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White Blood Cell Count as an Indicator of Formaldehyde Exposure

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Formaldehyde is an important solvent which is widely used in hospitals and industry. In hospitals, it is used for pathology work, hemodialysis and in medical technology units. According to the US EPA (1984), formaldehyde is classified as a possible carcinogen. Based on this classification, permissible levels for formaldehyde have been decreasing. OSHA has set 0.75 ppm as the permissible exposure limit (PEL) for formaldehyde and a threshold limit value-ceiling (TLV-C) of 0.3 ppm is recommended by the ACGIH (1992). However, in Taiwan permissible levels for formaldehyde have been set at 5 ppm. Short term exposure to formaldehyde can irritate the upper respiratory tract and the eyes. Dermal irritation, lacrimation and respiratory effects are common after exposure to formaldehyde (Porter 1975; Shellow and Altman 1966). Chronic exposure to formaldehyde causes allergic dermatitis (Quinn and Kennedy 1965), ocular damage and damage to tissue of the gastric-intestinal tract (Bartone et al., 1968). In animal experiments, chronic formaldehyde inhalation at 15 ppm resulted in the induction of squamous cell carcinoma in the nasal cavities of Fisher 344 rats and B6C3Fl mice. (Kerns et al 1983). Formaldehyde can enter the blood stream through the respiratory tract and/or the GI tract. Once in the blood, formaldehyde goes through a reduction-oxidation reaction and combines with macromolecules including proteins, DNA and RNA causing irreversible cross-links (Casanov-Schmitz et al. 1983). Vargova et al. (1992) concluded that formaldehyde interfered significantly in the functions of the immune system in formaldehyde workers. Yan (1994) reported that exposure to formaldehyde caused increased levels of B cells and an increased CD4/CD8 ratio. Exposure also caused decreases in absolute levels of CD3, CD4 and CD8 cells. Cheng (1995) reported that long-term exposure to formaldehyde caused increases in the percentages of micronuclei in lymphocytes and nasal epithelium cells. Exposure to formaldehyde was found to cause morphological changes in lymphocytes and oral epithelium (Suruda et al., 1993).

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Antibodies against erythrocytes have been found in patients hemodialyzed with formaldehyde-sterilized dialyzer and there may be a relationship between formaldehyde exposure and the anti-erythrocyte response (Lynen et al., 1983). In the past, hemodialysis nurses in Taiwan have not been monitored for exposure to formaldehyde. Information on the effects of exposure and associated symptoms should allow for the development of tests to monitor nurses for early signs of the negative effects of formaldehyde exposure.

MATERIALS AND METHODS

Four teaching hospitals in central Taiwan were included in the study. 50 hemodialysis nurses were the study subjects. 71 ward nurses who did not work in the hemodialysis unit constituted the control group. A constructed questionnaire was used to gather information regarding the nurses' health history, demographic data, lifestyle and habits, knowledge of formaldehyde, occupational exposure to formaldehyde and symptoms including itching, dizziness, nausea and vomiting, fatigue, difficulty and/or lack of concentration, tearing, nasal discharge, cough and difficulty breathing. Symptoms were scored from 0-3; 0=never, l=seldom, 2=occasionally, 3=frequently. The symptom values were totalled and a score was recorded for each subject.

A Cell-Dyn 3000 was used to measure RBC, Hb, Ht, MCV, MCH , MCHC and PLT, by electrical impedance. Multiple angle polarization scattered separation was used to differentiate white blood cells into neutrophils, lymphocytes, eosinophil, basophil and monocytes. RBC, WBC and Hb values were tested two times. The first test was performed at the beginning of the study and the second test was approximately one year later at the end of the study. The other blood parameters were only tested once.

