Enterally Taken Chrysotile Asbestos Affects Gastric Mucosa of Rats

ENTERAL YOLLA VERİLEN KRİZOTİL ASBESTİN RATLARIN MİDE MUKOZASINA ETKİLERİ

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Abstract

Occupational and environmental asbestos exposure by inhalation causes pulmonary diseases such as asbestosis, pulmonary and pleural malignancies, pleural fibrosis and calcifications.

This study is designed to show the effects of orally taken asbestos to the gastric mucosa. Sixty Wistar-albino rats were separated into 3 groups. Group A(n:24) had taken 1.5 gr/lt chrysotile asbestos with water. Group B(n:24) had taken 3 gr/lt asbestos with water and Group C(n:12) as a control group had taken only water. Asbestos water solution or only water was given to the rats with baby's bottle. At every 3 months 6 rats from group A and B; 3 rats from group C were sacrificed. Samples from their gastric mucosa, intestine, liver, spleen and mesenterial lymph nodes were taken for histopathological examination.

Gastric dysplasia on incisura angularis was shown in the rats of group B at the end of third month. At the end of one year on the rats in group A and B significant dysplasia was demonstrated in comparison with control group($p<0.005$). Asbestos bodies were coexisted with subcapsular fibrosis in the spleen.

As a conclusion; it is shown that orally taken asbestos fibers made some changes on gastric mucosa that might lead to malignancies. Asbestos bodies which were seen in the spleen are the evidence of the involvement of reticuloendothelial system.

Key Words: Asbestos, chrysotile, gastric malignancy

Özet

Çevresel ve mesleksel asbest maruziyetinin akciğer ve plevrada maligniteye kadar varan patolojiler oluşturduğu bilinmektedir. Oral yolla alınan asbestin oluşturduğu patolojileri inceleyen çalışma sayısı çok azdır. Bu çalışma oral olarak alınan asbestin sindirim sisteminde oluşturduğu etkileri göstermek amacı ile planlanmıştır

Wistar albino cinsi 60 rat çalışmaya alınmış ve 3 gruba ayrılmıştır. Grup A(n:24) daki ratlara 1,5gr/lt krizotil asbest ve su karışımı; grup B(n:24) ye 3gr/lt krizotil asbest ve su karışımı; kontrol grubu olan grup C(n:12) ye ise sadece su biberonla verildi. Her 3 ayda bir grup A ve B'den 6 şar, grup C'den 3 er rat eter anestezi ile sakrifiye edildi. Karaciğer, dalak, bağırsak, mezenter lenf nodları ve mide mukozasından örnekler alınarak histopatolojik inceleme yapıldı.

Grup B'deki ratlarda 3. aydan itibaren incisura angularis'de mide displazisi tesbit edildi. Birinci yılın sonunda grup A ve B deki ratlarda kontrol grubuna göre önemli ve şiddetli displazi ve dalakta asbest cisimcikleri görülmüştür($p<0.005$). Ayrıca dalakta subkapsüler fibrozis oluşumu belirlenmiştir.

Sonuç olarak; ağız yoluyla ratlara verilen asbestin maligniteye yol açacak şekilde gastrik mukozada patolojik değişikliklere sebep olduğu gösterilmiştir. Ayrıca dalakta görülen asbest cisimcikleri ve patolojik değişiklikler retiküloendotelyal sistemin de sürece katıldığını düşündürmüştür.

Anahtar Kelimeler: Asbest, krizotil, mide karsinomu

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Asbestos is a natural mineral that is chemically and physically distinct and its industrial use is common. Sweden, Finland, Bulgaria, Greece, Pakistan and Turkey are some of the countries those have asbestos deposits. The asbestos deposits are mostly found in some rural parts of central and southeast Anatolia in Turkey. The type of asbestos in most of these regions is tremolite and chrysotile.[1-6] Pleural and pulmonary diseases occur in people due to occupational and environmental exposure to asbestos. It has been determined that 20% of individuals certified as having occupational asbestos exposure die of their pneumoconiosis in United States.[2]

The respiratory diseases caused by asbestos inhalation are well documented however there is not a well documented study about gastrointestinal system diseases related to enterally taken asbestos by the way of water and food. The purpose of this

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study is to evaluate the effects of orally taken asbestos to the gastric mucosa of rats.

