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Research Article

Wood Dust Exposure and Risk of Sinonasal and Nasopharyngeal Cancer: A Meta-Analysis

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Abstract

Objectives: In order to examine association between wood dust exposure and sin nasal and nasopharyngeal cancer.

Methods: We performed a systematic search of the literature. Both random and fixed effects were used to calculate odd ratios (ORs) and 95% confidence intervals (95%CIs) of each study.

Results: A significant increased risk of sinonasal and nasopharyngeal cancer was associated with wood dust exposure. The ORs for sinonasal cancer were 7.78 (CI: 2.97-20.25) among adenocarcinoma studies and 1.18 (CI: 0.64-2.19) among squalors cell carcinoma studies. Contrary to women (OR=2.11, CI: 0.71-6.32), an elevated risk of sinonasal cancer was observed among men (OR=2.29, CI: 1.55-3.41). The OR for nasopharyngeal cancer was 1.87 (CI: 1.57-2.38).

Conclusion: Wood dust exposure was a high risk associated with sinosnasal and nasopharyngeal cancer. Except for female and squalors cell carcinoma studies in sinosnasal cancer, all stratifications in our meta-analysis present a significant risk between sinosnasal or nasopharyngeal cancer and wood dust exposure.

Keywords: Wood Dust; Sinonasal; Nasopharyngeal; Cancer; Meta-Analysis

Introduction

Sinonasal and nasopharyngeal cancer had often been related to occupational exposure. Sinonasal cancer was a rare disease with annual incidence rates around 1 per 100000 in many countries [1]. The association between nasal cancer and wood dust exposure was first concentrated from a clustering of this rare cancer in High Wycombe, a furniture-making center in central England [2], and various studies have confirmed the finding from then on [3-6]. Exposure to wood dust was also recognized as a risk factor for nasopharyngeal [7]. The study in Britain and United States involving approximately 29000 wood workers revealed evidence of association between exposure to wood dust and the risk of nasopharyngeal cancer [8].

Wood dust was classified as a human carcinogen by the International Agency for Research on cancer in October, 1994 [9]. Wood workers did their jobs in different occupations such as carpenters; sawmill workers and small boat constructors. All of them were exposed to a certain amount of wood dust. A reanalysis of data from five cohorts of workers in wood-related industries confirmed the association between sinonasal cancer and wood dust exposure [8]. Especially nasal adenocarcinoma showed a strong correspondence with occupational exposure to hardwood dust in furniture industries [10]. Another Thai population study identified that wood dust might be associated with an increase risk of nasopharyngeal cancer [11]. Thomas [12] took a further analysis of exposure to wood dust which focused on the 142 cases of nasopharyngeal cancer. After adjusted for the main risk factor, there was only weak evidence of an association with ever working in a job with potential exposure (OR=1.5; 95% CI: 0.7 to 3.3). Hence we preformed a meta-analysis of all eligible case-control studies to derive a more precise estimation of the association to help us better understand that the wood dust exposure possible influence on sinonasal and nasopharyngeal cancer. Our study mostly referred to sinonasal and nasopharyngeal cancer occurring in an occupational setting.

Methods

Data source and searches

We searched articles with search term "sinonasa" or "nasopharyngeal", "cancer" or "carcinoma" and "case-control study", in the Medline database utilizing Pub Med engine, with the search from January 1, 1980 through April 1, 2013. We assessed all associated publications to retrieve eligible literature. And their reference lists were searched manually to identify other relevant publications. All of the results were limited to case-control study and English-language papers.

Data inclusion and exclusion criteria

We included studies which present original data from case control studies. The following inclusion criteria were used to choose studies for further analysis: (1) published in peer-reviewed journals, (2) described explicitly occupational expose to wood dust, (3) diagnosed sinonasal and nasopharyngeal cancer exactly and (4) provided odd ratios (ORs) or gave enough data to allow us to calculate it. Meanwhile we selected studies that analyzed data on wood workers as a subgroup analysis.

