The effects of cadmium on gastric mucosal barrier

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6 week -old male albino rats were received 15 \.\g/ml cadmium containing water and normal rat food for 30 days and on day 30, under urethane anesthesia, their stomachs were reached and the components of gastric barrier as well as cadmium content were compared with those of control animals.

In the cadmium exposed group blood cadmium levels increased from 3.89±1.45 to 9.42±3.02 ug/c/L *(p<0.001) and mucosal cadmium content increased fromX).070±0.047 to 0.197±0.033 pg/g dry wt (p<0.01).*

Elevated mucosal lesions were associated with diminished gastric mucin and PGE2 contents in rats exposed to cadmium. Increased hemoglobin content and diminished acid output in gastric luminal fluid gave a good evidence for the breakdown of gastric barrier due to high cadmium intake. However the mucosal phospholipid and cholesterol which are accepted as mucosal surfactant were not changed in cadmium exposed rats.

The present results suggested that oral exposure to high cadmium impaires the mucosal defence mechanism against noxious agents. [Turk J Med Res 1994; 12(2): 53-56]

Key Words: Cadmium, Mucosal barrier, Mucin, Phospholipid, Gastric ulcer, Prostaglandin E2 •

It has been known that gastric mucosal barrier prevents selfdigestion of mucosa by pepsin and acid via several components. Rich mucosal blood flow (1), secretion of bicarbonate ions (2) and prostaglandin E2 (3,4), cytoprotectivity of gastric mucosa as well as mucus layer (4,5) are included into the component of this barrier. Gastric mucin protects the underlying epithelial cells. Bicarbonat secretion neutralizes the secreted acid into lumen, prevents backdiffusion of hydrogen ions into inter or intracellular spaces and decreases acid induced cellular damage (6). Prostaglandin E2 production potentiates the protective capacity of gastric mucosa by increasing mucosal blood flow and bicarbonat secretion and inhibiting acid secretion (4). Gastric phospholipids forming a hydrophobic mucosal surface between luminal secretion repel the hydrogen Ions and keep the surface of epithelium dry and prevent the contact of epithelial surface with luminal acidity. That's why mucosal phospholipids are accepted as the other component of the barrier and named as gastric surfactant [1,7). It is well known that the destructive and protective capacities should 'be in well balanced for the functional integrity of the gastric mucosa. Any factor which causes a disequilibrium in the balance between these two capacities results in cellular lesions and is involved in the ethiology of gastric ulcer (7,8).

Cadmium has been recognized as one of the most toxic environmental pollutants due to its ability to induce severe alterations in the function of various organs following either acute or chronic intake. Exposure to high cadmium for human being seems unavoidable since numerous human activities increase gradually the release of cadmium to the environment which in turn increases the intake of cadmium via inhalation of polluted air or ingestion of food and drinking water. Tobacco is also an important source of cadmium intake for human (9,10).

Among the various hazardous affects of cadmium on biological systems, its ulcerogenic effect on intestinal mucosa has been demonstrated by Anderson et al and Tasarenko et al (11,12). The results of our previous study on cadmium induced hypoacidity (13) sug-

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gested that oral cadmium intake has also, some adverse influence on gastric functions. But the effects of cadmium on gastric mucosa, were not studied before.

In this experimental study we investigated the possibility of cadmium induced changes, the components of gastric mucosal barrier in rats subjected to high cadmium containing water for 30 days.

MATERIALS AND METHODS

20 male albino rats weighing 190-235 g were used in this experimental study. Ten of these animals were kept on normal food and tap water ad libitum for 4 weeks while the remaining 10 rats were received 15 ug/ml of cadmium as CdCte in their drinking water for the same period.

At the 30th day, following 24 h fasting, all animals were anesthetized with 1 g/kg of urathane i.p. and their abdomen were opened with a midline incision. The lowermost level of the oesophagus was tied by preserving vagal nerves and vessels. A catheher placed into their stomach through the duodenum was used for gastric flushing to remove the food remnant as well as sampling.

Using this catheter, after repeated washing of the stomach with 37°C saline, 2 ml of distilled water (pH: 7.0) at 37°C was given into the stomach and kept there for 30 min, and it was used for the measurement of secreted acid concentration by titration with 0.01 N NaOH and its hemoglobin content by the method of cyanmethemoglobin (14). Then the stomach were opened through lesser curvature and examined using a magnifier for the numbers of ulcers and petechial bleedings. When scoring of the ulcers three areas of petechial bleedings were accepted as one ulcer.

