Published by Oxford University Press on behalf of the International Epidemiological Association
International Journal of Epidemiology 2005;34:1118–1122
doi:10.1093/ije/dyi109

Regular use of hair dyes and risk of lymphoma in Spain

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Accepted 28 April 2005

Background The use of hair dyes has been inconsistently associated with an increased risk of lymphomas. We explore hair dye use and lymphoma risk in a case–control study in Spain.

Methods We studied 574 incident lymphoma cases and 616 hospital controls in a multicentric study in Spain. Information on hair dye use was obtained through a personal interview together with information on other known or putative risk factors for lymphoma. Unconditional logistic regression analysis was used to estimate odds ratio (OR) and 95% confidence intervals (95% CI). All ORs were adjusted for pathology center, sex, age, and house ownership.

Results Ever use of hair dyes was associated with a non-significant 20% increased risk of lymphoma (OR = 1.2, 95% CI 0.9–1.7) with a slightly higher risk observed for those using permanent hair dyes (OR = 1.3, 95% CI 0.9–1.9). No association was observed with duration of use or lifetime doses of hair dyes. Among all lymphomas categories, only chronic lymphocytic leukaemia (CLL) was significantly associated with the use of hair dyes (OR = 2.3, 95% CI 1.1–4.7). The risk of CLL increased with lifetime doses received.

Conclusions Ever use of hair dye products is unlikely to substantially modify the risk of lymphoma. The observed association with CLL needs to be replicated.

Keywords Hair dyes, lymphoma, case–control, chronic lymphocytic leukaemia

The most common hair dyes used for colouring hair consist of semi-permanent dyes and permanent oxidation dyes. Hair colouring products are known to contain chemical substances that have been reported to be mutagenic and carcinogenic to animals although the evaluation of the effect of hair dyes among regular users was considered to be inconclusive for their carcinogenic effect by the International Agency of Research on Cancer (IARC).[1]

The use of hair dyes has been inconsistently associated with the aetiology of lymphomas. In 1988, Cantor *et al*.[2] suggested an ~2-fold increased risk of leukaemia and of non-Hodgkin lymphoma (NHL) with long-lasting hair dye use (OR = 1.8 and 2.0, respectively) among men. Zahm *et al*.[3] reported an increased risk of NHL, Hodgkin disease, and of multiple myeloma (MM) but not of chronic lymphocytic leukaemia (CLL) among women using hair-colouring products. Other studies have not reported positive associations between ever use of permanent hair dye and haematopoietic cancers.[4–8]

A case–control study among women in Connecticut by Zhang *et al*.[9] reported a 30% increased risk of NHL for lifetime ever use of hair colouring restricted to women who started using hair dyes before 1980. The risk was 2-fold for those using darker hair colours. Within all NHL histologies, follicular lymphomas was the category with the highest risk (OR = 1.9).

In line with these observations, excess risks of haematological cancer has also been described among cosmetologists and hairdressers[10,11] but data are scarce.

We evaluated for the first time, in a Spanish population, the association between personal use of hair-colouring products and risk of lymphoid neoplasm.

Study population

The study subjects were recruited at four centres in Spain served by three pathology departments: Barcelona, Tortosa-Reus,

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and Madrid. Cases ($n = 591$) were defined as all consecutive patients having an initial diagnosis of lymphoid malignancy during the period 1998–2002. The diagnosis of lymphoma was verified by histology and 99% of them were supplemented by immunohistochemistry tests and flow cytometry. Controls ($n = 631$) were frequency matched to cases by age, sex, and hospital and were selected from admission lists excluding hospitalizations for cancer, organ transplant, systemic infection, or severe immunosuppression. Controls were synchronically included with the cases.

Information was requested through a structured face-to-face interview on sociodemographics, reproductive, familial and medical history including allergies and asthma, tobacco, alcohol and drug consumption, use of hair dyes, sun exposure, and occupational history.

Subjects were asked about their natural hair colour and whether they had ever used any hair-colouring products in their lifetime. For ever users, information included colour of the dye used (brown, black, red, blond, or others), dyeing method (permanent dye, wash out dye, bleaching, or others), age at first and last use, and frequency of hair colouring.

