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Electric blanket (EB) use and risk of thyroid cancer in the Women's Health Initiative (WHI) observational cohort

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Abstract

Thyroid cancer disproportionately affects more women than men. The aim of this study was to assess whether exposure to extremely low frequency electric magnetic fields from electric blankets (EB) was associated with development of thyroid cancer. We analyzed data from 89,527 women who participated in the Women's Health Initiative Observational Study and who responded to questions concerning prior use of EB. During a mean follow-up of 12.2 years, we identified 190 incident cases of thyroid cancer. We estimated the hazard ratio (HR) and 95% confidence interval (CI) of incident thyroid cancer associated with EB use by Cox's proportional hazard model, adjusted for selected covariates. A majority, 57%, of the women in the cohort reported ever use of EB while sleeping and/or for warming the bed before sleep. We found no association between ever use of EB and subsequent risk of thyroid cancer (HR= 0.98, 95% CI: 0.72–1.32). Duration of EB use measured in years, months or hours had no effect on risk. These results did not change when the cases were limited to papillary thyroid cancer, the most frequently occurring histologic type. The results of this study do not support possible health hazards of EB in regards to thyroid cancer risk.

Keywords

Thyroid cancer; cohort study; electromagnetic field; postmenopausal women

INTRODUCTION

Thyroid cancer disproportionally affects women more than men. Particularly for reproductive ages (i.e., 15–44), the female/male ratio of thyroid cancer incidence reaches or exceeds 4.0, and consequently thyroid cancer is ranked as the 5th most commonly diagnosed cancer in US women (Howlader et al. 2013). In addition, thyroid cancer incidence in the US has risen more rapidly than other frequently occurring cancers, specifically since 1996 (Howlader et al. 2013) in the absence of any screening efforts suggesting a potential role for new environmental risk factors.

Exposure to ionizing radiation is the best-established risk factor for thyroid cancer (IARC, 2000). On the contrary to well quantified carcinogenic risk of ionizing radiation to humans (IARC, 2000), the effect of nonionizing radiation (except UV) on cancer risk in general has been highly controversial. Nevertheless, two previous expert reviews organized by the International Agency for Research on Cancer classified non-ionizing radiation, namely extremely low frequency (ELF) and radiofrequency (RF) electric magnetic fields (EMF), as group 2B human carcinogens (possibly carcinogenic). These conclusions were based on the observations from epidemiologic studies on childhood leukemia and adult brain cancer (IARC 2002, 2013), but the data concerning thyroid cancer have been very limited to date.

A wide range of household and personal appliances produces non-occupational exposure to EMF, but the exposure rapidly declines with distance from appliances, by the inverse square to inverse cube of distance (IARC 2002). Among various appliances, use of electric blankets (EB) has raised concern about hazardous health effects because of the combined characteristics of close proximity and prolonged hours of use. Thus far, the primary interest in epidemiologic studies of EB use has been breast cancer risk, owing to postulated effects on reproductive hormones through reduced melatonin secretion by EMF exposure (Cohen, Lippman, and Chabner 1978). These studies have, however, produced inconclusive results (IARC 2002), while a more recent large-scale cross-sectional study in postmenopausal women revealed an association between EB use for 20 years and longer and endometrial cancer (Abel et al. 2007). While reproductive hormones stimulate thyroid growth (Rahbari, Zhang, and Kebebew 2010), investigators have also found that exposure to EMF induces morphological and functional changes in the thyroid glands of rodents (Wright et al. 1984, Rajkovic et al. 2003, Rajkovic, Matavulj, and Johansson 2005). Hence, it is plausible that EMF exposure may modulate thyroid cancer risk in humans, although age at exposure may be critical for thyroid carcinogenesis as with ionizing radiation (IARC 2000). This study was the first of which we are aware to examine the association between EB use and thyroid cancer incidence in a prospective cohort study.

MATERIALS AND METHODS

Study participants

The women included in this study were a subset of participants in the Women's Health Initiative (WHI). The WHI was designed to address major causes of morbidity and mortality in postmenopausal women consisting of both multicenter clinical trials and an observational study (OS). This study was based on the OS cohort only. Other publications have described the details of the scientific rationale, eligibility requirements, baseline participant characteristics and measurement reliability of the WHI OS participants (Hays et al. 2003, Langer et al. 2003). Briefly, participants were women 50–79 years of age, recruited at 40 clinical centers throughout the United States between September 1, 1993, and December 31, 1998. Institutional Review Boards at all 40 clinical centers and at the coordinating center and a study-wide data and safety monitoring board oversaw the study. All participants in the WHI gave informed signed consent. At enrollment, participants completed self-administered questionnaires to provide information concerning demographic, medical and reproductive and lifestyle factors. In addition, OS participants (not clinical trial participants) answered five questions about EB use, ever use, current use, use only to warm the bed before sleep, number of years used, and average number of months used per year. The definition of EB in this questionnaire was inclusive of electric heating pad, electric mattress pad and heated water bed in addition to blankets.

