Journal of Inflammation Research

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ORIGINAL RESEARCH

Effects of Repeated Doses of the Vero Cell Vaccine (SARS-Cov-2 Inactivated Vaccine) on Renal Functions in Balb/C Albino Mice

Şükran Köse[1], Canberk Yılmaz[2], Kazım Kıratlı[3], Çağlar Çelebi[4], Pınar Akan[5], Meltem Kumas Kulualp[6], Soner Duman[7], Osman Yılmaz[8]

[1]Department of Infectious Diseases and Clinical Microbiology, Faculty of Medicine, Dokuz Eylul University, Izmir, Turkey; [2]Department of Pediatrics, Faculty of Medicine, Health Sciences University, Izmir, Turkey; [3]Department of Infectious Diseases and Clinical Microbiology, Mogadishu Somalia Turkey Recep Tayyip Erdoğan Training and Research Hospital, Mogadishu, Somalia; [4]Department of Medical Biology, Institute of Health Sciences, Ege University, Izmir, Turkey; [5]Department of Medical Biochemistry, Faculty of Medicine, Dokuz Eylul University, Izmir, Turkey; [6]Department of Histology and Embryology, Faculty of Veterinary Medicine, Dokuz Eylul University, Izmir, Turkey; [7]Department of Internal Medicine, Faculty of Medicine, Ege University, Izmir, Turkey; [8]Department of Laboratory Animal Science, Institute of Health Sciences, Dokuz Eylul University, Izmir, Turkey

Correspondence: Kazım Kıratlı, Mogadishu Somalia Turkey Recep Tayyip Erdoğan Training and Research Hospital, Department of Infectious Diseases and Clinical Microbiology, Mogadishu, Somalia, Tel +252 611 522 947; +90 537 252 84 86, Email drkazimkiratli@gmail.com

Objective: Many of the vaccines developed for COVID-19 have been approved for clinical emergency use before their safety and preclinical studies have been completed. The main aim of this study was to investigate the effects of an inactivated SARS-CoV-2 virus vaccine (Vero cells) on renal function in Balb/C Albino mice.

Methods: 21 healthy, 6–8 week old BALB/c male mice were divided into three equal groups, and 0.10 mL of intramuscular saline equal to the vaccine dose volume was administered to the first group. To the second group, a single dose of 0.10 mL 120 U of Vero cell inactive SARS COV-2 vaccine was administered intramuscularly. Group 3 received two consecutive doses of 0.10 mL 120 U intramuscular Vero cell inactive SARS COV-2 vaccine, 14 days apart. After administration, the clinical status, fecal and urine status, nutritional status and kidney histopathology of the mice were evaluated.

Results: It was determined that no acute toxic symptoms were observed in the mice administered the vaccine, they were in good condition, and there was no significant stimulatory reaction related to the vaccine in the tissues of the injected local area. There was no difference in feed consumption, water consumption, and body weight gains between the control group, the groups that received a single dose of vaccine, and the groups that received two doses of vaccine ($p>0.05$). No difference was found between the groups when urine and feces amounts were compared ($p>0.05$). No difference was found between the groups when urinary urea, creatinine, and serum BUN, creatinine levels were compared ($p>0.05$). No difference was found in the histopathological evaluation of the kidneys between the groups ($p>0.05$).

Conclusion: In conclusion, single or repeated injections of the SARS-CoV-2 vaccine (Vero cells) into mice were found to have no adverse effects on the animals' overall clinical health, performance abilities and kidneys.

Keywords: COVID-19, vaccine, SARS CoV-2, adverse effect, kidney

Introduction

Impact of the COVID-19 epidemic continue. On December 13, 2023, the World Health Organization (WHO) received reports of 772.386.069 confirmed cases of COVID-19 worldwide, including 6.987.222 fatalities. A total of 13.595.721.080 vaccination doses have been given as of November 25, 2023. [1] These figures are increasing every day. The multifaceted damages caused by the pandemic to countries are increasing day by day. In addition to the economic, social, and psychological damages, the damages seen in terms of health, which is one of the most important problems, are progressing to a level that will affect each individual. In a very short period of time, vaccinations with a variety of molecular modes of action were created specifically for the Coronavirus in order to reduce these damages, and the WHO has authorized their use in an emergency. However, the types and levels of systemic and organ side effects of these vaccines are not fully known.[2]

