The Effects of Silicon on Serum Total Protein, Albumin, Urea and Creatinine Levels and Histological Structure of Kidney Tissue in Rats

SİLİKONUN SIÇANLARDA SERUM TOTAL PROTEİN, ALBUMIN, ÜRE VE KREATİNİN SEVİYELERİ VE BÖBREK DOKUSUNUN HİSTOLOJİK YAPISINA ETKİLERİ

Leyla ÇOLPAN*, İstem ÇİLLİ**, İsmet AYDIN

* Dept. of Biochemistry, Medical School of Dicle University, Diyarbakır,
** Dept. of General Surgery, Istanbul Hospital, Istanbul,
*** Dept. of Endocrinology and Metabolism, Dicle University, Diyarbakır, TURKEY

Summary.

Silicon has been widely used in different medical areas. In this study, 40 adult rats investigated to evaluate effects of silicone on kidneys. Animals were divided into four groups. First group was given 0.1 ml intraperitoneal saline, while second group received olive oil. Third group was medicated by silicon (2,2-dimethyl)-4-(chlorometyI)- 1,3-dioxa-2-silacyclopentane) at the dose of 7,5 mg/kg, while fourth group was treated with intraperitoneal silicon at the dose of 15 mg/kg for 28 days. At the end of this period, the body weights of the animals were determined and intracardiac blood samples were taken. Silicon medication caused a significant decrease in serum protein (p<0.05) and albumin (p<0.001), and an increase in serum urea levels(p<0.00l). Histopathological impairements characterized with glomerulotubular damage including cellular derangements at tubular brush border, heamoragic alterations in the glomerular area and epithelial protrusion towards the tubular lumens were remarkable in the third and fourth groups.

These results indicated that I) silicon has a dose related harmful effect on the renal structures. 2) Glomerulotubular damages may influence renal functions of the rats treated with silicon deeply.

Key **Words:** Silicon, Rat, Kidney, Total protein, Urea, Creatinine, Histopathological alterations

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Ozet

Silikon tıpta farklı alanlarda yaygın şekilde kullanılmaktadır. Bu çalışmada, 40 erişkin sıçanın böbreklerinde silikonun zararlı etkileri araştırıldı. Havyanlar 4 farklı gruba ayrıldı. Birinci gruba 0.1 ml serum fizyolojik, ikinci gruba intaperitoneal zeytinyağı verildi. Üçüncü gruptakilere 7,5mg/kg, dördüncü gruba da I5mg/kg günlük dozda silikon (2,2-dimethyl-4 (cholorometh yl)-l,3-dioxa -2- silacyelopentane), 28 gün boyunca intraperitoneal olarak uygulandı. Bu periyod sonunda hayvanların vücut ağırlıkları tespit edildi ve kalplerinden kan örnekleri alındı. Silikon uygulanması serum protein(P<0.05) ve albumin(P<0.001) düzeylerinde önemli düzeyde düşüşe, serum üre düzeyinde ise bir artışa(P<0.00I) neden oldu. Tubulusların fırçamsı kenarlarında hücresel düzensizliklere, glomerüllerde kanamaya ilişkin değişiklikler ve tübülar lümene doğru epitelyal çıkıntıları kapsayan glomerulotubular tahribatlarla nitelenen histopatolojik bozukluklar üçüncü ve dördüncü grupta belirgindi.

Bu sonuçlar; 1- Böbrek yapıları üzerinde silikonun doza bağımlı zararlı etkilerinin olduğunu, 2- Silikon uygulanan sıçanlarda böbrek fonksiyonlarını belirgin bir biçimde etkileyen glomerulotubular bozuklukların ortaya çıktığını göstermektedir.

Anahtar Kelimeler: Silikon, Sıçan, Böbrek, Total protein, Albumin, Üre, Kreatinin Histopatolojik değişiklikler

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Correspondence: Leyla ÇOLPAN
Dept. of Biochemistry
Medical School of
Dicle University
Diyarbakır, TURKEY

Silicon compounds are the most abundant and important constituents of the earth's crust (1). Silicon is an abundant element in nature, foods and man-made products. It is also used in medicine widely and safely, for example in lnammoplasty,

dental procedures, penile prothesis, plastic reconstructive surgery (1-5). The most important pathway f°' metabolism of silicon is renal excretion as silicic acid and reabsorbtion of remained portion (6 7) The previous studies demonstrated that silicon was a material which could damage tissues in the body, including kidneys (6-11). The harmful effect of silicon has not been well investigated and evaluated (11-13).