Material and Methods

This experimental study is done in the animal laboratory of Ankara Training and Research Hospital by the permission of Hospital Ethical Committee. Sixty wistar-albino rats; 10 to 12 weeks old were included in the study.

White asbestos (chrysotile) used in the study had been taken from the asbestos mine of Kangal-Kamper district of Sivas in the middle Anatolia. The samples were purified from other materials and pure chrysotile asbestos was prepared in the Chemistry Faculty of Inonu University. The physicochemical and elementary properties of this material were evaluated by DTA (Differential Thermal Analyzer), DSC (Differential Scanning Colorimeter) and XRD (X-ray difractometer).

Rats were separated into 3 groups. Group A (n:24) had taken 1.5 gr/lt water with chrysotile asbestos. Group B (n:24) had taken water with 3 gr/lt asbestos and Group C (n:12) as a control group had taken only water. Water was from Ankara's tap water. Asbestos + water solutions were prepared outside the room where rats were kept. Rats were in cages and were fed by rat food and feces of the rats were removed and cleaned immediately. The environment was free from asbestos. Water need of rats is 15-20 ml per day. Rats sucked asbestos water solution or water from 250 ml feeding bottles. Dummies were periodically purified and controlled. At every 3 months 6 rats from group A and B; 3 rats from group C were sacrificed after ether anesthesia with median incision. Samples were taken from gastric mucosa, intestine, liver, spleen and mesenterial lymph nodes for histopathological examination. Gastric samples were taken after washing stomachs of the sacrificed rats by 0.15 mol/l NaCl solution. After searching all the gastric mucosa for a lesion, according to the Sidney system, 2 samples from antrum and corpus and 1 sample from incisura angularis were taken. The samples were fixed by 10% formaldehyde solution and blocked with paraffin. Five microslices were taken and dyed with hematoxylin eosin and histopathological evaluation was done.

Statistical analyzes were done by SPSS using Spearman's test for correlation, comparison of groups by Kruskal Walls and comparison in a group by Mann Whitney tests.

Results

Study was completed in 12 months. During this period none of the rats became ill and none of them died. None of the rats had any macroscopically seen mass, ascite or lymphadenopathy. Histopathological examination showed gastric mucosal dysplasia in the rats of group B (taken high dose asbestos) at the end of 3rd

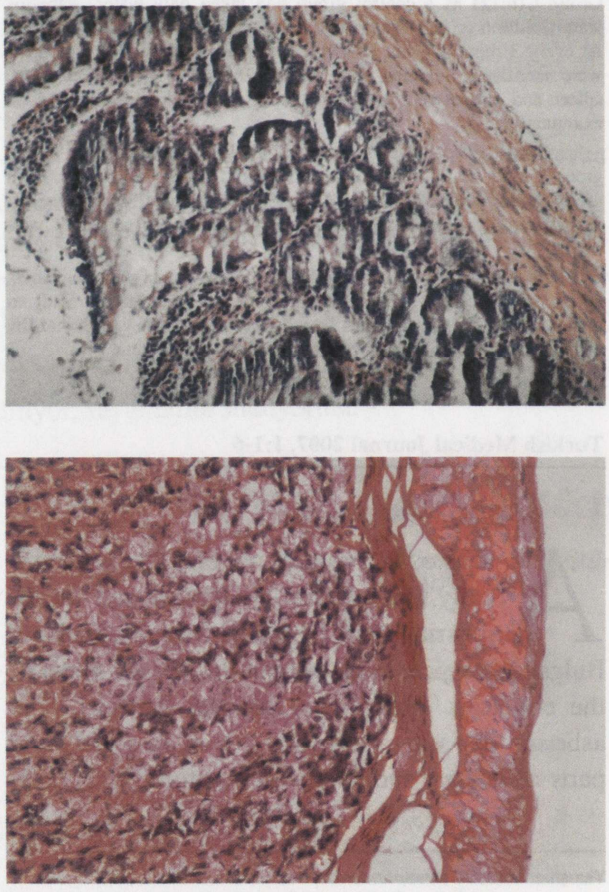

Figure 1. Dysplasia in the rat's gastric mucosa of incisura angularis in the group B at the end of 3rd month A (H&E 20x) and B (H&E 200x).