Received: 19 December 2023
Accepted: 20 April 2024
Published: 8 May 2024

Vero Cell is a fully inactivated COVID-19 vaccine (SARS-COV-2 virus inactivated vaccine) created by the Chinese business Sinovac Biotech.[3] Clinical trials in phase three have been carried out in Chile, Brazil, the Philippines, Indonesia, and Turkey. It can be stored between 2–8 °C without freezing. The inactivated polio vaccine-like technology used by Vero Cell is more traditional. In the beginning, a SARS-CoV-2 sample was utilized to produce a significant amount of the virus in Vero cells. The relevant genes are bound to by the beta-propiolactone that the viruses are encased in, deactivating them. Some viral components are still intact. The adjuvant aluminum hydroxide is subsequently incorporated with the inactivated viruses. Tanriover et al's findings from Turkey's phase III clinical study, which included 10,218 participants, were published in the Lancet in June 2021, and they demonstrated an 84% effectiveness rate. In every single case, the vaccination avoided the need for hospitalization and stopped the disease's progress to a serious level. On June 1, 2021, the WHO authorized its usage in an emergency.[4–6]

Huang et al[7] employed the rat strain to examine the toxicity of repeated injection in their preclinical safety assessment of the SARS CoV-2 inactivated vaccine. The animals most usually employed in general toxicity investigations of vaccines are Sprague Dawley rats, which were used in this study.[8–10] The repeated dosage toxicity research used Sprague Dawley rats that were sexually mature and 5–6 weeks old because the Vero cell SARS CoV–2 inactivated vaccine was intended to be given to people over the age of 18. We used 6–8-week-old young adult mice in our study.

Vero cell vaccine contains 600 SU in 0.5 mL (600SU, Spike Unit, 1μg of Antigen equals 200SU). According to Huang et al,[7] intramuscular administration of the SARS-CoV-2 inactivated vaccine in the low dosage vaccination group (100 U 0.5 mL/dose) and high dose vaccine group (150 U 0.5 mL/dose) did not cause any adverse effects in Sprague Dawley rats.

In light of the COVID-19 pandemic and the current lack of knowledge regarding the systemic and organ side effects of quickly developed vaccines, the purpose of this study was to investigate potential effects on kidney cells of mice given single or multiple doses of the inactive SARS-COV-2 vaccine.

Materials and Methods

Before starting this study, ethics committee approval was obtained from Dokuz Eylul University (DEU) Animal Experiments local ethics committee with approval number 0244/29.04.2021. This study was performed in the Multidisciplinary animal laboratory of DEU Faculty of Medicine and animals utilized were 21 healthy, 6- to 8-week-old BALB/c male mice grown in the same lab. The Vero cell Sars Cov-2 inactivated vaccine is advised for use in adults above the age of 18, hence adult mice were chosen. The investigation was carried out at the Dokuz Eylul University Animal Experiments Laboratory, a conventional center for the production and usage of animals. Mice at this facility were kept in air-conditioned rooms with continuous ventilation, 50–55% humidity, and a temperature of 22±2 °C. Mice used in the experiment were housed in standard mouse cages and randomly divided into 3 groups. Each cage held three to four mice, and the bedding was replaced twice a week. The standard mouse cages used in the study for the control and experimental groups were made by International Tecniplast and had non-ionizing makrolon plastic on the bottom and steel on top. The floor of the cage was covered with wooden commercial cage litter. They were given access to standard mice chow at all times during the trial, and automatic lighting was used to maintain their circadian rhythm of 12 hours of light and 12 hours of darkness. During the trial, regular rat pellet meal was provided ad libitum to the mice in both the experimental and control groups. Since there was always pellet food and water in the mouse cages, they consumed as much food and water as they wanted. Automatic lighting was used to maintain their circadian rhythm of 12 hours of light and 12 hours of darkness. Huang et al[7] used the Vero cell vaccine intramuscularly as 0.5 mL 100–150 U in a study conducted in rats. The vaccine dose was calculated as 0.1 mL 120 U per mouse we used in our study. (Vero cell vaccine content, 0.5 mL contains 600 SU (600SU-Spike Unit).

The experiment consists of three groups of mice. As the experimental design, 0.10 mL (intramuscular- IM) saline was administered to the first group (n: 7) as the volume of the vaccine dose. The second group (n: 7) got a single dose of 0.10 mL 120 U of the Vero cell inactive SARS COV-2 vaccine intramuscularly. In the 3rd group (n:7), two consecutive doses of 0.10 mL 120 U intramuscular Vero cell inactive SARS COV-2 vaccine were administered with an interval of 14 days. 0.10 mL volume injections were administered into the musculus semitendinosus and m. gluteobiceps femoris muscles with an insulin injector to prevent negative effects on the muscles. Since the neutralizing antibody test

experiment of Huang et al[7] could be detected 14 days after the first vaccine administration, we chose to administer the second dosage of the vaccine in our trial 14 days following the first dose.

