SISTER CHROMATID EXCHANGES IN LYMPHOCYTES IN OPERATING ROOM PERSONNEL
Anestezik gazlara ve atıklarına maruz kalan ameliyathane personelinde KKD oranları

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Summary: *The potential mutagenicity of anaesthetic gases was investigated by the sister chromatid exchange (SCE) test using lymphocytes in peripheral blood from hospital personnel exposed to anaesthetics as well as from persons not exposed. Sister chromatid exchange was carried out in 19 operating room personnel (anaesthetists M.D. and anaesthesia unit technicians) exposed to waste anaesthetic gases such as halothane, nitrous oxide and isoflurane and in 20 healthy unexposed controls. The SCE frequencies were increased significantly in smoking operating room personnel as compared to non-smoking operating room personnel ($p<0.001$). A significant increase in SCEs was found in non-smoking operating room personnel as compared to non-smoking controls ($p<0.01$). The difference between the SCE frequencies of smoking exposed subjects and smoking controls was not found significant ($p>0.05$). It was concluded that there is an association between occupational exposure to waste anaesthetic gases and an increase in SCEs in lymphocytes.*

Key Words: *Halothane, Isoflurane, Nit ous oxide, Sister-chromatid exchanges*

Özet: *Anestezik gazların olası mutajenitesi bu gazlara maruz kalan hastane personelinin ve maruz kalmayan kişilerin periferik kan lenfositleri üzerinde kardeş kromatid değişim (KKD) testi kullanılarak araştırılmıştır. Halotan, azot protoksid ve izofloran gibi inhalasyon anesteziklerine ve bunların atıklarına maruz kalan 19 ameliyathane personelinde ve herhangi bir şekilde anestezik maddeye maruz kalmamış, sigara kullanan ve kullanmayan 20 kontrol kişide kardeş kromatid değişim değerleri incelenmiştir. Ameliyathane personelinin sigara kullanan grubu, kullanmayan personele oranla KKD açısından anlamlı bulunmuştur ($p<0.001$). Sigara kullanmayan ameliyathane personelinde, sigara kullanmayan kontrollere oranla KKD açısından anlamlı bir artış gözlenmiştir ($p<0.01$). Sigara kullanan ameliyathane personeli ile sigara kullanan kontroller arasında anlamlı fark bulunamamıştır ($p>0.05$). Lenfositlerdeki bu KKD artışı ile anestezik gaz atıklarına mesleksel maruz kalma arasında bir ilişkinin olduğu sonucuna varıldı.*

Anahtar Kelimeler: *Halotan, İsofloran, Azot protoksid, Kardeş kromatid değişimleri*

Many studies about the toxic and potential mutagenic effects of inhalation anaesthetics has been made (1-4). Experimental and epidemiological studies revealed that there is no direct evidence about chronic exposure to waste anaesthetic gases being responsible for the higher incidence of spontaneous abortion or for the suggested increases in incidences of malignancies in the operating room personnel (5,6). As a result, the causal relationship has never been established (7). DNA exchanges between the two chromatids in the somatic cells can be the causal factor. The number of DNA exchanges between the two sister chromatids (SCE) is used as a tool for mutagenity testing (8,9). An increase in the number of such SCEs reflects the effects of mutagens that are being investigated (10).

The effects of short-term exposure to fluroxene, halothane and isoflurane were investigated in anaesthetized patients by SCE frequencies and no

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Geliş tarihi. 3 Ekim 1995

elevation in SCE values was determined (7,9,11). Also occupational exposure to these compounds did not reveal any elevations in SCE values (12-14). The purpose of the present study was to investigate the interaction of inhalation anaesthetics and smoking in 19 individuals of the operating room personnel working at the Gazi University Department of Anaesthesia for 1.5-26 years by using SCE as a mutagenity test.

METHODS

The study was carried out in 19 operating room personnel (anaesthetists and anaesthesia unit technicians) who had been occasionally exposed to inhalation anaestfietics and the results were compared to a control group. The exposed group consisted of 11 anaesthetists and 8 anaesthesia unit technicians who agreed to participate in the study. All were in good health and none of them were taking regularly dosed medication. Both the exposed persons and the control group were asked about their habits, addictions (like cigarette smoking, caffeine, oral contraceptives, etc) and occupational exposure. They were also asked to state whether they were exposed to radiation or chemicals used in laboratories or in disinfection and sterilization units. Drug consumption, viral diseases, recent vaccinations, coffee drinking and radiodiagnostic examinations were also taken into account.