Follow-up and ascertainment of cases

Incident thyroid cancer cases were identified by self-administered questionnaires annually throughout the study, with all cases confirmed by medical record review (Curb et al. 2003). All primary thyroid cancer cases were coded centrally in accordance with the Surveillance Epidemiology and End Results (National Cancer Institute) coding guidelines. For these analyses, participants were followed up to first thyroid cancer diagnosis, date of death, loss to follow-up, or end of WHI clinical trial or observational study follow-up (September 30, 2012), whichever occurred first. Only 2.35% of the cohort was lost to follow up at the end of the follow-up.

Statistical analysis

We computed hazard ratios (HR) and 95% confidence intervals (CI) using the Cox proportional hazard model. We tested potential covariates one at a time in a model that also included an indicator variable for participation in the extension study period. We selected these explanatory variables because they were basic demographic variables or a known strong risk factor (benign thyroid disease) or were reported as potential risk factors for thyroid cancer or as causal confounders with electric blanket use in earlier studies (Dal Maso et al. 2009, Abel et al. 2007, Kabat et al. 2012, Kitahara et al. 2012, Rahbari, Zhang, and Kebebew 2010). The “final” multivariable model included potential risk factors that altered the regression coefficient for the main exposure variable, electric blanket use, by at least 10% in addition to a known strong risk factor, a history of benign thyroid disease. We computed summary exposure indices (cumulative months/hours of use) using median values of each category of the number of years of use (<1, 1–4, 5–9, 10–19, ≥20), months of use per year (<1, 1–3, 4–6, 7–9, 10–12) and hours of sleep per day, because these data were

originally provided as categorical variables. For the bottom and top categories, we used the upper and lower bounds of these categories. We calculated these indices for women who used EB while sleeping (not warming before sleep only). Then, we grouped the main exposure variables into quartile levels to calculate the HR for each level, compared with the lowest quartile as the reference. We performed tests for linear trend in HRs for these variables using ordinal scores of each category as well as a continuous variable. After the exclusion of women who did not answer questions about EB use, those with missing covariates or with prevalent thyroid cancer, 89,527 (95.6%) of the original OS cohort remained in the analyses. We repeated analyses by limiting the cases to those diagnosed with papillary type thyroid cancer, the most frequently occurring type of thyroid cancer, excluding other types of thyroid cancer from the study population.

RESULTS

During 1,092,578.45 person-years (PY) of follow-up (average 12.2 years), a total of 190 incident thyroid cancer cases were diagnosed. The vast majority (79%) were papillary, followed by follicular/oxyphilic (12%) and medullary (5%) types.. Ever users of EB tended more to be white, from Western rather than Northeastern regions, lean and tall, menopausal hormone users and never users of oral contraceptives (Table 1). All characteristics tested were statistically significantly different between the two users and non-users of EBs.

Thyroid cancer incidence in this cohort decreased with age. The HR for an increase in age by 10 years was 0.79 (95% CI 0.55–0.97). The women who were enrolled in the northeast region of the US had a significantly higher incidence of thyroid cancer compared with those in the west region (HR=1.60, 95% CI 1.08–2.36). Other sociodemographic factors were not associated with thyroid cancer risk. History of any type of benign thyroid disease significantly increased the subsequent incidence of thyroid cancer (HR=1.56, 95% CI 1.16–2.11), while the HR progressively increased with increasing body height (HR for 10 cm increase in height = 1.40, 95% CI 1.12–1.75). Other reproductive histories and alcohol use had modest insignificant associations with thyroid cancer risk (Table 2).

Ever use of EBs at baseline was reported by 57% of the cohort. The bivariable HR associated with ever use of EBs was 0.96 (95% CI 0.72–1.27). Among the potential covariates that were tested in the bivariable model one at a time, race, location of recruitment, family income level, body height (continuous), body mass index categories, menopausal hormone and oral contraceptive use modified the regression coefficient for EB use by at least 10% and thus remained in the subsequent multivariable model in addition to the established risk factor, a history of benign thyroid diseases. The final multivariable adjusted HR for thyroid cancer risk associated with EB use was not significantly different from unity (HR=0.98, 95% CI; 0.72–1.32) (Table 3).