Method of Assessment

General and Local Clinical Observations

All mice included in the vaccine study were examined by a veterinarian and completely healthy animals were included in the study. Clinical observations were performed four times on vaccine administration days at 1 hour, 6 hours, 12 hours, and 24 hours after vaccine administration. On the following days, all animals were clinically observed once a day.

Live Body Weight, Feed and Water Consumption Measurement

After the vaccine application, live body weight, and feed consumption in the cage were weighed on a CAS brand (ED-H model) scale, and water consumption was measured once a day.

Fecal and Urine Routine Analysis

On the 41st day after the first dose of vaccine administration, 24-hour urine of all mice was collected by placing them in the metabolism cage.

Blood and Urine Analysis

In the functional examination of the kidneys, urea, and creatinine were measured in blood and urine. Mice in all groups were anaesthetized with 50 mg/kg ketamine + 10 mg /ketamine xylazine intraperitoneally on the 42nd day after the first vaccine administration. Blood was collected from the vena cava caudalis of all mice under anesthesia and hemogram, serum BUN, and creatinine levels were measured.

Blood (1 mL) was collected from the vena cava caudalis of the mice in the experimental group 3 and 14 days after the last application (EDTA-2K anticoagulation). Blood cells were counted after the samples were split into plasma and spun at 3000 rpm for 10 minutes.

Blood samples from the vena cava caudalis of the experimental group of mice at 42 days were centrifuged at 3000 rpm for 10 minutes to separate the serum. About 100 µL of serum were taken 3 and 14 days following the last treatment for the purpose of detecting antinuclear antibodies (ANA). An automated biochemical analyzer from Olympus, model number AU400 (Olympus Corporation, Japan), was used to find the remaining serum.

Histopathological Examination

On the 42nd day after the first vaccine administration, all mice were anaesthetized with 50 mg/kg ketamine + 10 mg / ketamine xylazine intraperitoneally. The kidneys were removed after blood sampling under anesthesia. The removed kidney tissues were fixed in 10% formalin solution for 48 hours for histopathological examinations. After fixation, they were dehydrated by passing through increasing alcohol series. Mayer's hematoxylin was used to segment paraffin-embedded blocks at a thickness of 5 µm (Merck; catalogue no. 05–06004/L) - Eosin (ThermoFisher Scientific; catalogue no. 6766007), Masson's trichrome stain (Bio-optica; catalogue no. 04–010802) and Periodic acid Schiff stain (Bio-optica; catalogue no. 04-130,802).

Hematoxylin & Eosin (H&E) staining technique was used to detect pathological changes such as proximal/distal tubular vacuolization, tubular dilatation, tubular atrophy, congestion, inflammation, hemorrhage, and infiltration.

Interstitial and glomerular fibrosis were detected and their severity was assessed using the Masson's trichrome staining technique.

Periodic Acid Schiff staining technique was used to detect pathological changes in the proximal tubules such as loss of brushy edge, disruption of basement membrane integrity, thickening of Bowman's capsule, and formation of hyaline cast.

Scoring System for the Assessment of Kidney Damage

The levels of tubular, glomerular, interstitial, and vascular damage were each assessed independently in order to determine renal injury.

In order to determine tubular damage, the presence of significant pathological changes in tubules such as tubular vacuolization, tubular dilatation/atrophy, loss of the proximal tubular brush border and hyaline cast formation were investigated.

To determine glomerular damage, the presence of significant pathological changes in glomeruli such as thickening of Bowman's capsule and glomerular fibrosis were investigated.

To determine interstitial damage, the presence of significant pathological changes in the renal interstitium such as interstitial fibrosis, inflammation, hemorrhage, and mononuclear cell infiltration was investigated.

The presence of congestion in capillary vessels was investigated to determine vascular damage.

The specimens were examined and scored under a light microscope (Carl Zeiss, Axiolab 5, Suzhou, China). Pathological changes detected in each kidney section: 0 = none (<10%), 1 = minimal change (<10%-25%), 2 = mild change (26%-50%) and 3 = severe change (>50%).