This study is based on the morphological evaluation of the kidney and the variation of some biochemical parameters, reflecting the alterations in the renal functions.

Material and Methods

In this study randomly selected 40 adult Sprague-Dawley rats, weighing in the range of 250-270 grams were investigated following silicon treatment. Animals were divided into four groups. 0.1 ml. saline to the first group, 0,1 ml. Olive oil to the second group, silicon suspension in olive oil at the dose of 7,5 mg/kg to the third group and at the dose of 15 mg/kg to the fourth group were injected intraperitoneally as daily doses for 28 days. A11 animals were housed in the room temperature and fed with standard chow pellet. At the end of the treatment the body weights of rats were determined, then intracardiac blood samples were drawn to measure their biochemical parameters including serum total protein, albumin, urea and creatinine. Tissue samples from the kidneys were taken and fixed by bouin solution and then embedded in paraffin. Paraffin sections were stained with haematoxylen eosin and Mallory- Azan dye (14).

Enzymatic methods in autoanalyzer have been used to assay, serum total protein, albumin and urea levels. The measurement of serum creatinine was carried out by the colorometric method in autoanalyzer. Globulin level was accounted considering serum values of total protein and albumin. Histopathological evaluation was based on the examination by light microscope.

For comparison of the results, the student's t-test was used. The value of PO.05 has been accepted statistically meaningful.

Results

Morphological Findings

The body weight changes of the groups are shown in Table 1. The olive oil given rats were significantly got heavier according to the other groups. Whereas when compared with control group (P<0,001), the body weights of silicon treated animals were significantly decreased.

Histopathological examination in silicon medicated animals by light microscope revealed glomerulotubular lesions characterized with derangament in the tubular epithelial cells. The cubic epithelial cells of proximal and distal tubules located in the renal cortex were swollen and their undefined borders were prominent. Cellular damage at the tubular brush border of proximal tubules was remarkable in most of the histopathological sections (Figure 1). Changes in staining caused by chromosomal separations in the nucleus were ramarkable, especially in the medullar epithelial cells (Figure 2). Some hemorrhagic changes in glomerules or in some injured areas close to glomerules have been observed frequently (Figure 3). Glomerular enlargement and obstruction in the space of Bowman's capsule forming by capillary vessel structures were the additional morphological changes. The collector ducts situated in the renal medullary section revealed swollen epithelial cells. Epithelial protrusion towards the tubular lumens

Table 1. The mean and standart deviation values and statistical comparison of the pre and post treatment body weights of the groups.

	Pretreatment weigt		Posttreatment weigt		
	X	SD	X	SD	P
1. Group	262.6	7.849	261	8.097	P>0.05
2. Group	261.6	6.995	294	10.488	PO.001
3. Group	262.8	6.339	221.5	12.030	PO.001
4. Group	260.5	8.317	215	8.497	PO.001

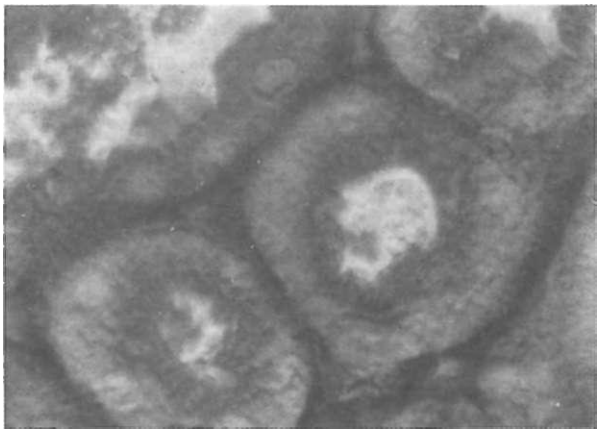

Figure 1. Undefined borders at the epithelial cells lining tubular lumens and derangement at tubular brush border. (M.Azan x640)