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Table 1. Histopathological examination of gastric mucosa and spleen of the rats

	Metaplasia	Dysplasia	Gastric Ca.	Spleen Asbestos
3rd month				
Group A	0/6	0/6	0/6	0/6
Group B	0/6	2/6	0/6	0/6
Group C	0/3	0/3	0/3	0/3
6th month				
Group A	0/6	5/6	0/6	4/6
Group B	0/6	6/6	0/6	5/6
Group C	0/3	0/3	0/3	0/3
9th month				
Group A	0/6	4/6	0/6	2/6
Group B	0/6	5/6	0/6	2/6
Group C	0/3	0/3	0/3	0/3
12th month				
Group A	0/6	4/6	0/6	6/6
Group B	2/6	5/6	0/6	6/6
Group C	0/3	0/3	0/3	0/3

month. Dysplasia was seen on incusura angularis (Figure 1).

After 6 months statistically significant gastric dysplasia was found in both of group A and B. All the rats in control group were normal (Table 1).

At the end of 9 months, the rats in group B had significantly more dysplasia then group A (p: 0.019). Also spleen had more asbestos bodies in group B rats then group A rats (p: 0.008). Gastric metaplasia was only shown in 2 rats in group B at the end of 12 months. Severe dysplasia in one B group rat is seen in Figure 2.

Gastric dysplasia localization of all cases that had dysplasia was mostly on incusura angularis. Asbestos in the spleen was seen mostly with subcapsular fibrosis (Figure 3, 4).

At the end of 12 months; difference of total gastric dysplasia between group A and B was not significant. The histopathological evaluation of liver, intestine and mesenterial lymph nodes were found to be normal (Table 1).

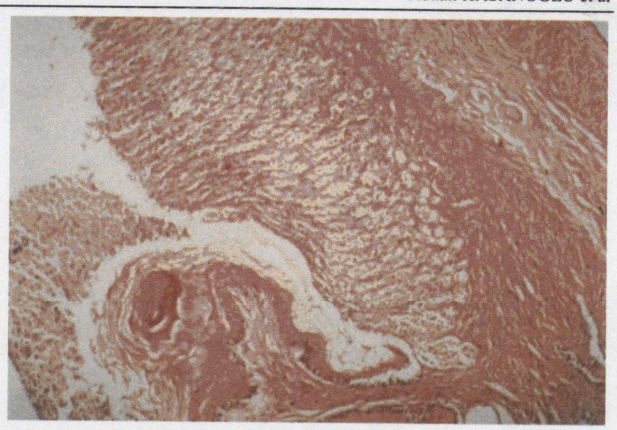

Figure 2. Gastric squamous metaplasia in the rat in group B at the end of 12th month (H&E 20x).

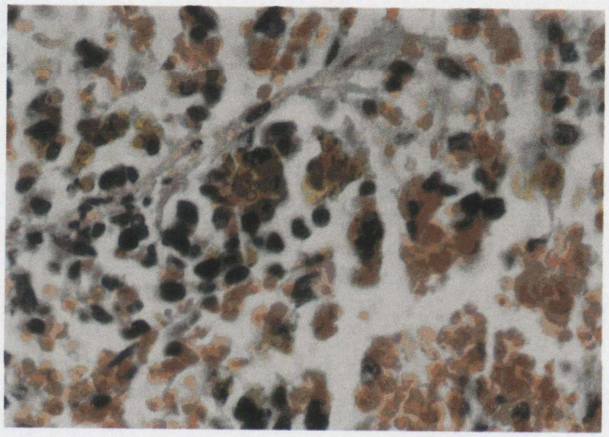

Figure 3. Asbestos in the spleen (H&E, 1000x).

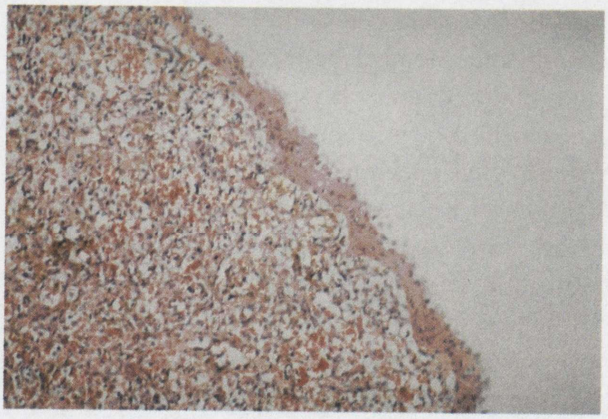

Figure 4. Subcapsular fibrosis and mesothelial proliferation in the spleen (H&E, 40x).