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Data extraction and quality assessment

Two reviewers abstracted information from all eligible publications independently, according to the inclusion and exclusion criteria mentioned above. The same two reviewers accessed the quality of the studies independently according to the predefined score scale for quality assessment (Table1). These scores were based on traditional epidemiological considerations, cancer genetic issues and Newcastle-Ottawa scale [13-15]. Both reviewers resolved any disagreement by discussion. Total scores ranged from 0 (worst) to 15 (best). Reports scoring <10 were classified as "low quality", and those 10 as "high quality".

Statistical analysis

Crude odd ratios (ORs) and 95% confidence intervals (CIs) were used to access the strength of association between sinonasal and nasopharyngeal cancer and wood dust exposure in each case-control study. We then pooled them together to be in a subsequent study. The pooled ORs were performed according to both fixed and random effects. We also preferentially used the latter when heterogeneity was present. The fixed effects model assumed that the results and that their variations were due to sampling only, and that was to say no variance between studies. The random effects model, on the contrary, assumed that study results are heterogeneous. The random effects model yields pooled results have wider confidence intervals which are less precise in nature but are closer to the true value if heterogeneity exists [15]. DerSimonian and Laird Q test was used to check for heterogeneity. The null hypothesis of the test is absence of heterogeneity. To quantify it, we subsequent calculated the proportion of the total variance depend on "between-study variance (Ri statistic)" [16]. We also analyzed the subgroup of studies defined by study characteristics such as type of controls (hospital-based or population-based), gender and ethnicity.

Table1. Scale for quality assessment.

Criterion	score
Source of cases	
Selected from population or cancer registry	3
Selected from hospital	2
Selected from pathology archives, but without description	1
Not described	0
Source of control	
Population-based	3
Neighborhood or volunteers	2
Hospital-based	1
Not described	0
Wood dust exposure	
Assess through job matrix	3
Assess through questionnaire	0
Regulation	
Adjusted by age, sex, and smoking	3
Not Adjusted by age, sex, and smoking	0
Total sample size	
≥1000	3
≥500 and <1000	2
≥200 and <500	1
<200	0

We used Egger's linear regression test by visual inspection of the funnel plot to estimate potential publication bias. $P<0.05$ was considered representative of statistically significant publication bias [14,17]. All of the statistical tests were performed with the STATA software, version 11.0 (State Corporation, College Station, TX).

Results

We retrieved 409 articles and finally included 20 case-control studies that met our criteria. They were published from 1980 to 2010 and carried in 10 countries, contained 10 sinonasal cancer studies and 10 nasopharyngeal cancer studies. During the extraction of data, two studies were excluded, one was lack of data to calculate OR and 95%CI for us [18], another was conducted by the same first author from France [19].

The characteristics of these 20 case-control studies were summarized in Table 2. The amounts of the sinonasal and nasopharyngeal cancer studies were equal. Approximate two thirds of cases source were from hospital. Table 3 showed that, two types of cancer pooled together in the meta-analysis, and there was a significant association between the risk of sinonasal and nasopharyngeal cancer and wood dust exposure (random effect pooled OR=2.30, 95%CI: 1.83-2.91). In spite of heterogeneity was high when all studies pooled together, the two different effect estimate methods were similar with each other and showed a significant increase in the risk. Cases source from hospital showed a random effect pooled OR which was higher than that from population (OR=2.52, 95%CI: 1.83-3.47 for hospital cases and OR=1.99, 95%CI: 1.39-2.86 for population). Meanwhile Caucasians also indicated a higher risk associated with sinonasal and nasopharyngeal cancer than Asians (OR=2.59, 95%CI: 1.71-3.92 for Caucasians and OR=2.03, 95%CI: 1.69-2.44 for Asians). Except for Asians case–control pooled studies, heterogeneity did not subside when we strained our data according to study design. Furthermore, we performed subgroup analysis according to quality score scale of all studies. A risk associated with wood dust exposure and sinonasal and nasopharyngeal cancer was observed in both high and low quality