Air levels of formaldehyde were tested according to NIOSH protocols (NIOSH 1989). XAD-2 coated with a 10% solution of 2-hydroxyl-methyl-piperidine was used as the solid sorbent. The sampling rate was 100 mL/min and the sampling volume was 18-24 liters. A mixture of 95% n-hexane and 5% methanol was used to desorb the formaldehyde. Meta-xylene was used as the internal standard. The detection limit was found to be 1.29 µq/ml. The gas chromatograph was tested at three levels: 39 µg, 78 µg and 156 µg. At all three levels, the coefficient of variance was less than 1%. Nine formaldehyde solutions were used to establish a calibration curve and the correlation coefficient was 0.999.

RESULTS AND DISCUSSION

Table 1 is a comparison of the demographic data between the control group and the exposure group. Significant differences were found for age, marital status and incidence of allergic rhinitis, however no other significant differences were noted in this table. The control group was found to be younger, less likely to be married and more likely to have allergic rhinitis. In the past three months, as reported by the subjects, twenty-four percent of the exposure group was found to have had an incidence of the common cold, as opposed to eleven percent of the control group. The average duration of employment for both groups was approximately three years.

Table 1. Basic information for the control and exposure groups.

variable	control group n (%)	exposure group n (%)	p value
Age (years)			
< 25	31 (43.7)	3 (6.0)	<0.01
25-30	26 (43.7)	26 (52.0)	
> 31	9 (12.7)	21 (42.0)	
Marital status			
unmarried	52 (80.0)	23 (44.0)	<0.01
married	14 (19.7)	26 (54.0)	
other	0 (0.0)	1 (2.0)	
Duration of employment (years)			
< 1	26 (36.2)	15 (33.3)	0.76
1-3	17 (23.3)	12 (23.3)	
3-10	24 (34.4)	18 (34.6)	
> 10	4 (5.9)	5 (8.6)	
Health status			
chronic cough	2 (4.0)	3 (6.0)	0.39
allergic rhinitis	13 (26.0)	2 (4.0)	0.02
dermatitis	5 (10.0)	9 (18.0)	0.65
liver disease	3 (6.0)	2 (4.0)	0.95
common cold	8 (11.4)	12 (24.0)	0.07

A comparison of the frequency of symptoms is shown in Table 2. The exposure group was found to have significantly increased incidence of dizziness, nausea, difficulty concentrating, tearing, nasal discharge, cough and difficulty breathing. No significant differences were found for stomach pain or toothache, the two dummy variables. These symptoms may be related to exposure to formaldehyde or sodium perchlorate, as these are substances used during hemodialysis. Because of formaldehyde's impact on the central nervous system, the symptoms of dizziness, nausea, fatigue and difficulty

concentrating are associated with formaldehyde exposure. Symptoms such as nasal discharge or cough may be more related to sodium perchlorate which is a stimulant and irritant.

Table 2. A comparison of formaldehyde-related symptom frequency in the control and exposure groups.

variable	control group	exposure group	p value
itching	1.64±0.87	1.94±0.89	0.07
dizziness	1.49±0.67	2.14±0.88	<0.01
nausea	1.44±0.67	1.82±0.78	0.01
fatigue	2.14±1.09	2.38±1.05	0.23
difficulty concentrating	1.65±0.79	1.96±0.88	0.04
tearing	1.28±0.56	2.12±0.92	<0.01
nasal discharge	1.45±0.75	1.86±0.81	<0.01
cough	1.52±0.71	1.82±0.85	0.04
difficulty breathing	1.23±0.45	1.76±0.80	0.04
stomach pain	1.46±0.71	1.60±0.88	0.35
tooth pain	1.30±0.60	1.32±0.62	0.83

Table 3. Correlation matrix for complete blood count (second test), formaldehyde concentration, symptom score and work duration.