We found no differences in the HRs with either past or current use of EB at the time of enrollment, or either use while sleeping or use for only warming the bed before retiring for sleep (Table 3). When we computed the HRs according to cumulative exposure indices for those who used EB while sleeping, we did not find any indication that the risk of thyroid cancer increased with the total years of use, total months of use, or total hours of use. These

results did not change when we limited the cases to papillary thyroid cancer only. For example, the HR associated with ever use associated with papillary thyroid cancer was 0.99 (95% CI 0.71, 1.39).

DISCUSSION

The results of this prospective cohort study did not support the hypothesis that exposure to ELF/EMF through EB use increased the risk of developing thyroid cancer. EB use was fairly frequent in this cohort (57%), but we did not find any indication that prolonged or more robust exposure was associated with the risk of thyroid cancer. On the other hand, Lope et al reported a significantly elevated standardized incidence ratio for thyroid cancer among female electric installation workers in a Swedish census cohort, whose median age at diagnosis was approximately 55 years (Lope et al. 2005), although a subsequent study based on job exposure matrixes did not confirm the direct association with estimated exposure levels to thyroid cancer incidence (Lope et al. 2006). Moreover, the recent data from the WHI cohort revealed an association between sleep disturbance and thyroid cancer risk, suggesting a possible link to melatonin (Luo et al. 2013).

We acknowledge several limitations that were present in this study. First, although this was a prospective study, the information about EB use was based on retrospective recall and thus subject to large measurement error, which may have attenuated the risk estimates.

Furthermore, we did not collect the information about the exact timing of exposure in terms of age and calendar years. In addition, the WHI questionnaire did not ask about age at first use, and recorded the duration in categories with the highest category including the duration of 20 years or longer altogether. In response to public controversy about health hazards from use EBs, manufacturers have improved their technologies to reduce EMF exposure in newer models of EBs, while some older models may produce a significant EMF even when turned off (if not unplugged) (Woodward 2013). Hence, EB use limited to more recent years was likely to lead to lower exposure. Second, age at exposure may be critical for thyroid carcinogenesis as documented for the association of ionizing radiation with thyroid cancer, indicating the excess risk limited to exposure before age 20 years (IARC 2000). Age-dependent susceptibility may be modulated through the interactions with host hormonal milieu, e.g., growth hormone and sex steroids. Also, body height has been consistently positively associated with thyroid cancer risk in epidemiologic studies (Dal Maso et al. 2009, Rinaldi et al. 2012), including in this study. These observations suggest that the thyroid gland is more vulnerable during a period of growth. If this is the case, a substantial proportion of our cohort members who were born in the period 1914–1948 did not have exposure during and before puberty, as EBs were not widely available until the late 1930s (Woodward 2013). Even if EBs had been available, the reliability of memory regarding assessing exposure in such a distant past may have posed a recall problem. The lack of exposure information in the etiologically more relevant period (10–25 years ago) would have reduced the strength of the association, if any.

An additional important limitation of the study was the lack of EMF dosimetry data. In contrast to studies on ionizing radiation, the use of personal dosimeters for EMF has been limited in research studies (Swanson and Kaune 1999). While investigators have often

assessed occupational exposure to EMF in the form of a job-exposure matrix (Feychting 2013), the measurement of residential exposure from home appliances and wiring has largely relied on portable magnetic field dosimeters in participants' bedrooms and other home locations for a limited time period, e.g., spot measurements or measuring from 24 hours to 7 days (Swanson and Kaune 1999). These measurements did not necessarily include EMF from EBs because EB use is highly dependent on seasons of the year. In other cases, investigators obtained direct measurements of EMF from EBs in a laboratory setting using a limited number of EBs, but the data seemed to vary with blanket types and manufactured years (Wilson et al. 1996, Lee et al. 2000, Florig and Hoburg 1990). To date, the vast majority of epidemiologic studies concerning EB use and cancer have been based on questionnaire data only, except one population-based case-control study on breast cancer in Seattle, which incorporated bedroom magnetic field measurements (Davis, Mirick, and Stevens 2002). Similar to other studies, our study did not compile information to grade relative exposure intensity, such as EB brand, date of purchase, and typical mode of setting (high, medium or low).

