Original article

Scand J Work Environ Health 1980;6(4):299-301

doi:10.5271/sjweh.2605

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This article in PubMed: www.ncbi.nlm.nih.gov/pubmed/7233118

Scand j work environ health 6 (1980) 299—301

Increased sister chromatid exchange frequencies in lymphocytes of nurses handling cytostatic drugs

by Hannu Norppa, LSc,[1] Marja Sorsa, PhD,[1] Harri Vainio, MD,[1] Pentti Gröhn, MD,[2] Erkki Heinonen, MD,[2] Lars Holsti, MD,[2] Eeva Nordman, MD [3]

NORPPA H, SORSA M, VAINIO H, GRÖHN P, HEINONEN E, HOLSTI LR, NORDMAN E. Increased sister chromatid exchange frequencies in lymphocytes of nurses handling cytostatic drugs. *Scand j work environ health* 6 (1980) 299—301. In oncology units, personnel handling chemotherapeutic drugs may occasionally be exposed to small amounts of genotoxic agents. This exposure was obviously the cause of the increased frequencies of sister chromatid exchange (SCE) observed in nurses in daily contact with cytostatics (N = 20, mean SCEs/cell ± SE 9.4 ± 0.3) as compared to a group of office workers (N = 10, mean SCEs/cell 8.1 ± 0.3). The oncology nurses also had a higher SCE frequency than other hospital nurses (N = 10, mean SCEs/cell 8.7 ± 0.2), but this difference was not statistically significant. The SCEs of patients under chemotherapy were about five times higher (mean SCEs/cell 36.8 ± 0.6) than those of healthy subjects.

Key terms: carcinogens, chemotherapeutic drugs, chromosome damage, mutagens, occupational exposure.

Nurses working with cytostatic drugs in an oncology unit have increased mutagenicity in their urine, as detected by a sensitive bacterial fluctuation test (2). Since this mutagenicity is obviously due to the uptake of very small amounts of cancer chemotherapeutic drugs, it was necessary to study whether such a low exposure would cause any biological response in the nurses. The analysis of sister chromatid exchanges (SCEs) in cultured blood lymphocytes of groups of people exposed in vivo to suspected genotoxic chemicals in the environment has recently offered a promising tool for the biological monitoring of specific occupational exposures (5). A specific case of such exposure is the handling of cytostatic drugs, many of which are known mutagens, carcinogens, and inducers of SCE (1, 6, 7, 8, 10, 11, 12, 13).

Subjects and methods

The exposed subjects of the study comprised 20 nurses working in three oncology units with daily or almost daily contact with cytostatic drugs (preparation of solutions and syringes for infusion), the five most frequently used drugs being cyclophosphamide, 5-fluorouracil and analogs, methotrexate, adriamycin and cisplatinum. The following reference groups were used: ten hospital nurses working in different bedside units of the same hospital and ten persons working in various offices with no known chemical exposure. In addition five patients under therapy (cyclophosphamide as the main drug) were used

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0355-3140/80/040299-3

Table 1. Sister chromatid exchange frequencies in lymphocytes of patients, hospital nurses and office personnel.

Group of subjects	Number of subjects	Number of cells analyzed	SCEs/cell (group mean ± SE)	Statistical significance (t-test)
A. Patients	4	120	36.8 ± 0.6	< 0.001 (A to all groups)
B. Oncology nurses	20	600	9.4 ± 0.3	< 0.1 (B to C) < 0.01 (B to D, B to E)
C. Other nurses	10	300	8.7 ± 0.2	< 0.1 (C to D)
D. Office personnel	10	300	8.1 ± 0.3	—
E. All referents (C + D)	20	600	8.4 ± 0.2	—

as positive controls. All the subjects were nonsmokers, except one person in the office group and one of the oncology personnel, who smoked about 10 cigarettes daily. According to blood counts and a personal interview, all the referents were healthy and had not been exposed previously to known SCE-inducing agents.

The whole-blood microculture method was used as described earlier (4, 9), bromodeoxyuridine (Calbiochem) being added in a concentration of 5.0 μg/ml for the whole culture time of 68 h. The samples were cultured in two groups and analyzed by one person on coded slides, 30 harlequin-stained metaphases from each subject.

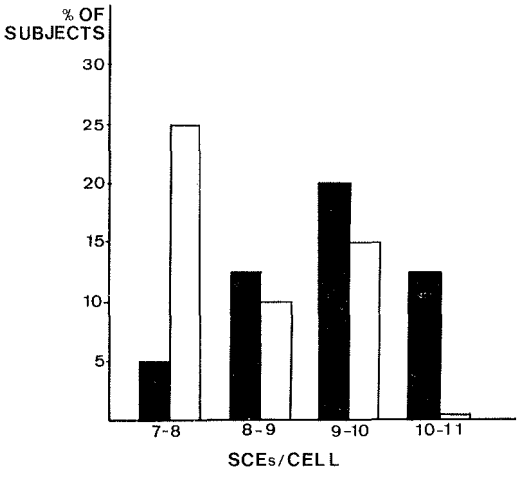

Fig 1. Distribution of individual sister chromatid exchange (SCE) frequencies for 20 oncology nurses (filled columns) and 20 referents, 10 nurses and 10 office workers (unfilled columns).

Results

The SCE frequencies of the four groups of subjects are given in table 1. The SCEs of the patients under therapy were five to six times higher than those of the other subjects (no result could be obtained from one patient). Also the oncology nurses generally had higher SCE frequencies than the office personnel, their group mean of SCE/cell deviating significantly ($p < 0.01$, one-tailed Student's t-test) from that of the office workers but not significantly ($p < 0.1$) from that of the other hospital nurses. Also the distribution of individual mean SCE frequencies/cell (fig 1) clearly revealed a tendency towards higher individual SCE rates among the nurses handling cytostatics as compared with the two groups of referents.

Discussion

The previous findings of increased mutagenicity in the urine of nurses (2) suggested that some exposure to anticancer drugs may occur. Many of the chemotherapeutics used, eg, adriamycin (10, 11), 1-[2-chloroethyl-3-(4-methyl-cyclohexyl)]-1-nitrosourea (CCNU) (7, 8), cyclophosphamide (10, 12), and cis-platinum (13) have been shown to be potent inducers of

SCE in patients or in experimental systems, and thus the increased SCE frequencies among nurses handling cytostatic drugs can be attributed to this occupational exposure. In the present study the increased frequency of SCEs in the blood lymphocytes of nurses handling cytostatics was of the same order of magnitude as that found earlier for smoking subjects (4). Another recent study (14) revealed an increase not only in SCEs, but also in chromosome aberration frequencies among nurses handling cytostatic drugs.

Hospital work as such may involve some exposure to mutagenic chemicals (eg, drugs, sterilizing agents, solvents). Personnel in hormone and research laboratories have been reported to have increased SCE frequencies in comparison to referents (3). In the present material, the SCE frequency of the oncology nurses and the nurses from other hospital departments did not differ statistically significantly, neither did the hospital referents show a statistically higher SCE frequency than the office personnel.

The biological response in the SCEs of oncology nurses points to a possible genotoxic hazard and to the need for careful hygienic measures during the handling of cytostatic drugs.

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Received for publication: 10 October 1980