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Original article

Dermatological exposure to coal tar and bladder cancer risk: A case-control study

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Abstract

Objective: Coal tar ointments are used as treatment of various skin diseases, especially psoriasis and eczema. These ointments contain several carcinogenic polycyclic aromatic hydrocarbons. Metabolites of these polycyclic aromatic hydrocarbons are excreted in the urine and therefore, dermatological use of coal tar may be associated with an increased risk of bladder cancer. The objective of this study was to evaluate the association between dermatological use of coal tar ointments and bladder cancer.

Material and methods: A population-based case-control study was conducted including 1,387 cases diagnosed with bladder cancer and 5,182 population controls. Information on the use of coal tar, history of skin disease, and known risk factors for bladder cancer was obtained through postal questionnaires. Logistic regression analyses were performed to estimate the risk of bladder cancer after coal tar treatment, adjusted for age, gender, smoking status, duration of smoking, and intensity of smoking.

Results: The use of coal tar ointments was approximately equal among cases and controls (3.8% vs. 3.0%, respectively). Dermatological application of coal tar was not significantly associated with bladder cancer (adjusted odds ratio = 1.37, 95% CI: 0.93–2.01). An inverse association between bladder cancer and a history of skin disease was observed (adjusted odds ratio = 0.74, 95% CI: 0.61–0.90).

Conclusion: This is the first study with a specific aim to study the association between the use of coal tar preparations and bladder cancer. The results suggest that there is no reason for safety concerns with respect to the risk of bladder cancer after the use of coal tar preparations in dermatological practice.

Keywords: Coal tar; Polycyclic aromatic hydrocarbons; Bladder cancer; Psoriasis; Eczema; Case-control

1. Introduction

Coal tar is an effective therapy in the treatment of chronic skin diseases, such as psoriasis and eczema [1]. It contains more than 10,000 compounds, including polycyclic aromatic hydrocarbons (PAHs), in high concentrations. Some PAH, such as benzo(a)pyrene are classified as human carcinogens [2,3]. Because of the carcinogenic potency of PAHs, concerns have been raised about the risk of cancer after coal tar treatment in patients with skin diseases. The skin is an important route of uptake after dermatological exposure to coal tar [4]. Several studies have therefore investigated the risk of skin cancer after coal tar treatment but most studies [5–8], except one of Stern et al. [9], did not observe an increased risk. After application, coal tar is absorbed and metabolized in the skin and body. After metabolization, several metabolites of PAHs are excreted in the urine [10]. Therefore, dermatological use of coal tar might be associated with an increased risk of nonskin cancer, especially bladder cancer. The risk of nonskin cancer in patients treated with coal tar was investigated in only a few studies and most of these studies did not observe an increased risk of internal malignancies [6,11–13]. However, none of the previously performed studies had a specific aim to test the association between bladder cancer

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and dermatological application of coal tar preparations. In this case-control study, we examined the risk of bladder cancer after exposure to coal tar ointments used in the dermatological practice.

2. Material and methods

2.1. Study population and data collection

Patients were identified by the Department of Registry and Research of the Comprehensive Cancer Centre, Nijmegen, the Netherlands. All patients with bladder cancer who were diagnosed between 1995 and 2006, younger than 75 years, in this region, and alive at time of data collection were invited to participate in a study on genetic susceptibility and environmental risk factors for bladder cancer [14]. Patients filled out a detailed postal questionnaire concerning topics such as demographic factors, life style, history of diseases (e.g., cancer), and medication use. The response rate was 62%. For the current study, only bladder cancer cases with urothelial cell carcinoma were included ($n = 1{,}501$). Patients with missing data on skin disease, smoking status, or use of coal tar ointments were excluded ($n = 114$). A total of 1,387 cases were included in the analyses.

Controls were obtained through the Nijmegen Biomedical Study, a population-based survey conducted by the Radboud University Medical Centre in 2002 [15]. A random selection of inhabitants of Nijmegen were invited to participate in a study on risk factors for (any) disease by filling out a detailed postal questionnaire. In 2008, an additional questionnaire, more specifically aimed at potential risk factors for bladder cancer was sent to all participants of the Nijmegen Biomedical Study who gave consent for further research and were still alive then. A total of 5,613 (64%) persons returned this second questionnaire. Persons who were diagnosed with cancer (except for basal cell carcinomas of the skin) at the time of data collection were excluded ($n = 303$), as well as controls with missing data on smoking status and skin disease ($n = 128$). Coal tar exposure was measured as "yes" vs. "no." People with missing data on this variable ($n = 1{,}481$) were included in this category as well (assuming that persons who did not answer yes to this question did not use these preparations). A total of 5,182 controls were included in the analyses. All patients and controls gave written informed consent. The study was approved by the Institutional Review Board of the Radboud University Medical Centre.

2.2. Statistical analysis

Descriptive analyses were performed to provide insight into the characteristics of the patients and controls. Logistic regression analyses were performed to estimate odds ratios (ORs) and 95% CI for the association between the use of coal tar ointments and bladder cancer. These analyses were adjusted for age at completion of the questionnaire, gender, and smoking. Smoking and male gender are strong risk factors for bladder cancer. To exclude the effect of smoking in the association between coal tar and bladder cancer, subanalyses in nonsmokers were performed. In addition, subanalyses in men and women were performed. We also analyzed the association between occurrence of skin disease and bladder cancer because coal tar ointments are applied in patients with skin diseases. Models were not adjusted for height, weight, use of temporary or permanent hair dyes or both, and educational level because these variables did not alter the effect estimates in the models. All statistical analyses were performed in SAS (SAS system for Windows, version 9.2, SAS institute, Cary, NC).

3. Results

This study included 1,387 patients and 5,182 controls (Table 1). Patients were older at the time of completing the questionnaire compared with controls (67 y vs. 57 y). Smoking, both current and former, was more frequent in patients. Among current and former smokers, the patients had smoked for a longer period of time and the intensity of smoking was higher. Education level among patients was lower compared with controls. The use of coal tar ointments was approximately equal in both groups (3.8% vs. 3.0%). Among individuals exposed to coal tar, skin diseases were

Table 1
Characteristics of the study population

	Cases ($n = 1{,}387$)	Controls ($n = 5{,}182$)
Age at completion of the questionnaire, y[a]	67.3 ± 9.4	57 ± 16
Gender (% men)	84	46
Smoking status		
Never smokers, %	10.7	36.2
Former smokers, %	64.9	47.6
Number of cigarettes, cigarettes/d[a]	15.4 ± 4.5	12.6 ± 8.7
Smoking duration, y[a]	29.2 ± 13.7	20.4 ± 13.6
Age at start smoking, y[a]	17.5 ± 4.5	17.7 ± 4.6
Current smokers, %	24.4	16.2
Number of cigarettes, cigarettes/d[a]	15.3 ± 5.1	13.7 ± 8.1
Smoking duration, y[a]	42.7 ± 13.1	32.1 ± 15.2
Age at start of smoking, y[a]	17.6 ± 5.1	17.4 ± 5.0
Educational level, %		
Primary school	15.9	7.2
Technical/professional school	52	53.1
Secondary school	22.3	21.9
University degree	9.8	17.8
Use of temporary or permanent dyes or both, %	13.9	44.9
Skin disease, %	14.4	18.8
Use of coal tar ointments, %	3.8	3.0

[a]Mean ± standard deviation.