Sister chromatid exchange (SCE)

Peripheral blood samples were taken from each subject and 72-h culture was done. Basal medium was Medium 199 (Seromed Biochrom KG, Berlin, Germany) supplemented with 20 % heat-inactivated fetal calf serum (Seromed) (30 min at 56 °C), 100 U/ml penicillin, 100 µg/ml streptomycin (Seromed), 1.5 ml phytohaemagglutinin (Seromed) and 1 ml L-Glutamine (Seromed). At the 24th hour, 5-Bromodeoxyuridine (Sigma Chemical Co., St.Louis, MO, U.S.A.) of a 20 µg/ml final concentration was added to the cultures and they were incubated in the dark at 37 °C for 48 hours more. 0.5 µg/ml colchicine (Seromed) was added to the cultures for the last 3 hr of incubation. The cultures were harvested and preparations were made according to the routine protocol. Differential staining of sister chromatids was by means of the slightly modified procedure of Wolff and Perry (15). SCEs were analyzed in at least 30 cells containing 46 chromosomes in each preparation.

Statistical methods

Student's t-test was used to evaluate the data concerning the mean numbers of SCE, age, exposure time, cigarette smoking and various exposed groups.

RESULTS

Table 1 shows the frequencies of SCEs in exposed personnel correlated with age, occupation, duration of exposure and smoking habits. The correlation between the duration of occupational exposure and the SCE frequency was significant ($p<0.02$). The mean values of SCEs were significant in both anaesthesia doctors and anaesthesia unit technicians (respectively $p<0.01$ and $p<0.05$). Again smokers and non-smokers differed significantly ($p<0.001$) in these groups (Table I). No significant relationship was found between age and SCEs. In table II the mean number of SCEs/cell and the standard deviation (SD) of the total of exposed and control subjects are given. The difference between the SCE frequencies of smoking exposed subjects and smoking controls was not found significant ($p>0.05$) while the difference between exposed non-smokers and non-smoker controls was found to be significant ($p<0.01$). The SCE frequencies seemed to be significantly higher among exposed smokers than exposed non-smokers ($p<0.001$).

Table I. Age, occupation, duration of exposure to anaesthetic gases and smoking habits of 19 operating room personnel in whom sister chromatid exchanges were counted in lymphocytes from peripheral blood

Group	n	Age (years) Mean ± SD	Occupational Exposure (years) Mean ± SD	SCE / cell Mean ± SD
Total Operating Room Personnel	19	30.26 ± 7.94	6.82 ± 6.48	11.11 ± 1.23
Non-Smokers	13	30.08 ± 6.55	5.31 ± 4.54	10.55 ± 0.76
Smokers	6	30.67 ± 11.13	10.08 ± 9.10	12.33 ± 1.23
Anaesthetists M.D.	11	32.64 ± 9.15	6.14 ± 8.09	11.36 ± 1.29
Anaesthesia unit technicians	8	27.00 ± 4.66	7.75 ± 3.58	10.77 ± 1.13

Table II. Mean sister chromatid exchange (SCE) number in lymphocytes of exposed operating room personnel and control subjects as a function of smoking status

	SCE / cell Mean ± SD					
	n	Exposed	n	Controls	t	p
Smokers[a]	6	12.33 ± 1.23	10	12.57 ± 1.02	0.35	>0.05
Non-smokers	13	10.55 ± 0.76	10	9.07 ± 1.14	3.23	<0.01
t		3.91		5.11		
p		<0.001		<0.001		

n, number of subjects
[a] *> 10 cig./day in both exposed and controls*

DISCUSSION

Smoking plays a causative role in SCE elevations in both controls and the exposed group (16). In various reports, increased levels of SCE in peripheral lymphocytes of smokers were confirmed (17-19). Also in this study, we found that the difference between the smoker and non-smoker controls is significant ($p<0.001$). The results of the present study differs from previous SCE studies by Husum et al., (8,12-14) with negative results concerning the SCE test in exposure to inhalation anaesthetics. On the other hand our findings are in agreement with the previous study by Sardaş et al. (16). They also found a difference between SCE in lymphocytes from operating room personnels and from unexposed control persons.

Since there is a large number of confounding factors such as the level and duration of exposure, biological factors and protective measures taken vary in the different studies, a comparison among them is difficult. Nevertheless some generalised comparisons with the previously published works could be drawn.

We conclude that by examination of sister chromatid exchanges in lymphocytes from peripheral blood in operating room personnel, we have found indication of a mutagenic effect of long-term exposure to waste anaesthetic gases such as halothane, nitrous oxide and isoflurane.

Acknowledgements

We thank Gazi University, Faculty of Medicine, Department of Anaesthesia for helpful contribution.

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