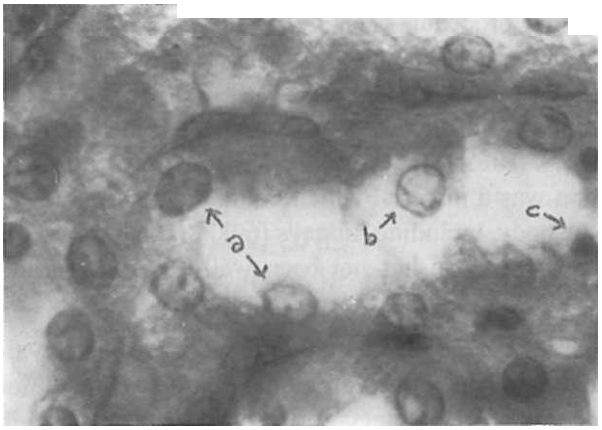

Figure 2. In the medullar section of the kidney; a) staning differences at nucleus, b) Desquamation at the epithelial cells, c) Picnotic appearance at the nucleus of the epithelial cells. (H.E. x640)

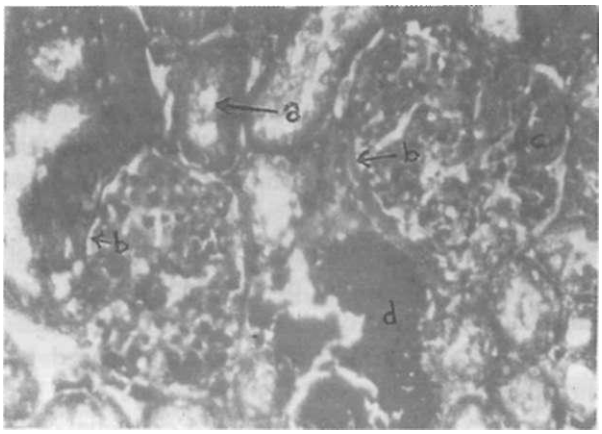

Figure 3. In the cortex; a) Stickness and thickness at the brush border, b) Stickness at the parietal and visseral sheets of the Bowman's capsule, c) Intraglomerular hemorrage, d) Hemorrhagic areas around the glomerular structures. (M.Azan x 160)

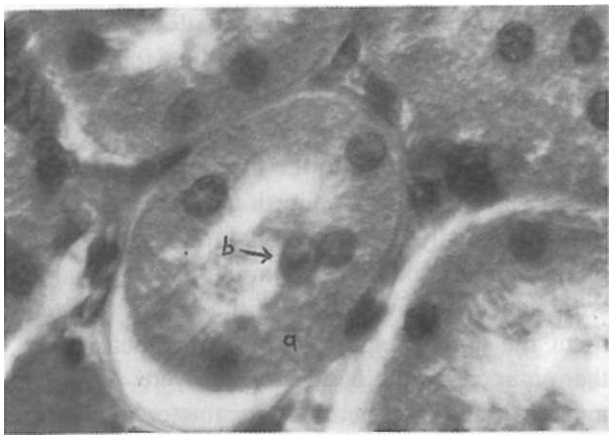

Figure 4. At the renal cortex; a) Hypertrophy of the epithelial cells lining tubular lumens, b) Nuclear protrusion into tubular ducts. (H.E. x 640)

which was considered as a nucleic formation, were remarkable, especially in the rats exposed to high doses of silicon (Figure 4). In the mallory-Azan stained sections the alterations in the Bowman's capsule associated with stickness and thickness of visceral and parietal sheets were other important histopathological deteriorations (Figure 3). The nuclei of the cells lining tubuler lumina projected into ductal lumen and some of them showed epitelial desquamation (Figure 5).

Biochemical Findings

As presented in Table 2, the biochemical values of the rats receiving only saline or olive oil, did not show any significant alterations. In the low dose (7.5mg/kg) silicon treated group, the values of albumin ($P<0.001$) and albumin/globulin (A/G) ratio($P<0.01$) were significantly lower than control group. In contrast, serum urea level was significantly higher as compared with the control group ($P<0.001$). The biochemical values in the high dose (15mg/kg) silicon treated rats were also significant-