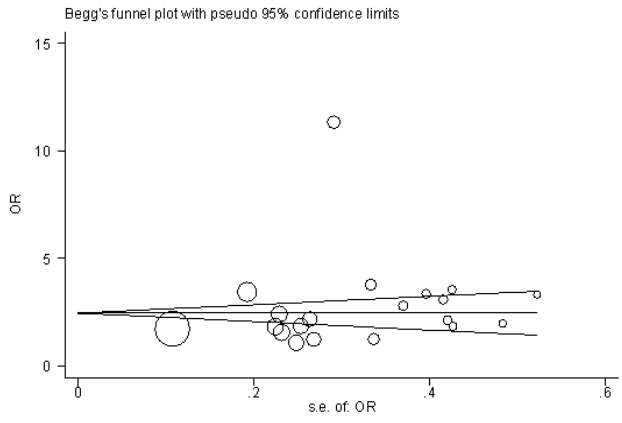

Figure 1: Begg's funnel plot of wood dust exposure and sinonasal and nasopharyngeal cancer risk for homozygote comparison. Each circle size indicates proportional to the sample size.

Table2: Baseline characteristics and summary OR of studies included in the meta-analysis.

First author, year	country	Year of study	OR (CI95%)	Source of cases	Source of control	Type of interview	Case/Control cases
[1]	Italy	1996-2000	11.4(6.29-20.74)	H	H	In person	113/336
[25]	Germany	1996-2000	11.2(5.4-27.8)	H	H	In person	58/85
[26]	Germany	1994-2003	2.69 (1.24-5.81)	P	P	In person	86/204
[22]	European*	1970-1989	1.73(1.40-2.14)	P	P	In person	555/1705
[3]	Netherland	1978-1981	1.7(1.0-2.9)	H	P	In person	91/195
[27]	USA	1935-1975	4.0(1.5-10.8)	H	P	In person	301/857
[6]	USA	1979-1987	7.3(1.4-34.2)	P	P	In person	465/1099
[28]	Germany	1986-1988	3.44(2.36-5.02)	p	p	In person	135/747
[29]	Italy	1982-1987	2.79(1.35-5.75)	H	H	In person+mail+telephone	78/254
[30]	China	1988-1990	1.9(0.7-5.0)	P	P	In person	60/414
[31]	USA	1982-1998	2.15(0.98-4.72)	H	H	In person	90/1522
[32]	USA	1987-1993	1.5(0.7-3.3)	p	p	Telephone	142/244
[33]	China	1991-1994	1.7(1.0-3.0)	H	N	In person	375/325
[34]	China	1986	5.4(1.5-19.8)	P	N	In person	88/176
[35]	Thailand	1987-1990	8.0(2.3-28.2)	H	H	In person	120/120
[36]	China	2001-2004	5.82(2.5-13.6)	H	H	In person	1049/785
[11]	Thailand	2007-2008	1.63(1.02-2.61)	H	P	In person	327/327
[24]	China	1996	1.23(0.73-2.08)	H	H	In person	323/1119
	Malaysia	1990-1992	2.36(1.33-4.19)	H	N	In person	282/282
[37]	Malaysia	1990-1992	2.36(1.33-4.19)	H	N	In person	282/282
[38]	Malaysia	1973-1980	1.84(0.80-4.25)	H	N	In person	100/100

*Including Netherlands, France, Germany and Sweden.
H=hospital; P=population; N=neighborhood.

Table 3: Pooled odds ratios (ORs) and 95% confidence intervals (CIs) of sinonasal and nasopharyngeal among exposed wood dust people.

