

Are serum aluminum levels a risk factor in the appearance of spontaneous pneumothorax?

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Aim: To investigate the relationship between aluminum and spontaneous pneumothorax (SP) development.

Materials and methods: A patient group and a control group were formed with 100 individuals in each. The serum aluminum levels of the groups were determined and statistically compared.

Results: The mean serum aluminum levels were 5.6 ± 2.4 µg/L (1.6-11.9) and 23.2 ± 15.4 µg/L (2-81) in the control and SP groups, respectively ($P < 0.001$). The specificity and sensitivity of the measurement of aluminum level were 74.4% and 86.4% in the SP group. The risk of SP development was found to be 18 times higher in individuals with high serum levels of aluminum compared to that in individuals with low serum levels of aluminum.

Conclusion: A high level of aluminum is a risk factor for the development of SP.

Key words: Aluminum, pneumothorax, public health

Spontan pnömotoraks gelişiminde serum alüminyum seviyeleri bir risk faktörü müdür?

Amaç: Bu çalışmada spontan pnömotoraks (SP) gelişimi ile serum alüminyum düzeyleri arasındaki ilişkinin analiz edilmesi amaçlandı.

Yöntem ve gereç: Yüz SP hastasından oluşan hasta grubunun yanı sıra 100 kişiden oluşan sağlıklı kontrol grubu çalışmaya dahil edildi. Gruplar serum alüminyum düzeyleri açısından istatistiksel olarak kıyaslandı.

Bulgular: Ortalama serum alüminyum düzeyleri SP ve kontrol grupları için sırasıyla $5,6 \pm 2,4$ µg/L (1,6-11,9) ve $23,2 \pm 15,4$ µg/L (2-81) bulundu ($P < 0,001$). SP grubunda serum alüminyum düzeyinin özgüllüğü % 74,4 iken duyarlılığı % 86,4 bulundu. Serum alüminyum düzeyi yüksek olan bireylerde, düşük tespit edilen bireylere kıyasla SP gelişme riski 18 kat yüksek tespit edildi.

Sonuç: Yüksek serum alüminyum düzeyleri SP gelişiminde bir risk faktörü olabilir.

Anahtar sözcükler: Pnömotoraks, alüminyum, halk sağlığı

Introduction

Aluminum is the third most common element after oxygen and silica (1). It has recently been shown to have adverse effects upon human health. Contact with aluminum cannot be avoided

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because it comprises about 8% of the earth's surface (2).

It was first reported in 1934 that the inhalation of aluminum dusts caused pulmonary diseases. Fourteen years later, 11 people with vocational pneumo-infections due to bauxite inhalation were reported (3). It was also reported that Shaver's disease involving fibrosis with large bubbles and the symptoms of potroom asthma had developed in workers employed in the manufacture of aluminum (3). Aluminum is known especially to play a role in Alzheimer's disease and also affects the other organ systems. However, there has been no study concerning its causing of bullae formation or spontaneous pneumothorax evolution.

In our first study, the relationship between aluminum and spontaneous pneumothorax (SP) development was shown (4). The present study aimed to show this relationship again with a large series and to demonstrate serum aluminum level as a risk factor in SP.

Materials and methods

The patient group consisted of 100 patients who presented to our clinic with the diagnosis of SP between 2002 and 2008, and the control group consisted of 100 healthy individuals who had no complaints. Both groups underwent a physical examination. The history of the subjects in both groups was obtained, and all underwent routine blood evaluations. X-rays and thoracic computed tomography (CT) of all the subjects were also performed. The serum aluminum levels of the subjects were measured twice in the same laboratory. The blood samples were taken after the patients had been admitted to the clinic during the treatment. Blood samples were taken into vacuumed tubes not containing gel to avoid aluminum contamination and were not opened before centrifugation. After centrifugation serum materials were put into clean tubes and stored at -80 °C. Atomic absorption spectrometry (AAS) was used to determine the serum aluminum levels.

The treatment options for SP are conservative management, needle aspiration, percutaneous catheter for drainage (Heimlich valve, etc.), tube

thoracostomy, thoracotomy, and video assisted thoracic surgery (VATS).

Thoracic CTs were performed after expansion of the lung. The structure of the pulmonary parenchyma was evaluated. Postoperative morbidity and mortality were determined.