Statistical Analysis

The suitability of each group for normal distribution was checked with the Shapiro–Wilk test. All data showed normal distribution. Statistics were examined using SPSS 24.0. The data were presented as the mean and standard deviation. Since parametric conditions were met, ANOVA *F*-test was used for comparisons between groups. Since the ANAOVA *F*-test was found to be > 0.05 in all comparisons, post hoc tests were not applied.

Results

General and Local Clinical Effects of Vaccine Administration in Mice

In the clinical follow-up of the mice in each group included in the study, clinical examination was performed 2–3 times in the first 24–48 hours after the application. It was observed that there was no redness, swelling, bruising, hardening, abscess, inflammation, local reaction, or pathology related to the vaccine at the local injection site in each group in their own cages. No obvious abnormalities were observed such as mobility of the mice in the cage, limping in the injected hind legs, confusion, and erection of the feathers. In some mice in the 2nd and 3rd groups, stagnation and tangling of feathers were observed. This clinical condition resolved spontaneously in 2 to 3 days.

Evaluation of the Effects of Vaccination on Live Body Weight

The live body weights of the mice included in the study were measured daily. All groups' live body weights increased steadily throughout the experiment, and when the live body weight changes of the control group, the groups receiving a single dose of the vaccine, and the groups receiving repeated vaccination were compared, there was no statistically significant difference between the groups. Table 1 shows the mean live body weights and standard deviations of the three groups before the experiment, on the 7th day, 21st day, and 40th days after vaccination. The live weights of the three groups before the experiment and the live weight increases at the end of the experiment were 74% in the control group, 73% in the group receiving the single-dose vaccine, and 74% in the group receiving the double-dose vaccine. Between the three groups, there was no statistically significant difference in the rate of body weight gain ($p > 0.05$).

Evaluation of the Effects of Vaccination on Feed Consumption

Feed consumption of mice in daily cages was measured before vaccination and on the 7th, 21st, and 40th days after vaccination in the three groups included in the study. Table 2 shows the average feed intakes before the experiment and at 7, 21, and 40 days after vaccination. In terms of the groups' feed consumption throughout the experiment, there was no statistically significant difference ($p>0.05$).

Evaluation of the Effects of Vaccination on Water Consumption

The water consumption of the mice in the cages was measured daily before, 7, 21, and 40 days after the vaccine administration of the three groups included in the study. Table 3 shows the averages of water consumption before the experiment, 7, 21, and 40 days after vaccination. The groups' water consumption during the trial did not differ statistically significantly from one another ($p>0.05$).

Table 1 Live Weight Increase Values (CA Average ±SD Gr)

Groups	Average Live Weight Before Vaccination (g)	CA Average on Day 7 after Vaccine Administration (g)	Average CA on the 21st Day After Vaccine Administration (g)	CA Average (g) at 40 Days After the First Application	Increase in Live Body Weight Between the Beginning and the End of the Experiment (%)
Control Group	27.83±1.34	29.83±0.68	34.83±0.75	37.83±0.75	% 74
Single Dose vaccine group	27.33±1.21	29.33±1.37	35.33±0.74	37.50±0.76	% 73
Double dose vaccine group	27.66±1.49	29.66±1.24	34.66±0.47	37.33±0.51	% 74

Notes: Live weight gain / (%) = Live weight before the experiment x 100 / Live weight at the end of the experiment.

Table 2 Feed Consumption Amounts (Average Feed Consumption ±SD g)

Groups	Average Feed Consumption Before vaccination (g)	Average Feed Intake on the 7th Day After Vaccination (g)	Average feed Intake on the 21st Day After Vaccination (g)	Average feed Consumption in 40 Days After the First Application (g)
Control Group	5.5±0.2	5.8±0.1	6.3±0.4	6.6±0.3
Single Dose vaccine group	5.3±0.3	6.1±0.4	6.0±0.2	6.9±0.5
Double dose vaccine group	5.1±0.2	5.9±0.3	6.6±0.1	6.5±0.3

Table 3 Water Consumption Amounts (Water Consumption Average ±SD Ml)

Groups	Average Water Consumption Before Vaccination (mL)	Average Water Consumption on the 7th day After Vaccination (mL)	Average WATER consumption on the 21st day After Vaccination (mL)	Average Water Consumption in 40 Days After the First Application (mL)
Control Group	10.5± 0.7	10.5± 0.7	9.4± 0.9	9.8± 0.5
Single Dose vaccine group	9.6± 0.6	11.2± 0.5	10.6± 0.6	10.9± 0.7
Double dose vaccine group	9.5± 0.8	11.4± 0.6	10.5± 0.8	11.5± 0.4