The distribution of the medical conditions of the controls included: 14.7% surgical procedures, 14% ocular diseases, 15.6% diseases of the circulatory system, 12% injury and poisoning, 9.1% diseases of the respiratory system, 8.9% diseases of the urogenital system, 8.2% diseases of the gastrointestinal system, 4.1% diseases of the gynaecological system, 3.3% infections, 2.6% skin disorders, 2.4% diseases of the liver, 1.9% behavioural problems, 1.4% diseases of the endocrine system, 0.2% diseases of the haematological system, and 1.6% diseases of the cerebral system. Further details of the study have been described elsewhere.[12]

Data analysis

Ever users were considered as those who at least reported to having dyed their hair more than 10 times in their lifetime. Subjects with missing data on hair dye use or with missing data on lifetime exposure were excluded from the analysis (15 controls and 17 cases). The study population finally consisted of 574 cases and 616 controls.

Ever users of hair colouring products were compared with never users. Further analysis included colour and method used. In the category of dark colour we included those reporting black and brown colours and in the light colour category included blond dyes. Permanent type of colouring included permanent dyes and hair bleaching, semi-permanent included wash-out dyes. Year at start using hair dyes, lifetime dose, time of exposure, and mean annual dose were estimated. Categorization of these variables was based on the quartile distribution among controls. For those subjects who have been using different types of colours and/or methods of colouring during the same period, the exposure time for each of these colours and/or methods of dying was estimated as inversely proportional to the number of different colours and/or types.

Unconditional logistic regression was used to estimate the association between hair dye use and risk of haematological disease. The potential confounding variables included in the final model were sex, age (⩽42, 43–56, 57–67, 68–74, and >74 years), centre of recruitment, and house ownership. Adjustment for

Table 1 Distribution of cases and controls by sociodemographic characteristics

	Control *n* (%)	Cases *n* (%)
Recruitment centre		
Barcelona	514 (83.4)	457 (79.6)
Madrid	53 (8.6)	67 (11.7)
Tarragona	49 (8)	50 (8.7)
P-value	0.173	
Sex		
Men	327 (53.1)	325 (56.6)
Women	289 (46.9)	249 (43.4)
P-value	0.221	
Age		
⩽42	137 (22.2)	105 (18.3)
43–56	128 (20.8)	118 (20.6)
57–67	126 (20.5)	112 (19.5)
68–74	117 (19)	126 (22)
>74	108 (17.5)	113 (19.7)
P-value	0.351	
Highest educational level attained		
Primary school	238 (38.6)	235 (40.9)
Secondary school	60 (9.7)	40 (7)
High school	17 (2.8)	19 (3.3)
University degree	41 (6.7)	46 (8)
Other studies	47 (7.6)	39 (6.8)
No degree reached	148 (24)	121 (21.1)
No schooling	65 (10.6)	74 (12.9)
P-value	0.323	
House ownership		
Yes	444 (72.5)	470 (82)
No	168 (27.5)	103 (18)
P-value	<0.001	
Marital status		
Single	108 (17.5)	68 (11.8)
Married	386 (62.7)	401 (69.9)
Divorced	25 (4.1)	23 (4.0)
Widowed	97 (15.7)	82 (14.3)
P-value	0.03	
Natural hair colour		
Light	56 (9.1)	54 (9.4)
Dark	560 (90.9)	520 (90.6)
P-value	0.850	
Hair dye use in their lifetime[a]		
Never	429 (69.6)	395 (68.8)
Ever	187 (30.4)	179 (31.2)
P-value	0.757	

[a] People with <11 doses in their lifetime have been considered as non-exposed.