The acidic mucopolysaccharide as an indicator of gastric mucosal barrier was measured by the method of Come et al. which was based on the alcian blue binding capacity of gastric mucosa (19).

The lipids of mucosal scrapings were extracted by the method of Radin (2). The blood and the mucosal extracts were used for the analysis of cholesterol (4) and phospholipid (15), mucin (19) as well as cadmium. The PGE2 content of the gastric mucosa were measured by using HPLC (Varian 5020) by the method of Cockrell and Ellis (16).

The mucosal scrapings were dried overnight at 70°C and dissolved in nitric and perchloric acid (6:1 V/v). The graphite furnace of Atomic Absorbtion Spectrophotometry (Hitachi Z 8000) was used for cadmium analysis in the mucosa and blood samples taken from the heart. The cadmium content were expressed as ug/g dry weight (wt), tissue and ug/L for blood.

The results were expressed as mean ± SD, and "student t test" was used for the statistical analysis.

RESULTS

Blood cadmium level was found to be 3.89±1.45 ug/dL in control rats. Addition of 15 ug/ml Cd Cl2 into the drinking water for 30 days caused a significant increase in blood cadmium levels of animals (9.42±3.02 ug/dL, p<0.001) (Figure 1). The mean cadmium content of mucosal scrapings were also increased from 0.070+0.047 to 0.197±0.033 ug/g dry wt due to high cadmium intake (p<0.01).

Chronic cadmium intake caused to decrease in gastric acid output. The mean acid was 37.84±6.02 mEq/h and 25.64+6.93 mEq/h in control and treated rats, respectively (p<0.01) (Figure 1). Hemoglobin content of gastric fluid increased from the control value of

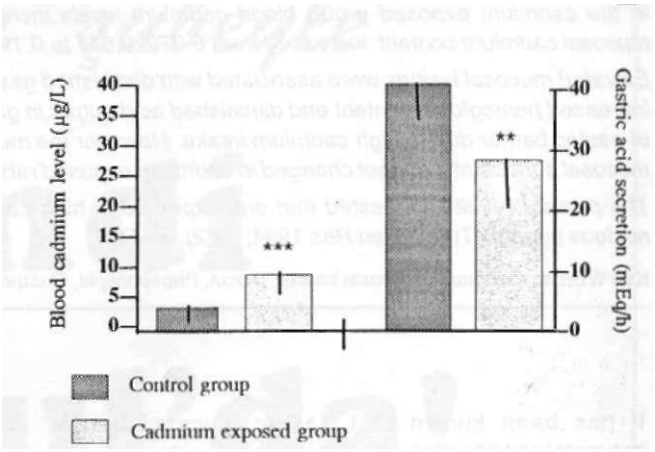

Figure 1. The changes of cadmium level of blood and gastric acid secretion.

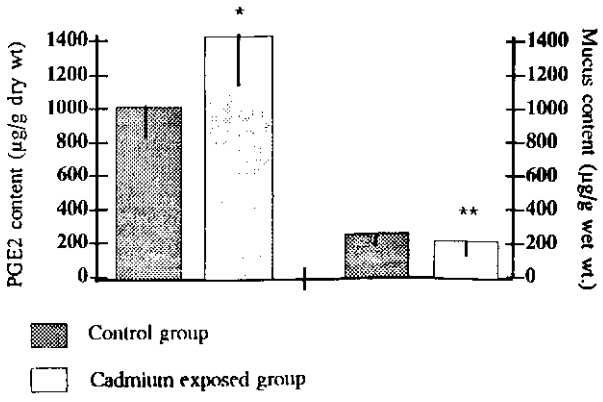

Figure 2. The changes of PGE_2 and mucus content in gastric mucosa.

Table 1. The levels of phospholipid and cholesterol in blood and gastric mucosa of rats exposed to cadmium

	Control group	Cadmium exposed group
Blood		
Cholesterol (mg/dl)	67.91+7.23	63.58±8.95
Phospholipid (mg/dl)	121.48±14.01	124.06+13.10
Gastric mucosa		
Cholesterol (mg/g wet wt.)	2.84±0.41	2-.52+0.42
Phospholipid (mg/g wet wt.)	6.59±0.45	6.65+0.93

3.39±1.42 ug/ml to 4.47±1.33 ug/ml in animals receiving high cadmium.