None of the rats in control group in any period showed any pathological change in the gastric mucosa or in spleen.

Discussion

Recently, etiology of gastric malignancy became very important to avoid from cancer. H. pylori, N-nitrozo compounds, smoking, salted food, and heredity are well known risk factors (predisposed factors) for gastric cancer. Environmental and occupational exposure of some carcinogens is also shown to cause malignancies in a long period. Asbestos is one of these environmental and occupational factors that is well studied. It is shown that asbestos exposure leads to pleuropulmoner malignancies.[3-9] Some studies also showed statistically significant elevations in esophageal, stomach and total gastrointestinal tract cancer in all asbestos exposed workers.[10,11]

Most of these studies are retrospective evaluation of workers that were occupationally exposed to asbestos.[10,11] Epidemiological studies are mostly performed in Canada and USA to assess the effects of asbestos covered water pipes to the population.[12,13] Some of these studies demonstrated a relationship between ingested asbestos and gastric malignancy.[14,15]

Experimental studies about gastric malignancy and asbestos is very rare. Thomas et al gave the rats drinking water with chrysotile asbestos for 1.5 year and compared with control group. The study results suggested that chronic exposure to asbestos decreased ability of the intestine to absorb some nonmetabolizable sugars.[16] Another study showed that chrysotile asbestos had carcinogenetic potential on intestinal system of the rodents.[17] A synchronic gastric and intestinal malignancy in a patient who had a severe exposure to asbestos was reported. The histopathological evaluation of lungs of this patient revealed asbestos bodies but there were none in the gastrointestinal system.[18] Correa et al suggested a cascade that shows gastric cancer formation after precancerous changes in a time period.[19-21] This period for asbestos exposure was supposed to be 1 to 10 years in the studies.[22-24] Our study showed that 1 year enteral exposure to asbestos made some changes according to this cascade; dysplasia and metaplasia while rats in control group showed no changes. None of the rats developed gastric cancer but most of them showed precancerous changes mostly on incisura angularis in one year period. In a longer time interval these changes are supposed to develop gastric cancer.

Prospective randomized studies demonstrated that gastric cancer occurs on 20 to 80% of gastric dysplasies.[25,26] In another experimental study white asbestos covered with polyethylene was located on the major curvature of stomach of rats. After 25 months of follow-up, gastric cancer occurrence was reported. Spleen and liver were not histopathologically evaluated in this study.[23] Another fact is that, rats exposed to more asbestos demonstrated more pathological changes than the rats in the group given less asbestos.

Some studies showed that the malignancy potential of asbestos is because of fibrogenetic effects of the fibers.[27] It is shown in epidemiological studies about mesothelioma and lung cancer that when the exposure period is longer and more; diseases due to asbestos, especially malignancy develops more.[3,5,7,8] While asbestos bodies could be shown in pleural mesothelioma and lung cancer in many studies, there is only one study that shows asbestos fibers in gastric malignancy. Ehrlich et al evaluated colon cancer patients and showed asbestos bodies or fibers on the colon segments of 12 patients that were exposed to asbestos. It was not seen in the colon cancer group that was not exposed to asbestos.[28] In this experimental study we could not demonstrate asbestos in the mucosal samples from stomach but we demonstrated asbestos fibrils in the samples taken from spleen. This may be an evidence of asbestos transmission to lymphohematogenic stream. After transmitted to lymphohematogenic stream asbestos fibers were arrested by spleen which is the main organ of reticuloendothelial system. In a study which was done by necroscopic evaluation

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of the patients who were exposed to asbestos; fibers were also shown in the spleen.[27] The evidence demonstrating the transport of test substances in the micrometer size range across the adult intestinal barrier is examined for a number of food substances and environmental contaminants. Macromolecules can be transported across the barrier by endocytosis; by uptake into the gut-associated lymphoid tissue.[29] Finally this may lead to a passage to lymphohemathogenic pathway.

As a result, orally taken chrysotile asbestos induced dysplasia and metaplasia on the gastric mucosa of rats in one year period of exposure. So it is suggested that asbestos makes carcinogenetic changes by its fibrogenetic and cytotoxic effects which were well documented by the studies done before about pleura and lung cancer.

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