Occupational exposure to polyvinyl chloride as a risk factor for testicular cancer evaluated in a case-control study

Lennart Hardell*, Carl-Göran Ohlson** and Mats Fredrikson***

*Department of Oncology, Örebro Medical Center, S-701 85 Örebro
**Department of Occupational and Environmental Medicine, Örebro Medical Center, S-701 85 Örebro
***Department of Occupational and Environmental Medicine, University Hospital, S-581 85 Linköping, Sweden

Introduction

The Swedish age-adjusted incidence of testicular cancer increased with 2.8% annually during the time period 1976-95 (1). It is the most common cancer among young men. The etiology is poorly understood. Cryptorchidism is the only established risk factor and the risk has been reported to be increased also for the descendent testis (2). Common risk factors for both cryptorchidism and testicular cancer have thus been suggested (2). Prenatal exposures have been discussed to be of etiological significance. Especially exposure to some environmental pollutants with estrogenic potency have been of concern during recent years (3). Testicular cancer is usually not regarded to be an occupational disease. The aim of this study was to investigate occupational risk factors in the etiology of testicular cancer.

Material and Methods

Case ascertainment: Cases with testicular cancer 30 to 75 years old and reported to the Swedish Cancer Registry during the time period 1989-92 were identified. The cases were living in the middle and northern part of Sweden. The study encompassed 163 cases, 109 with seminoma testis and 54 with embryonal cancer.

Control ascertainment: Twice as many male controls as cases were used. They were sampled from the Swedish Population Registry by selecting the next subject in birth registration number (born the same year) as the cases. We were not able to get in contact with 37 of the 326 control subjects and therefore they were exchanged with the next following subjects in the Population Registry fulfilling the inclusion criteria, *i.e.*, birth registration number and sex.

Assessment of exposure: A 22 pages questionnaire was mailed to each case and control. Lifetime working history was asked for. It also contained a number of questions on specific occupations and occupational histories. The questionnaires were supplemented over the phone if the answers were unclear. These interviews, as well as coding of the questionnaires, were made without knowing the group status.

Exposure to plastics, mostly to styrene, was reported by 44 subjects. Exposures to polyvinyl chloride (PVC) plastics were confirmed by contact with the employers or the production managers. Nine subjects reported exposure to PVC and eight were confirmed. For one subject, a case, the company could not be contacted. However, he clearly stated PVC exposure in 1957-60 in the production of plastic carpets and was included among the exposed subjects. Also jobs with potential exposure to PVC were checked. No additional case or control with such exposure could be identified thereby.

Cumulative exposure was calculated by multiplying exposure level, part of day (half day = 0.5, whole day = 1) and number of years of exposure. The exposure level was arbitrarily taken as 0 = no exposure, 1 = low grade exposure and 2 = high grade exposure.

Statistical methods: A conditional logistic regression model for matched studies was employed to obtain exact odds ratios (OR) and 95% confidence intervals (CI) (EGRET, Statistics and Epidemiology Research Corporation, Seattle, USA, 1990).

Results

Of the 163 cases 148 (91%) answered the questionnaire. compared to 315 (87%) of the finally enrolled 363 controls.

The mean age for both cases and controls was 41 years. For cases with seminoma (n=101) the mean age was 43 years compared to 38 years for cases with embryonal cancer (n=47).

Occupational plastic work gave OR 2.9, CI 1.3-6.5. No increased risk was found for plastic work during leisure time, OR 0.7, CI 0.1-3.3.

A summary of the exposure to PVC is displayed in Table 1. Six of the seven exposed cases had seminoma. An OR of 6.6, CI 1.4-32, was obtained for such exposure, Table 2. For other types of plastics no significantly increased risks were found.

Only one case with exposure to plastic (polystyrene) reported cryptorchidism in his youth. If subjects with self reported cryptorchidism were excluded the risk increased further. Thus, exposure to PVC yielded OR 14.0, CI 1.7-114, for all testicular cancer. One case with exposure to PVC reported that he had had orchitis. If all cases with self-reported orchitis were excluded exposure to PVC yielded OR 10.0, CI 1.2-87. The ORs for exposure to other types of plastics were not significantly changed in similar calculations.

Regarding cumulative exposure to PVC, cases and controls were divided in two groups with 3 cases and 2 controls in the group with low exposure yielding OR 2.6, CI 0.3-32. Four cases and no control were found in the group with high exposure and no OR could be calculated. For polystyrene, OR 0.5, CI 0.0-5.5, versus OR 0.7, CI 0.1-3.1 were calculated in the group with low and high exposure, respectively. For the other plastic exposures dose-response calculations were not carried out due to low numbers of exposed subjects.