Other potential limitations included the lack of information concerning an established risk factor for thyroid cancer, i.e., ionizing radiation. However, unless ionizing radiation exposure was inversely associated with EB use, we cannot explain the null association by a failure to incorporate ionizing radiation exposure into the model. Furthermore, our cohort consisting of postmenopausal women did not allow us to investigate thyroid cancer occurring before the age of 50 years. This could reduce the excess risk from exposure to some extent, although effects of ionizing radiation persist for more than 50 years (Furukawa et al. 2013). In addition, WHI did not collect information regarding the use of other electronic items in one's daily life, such as vibrating massagers, electric shavers, audio systems, personal computers, cell phones, TV, humidifiers, microwave ovens, electric stoves, hair dryers, etc., which may have cumulatively contributed to women's EMF exposure. Finally, we are aware that the number of incident cases of 190 was not sufficient to detect a modest effect size (i.e., $HR < 1.5$), even in the absence of measurement error, and the 95% CIs from this study did not enable us to rule out a small effect. Collectively, non-differential measurement errors in combination with the relatively small number of cases would have attenuated or hidden any real effect (if one existed).

On the other hand, this study had several strengths, including a large cohort consisting of geographically and ethnically diverse populations, the prospective study design in which exposure information was less likely to be biased and less likely to be affected by the presence of the disease, high quality data, high completeness of follow up and availability of information about a wide range of potential confounders.

Although only a few epidemiologic studies have specifically addressed the association between ELF/EMF exposure and thyroid cancer risk, the accumulated data to date from studies on breast cancer, which is also a hormone-sensitive cancer, corroborate the absence of an association (Feychting 2013). In addition, we are aware of no new experimental findings in support of the specific effect of use of EBs on the thyroid gland. Thus, given progress in the technology in reducing EMF emitted from EBs, it is unlikely that the use of these heating devices, particularly in recent models, poses serious carcinogenic risks to

human adults. Rather epidemiologic surveillance efforts should be redirected toward new personal/home appliances and products that may introduce other types of physical, chemical or biological exposure into our environments and to focus on risks associated with ELF/EMF exposures that occur at vulnerable times, e.g., during growth periods.

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Table 1

Characteristics of WHI study participants according to electric blanket use status

Variables	Categories	Electric blanket use	
		Never user	Ever user
Age (years)	50–59	12180(31.84%)	16254(31.70%)
	60–69	17102(44.71%)	22308(43.50%)
	70–79	8966(23.44%)	12717(24.80%)
Race	White	28739(75.14%)	46116(89.93%)
	Non-white	9509(24.86%)	5163(10.07%)
Region	Northeast	10507(27.47%)	10049(19.60%)
	South	10242(26.78%)	12906(25.17%)
	Midwest	8599(22.48%)	11160(21.76%)
	West	8900(23.27%)	17164(33.47%)
Annual Family income	Missing	3061(8.00%)	3434(6.70%)
	< \$20,000	6516(17.04%)	6640(12.95%)
	\$20,000 – \$34,999	8240(21.54%)	11089(21.62%)
	\$35,000 – \$49,999	6822(17.84%)	9930(19.36%)
	\$50,000 – \$74,999	6831(17.86%)	9961(19.43%)
	\$75,000 +	6778(17.72%)	10225(19.94%)
History of Benign thyroid disease	Missing	250(0.65%)	303(0.59%)
	No	29457(77.02%)	37311(72.76%)
	Yes	8541(22.33%)	13665(26.65%)
BMI (kg/m ²)	<25	14492(37.89%)	22180(43.25%)
	25 – <30	13063(34.15%)	17378(33.89%)
	30	10693(27.96%)	11721(22.86%)
Height (cm)	< 160	15962(41.73%)	18269(35.63%)
	160–170	18872(49.34%)	27439(53.51%)
	170+	3414(8.93%)	5571(10.86%)
Ever Oral contraceptive use	Yes	13798(36.08%)	22254(43.40%)
	No	24450(63.92%)	29025(56.60%)
Ever Menopausal hormone use	No	18262(47.75%)	17889(34.89%)
	Yes	19986(52.25%)	33390(65.11%)

Table 2

Number of cases, incidence rates (per 100,000 person years), and bi-variable hazard ratios (HR) of thyroid cancer and 95% confidence intervals (CI) according to potential confounding factors