Statistical analysis

The statistical analyses of the data were performed using SPSS for Windows 11.5. In the evaluation, Student's t-test, Spearman rank correlation analysis, chi-square test, and Fisher's exact test were used. In addition, receiver operating characteristic (ROC) analysis was performed in order to determine the level that best identified the aluminum levels in both the control and patient groups, and this best level was determined to be 6.95 µg/L (AUC: 0.904 ± 0.028, P < 0.001, Figure). Considering this value, odds ratio (OR) was also calculated to determine the results of the risk (5,6). Mean ± standard deviation values were calculated as descriptive statistics. P < 0.05 was considered significant.

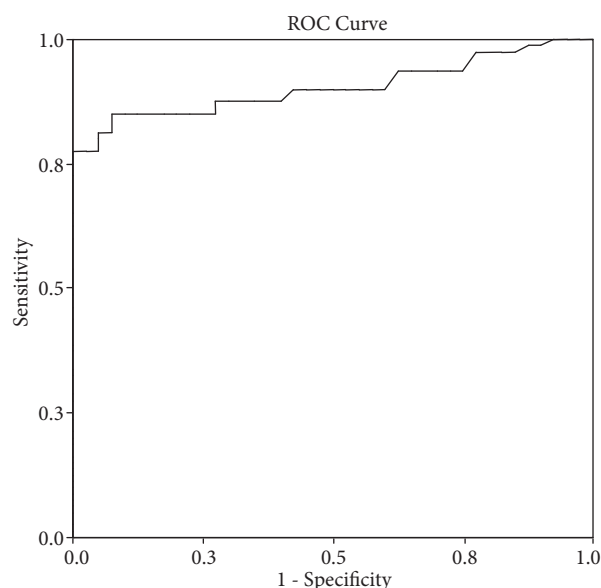


Figure. ROC analysis of sera aluminum levels.

Results

The mean age of the patients in the SP group was 32.25 ± 13.72 years (14-77 years). Ninety-five of the patients (95%) in this group were male. The male

predominance was statistically significant in the SP group ($P < 0.001$). The mean age of the subjects in the control group was 24.80 ± 7.59 years (17-47), and 60% of the subjects in this group were male. The mean level of aluminum in the blood samples of the SP group was 23.2 ± 15.4 $\mu\text{g/L}$ (2-81 $\mu\text{g/L}$) and the level of aluminum in the control group was 5.6 ± 2.4 $\mu\text{g/L}$ (1.6-11.9 $\mu\text{g/L}$, Table 1).

SP was on the right in 64 patients (64%), and the mean aluminum level on the right was 25.8 $\mu\text{g/L}$ and the mean aluminum level on the left was 18.6 $\mu\text{g/L}$ in the patients with SP. The difference between the 2 values was statistically significant ($P < 0.05$, Table 2). Seventy-one (71%) of the SP patients had bullous lesions on the thoracic CTs and the mean aluminum level of these patients was 25.8 $\mu\text{g/L}$, while it was 16.7 $\mu\text{g/L}$ in the patients with no bullous lesions. The difference was statistically significant ($P < 0.05$, Table 2), and none of the subjects in the control group had bullous lesions, and all the other results of the control group were normal.

The mean time since the onset of symptoms in the patients with SP was 4.33 ± 17.02 days (1-150). It was 1 day in 67% of the patients. Recurrent SP developed in 11 patients (11%), and we performed VATS in 6 patients (6%).

The serum levels of aluminum in the patients with SP were higher ($P < 0.001$). According to ROC analysis performed, the level that was able to best identify the patient and control groups was 6.95 $\mu\text{g/L}$. The risk of SP development in the patients with higher than 6.95 $\mu\text{g/L}$ serum aluminum level was 18 times that of the controls (OR=18.46, 95% CI: 7.07-48.18). In the patient group, there was not a significant difference between the amount of aluminum in males and females. Seventy-eight of the patients were smokers (78%). Serum aluminum level in SP patients who were smokers was 25 $\mu\text{g/L}$ while the level was 16.9 $\mu\text{g/L}$ in the non-smokers; the difference between them was statistically significant ($P < 0.01$, Table 2). Twenty-four of the controls were smokers (24%). Serum aluminum level in the controls who were

Table 1. The results of 3 studies on patients with spontaneous pneumothorax and healthy controls.

Study	N	Serum Aluminum Levels ($\mu\text{g/L}$)		P
		SP Mean \pm SD	Control Mean \pm SD	
Han (2004)	60	18.4 \pm 14.6	2.7 \pm 0.8	<0.001
Leo (2005)	20	3.8 \pm 1.2	4.6 \pm 1.8	0.19
Han (2008)	200	23.2 \pm 15.4	5.6 \pm 2.4	<0.001

Table 2. Relationship between side of pneumothorax, bullous lesions on computed thorax tomography, smoking, and aluminum level in the patient group.