Discussion

A significantly increased risk was found for exposure to PVC. The induction latency period varied between 11 to 35 years with a median time of 22 years. Six of the seven exposed cases had seminoma. Furthermore, the case with embryonal cancer had a low cumulative exposure. It is unclear why the increased risk was seen only for seminomas.

The chemical composition of PVC has two features. First, PVC is the only type which contains chlorine, about 56% of the molecular weight (4). Second, plasticizers, e.g. phtalates, are used in PVC. Almost all phthalates are used in PVC production. Estrogenic effects have been reported for some phthalates (5).

The additive bisphenol A is used as an antioxidant in plastics. It is of interest since estrogenic potency has been reported in experimental studies for bishpenol A (6). However, it is used in several types of plastics whereas we found increased risk only for exposure to PVC.

To conclude, in this case-control study of testicular cancer a somewhat surprisingly high risk was observed for exposure to PVC plastics. The shortcomings of retrospective assessment of exposure by a self-administered questionnaire are evident and a spurious association between PVC exposure and seminoma can not be ruled out. Therefore, the results must be regarded as hypothesis generating and warrants further studies. The results of this study have been published elsewhere (7).

Acknowledgements

Supported by grants from Telehjälpen, The Swedish Cancer Society and Örebro County Council Research Committee. The assistance of Miss Iréne Larsson in the data collection is acknowledged.

References

1. National Board of Health and Welfare. Cancer Incidence in Sweden 1995. *The National Board of Health and Welfare. Centre for Epidemiology. Stockholm, Sweden,* 1997.
2. Henderson BE, Benton B, Jing J, Yu MC, Pike MC. Risk factor for cancer of testis in young men, *Int J. Cancer*, 1979;23,598-602.
3. Toppari J, Skakkebaek NE, Larsen JC (eds). Male Reproductive Health and Environmental Chemicals with Estrogenic Effects. *Danish Environmental Protection Agency, Copenhagen, Denmark. Miljöprojekt nr. 290*, 1995.

4. KemI. Plastic Additives Project. Rapport från kemikalieinspektionen. *The Swedish National Chemicals Inspectorate, Stockholm* 15/95, 1995. In Swedish, English summary.
5. Joblin S, Reynolds T, White R, Parker MG, Sumpter JP. A variety of environmentally persitent chemicals, including some phatalate plasticizers, are weakly estrogenic. *Environ Health Perspect* 1995;103,582-587.
6. Krishnan AV, Stathis P, Permuth SF, Tokes L, Feldman D. Bisphenol-A: an estrogenic substance is released from polycarbonate flasks during autoclaving. *Endocrinology,* 1993;132:2279-86.
7. Hardell L, Ohlson CG, Fredrikson M. Occupational exposure to polyvinyl chloride as a risk factor for testicular cancer evaluated in a case-control study. *Int J Cancer*, 1997;828-830-

Table 1. Exposure to PVC for cases and controls.

Birth year	Cumulative exposure	Year of first exposure	Year of diagnosis	Type of cancer
1930	6	1957	1992	Seminoma
1931	4	1967	1989	Seminoma
1939	12	1977	1989	Seminoma
1945	8	1965	1991	Seminoma
1947	5	1969	1991	Seminoma
1953	<1	1978	1989	Embryonal
1956	2	1974	1992	Seminoma
1952	<1	1964		Control
1958	2	1979		Control

Table 2. Exposure to plastic in cases and controls. Number (No) of exposed cases/controls, Odds ratios (OR) and 95% confidence intervals (CI) are given.

	All cancer			Seminoma			Embryonal carcinoma		
Agent	No	OR	CI	No	OR	CI	No	OR	CI
Polyvinyl chloride	7/2	6.6	1.4-32	6/2	5.6	1.1-196	1/2	-	-
Styrene	4/15	0.6	0.2-2.0	2/15	0.5	0.1-2.3	2/15	1.0	0.2-6.4
Urethane	4/5	1.5	0.4-5.6	2/5	1.0	0.2-5.5	2/5	3.2	0.3-37
Acrylate	2/1	3.2	0.3-37	0/1	-	-	2/1	3.2	0.3-37
Plastic, unspeci-fied	4/3	4.3	0.8-24	1/3	2.5	0.2-40	3/3	6.0	0.6-58