Routine Physical Examination of Feces and Urine

Each of the mice housed in 24-hour metabolism cages had urine and feces collected on the 41st day following the administration of the Vero cell SARS-CoV-2 inactivated vaccination. The mean 24-hour urine amount of each group was 1.61±0.08mL, 1.57±0.07mL, and 1.54±0.07mL in the control group, single-dose vaccine group, and double-dose vaccine group, respectively. The mean value of each group's 24 h feces amount was 6.01±0.63 g in the control group mice, 6.49 ±0.38 in the group receiving single-dose vaccine, and 6.11±0.49 g in the group receiving double dose vaccine (Table 4).

Table 4 24-Hour Urine and Feces Quantities (Mean ± SD)

Groups	Average Urine volume (mL)	Average Amount of Feces (g)
Control Group	1.61±0.08	6.01 ±0.63
Single Dose vaccine group	1.57±0.07	6.49±0.38
Double dose vaccine group	1.54±0.07	6.11±0.49

When the mean urine amounts of the three groups were compared, no appreciable difference was discovered ($p > 0.05$). Comparing 24-hour feces quantities revealed no statistically significant variation ($p > 0.05$). Figure 1 shows that neither the amount of urine and feces collected over the course of 24 hours nor the color of the urine and feces significantly differed across the groups.

Examination of Blood and Urine

The mean urea and creatinine values in blood and urine of the three groups in terms of renal function evaluation are given in Table 5. In terms of renal function, no statistically significant difference was found when the mean values of BUN and creatinine in blood serum and urea creatinine in urine were compared in the three groups ($p > 0.05$). It is possible to say that the vaccine does not impair renal function when the urea and creatinine values in the blood and urine of the three groups are evaluated.

No statistically significant difference was found when the hemogram values of the three groups were compared ($p>0.05$).

Histopathological Results

The results of histopathological scores of all groups are given in Table 6. Minimal vacuolization, dilatation, and loss of the proximal tubular brush border were detected in renal tubules in both single and double-dose vaccine groups. Similar changes were observed in the control groups (Figure 2a-c, f, h and i). Less than 25% of the tissue displayed tubular alterations, and there was no discernible difference between the groups in terms of tubular damage (Table 6). Additionally, significant tubular damage