variable	formaldehyde	symptom score	work duration
RBC	0.07	0.09	0.04
WBC	-0.33*	-0.23*	-0.18
Ht	-0.08	0.00	-0.18
MCV	-0.04	-0.02	-0.06
MCH	-0.04	-0.10	-0.20
MCHC	0.03	-0.21	-0.17
PLT	-0.03	-0.09	-0.02
neutrophil	-0.16	0.02	0.15
lymphocyte	0.10	-0.09	-0.12
monocyte	0.16	0.24	0.10
eosiphil	0.18	0.06	-0.05
basophil	0.10	0.20	-0.09

* $p<0.05$

Table 3 is a correlation matrix between the total blood count (as determined from the second blood test), airborne formaldehyde concentration, symptom score total and work duration. A significant positive correlation was found between airborne formaldehyde concentration and total symptom score. Work duration was also found to be negatively correlated, but this correlation was not significant. Other variables were not found to be

significant. However, no association between formaldehyde exposure and blood analysis was found in the first blood count levels. There was a decrease in WBC counts from the first blood test to the second blood test. Other changes were not found.

A multiple regression, in Table 4, shows the factors influencing WBC count. It was found that the exposure group's WBC count was significantly lower than the control group. Secondly, the higher a subject's total symptom score, the lower her/his WBC count. Age, work duration and common cold were not found to be correlated with WBC count. It has been reported that some chemicals can combine with neutrophils to form complexes which stimulate the production of antibodies. Following the production of these antibodies, the host WBC count decreases due to an inhibitory mechanism (Bruckart et al., 1981; Neftel et al., 1983). Anti-formaldehyde antibodies can be found in the blood of hemodialysis patients who are treated with a reusable dialyzer sterilized with formaldehyde. These authors concluded that patients treated with formaldehyde-sterilized reusable dialysis equipment may on occasion have a positive direct antiglobulin test result and have an eluate that is nonreactive with the use of standard reagent cells but reactive with formaldehyde-treated cells (Dzik & Darling 1989).

Table 4. Multiple regression to explain the variance in WBC count.

variables	B (S.E.)	p value
group (exposure=1)	-96.3(37.2)	0.01
age (years)	-18.9(36.1)	0.62
symptom score	-9.83(3.34)	<0.01
work duration(year)	0.04(0.36)	0.90
common cold(yes=1)	23.1(47.4)	0.63

Table 5 shows sample values for both personal and area sampling of formaldehyde in four hospitals. The variation in formaldehyde levels was very high, although all the hospitals were found to be in compliance with government standards. The current acceptable formaldehyde level in Taiwan is 5 ppm. Formaldehyde levels are highly variable because when nurses are working with formaldehyde solutions, there may be accidents where some formaldehyde is spilled, or the lid of a container may not be properly closed. Formaldehyde vaporizes easily and for a short period of time the formaldehyde levels may be increased. There is no vapor hood in the dialysis unit, so vaporized formaldehyde may remain in the air for a long period of time. About ninety percent of the exposure group reported

that they never use a respiratory mask, they only use gloves. Nurses exposed to formaldehyde over a long period of time may have decreased WBC counts as a result of this exposure. In general, hospital administrators have not been concerned with this type of chemical hazard. All hospital personnel should have a periodic health examination including routine blood work. If a nurse's WBC count is found to be decreased, appropriate action should then be taken to minimize exposure.

Table 5. Personal and area sampling of formaldehyde levels (ppm) in the hemodialysis units of four teaching hospitals.

	A Hosp. site 1	A Hosp. site 2	B Hosp.	C Hosp.	D Hosp.
personal sampling					
N	4	3	3	2	2
mean	0.015	ND	0.017	0.033	0.054
median	0.060	ND	0.078	0.033	0.058
lowest	ND	ND	ND	0.033	0.038
highest	0.082	ND	0.089	0.033	0.078
area sampling					
N	6	5	5	5	6
mean	0.231	0.022	0.219	0.006	0.237
median	0.098	0.091	0.133	0.043	0.058
lowest	0.054	0.082	0.051	ND	ND
highest	0.082	0.101	2.800	0.079	1.168

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