Table 2 Risk of lymphoma associated with ever use of hair dyes by subtype

	Never/ever	OR[a] (IC 95%)
Controls	429/187	Reference
All lymphoma	395/179	1.2 (0.9–1.7)
B-Cell	311/153	1.3 (0.9–1.9)
Chronic lymphocytic leukaemia	86/37	2.3 (1.1–4.7)
Lymphoplasmatic lymphoma	16/3	0.5 (0.1–2.2)
Splenic marginal zone lymphoma	14/10	1.8 (0.5–6.0)
Plasma cell myeloma	56/26	0.9 (0.5–1.7)
Marginal zone B-cell lymphoma	23/8	0.8 (0.3–2.1)
Follicular lymphoma	26/17	1.8 (0.7–4.5)
Difusse large-cell lymphoma	61/37	1.4 (0.8–2.5)
Other B-cell lymphoma	29/15	2.4 (0.9–6.2)
Hodgkin lymphoma	47/19	1.7 (0.8–3.7)
T-cell	37/7	0.3 (0.1–0.9)
Mycosis fungoide/serazy	18/4	0.7 (0.2–3.1)
Other T-cell	19/3	0.2 (0.1–0.8)

[a] ORs are adjusted by sex, age (continuous), centre of recruitment and house ownership.

other variables such as educational level, natural colour of hair, family history of haematological disease, smoking status, and alcohol consumption did not modify the observed associations and were not included in the final model. Odds ratio (OR) and 95% confidence intervals (CIs) were calculated using the statistical package SPSS 9.0.

Results

The average age at entry was 60 years among cases and 58 years among controls. Ever use of hair dyes was more prevalent among women than among men (79 and 8%, respectively). Among women, hair dye use was reported more frequently among cases than controls (82 vs 76%, respectively $P = 0.07$) while among men there was no significant difference in use among cases and controls (8 vs 7.3%, respectively $P = 0.769$).

Table 1 describes the distribution of all subjects by age, recruitment centre, highest educational qualification attained, house ownership, marital status, natural hair colour, and ever use of hair colouring methods. Married subjects and being owner of the house in which they live were significantly more common among cases than among controls.

Table 3 Risk of all lymphoma and of CLL associated with different characteristics of hair dye use

	All lymphomas/ controls	OR[a] (IC 95%)	CLL/Controls	OR[d] (IC 95%)
Use of hair dyes				
Never	395/429	Reference	86/429	Reference
Ever	179/187	1.2 (0.9–1.7)	37/187	2.3 (1.1–4.7)
Starting period				
Before 1980	95/91	1.3 (0.8–1.9)	27/91	3.5 (1.5–7.8)
After 1980	84/96	1.2 (0.8–1.7)	10/96	1.5 (0.6–3.6)
Hair dye colour[b]				
Dark colour	107/117	1.1 (0.8–1.6)	24/117	2.3 (1.1–4.9)
Light colour	76/81	1.2 (0.8–1.9)	17/81	2.9 (1.3–6.8)
Hair dye method[b]				
Permanent	161/160	1.3 (0.9–1.9)	35/160	3.4 (1.4–7.8)
Semi permanent	14/27	0.6 (0.3–1.3)	3/27	1.6 (0.4–6.6)
Time exposed				
⩽10	67/73	1.2 (0.8–1.8)	6/73	1.1 (0.4–3)
11–24	50/52	1.3 (0.8–1.9)	12/52	3.2 (1.3–8.2)
⩾25	62/62	1.2 (0.8–1.9)	19/62	3.7 (1.5–8.9)
P-value linear trend[c]		0.776		0.04
Lifetime dose				
⩽67	59/63	1.2 (0.8–1.9)	8/63	1.7 (0.7–4.4)
68–238	66/58	1.5 (1–2.3)	10/58	2.4 (0.9–6.2)
⩾239	54/66	1 (0.6–1.5)	19/66	2.8 (1.3–6.3)
P-value linear trend		0.4		0.183
Annual dose				
⩽12	78/90	1.1 (0.7–1.7)	16/90	2.3 (1–5.3)
>12	101/97	1.3 (0.9–1.9)	21/97	2.4 (1.1–5.1)
P-value linear trend		0.524		0.777

[a] ORs are adjusted by sex, age (⩽42, 43–56, 57–67, 68–74, and >74 years), centre of recruitment and house ownership.

[b] Subjects could be included in both categories if they have used both colour types.

[c] Trend analysis has been carried out among exposed.

[d] ORs are adjusted by sex, age (continuous), centre of recruitment, and house ownership.