In cadmium treated rats, gastric mucosa lost its integrity and increased petechial bleedings were observed in spite of its bright color and inteprity in control rats. The ulcer number was 0.45+0.32 in rats exposed to oral cadmium. While the mean alcian blue binding capacity which shows the acidic mucopolysaccharide content of gastric mucin was 188.06+10.76 ug/g wet wt in control rats, Its level decreased significantly to 158.41 ±22.74 ug/g wet wt after the high cadmium intake ($p<0.01$) (Figure 2).

The mean PGE2 levels decreased from 1321.92±271.65 ug/g wet wt. to 1030.50±278.51 ug/g wet wt. ($p<0.05$) in cadmium treated rats (Figure 2). As depicted in Table 1 neither cholesterol nor phospholipid content of both mucosa and blood changed in rats exposed to high cadmium.

DISCUSSION

Our findings showed that in rats receiving high cadmium containing water for 30 days, cadmium levels increased significantly in blood and gastric mucosa. Becaue of its cumulative nature cadmium accumulates in most tissues of the body including kidney and liver (10,17). The results of present study showed that gastric mucosa can also be included into the list of organs which are prefered by cadmium. Togetherness of mucosal erosions such as ulcer and petechial bleedings and high cadmium in the gastric mucosa gives an impression that accumulation of cadmium in the gastric mucosa may be accounted for the breakdown of mucosal barrier. Gastric mucus gel adhering to the gastric mucosal surface plays an important role in the protection of the underlying epithelium against acid, pepsin and mechanical damage (5,6).

It has been reported by many authors that a decrease in gastric mucus content results in a breakdown of mucosal barrier (6,7,8). Increased lesions and petechial bleedings were associated with decreased gastric acid output and increased hemoglobin leakage into gastric lumen. Positive correlation between ulcer and luminal hemoglobin was obvious evidence of breakdown of mucosal barrier. Despite of its mechanism is unclear, the presence of significant negative correlation between decreased acid output and increased mucosal cadmium ($r=-0.764$, $p<0.01$) supports the results of our previous in vitro study indicating cadmium induced hypoacidity (10). In the present study cadmium induced hypoacidity may be explained by an increase in hydrogen ion backdiffusion as demonstrated in the broken gastric barriers by Davenport et al (20).

These cadmium induced changes in gastric mucosal barrier were also supported by a significant decline in mucosal PGE2 levels. The presence of significant negative correlation between mucin and cadmium levels of mucosa ($r= -0.749$, $p<0.01$) and PGE2 and cadmium content ($r= -0.908$, $p<0.001$) in this study support that the functions of mucosal epithelial cells are sensitive against the accumulation of cadmium . Exposure to high cadmium produces a severe impairment in gastric mucosal integrity.

The other component of mucosal barrier is the hydrophobic capacity of mucosa, in other word mucosal phospholipid content (1,7). Cadmium accumulation in the mucosal cell has changed neither phospholipids nor cholesterol content of the gastric mucosa of rats exposed to high cadmium. These findings are in of accord with the results of Amanuma and Suzuki who showed no cadmium induced alteration in the content of lung surfactant which has close structural similarities with gastric mucosal phospholipids (18).

In conclusion, these results suggest that exposure to high cadmium from polluted environment via inhalation of air, ingestion of contaminated food, smoking or drinking water by weakening gastric mucosal barrier against noxious agents, facilitates the occurrence of mucosal lesions and may increase the susceptibility of gastric ulcer in the population. However more and detailed studies are needed in this topic.

Kadmiyumun mide mukoza bariyerine etkisi

Kadmiyumun, midedeki mukozal bariyere etkisini incelemek amacıyla yapılan bu çalışmada, 30 gün süre ile 15 \\gjml Cd^{++} içeren su verilen sıçanların bulguları kontrol hayvanlarınki ile karşılaştırılmıştır. Beslenme süresinin sonunda, kanda ve mide mukozasında artan kadmiyumun, bazal asit salgısını

ve *müküs miktarını azalttığı ve belirgin ülser oluşumuna yol açtığı gözlenmiştir.*

Kadmiyum alan sıçanlarda kan ve mide mokuzasındaki kolesterol ve fosfolipid miktarının değişmemesine karşın, mukoza kazıntısındaki PGE2 düzeyinin azaldığı da dikkati çekmiştir.

Sonuç olarak, bulgularımız, oral kadmiyum alınmasının mide mukoza barlyerini zayıflatarak, ülsere eğilimi arttıracağını düşündürmektedir. [TurkJMed Res 1994; 12 (2): 53-56]

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