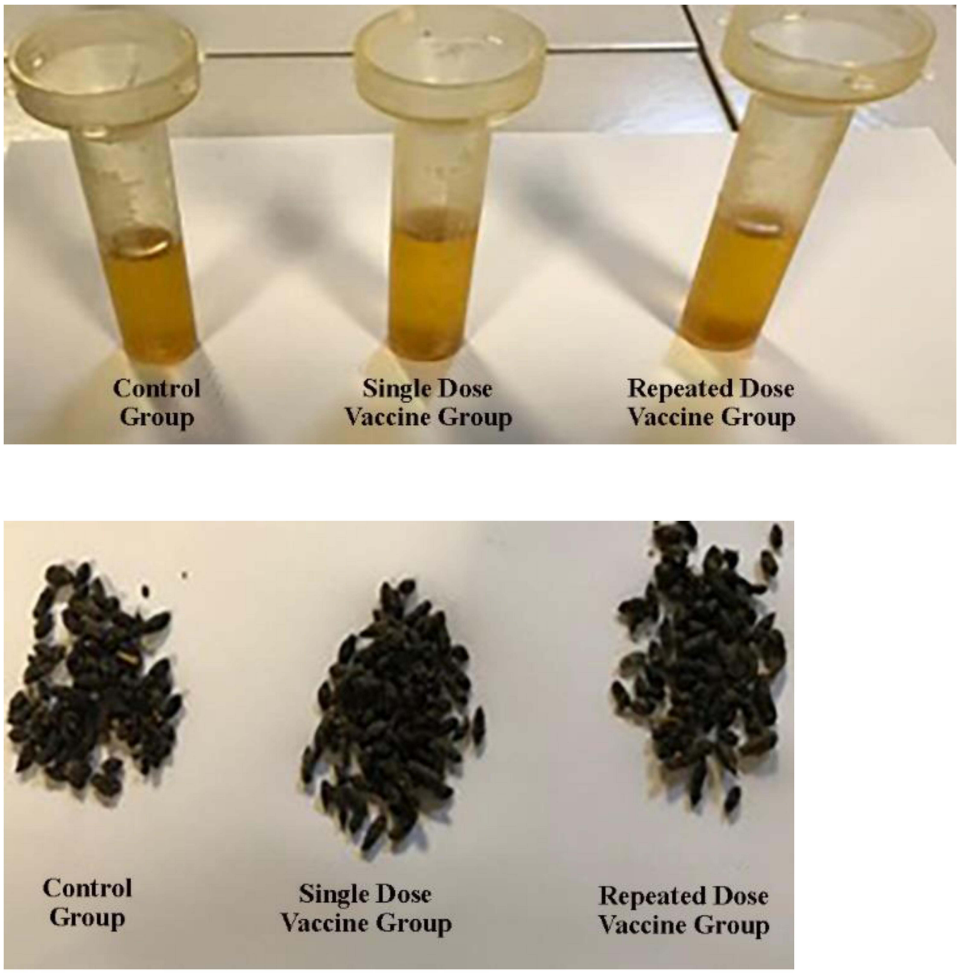

Figure 1 Urine and feces were collected for 24 hours.

Table 5 Mean Values of BUN, Creatinine in Blood, and Urea Creatinine in Urine (Mean ± SD)

Groups	In Blood		In Urine	
	BUN (mg/dL) (mean±SD)	Creatinine (mg/dL) (mean±SD)	Urea (mg/dL) (mean±SD)	Creatinine (mg/dL) (mean±SD)
Control Group	30.38±4.9	0.178±0.21	2608.5 ± 500.3	29.72±2.6
Single Dose vaccine group	34.20±4.8	0.19±0.09	2581.1± 437.3	32.93±4.3
Double dose vaccine group	31.15±5.6	0.18±0.07	2372.5±144.9	32.23± 2.2

Table 6 Summary Statistics of Histopathological Parameters Evaluated in All Groups. The Data are Expressed as Median and Interquartile Range (IQR), and Compared Using Kruskal–Wallis Test

Histopathological Parameters	Control Group	Single Dose Vaccine GROUP	Double Dose vaccine Group	P value
Tubular vacuolization	0 (0.25)	1 (1)	1 (0.25)	0.063
Tubular dilatation and atrophy	0 (0.25)	0.5 (1)	1 (1)	0.226
Loss of the proximal tubular brush border	0 (0.25)	1 (1)	1 (0.25)	0.063
Congestion	0 (0.25)	0.5 (1)	1 (1.25)	0.190

indicators including the shedding of cells into the tubular lumen and the separation of tubular epithelial cells from the basement membrane, and hyaline cast formation were not observed in any group (Figure 2e). No damage to the renal interstitium and glomeruli was observed in any group. Fibrosis development was not detected in both kidney sections (Figure 2g-i). Glomeruli