Table 2 summarizes the risk for different lymphoma types associated with ever use of hair dyes. The risk for all lymphomas associated with ever use of hair dyes was OR = 1.2 (95% CI 0.9–1.7). Among all lymphoma entities, ever use of hair dyes was associated with a 2-fold increased risk of CLL (OR = 95% CI 1.1–4.7). The OR for other lymphoma categories was 0.9 (95% CI 0.5–1.7) among plasma cell myeloma, 2.4 (95% CI 0.9–6.2) among other B-cell lymphoma, 0.3 (95% CI 0.1–0.9) for T-cell lymphomas, and 1.7 (95% CI 0.8–3.7) for Hodgkin lymphoma.

Table 3 summarizes the analysis of lymphoma risk and characteristics associated with the use of hair dyes. First use of hair dye products before 1980 was associated with a 20% increased risk. Compared with never users of hair dyes, the OR associated with permanent dye use was marginally significant (OR = 1.3, 95% CI 0.9–1.9). No changes in risk were observed related to number of years being exposed, lifetime doses received, or average annual doses.

The risk of CLL increased with lifetime doses received as compared with never users (OR $<$ 68 doses = 1.7, 95% CI 0.7–4.4; OR 68–238 doses = 2.4, 95% CI 0.9–6.2; OR $>$ 238 doses = 2.8, 95% CI 1.2–6.3; P for linear trend among exposed $P = 0.183$). The risk of CLL was higher for those starting to dye their hair before 1980 as compared with those starting after 1980.

Among all subjects, we identified 5 cases and 6 controls who reported having worked as hairdressers (OR = 0.9, 95% CI 0.3–3).

Discussion

Our data indicate that overall no major differences in use of hair colouring products were observed between cases and controls. However, hair dye use was associated with a 2-fold increased risk of CLL, the risk increasing with number of lifetime doses received.

Our data are consistent with Zhang *et al*.[9] in identifying an association with an earlier period of use of hair dyes. However, while Zhang *et al*.[9] identified an elevated risk associated with the period of use for NHL we could only observe this period effect for CLL cases. This increased risk of CLL and hair colouring was not modified by adjusting the models for potential confounders including occupational exposures or medical history of allergies. Epidemiological studies that have linked hair dyes and lymphoma have mainly explored the association with NHL. The studies that have explored the association between hair dyes and CLL have been mainly negative[13] or based on few numbers.[3] Recently Rauscher *et al*.[14] have reported a 50% increased risk of adult acute leukaemia associated with ever use of permanent dyes. Unfortunately the recent report by Tavani *et al*.,[7] a mainly negative study, does not include CLL as a distinctive histology.

In our data, for use ever category, being a hairdresser was not associated with an increased risk; however, the number of exposed subjects in this professional category was very small and our estimates were not precise.

As in any hospital-based case–control study, selection and recall bias are of concern. We had a high participation rate of cases and controls. It is unlikely that the small proportion of non-respondents could be differentially associated with the use of hair dyes, particularly because our cases and controls were frequency matched for age and sex. Our estimates could be affected by a differential recall bias if subjects had known that there could be an association between hair dye use and lymphoma. However, this is unlikely as most subjects were unaware of this association.

The mechanisms through which hair dyes could act in producing lymphomas are unknown. DNA damage in lymphocytes has been reported to be slightly higher in volunteers after hair dyeing.[1,15] The complex mixture of chemical components found in hair dyes has changed over time. During 1978–1982, all oxidative dye products were reformulated to eliminate some ingredients that had been reported to produce tumours in bioassays.[16] Whether the resultant compounds could still induce carcinogenesis or affect the overall immune response is not known and need careful monitoring as any increase in risk, even if moderate, for use of hair dyes could have a great public health impact because of the highly prevalent exposure.

We conclude that ever use of hair dye products is unlikely to substantially modify the risk of lymphoma. The observed association with CLL needs to be replicated.

Acknowledgements

This work was supported by the Spanish Ministry of Health grant 04-0091 and ISCIII C03/09 and also by the 5th frame Quality of Life Program QLK4-CT-2000-00422. This case–control study was undertaken within the framework of the EPILYMPH international study.

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