Variables	Categories	No. Cases	Person-years	Rate	HR (95% CI)
Age (years)	50–59	76	373735.03	20.4	Ref
	60–69	88	483678.63	18.2	0.88 (0.65, 1.20)
	70–79	26	235164.80	11.1	0.55 (0.35, 0.85)
	Trend, per 10 year increase				0.79 (0.65, 0.97)
Race	White	170	938709.86	18.1	Ref
	Non-white	20	153868.59	13.0	0.76 (0.47, 1.21)
Region	Northeast	59	259768.01	22.7	1.60 (1.08, 2.36)
	South	52	276363.76	18.8	1.33 (0.89, 1.99)
	Midwest	35	242573.20	14.4	1.01 (0.65, 1.58)
	West	44	313873.48	14.0	Ref
Annual Family income	Missing	15	72445.035	20.7	1.69 (0.85, 3.39)
	< \$20,000	17	140364.97	12.1	Ref
	\$20,000 – \$34,999	31	229017.94	13.5	1.09 (0.60, 1.97)
	\$35,000 – \$49,999	34	207879.23	16.4	1.30 (0.73, 2.33)
	\$50,000 – \$74,999	43	215745.47	20.0	1.58 (0.90, 2.77)
	\$75,000 +	50	227125.81	22.1	1.73 (1.00, 3.01)
	Trend by categories				1.09 (0.99, 1.20)
History Benign thyroid disease	No	123	815763.28	15.1	Ref
	Yes	64	270806.61	23.7	1.56 (1.16, 2.11)
BMI (kg/m ²)	<25	71	460982.06	15.4	Ref
	25 – <30	68	371965.81	18.3	1.19 (0.85, 1.66)
	≥30	51	259630.59	19.7	1.30 (0.91, 1.86)
	Trend by categories				1.14 (0.96, 1.37)
Height (cm)	< 160	65	403326.13	16.1	Ref
	160–170	97	574649.34	16.9	1.04 (0.76, 1.42)
	170+	28	114602.98	24.5	1.50 (0.96, 2.33)
	Trend, per 10 cm increase				1.40 (1.12, 1.75)

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Variables	Categories	No. Cases	Person-years	Rate	HR (95% CI)
Ever Oral contraceptive use	Yes	87	462363.86	18.8	1.14 (0.86, 1.52)
	No	103	630214.59	16.4	Ref
Ever Menopausal hormone use	No	84	424697.73	19.7	Ref
	Yes	107	667880.72	16.0	0.80 (0.60, 1.06)

Adjusted for participation in the extension phase.

Number of cases, incidence rates (per 100,000 person years), and multivariable hazard ratios (HR) of thyroid cancer and 95% confidence intervals (CI) according to electronic blanket (EB) use

Table 3

Variables	Categories	No. Cases	Person-years	Rate	HR (95% CI)
Ever Use	No	80	452153.49	17.7	Ref
	Yes	110	640424.96	17.2	0.98(0.72,1.32)
Former/Current Use	Never	80	452153.49	17.7	Ref
	Former	65	368658.62	17.7	1.00(0.71,1.40)
Type of use	Current	45	270805.61	16.6	0.95(0.65,1.39)
	Never	80	452153.49	17.7	Ref
Years of use	Warning only	37	170755.45	21.7	1.23(0.82,1.83)
	Most of the time	73	468240.04	15.6	0.89(0.64,1.23)
Total months of use	Never/Warning only	117	622908.94	18.8	Ref
	< 1	9	28048.09	32.1	1.71(0.87,3.38)
Trend	1–4	18	119540.25	15.1	0.79(0.48,1.31)
	5–9	16	108879.03	14.7	0.77(0.46,1.31)
Total hours of use	10–19	12	106091.99	11.3	0.60(0.33,1.10)
	20+	18	105489.14	17.1	0.92(0.55,1.52)
Total months of use	Never/Warning only	117	622908.94	18.8	Ref
	Q1: 0–12.5	19	100664.20	18.9	1.00(0.62,1.63)
Trend	Q2: 12.5–35	16	109712.32	14.6	0.77(0.45,1.30)
	Q3: 35–100	18	131928.04	13.7	0.72(0.44,1.20)
Total hours of use	Q4: 100–220	20	125350.68	16.0	0.86(0.53,1.40)
	Trend				0.93 (0.84, 1.03)
Total months of use	Never/Warning only	117	622908.94	18.8	Ref
	Q1: 0–2520	23	107240.80	21.4	1.13(0.72,1.78)
Trend	Q2: 2520–7350	13	105961.16	12.3	0.65(0.36,1.15)
	Q3: 7350–18000	18	105629.26	17.1	0.91(0.55,1.50)
Total hours of use	Q4: 18000–66000	16	120242.89	13.3	0.72(0.42,1.23)
	Trend				0.92 (0.83, 1.03)

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Adjusted for participation in the extension phase, race, region, family income level (ordinal), family income unknown, body height (continuous), BMI level (ordinal), menopausal hormone use, oral contraceptive use and history of benign thyroid disease.