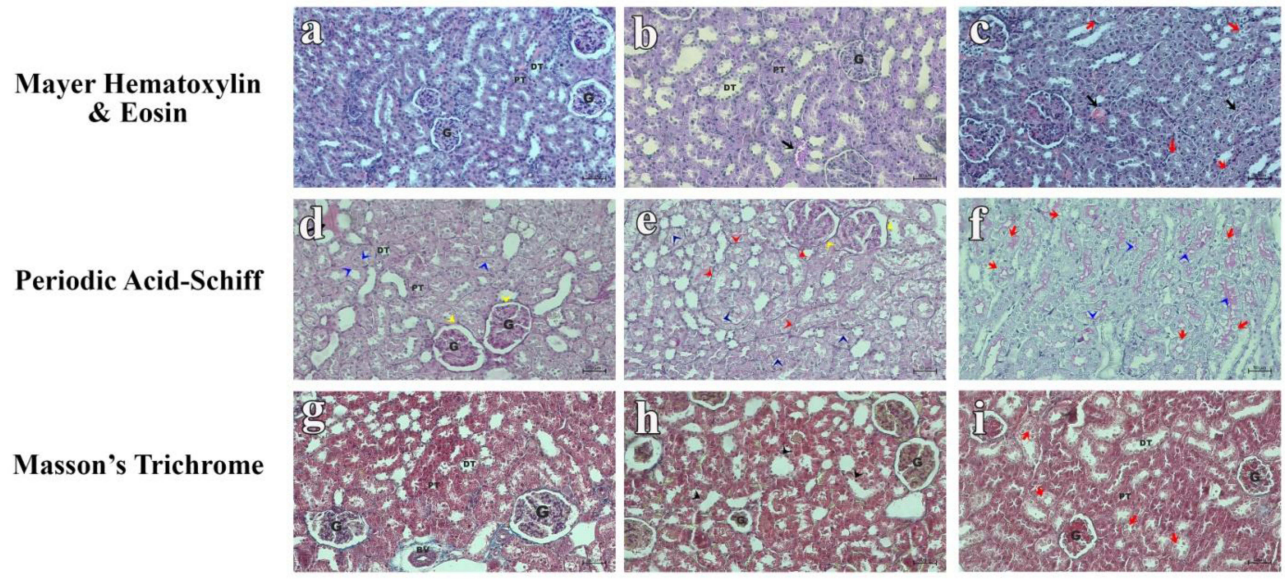

Figure 2 (**a-c**) Light microscopic view of renal cortex stained with Masson Hematoxylin &Eosin technique, in all experimental groups. (**a**) The control group shows normal histological structure. Glomeruli (G), proximal convoluted tubules (PT), and distal convoluted tubules (DT) are intact. (**b**) Histological structure of renal cortex is almost similar to controls, only minimal congestion (black arrows) is observed in single-dose vaccine group. (**c**) Tubular vacuolization (red arrows) is slightly observed in renal cortex of double-dose vaccine group. (**d-f**) Light microscopic view of renal cortex stained with Periodic Acid Schiff kit in all experimental groups. (**d**) The thickening of the Bowman capsule (yellow arrowheads) and integrity of the basal membrane shows normal histological structure, and brush border of proximal tubules (blue arrowheads) is intact in control group. (**e** and **f**) Thickening of the Bowman capsule (yellow arrowheads) and integrity of the basal membrane are also normal in vaccine treated groups. Minimal tubular dilation and vacuolization (red arrows) are observed, and loss of brush border is slightly recorded in vaccine treated groups. (**g-i**) Light microscopic view of renal cortex stained with Masson's trichrome stain kit in all experimental groups. Interstitial and glomerular fibrosis was not observed in any experimental group (black arrowheads: tubular dilation).
Abbreviation: BV, blood vessel.

were found to have normal histological appearance in both vaccine groups similar to the control group. Bowman's capsule was found to be intact in all groups and no narrowing or widening of Bowman's distance was determined. This metric did not differ across the groups, despite the fact that the renal interstitium had only slight congestion (Figure 2b-d, $p>0.05$). As a result, no significant pathological changes were found in all kidney sections evaluated in the vaccinated groups.

Discussion

The most efficient and cost-effective method of preventing and controlling numerous infectious diseases is vaccination.[11,12] The continuous pandemic issue poses a serious risk to the world's immune system. Due to their weakened health, seniors in particular are more at danger. Health risks during COVID-19 are caused by several causes, including comorbidities like obesity, diabetes, and hypertension. Somehow, the weakened immune response is connected to these disorders.[13]

One of the concerns that must be taken into account during the pandemic is vaccination-related side effects, with age, gender, and the kind of vaccine being the most significant predictors of these adverse effects.[14] The public may grow afraid of COVID-19 vaccinations and anti-vaccine as a result of the new COVID-19 vaccines being created and the withdrawal of the vaccines' negative effects.[15] The most frequent adverse response or occurrence in clinical trials—which frequently affected more than 10% of patients—was pain at the injection site.[16] The safety requirement should be higher than for drugs considering that vaccines used for immunization are used for healthy humans or animals. The preclinical safety assessment of new vaccines to be used is one of the most important stages. Due to sudden epidemics that affect the whole world, such as the COVID-19 pandemic, it may become mandatory to use the SARS-CoV-2 inactivated vaccine before a preclinical safety assessment has been made. To stop the spread of speculative information regarding vaccines, some safety studies are required, including pre-clinical controlled studies and investigations into the precise effects of vaccines on organs. As a result, society will have more faith in the vaccination, which will also make it safer.[17]

The SARS-CoV-2 inactivated vaccine, given to a macaque monkey at a dose of 6 µg, had no negative side effects, changes in appetite, or mental state in the research by Gao et al.[18]