	Number of studies	OR(95%CI) fixed effect	OR(95%CI) random effect	Ri*	Test for Heterogeneity *P*
all studies	20	2.12(1.90-2.37)	2.30(1.83-2.91)	0.182	0.000
Population based	7	1.93(1.66-2.25)	1.99(1.39-2.86)	0.151	0.002
Hospital based	13	2.35(2.01-2.75)	2.52(1.83-3.47)	0.236	0.000
Caucasians	10	2.19(1.91-2.51)	2.59(1.71-3.92)	0.349	0.000
Asian	10	2.03(1.69-2.44)	2.01(1.67-2.42)	0.000	0.620
Quality score<10	11	2.41(2.01-2.89)	2.56(1.73-3.79)	0.324	0.000
Quality score≥10	10	1.98(1.72-2.27)	2.07(1.67-2.73)	0.11	0.003
Sinonasal	10	2.32(2.10-2.67)	2.83(1.88-4.27)	0.335	0.000
ADs**	6	8.67(6.64-11.32)	7.78(2.97-20.25)	1.102	0.000
SCCs**	6	0.89(0.69-1.14)	1.18(0.64-2.19)	0.380	0.001
Male only	4	1.92(1.59-2.32)	2.29(1.55-3.41)	0.093	0.058
Female only	2	2.11(0.71-6.32)	2.11(0.70-6.35)	0.000	0.764
Population based	5	1.98(1.68-2.32)	2.14(1.37-3.35)	0.188	0.001
Hospital based	5	3.90(2.93-5.25)	3.86(1.95-7.68)	0.473	0.001
Caucasians	8	2.34(2.02-2.71)	3.05(1.85-5.02)	0.418	0.000
Asian	2	2.14(1.36-3.37)	2.13(1.36-3.36)	0.000	0.860
Nasopharyngeal	10	1.87(1.57-2.38)	1.85(1.54-2.23)	0.005	0.395
Population based	3	1.64(1.05-2.57)	1.63(1.04-2.56)	0.034	0.545
Hospital based	7	2.00(1.63-2.47)	1.99(1.58-2.52)	0.010	0.318
Caucasians	2	1.45(1.00-2.11)	1.45(1.00-2.11)	0.000	0.580
Asian	8	2.05(1.64-2.55)	2.04(1.59-2.61)	0.016	0.325

*Proportion of total variance due to between-study variance.
**ADs= Adenocarcinomas, SCCs= Squamous cell carcinomas

score, however, the OR of high quality score studies was a slightly smaller than that of low quality score studies(OR=2.56, 95%CI: 1.73-3.79 for low quality score and OR=2.07, 95%CI: 1.56-2.73 for high quality score).

The funnel plot (Figure1) seemed to be slightly skewed to one side. However, we found no further evidence of publication bias through Egger's test (P=0.312). Neither Bag's funnel plot nor Egger's test detected any obvious evidence of publication bias in any subgroup analysis (data not shown).

Sinonasal cancer

We examined wood dust exposure associated with the risk of sinonasal cancer, which indicated that the risk of snonasal cancer was higher among wood dust exposure than the general population (OR=2.83, 95%CI: 1.88-4.27). Then we accessed two histologic types of sinonasal cancer, adenocarcinoma and squalors cell carcinoma. The former one had a high risk association with wood dust exposure (OR=7.78, 95%CI: 2.97-20.25). On the contrary, the latter one presented no evidence of a significant association (OR=1.18, 95%CI: 0.64-2.19). For gender analysis, male had a risk of sinonasal cancer associate with exposing in wood dust (OR=1.92, 95%CI: 1.59-2.32), but female did not (OR=2.11, 95%CI: 0.71-6.23). As the above, cases source from hospital showed a random effect pooled OR that was higher than that from population (OR=3.86, 95%CI: 1.95-7.68 for hospital cases and OR=2.14, 95%CI: 1.37-3.35 for population cases). So did ethnic analysis, Caucasians showed a higher OR than Asians (OR=3.05, 95%CI: 1.85-5.02 for Caucasians and OR=2.14, 95%CI: 1.36-3.37 for Asians).

Nasopharyngeal cancer

We pooled 10 nasopharyngeal cancer case-control studies to assess the risk of wood dust exposure. Pooled analysis indicated that wood dust exposure was a significant risk in nasopharyngeal cancer (OR=1.87, 95%CI: 1.57-2.38). Contrary to sinonasal cancer, Caucasians showed a lower OR than Asians (OR=1.45, 95%CI: 1.00-2.11 for Caucasians and OR=2.05, 95%CI: 1.64-2.55 for Asians). Cases from hospital and population showed a high risk in nasopharyngeal cancer associated with wood dust exposure (hospital based: OR=2.00, 95%CI: 1.63-2.47; population based: OR=1.64, 95%CI: 1.05-2.57).

