sedentary.

Received 30 August 2013, accepted 30 October 2013, published online 19 December 2013

Introduction

Vaccination is considered the most effective way to prevent primary human papillomavirus (HPV) infection by enhancing the immune system[1,2] and, to some extent, inhibiting the progression to high-grade cervical intraepithelial neoplasia (CIN). Certain lifestyle factors, such as dietary intake, cigarette smoking, alcohol consumption and physical activity, can affect the immune system and consequently modify the risk of CIN including cervical cancer.[3–5] In particular, physical activity engagement is known to improve the immune system through inhibition of the inflammatory pathways.[6,7] Physical activity also increases the circulating levels of anti-inflammatory cytokines,[8] and affects the levels of endogenous sex hormones.[7,9,10] Since the cervix epithelium is hormone-dependent,[11] increasing the metabolism of oestrogen by physical activity may affect the mechanism of HPV on the cervical tissue and the risk of high-grade CIN.[7,9,10]

Despite the apparent protective effect of physical activity, the underlying mechanism is different to that of physical inactivity or sedentary behaviour.[12–14] In particular, the impact of sitting is unknown. With increasing numbers of the population living a sedentary lifestyle and engaged in approximately 10 h of sitting time per day,[15] it is important to investigate the role of prolonged sitting in the development of CIN. The present study aimed to ascertain the relationship between sitting time, physical activity level, lifetime physical activity exposure and the risk of CIN in Australian women.

Materials and methods

Participants

During the period of 2007 to 2010, 600 community-dwelling adult women residing in metropolitan Perth, Western Australia, who had had a Papanicolaou (Pap) smear test at one of five medical centres and clinics (Parkwood Medical Centre; Murdoch Health and Counselling Service; Fremantle Women's Health; Women's Health Services, Northbridge; Women's Health Service Incorporation, Gosnells), were approached by their general practitioners to participate in the present study. Initially, eight medical centres were randomly selected from a list of clinics that provide health services to women within metropolitan Perth, but only five of them agreed to take part in the study. Females below 18 years of age, temporary residents, women who had a history of breast, ovarian or endometrial cancer, and those with a chronic debilitating disease, were excluded during the recruitment process. Following consecutive referrals from general practitioners, further screening and withdrawals, 348 women were eventually recruited and signed the written informed consent form, giving a final response rate of 58%. All subjects were assured of confidentiality and blinded to the research hypothesis. The study protocol was approved by the participating clinics and the Human Research Ethics Committee at Curtin University (approval number HR 118/2006).

Instrument and exposure measurement

A structured questionnaire was used to collect self-reported information at the face-to-face interview conducted by the third author. The first section solicited demographic, lifestyle and reproductive characteristics, including age, weight, height, education level, annual family income, alcohol consumption, cigarette smoking, use of contraceptive, use of hormone replacement therapy, number of live births and current use of condom to prevent infection. Information on sitting time and physical activity was obtained using the International Physical Activity Questionnaire (IPAQ) – short form.[16] Sitting time was measured by the question on 'total minutes spent sitting during the last seven days at work, at home, while doing course work and during leisure time, such as sitting at a desk, visiting friends, reading, or sitting or lying down to watch television'. Physical activities recorded included walking and moderate and vigorous activities undertaken in the past week that exceeded 10 min in duration. The level of physical activity was quantified in terms of metabolic equivalent tasks (MET), defined as the amount of energy or effort a person expends in performing the activity, with intensity codes 3.5, 5.0 and 7.5 MET assigned to walking, moderate and vigorous activities respectively. Total physical activity was then calculated by summing the product of MET score and activity duration over the three intensity levels.[17] Lifetime physical activity exposure was defined as 'doing active sports or vigorous exercise long enough to get sweaty, at least twice a week' throughout the life course. Participants were asked to rate their lifetime physical activity exposure on five levels: 'never been much involved'; 'previously active but not anymore'; 'active just recently'; 'intermittently active'; and 'always been involved'.[18]

The Pap smear test status was classified as either 'normal' or 'CIN' according to the result reported by the accredited St John of God Pathology, Murdoch, Australia. The classification was defined by the Australian Modified Bethesda System 2004, where abnormal Pap smear result indicating CIN includes squamous atypia, low-grade squamous intraepithelial lesion, high-grade squamous intraepithelial lesion and squamous cell carcinoma.[19] The participants were informed that their pathology tests would be accessed at the time of recruitment by their general practitioners.