20.3% of 300 participants in the 0–14 day program and 10.3% of 31 individuals in the 0–28 day program in the Phase 2 trial of the SARS-CoV 2 inactivated vaccine reported discomfort at the injection site. However, this adverse effect subsided within three days and none of the participants experienced any severe grade 3 side effects.[19] According to preliminary findings from the Phase 3 vaccination research in Turkey, 11 of 10,214 participants (0.1%), including six (0.1%) of 6646 participants in the vaccine group and five (0.1%) of 3568 participants in the placebo group, suffered major adverse effects after receiving the second dose of CoronaVac.[5]

The most frequent diagnoses were identified as minimal change disease (MCD), IgA nephropathy (IgAN), antineutrophil cytoplasmic autoantibody (ANCA) vasculitis, and acute interstitial nephritis (AIN) in a research that examined the renal side effects of all COVID-19 vaccinations in the literature. A total of 128 individuals were compiled, comprising 39 cases of recurrence and 89 cases of newly diagnosed renal involvement. MCD, by far the most typical renal adverse effect of the COVID-19 immunization, was detected in 41% of them, while IgAN, with a prevalence of 37.5%, was the second most typical disease. Following this were ANCA with 12.5% and AIN with 9.0%. Among the 128 individuals who experienced renal adverse effects, only 3 (2.3%) had received the inactive CoronaVac vaccination. Furthermore, symptoms appeared in 39% of patients following the first dosage and 61% following the second.[20]

This is a more specific study to investigate the function of the kidneys and whether kidney tissue is damaged by repeated vaccination. According to the WHO's guidelines on vaccine toxicology studies, it is recommended that at least one person should receive the dose, regardless of which animal model is used.[17]

In our investigation, administering the vaccination in single or double doses had no adverse effects on the mice's feed and water intake or rate of weight gain. These results support the results obtained by Huang et al[7] in repeated vaccination in rats with Vero cell SARS CoV-2 vaccine.

It has been determined that the administration of the vaccine has no adverse effect on urine and feces quantities. There is no negative effect on urea and creatinine values in the urine and blood.

Histopathological examination of the kidney revealed no significant pathological findings in the tubular, glomerular, interstitial, and vascular areas of the kidney. The histological appearance of all kidney sections examined in the vaccine-treated

groups was close to the control group. It was not determined that vaccine administration has a negative pathological effect on the kidneys of the subjects.

According to a Charles River Laboratory analysis of histological results in 4–26-week-old Sprague Dawley rats, male or female rats were more likely to experience pathological abnormalities in the heart, liver, kidney, and lung than in other organs.

The study on the safe administration of the SARS-CoV-2 vaccine will continue. No significant systemic toxicity was observed in mice in our study evaluating the effects of repeated vaccine administration on renal function in mice of the SARS-CoV-2 inactivated vaccine developed by Wuhan Institute of Biological Products Co. Ltd. According to these results, similar to the study of Wang et al.[21] The kidney tissues and organs of mice did not exhibit any major histopathological changes after receiving the SARS-CoV-2 inactivated vaccine several times.

Strengths and Limitations

Our study's strengths include the topic's urgency and currentness, as well as the dearth of studies on vaccine adverse effects. As a result of the nature of animal studies, our work is also valuable since it can yield highly beneficial conclusions for humanity, it also demands a larger team, intensive-labor and time-consuming. One potential limitation of our research could be the small sample size.

Conclusion

The ability to be used safely in clinical settings is one of the most crucial characteristics that recently created vaccines must possess. Using the inactive COVID-19 vaccination in single or double doses, we found no adverse effects on the mice's food/water intake, urine/fecal output, or pathological abnormalities on their kidney tissues. The results indicate that the inactive vaccination may still be administered safely and corroborate earlier research on the topic. In order to properly manage patients who report with symptoms like hematuria, edema, or foamy urine, healthcare practitioners must be alert to these side effects as soon as they appear. It is clear that additional research is required to fully comprehend the pathogenesis of kidney illness that arises following COVID-19 vaccination.

Ethics Committee

This study was approved by the local ethics committee of Dokuz Eylul University Multidisciplinary Laboratory Animal Experiments (Dokuz Eylul University Multidisciplinary Laboratory Animal Experiments Ethics Committee Decision Form: 0244/29.04.2021).

Animals Guideline

The authors clearly indicate that the National Research Council's Guide for the Care and Use of Laboratory Animals (EU Directive 2010/63/EU for animal experiments) have been followed.

Acknowledgments

This article is an original work and was not fully or partially published elsewhere or submitted for publication prior to submission to the journal.

Funding

No financial support was received from any institution or person for our study.

Disclosure

The authors declared no conflict of interest regarding this article.

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