Discussion

The results of this meta-analysis, based on 20 independent studies totaling 15214 samples, suggested that wood dust exposure was a risk factor to sinonasal and nasopharyngeal cancer. We found that the result of relationship between wood dust exposure and squamous cell carcinoma of sinonasal cancer met the results of Demers' [20]. Their results present ambiguous picture of squamous cell carcinoma. A research group using census data on industry and occupation in Sweden found a no significant odds ratio for squamous cell nasal cancer for workers in wood industry [21]. Our 6 case-control pooled studies analysis indicated that there was no association between squamous cell carcinoma and wood dust exposure. But the result of relationship between wood dust exposure and adenocarcinoma of sinonasal cancer was opposite to Demers'. Excess risk observed for wood dust was particularly high for adenocarcinoma [1,22].

In contrast to the results for men, the result of women presented no relationship with sinonasal cancer and wood dust exposure. Even though based on small numbers, the relationship was available for wood dust exposure (test for heterogeneity: *P*=0.764). Blot [23] also indicated that women had no clear dose-response trend was seen with exposure levels, and the number of women who held wood-dust-related jobs was small. It was possible that the low prevalence of employment in wood-related worker for women induce no association. For further analysis, we will need more cases to assess the risk.

A Chinese research suggested that wood dust exposure might associate with an increased risk of nasopharyngeal cancer [24]. Indeed, wood dust exposure indicated a high risk in nasopharyngeal cancer when we pooled 10 studies together in our meta-analysis. Interestingly, stratification by ethnic origin showed that Asians present a higher risk than Caucasians in nasopharyngeal cancer. To the contrary, Asians present a lower risk than Caucasians in snonasal cancer. Some previous studies [11,24] indicated that nasopharyngeal cancer is rare in most populations (general<1 per 100,000) but common in Southern China and Southeast Asia (20 to 40 per 100,000). It suggested that the existence of interactions between genetic susceptibility to nasopharyngeal cancer and environmental factor. Otherwise, when we stratified cases source separately by hospital-based and population-based nasopharyngeal cancer studies, hospital-based studies had a higher risk than population-based studies in wood dust exposure. The difference suggested that selection bias was a major problem for studies of wood dust exposure of nasopharyngeal cancer. In these 10 studies, the source of controls was familiar with the source of cases. And hospital-based controls may not be truly representative of the general population. Therefore, a methodologically preferable design was a key to avoid selection bias, such as using non-related subjects which were recruited from the same source population as controls.

Our meta-analysis also had many limitations. First of all, all of the eligible studies were case-control studies and published in English. It was possible that some studies published in other language or some unpublished studies in English were missed. Thus, some publication bias was inevitable although the funnel plot suggested no remarkable publication in our meta-analysis. Second, we only performed 2 Asian studies in sinosnasal cancer and 2 Caucasian studies in nasopharyngeal cancer. Thus, more other studies were warranted to evaluate the risk. In our meta-analysis, we only included Asian and Caucasian, additional ethnic studied were needed for further analysis.

Despite some limitations, wood dust exposure is a significant risk associate with sinosnasal cancer, so did nasopharyngeal cancer. Except for female and squamous cell carcinoma studies in sinosnasal cancer, stratification by many subgroup such as histologic type, gender ,ethnic in sinosnasal cancer and case and control source ,ethnic in nasopharyngeal cancer indicates wood dust have little involvement in sinosnasal and nasopharyngeal cancer. Nevertheless, well designed studies including care assessment of ethnicity and more studies about female with large samples are warranted to confirm our findings.

Contributors

Qixing Zhu and Jiaxiang Zhang initiated the project, Jiaxiang Zhang and Feng Wang included and extracted all of the data. Jiaxiang

Zhang and Feng Wang analyzed the data. Each author took part in discussing the results and writing the article.

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