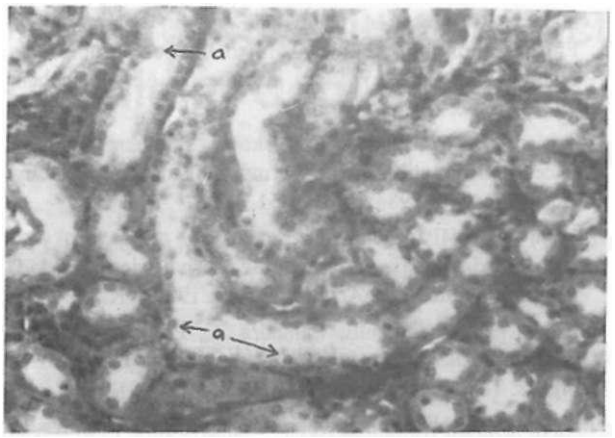

Figure 5. At the medullary section of the kidney; a) Ductal dilatation and protrusion of epithelial nucleus into tubular lumens. (**H**.E. x 160)

ly different from the values observed in first and second group animals. Serum total protein levels showed significant differences between third and fourth groups (P<0.01).

Discussion

Weight gain in the second control group might be caused by olive oil medication. On the contrary, reduced weight in the silicon treated animals might be related to the silicon induced metabolic disorders as reported before (3).

This concept is consistent with previous reports suggesting the repsonsibility of silicon related metabolic effects on the weight loosing (3).

Histopathological findings in the low dose silicon medicated animals confirmed previous observations (4,6,9,15). Silicon leads to the glomerulo tubular damages including cellular derangement in the tubular brush border, alterations in staining and formation of hemorrhagic areas in the renal structures (7,11,16,17). Epithelial protrusion into tubular lumens which are considered as a nucleic formation, were remarkable in the animals exposed to the high silicon medication. Excessive hemorrhagic lesions and epithelial cell degenerations seems to be dose related pathological developments. In this study morphological findings in the fourth group, are compatible with some other previous reports (3,6,7,18,19).

Firm conclusions cannot be drawn about biochemical alterations in animal models, since the biochemical parameters such as total protein, albumin, urea and creatinine levels in serum were not investigated well enough in the rats treated with silicon. The decreases in the serum total protein and albumin values may be due to hepatic injury including degenerative and necrotic changes as previously reported (1,2,7,8,20). However renal proteinuria considering to be related to renal deterioration, should be an additional reducing effect on serum protein levels. The weight loss in the animals medicated with silicon suspention might be responsible for increments in the serum urea levels.

According to Hosokawa, serum and erythrocyte Si levels were directly correlated with the markers of renal function (BUN, serum creatinine) and inversely with the markers of anemia. On the other hand correlated only with the markers of anemia (2). In our study, serum urea levels was significantly higher in the fourth group (PO.001). The fact that serum creatinine levels were normal in spite of high serum urea levels, implies prerenal azotemia caused by silicon related metabolic deprivity which leads to a decrease in serum protein and albumin levels. On the other hand glomerulotubular damages due to silicon implantation, separated microparticules into localized tissues, stimulates immun response(12). There is a good correla-

Table 2. The mean values and standard deviations of some biochemical parameters.

	Group-1		Group-2		Group-3		Group-4	
Protein	7.39	0.79	7.38	0.175	7.09	0.052	6.93	0.189*
Albumin	2.27	0.095	2.26	0.097	1.88	0.187***	1.75	0.127***
Globulin	5.11	0.191	5.12	0.193	5.27	0.323	5.28	0.469
A/G	0.44	0.092	0.44	0.052	0.35	0.053**	0.33	0.100**
Urea	42	4.497	46.8	4.76	75.8	4.917***	74.9	4.581***
Creatinin	0.33	0.108	0.36	0.113	0,37	0.173	0.42	0.161

*p<0.05 **p<0.01 ***p<0.001

tion between silicon amount and the severity of inflammation. All of this development caused increases in serum globulin levels (12,13). In a previous study, 25 mg/kg silicon injected rats showed no significant changes in blood enzymes and immunglobulin levels. Whereas silicon treatment at the dose of 50 mg/kg lead significant enhancement of serum globulin levels (7). A / G ratio appears to be crucial to the development of morphologic deterioration.

Increments in the serum urea levels might be correlated with metabolic deprivity caused by silicon.

In conclusion, silicon treatment leads to the dose related morphological alterations and renal function deterioration in the rats.

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