		N	Serum Aluminum Levels ($\mu\text{g/L}$)		P
			Mean \pm SD		
Side	Right	64	25.8 \pm 16.9		<0.05
	Left	36	18.6 \pm 11.2		
Lesions	Bullae (+)	71	25.8 \pm 16.2		<0.05
	Bullae (-)	29	16.7 \pm 11.1		
Smoking	(+)	78	25.0 \pm 16.7		<0.01
	(-)	22	16.9 \pm 7.3		

smokers was $6.1 \pm 2.9 \mu\text{g/L}$, while it was $5.4 \pm 2.2 \mu\text{g/L}$ in the non-smokers. There was no statistically significant difference between the smokers and nonsmokers in the control group ($P > 0.05$).

The mean serum aluminum levels were $24.9 \mu\text{g/L}$ and $19.5 \mu\text{g/L}$ in the patients whose period of symptoms was 1 day and longer than 1 day, respectively ($P > 0.05$). The mean serum aluminum levels were $24.0 \mu\text{g/L}$ and $16.6 \mu\text{g/L}$ in the patients with relapse and those with no relapse, and $23.4 \mu\text{g/L}$ and $20.7 \mu\text{g/L}$ in the operated and not operated patient groups for SP, respectively ($P > 0.05$, $P > 0.05$, respectively).

No postoperative complications or mortality occurred.

Discussion

It was first reported in 1934 that the inhalation of aluminum dusts caused pulmonary diseases. Fourteen years later, as a result of bauxite inhalation, 11 people with vocational pneumo-infections (Shaver disease) were reported (3,7). Pulmonary fibrosis and emphysema are known to have occurred in workers who were exposed to aluminum oxide and silica smog. In addition, it was reported that some granulomatous lesions developed in the respiratory bronchi in laboratory animals exposed to high concentrations of aluminum chlorohydrate used as aerosol antiperspirant (8). The clinical picture occurs in the form of dyspnea, cough, and pneumothorax, and nodular interstitial fibrosis develops as a histopathologic sign. In workers exposed to pure aluminum dusts, it has been reported that pulmonary fibrosis develops, which has been termed aluminosis (9,10). Aluminum may also cause Shaver's disease, which causes fibrosis and respiratory problems with large bullae, and SP is a frequently occurring complication (11). In workers employed in the manufacture of aluminum, potroom asthma symptoms were reported, but the exact etiology is not clear. In a 32-year-old worker employed for 8 years in an atmosphere containing aluminum dusts, development of sarcoid-like pulmonary granulomatosis was reported (12).

Because of its physical and chemical properties, aluminum has a very wide area of usage, including the

drug and cosmetic industries. The contact with aluminum occurs mainly with food and kitchen utensils and through many ways such as dietary, environmental, and therapeutic procedures (13). It is reported that the highest level of aluminum is found in the lungs, and it is 20 mg/kg in terms of age and weight. This has been attributed to the accumulation of insoluble compounds entering the lungs through respiration. Pulmonary aluminum concentration increases with age, depending on the continuation of the environmental contact and physiological changes (14,15).

Smoking is another factor that increases the body's burden of aluminum (16). In our study, the serum aluminum levels of the smokers were higher than those of the non-smokers; 78 of the patients (78%) were smokers, and the level of aluminum in the blood plasma of the SP patients who smoked was $24.98 \mu\text{g/L}$, while it was $16.94 \mu\text{g/L}$ in the non-smokers. The difference between the aluminum levels of these patients was statistically significant. None of our patients had chronic obstructive pulmonary disease or bronchial asthma according to lung function test results, all of which were normal.

None of our patients in the study group had any vocational history related to aluminum, and most of them lived in urban areas. Nevertheless, aluminum has such wide usage that it is impossible to avoid contact with it. It is clear that aluminum has a pathologic effect on the lungs and other systems, as shown in previous studies. In our study, the aluminum levels of the SP patients were significantly higher than those of the controls.

This study comprises our second report on this issue. Higher plasma concentrations of aluminum in patients with SP were reported (4); however, another study, from France, did not confirm the relationship between aluminum and SP (17).

Conclusion

Aluminum may play a role in SP etiology, causing the development of subpleural bleb and bullous lesions. It is obvious that it will give us a clear idea in the prognosis and treatment of SP and it can be supposed that a high level of aluminum in blood plasma is a risk factor for SP development.

Environmental agents or differences in the characteristics of different regions may have played an important role in establishing this relationship, but the findings of our study may be helpful for thoracic

surgeons in the treatment and follow up of SP and can be used for occupational decision-making and public health management.

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