Statistical analysis

Descriptive statistics were first used to summarise the characteristics of the participants. Chi-square and *t*-tests were then applied to compare women with normal and abnormal Pap smear status indicating CIN. To assess effects of sitting and physical activity on the CIN risk, separate unconditional logistic regressions were performed. Sitting time was categorised into three increasing levels of exposure based on the distribution of women with normal Pap smear status, as '<24.5 h per week', '24.5–42 h per week' and '≥42 h per week'. Total physical activity was similarly classified into '<76.75 MET-h per week', '76.75–255.15 MET-h per week' and '≥255.16 MET-h per week'. To facilitate analysis, lifetime physical activity exposure was recoded into three groups: 'never been much involved'; 'sometimes active'; and 'always been involved'.

Each fitted multivariable unconditional logistic regression model included terms for age (years), body mass index (BMI, kg m^{-2}), alcohol consumption (g day^{-1}), cigarette smoking (pack-year), education level (secondary school or below; tertiary), annual family income (<$15 000; $15 000–60 000; >$60 000), use of contraceptive (ever; never), use of hormone replacement therapy (ever; never), number of live births and current use of condom to prevent infection (yes; no). These variables were either plausible risk factors from the literature or associated with CIN based on our univariate analysis. Both crude and adjusted odds ratios (OR) and their 95% confidence intervals (CI) were calculated. All statistical analyses were performed using the SPSS package version 20 (IBM, Chicago, IL).

Results

Table 1 presents the characteristics of the 348 participants. The prevalence of CIN was found to be 15.8%. Lifestyle and reproductive characteristics were generally comparable between women with and without abnormal Pap smear results. Although total physical activity level and lifetime physical activity exposure were similar between the two groups, their reported mean sitting durations were significantly different ($P = 0.008$). On average, women with abnormal Pap smear results sat about 10 h longer per week than their normal counterparts.

Table 2 summarises the logistic regression results. After adjusting for confounding factors, women with prolonged sitting duration of

Table 1. Demographic and reproductive characteristics of participants by Pap smear status
CIN, cervical intraepithelial neoplasia; MET, metabolic equivalent tasks

Characteristics	Normal $n = 293$	CIN[A] $n = 55$	*P*-value[B]
Age: mean (s.d.), years	46.8 (13.7)	38.8 (15.2)	<0.001
Body mass index[C]: mean (s.d.), kg m^{-2}	26.1 (5.4)	25.1 (5.0)	0.223
Alcohol consumption: mean (s.d.), g day^{-1}	110.3 (143.9)	122.8 (159.0)	0.560
Cigarette smoking[C]: mean (s.d.), pack-year	26.0 (83.9)	46.38 (130.1)	0.351
Number of live births[C]: mean (s.d.)	1.7 (1.2)	1.4 (1.4)	0.212
Sitting time[C]: mean (s.d.), h per week	35.5 (20.2)	45.0 (24.3)	0.008
Total physical activity: mean (s.d.), MET-h per week	290.7 (404.4)	346.7 (589.7)	0.386
Education level: *n* (%)			0.897
Secondary school or below	205 (70.0)	38 (69.1)	
Tertiary	88 (30.0)	17 (30.9)	
Annual family income[C]: *n* (%)			0.019
<$15 000	14 (4.8)	7 (12.7)	
$15 000–$60 000	135 (46.6)	30 (54.5)	
>$60 000	141 (48.6)	18 (32.7)	
Alcohol drinking status, *n* (%)			0.928
Never drinker	44 (15.0)	8 (14.5)	
Ever drinker	249 (85.0)	47 (85.5)	
Smoking status, *n* (%)			0.143
Never smoker	187 (63.8)	29 (52.7)	
Current smoker	29 (9.9)	10 (18.2)	
Ex-smoker	77 (26.3)	16 (29.1)	
Use of contraceptive: *n* (%)			0.529
Ever	99 (33.8)	21 (38.2)	
Never	194 (66.2)	34 (61.8)	
Use of hormone replacement therapy[C]: *n* (%)			0.290
Ever	78 (26.8)	11 (20.0)	
Never	213 (73.2)	44 (80.0)	
Current use of condom to prevent infection: *n* (%)			0.366
Yes	35 (11.9)	9 (16.4)	
No	258 (88.1)	46 (83.6)	
Sitting time[C]: *n* (%)			0.033
<24.5 h per week	106 (36.2)	11 (20.0)	
24.5–42 h per week	85 (29.0)	16 (29.1)	
>42 h per week	102 (34.8)	28 (50.9)	
Total physical activity[C]: *n* (%)			0.278
<76.75 MET-h per week	43 (14.7)	8 (14.5)	
76.75–255.15 MET-h per week	27 (9.2)	9 (16.4)	
≥255.16 MET-h per week	222 (76)	38 (69.1)	
Lifetime physical activity exposure: *n* (%)			0.372
Never been much involved	17 (5.8)	5 (9.1)	
Sometimes active	154 (52.6)	32 (58.2)	
Always been involved	122 (41.6)	18 (32.7)	

[A]Abnormal Pap smear indicating cervical intraepithelial neoplasia.
[B]Chi-square test or *t*-test for difference between two groups.
[C]Missing data present.

more than 42 h per week had significantly increased risk of CIN (adjusted OR 3.49, 95% CI 1.12–10.88) than others who sat less than 24.5 h per week. Although the effect of total physical activity level was not apparent ($P = 0.408$), being always involved in physical activity during the entire life appeared to be inversely associated with CIN risk ($P = 0.036$).

Discussion

While epidemiological studies have linked prolonged sitting to poor health outcomes,[11–13,20] there is currently a lack of evidence with respect to CIN. The present study provides preliminary evidence on the potential relationship. Prolonged sitting is likely to inhibit vascular health[14,20] and lead to high homocysteine level, which in turn, increases the risk of high-grade CIN.[21] Preliminary results have suggested that this deleterious metabolic effect can be reduced by introducing breaks during the course of prolonged sitting.[22,23] Physical activity affects the insulin-mediated pathways as well as metabolic and cellular pathways, adiposity, adiponectin, hormone levels, inflammation and immune function.[4] Although physical activity level appeared to be inversely associated with the risk of CIN,

Table 2. Association between sitting time, physical activity level, lifetime physical activity exposure and abnormal Pap smear indicating cervical intraepithelial neoplasia for Australian women (*n* = 348)

MET, metabolic equivalent tasks

Variable	Crude OR (95% CI)	Adjusted OR[A] (95% CI)	*P*-value
Sitting time (h per week)			0.032
<24.5	1.00	1.00	
24.5–42	2.09 (0.89, 4.89)	2.29 (0.71, 7.33)[B]	
>42	3.41 (1.50, 7.77)	3.49 (1.12, 10.88)[B]	
Total physical activity (MET-h per week)			0.408
<76.75	1.00	1.00	
76.75–255.15	1.99 (0.67, 5.90)	1.21 (0.27, 5.50)[C]	
≥255.16	1.19 (0.50, 2.81)	0.69 (0.21, 2.31)[C]	
Lifetime physical activity exposure			0.036
Never been much involved	1.00	1.00	
Sometimes active	0.71 (0.24, 2.05)	0.61 (0.13, 2.76)	
Always been involved	0.50 (0.17, 1.53)	0.27 (0.06, 1.29)	

[A]Adjusted for age (years), body mass index (BMI, kg m^{-2}), alcohol consumption (g day^{-1}), cigarette smoking (pack-year), education level (secondary school or below; tertiary), annual family income (<$15 000; $15 000–60 000; >$60 000), use of contraceptive (ever; never), use of hormone replacement therapy (ever; never), number of live births, and current use of condom to prevent infection (yes; no).
[B]Additional adjustment for total physical activity (MET-h per week).
[C]Additional adjustment for sitting time (h per week).

the observed association did not attain statistical significance, which is consistent with previous studies.[13,24]

Conversely, our results suggest the likelihood of abnormal Pap smear indicating CIN could be reduced if women remained physically active during their entire life course. An ongoing active lifestyle, rather than irregular involvement, is required to maintain an effective innate immune system to guard against CIN. This protective effect is similar to the role of long-term physical activity in cancer prevention.[4,25–27]

Strengths of the study include the use of validated questionnaire to assess habitual physical activity exposure, classification using the Australian Modified Bethesda System and the use of accredited pathology for the confirmation of Pap smear status. The face-to-face interviews by a single investigator (third author) also eliminated inter-interviewer bias. A major limitation concerns the cross-sectional retrospective design, so that cause–effect relationship cannot be established. In addition to recruitment location bias, selection bias could not be avoided due to the large number of participant refusals and subsequent withdrawals, while randomisation was difficult to implement in the general practice setting. Another limitation is the one-off assessment of Pap smear status whereas HPV infection and CIN may regress. It is recommended to make regular assessments and collect information about lifetime sexual behaviour in future studies. While more research on physiology in relation to the immune and hormonal system is also needed to comprehend the underlying mechanism,[14] this preliminary investigation highlights another new area for health-promotion interventions to reduce the risk of CIN. Nevertheless, the findings are tentative in view of the study limitations, so that larger studies should be conducted before their generalisation to the broader community.

Conclusion

In conclusion, as with the importance of HPV vaccination and Pap smear screening, the potentially higher risk of CIN associated with prolonged sitting should be widely disseminated to women. The responsibility does not lie only on the general practitioners. All health professionals, particularly health-promotion practitioners, can implement some useful educational materials and health-promoting strategies to assist the women at risk.

Acknowledgements

The authors are grateful to the participants for taking part in the interview. The authors declare that no external funding was received and no financial or other potential conflicts of interest exist.

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