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The Effect of Sputnik V COVID-19 vaccine on the Body Weight of Mice

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ABSTRACT

Background and Aim: Efforts are being made to discover the proper vaccine against COVID-19. After discovering such a vaccine, its acceptance is an essential subject for disease control. The present study aims to determine the effect of weight gain of Sputnik V COVID-19 vaccine on mice compared to control group.

Materials and Methods: This experimental study was performed on mice weighing on average of 20 g, selected by random allocation method. The mice were divided into two groups of 12 (one control group and one case group), receiving 0.5 ml Sputnik V COVID-19 vaccine.

Results: The weight gain of mice among the two groups after 15 days was significantly higher compared to the control group ($p<0.05$).

Conclusion: The use of Sputnik V COVID-19 vaccine has a significant effect on body weight compared to the control group and could be related to the human adenovirus. Evaluating body composition or histopathological assessments are suggested.

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Introduction

Coronavirus disease 2019 (COVID-19) has spread rapidly to multiple countries through its infectious agent causing acute and severe respiratory syndromes [1,2]. The pandemic condition of coronavirus disease (COVID-19), caused by the novel respiratory syndrome coronavirus 2 (SARS-CoV-2), can take asymptomatic, mild, moderate or severe progression [3-5]. The present pandemic emphasizes the tremendous threat of these viruses [5-7]. COVID-19 affects primarily the respiratory airways leading to fever, dry cough, headache, myalgia, diarrhea and fatigue and can end up in interstitial pneumonia and severe respiratory failure. The entry of coronavirus into host cells is mediated by a transmembrane spike (S) glycoprotein that forms homotrimers at the exterior envelop (corona) of the virus [8-10].

Several vaccine platforms were developed to generate a rapid emergency response. Many conventional vaccines use whole viruses or parts of it to trigger an immune response. There are two main approaches. Live attenuated vaccines use a weakened form of the virus that can still replicate without causing illness. Inactivated vaccines use viruses whose genetic material has been destroyed not being able to replicate (Chinese vaccine: CoronaVac 600SU/0.5 mL IM) [11,12]. Subunit vaccines use pieces of the pathogen - often fragments of a protein - to trigger an immune response. This technique minimizes the risk of side effects, but it also weakens the immune response. This is why they often require adjuvants to help boost the immune response. Nucleic acid vaccines use genetic material either RNA (Pfizer–BioNTech COVID-19, Moderna, CureVac and Walvax vaccines) or DNA (e.g Sputnik V COVID-19, Oxford/AstraZeneca COVID-19 vaccines) to provide cells with instructions to make the antigen [13-16]. In the case of COVID-19, this is usually the viral spike protein. Once this genetic material had entered into the cells, it uses the cells' protein factories to produce the antigen that will trigger an immune response. The advantages of such vaccines are that they

are easy to make and cheap. Since the antigen is produced inside our own cells and in large quantities the immune reaction should be strong [12,17].

Gam-COVID-Vac is a viral two-vector vaccine based on two human adenoviruses, a common cold virus, containing the gene that encodes the full-length spike protein (S) of SARS-CoV-2 to stimulate an immune response. The recombinant adenovirus types 26 and 5 are both used as vectors in the vaccine. The adenoviruses are common pathogens of humans and cause a wide range of illnesses and symptoms such as common cold, enteritis, acute upper respiratory tract infections, or conjunctivitis [18]. They were biotechnology-derived and contain the SARS-CoV-2 S protein cDNA. Both of them are administered into the deltoid muscle: the Ad26-based vaccine is used in a first injection and the Ad5 vaccine is used in a second injection to boost the immune response [18].

Materials and methods

Experimental animals

Swiss Albino male mice (18 ± 3 g) were used for experiments. In order to reduce the contact caused by environmental alterations and handling during behavioral studies, mice were acclimatized to the Laboratory Animal Holding Center and laboratory surroundings for three days and at least one hour before the experiments, respectively. Mice were kept under standard conditions with food (low protein diet) and water available ad libitum. The animals were housed six per cage in a light-controlled room (12 h light/dark cycle, light on 07:00 h) at 27 °C and 65% relative humidity. All experiments were carried out between 11:30 and 14:00 h. Each test group consisted of 12 mice, and each mouse was used only once. All animal experiments were conducted according to guidelines set by Institutional Animal Ethics Committee of University of Tripoli.

Animal body weight changes test

Animal body weight changes were performed to investigate the weight changes using Sputnik V vaccine on experimental animals. The intend of performing these studies was to establish a therapeutic index of covid-19 vaccine using body weight parameters [19]. Male mice were randomly allocated into two groups (n=12). The first group served as control and was given 0.9% normal saline at 0.2 ml/kg body weight. The second group (n=12) was given a single dose of 0.5 ml (human dose) of Sputnik V COVID-19 vaccine.

Statistical analysis

The difference among various treated groups and control group were analyzed using one-way-ANOVA followed using unpaired Student's t test. The results were expressed as the mean ± SEM of the number of experiments done, with $P < 0.05$ indicating a significant difference between groups. All p values reported are for a one-tailed test. The significance level was chosen at $\alpha = 0.05$.

Results and discussion

None of the mice used in the study showed any sign of abnormality or ill health throughout the 15 days post-immunization observation. There was no weight loss and none died. A good quality vaccine should not (i) cause a decrease in the weight of the mice 3 days post-vaccination, (ii) produce a less than 60% mean weight gain per mice compared with the control at 7 days post-vaccination (iii) produce larger than 5% animal dead during the 7 days observation period nor any sign of illness of the animals [20-22]. As shown in Table 1, the mice immunized with the Sputnik V COVID-19 vaccine (15 days) showed on the average some increase in weight gain and the percentage weight gain compared with the mice immunized with 0.9% sodium chloride (the control) was greater than thousand times. At day 15 post-vaccination, the mice immunized with Sputnik V COVID-19 vaccine had significant weight gain while those injected with 0.9% sodium chloride had non-significant weight gain at $p < 0.05$.A two-way analysis of variance of the result of the body weight changes test showed that vaccine type and post-vaccination significantly affected the weight of the mice (p value <0.00001) but with 0.95 sodium chloride did not (p value = 0.425).

Table 1: Mice body weight changes test for Sputnik V COVID-19 vaccine

Injection type	Day after vaccination	Mice body weight (g)			p Value* (<0.05 = significant)
		Total Weight	Mean weight (n = 12)	Mean weight gain	
NaCl 0.9%	0	218.5	18.2	0.00	0.425
	15	221.4	18.45	0.25	
Sputnik V COVID-19	0	219.5	18.29	0.00	0.000016
	15	249.9	20.82	2.53	

Note: day 0 means before vaccination, * p value is for student t-test.

It has been reported that five human adenovirus subtypes, Ad5, Ad9, Ad31, Ad36, and Ad37, and a non-human adenovirus, SMAM1, are linked to increased adiposity in vitro or in vivo. Experimental infection with Ad5, Ad36, and Ad37 produced excess adiposity or weight gain in animals [23-25]. Ad9 and Ad31 increase fat storage in tissue culture but are not associated with animal or human obesity. Ad36 is the most extensively studied adipogenic adenovirus and is correlated with some measure of overweight/obesity in humans from multiple countries. The correlation is strongest and most consistent in children, but some studies have been negative in both children and adults. About 30% of overweight/obese children and adults and about 15-20% of lean individuals have Ad36 antibodies in epidemiologic studies. The mechanisms of action of Ad36 are due to the early gene 4, open reading frame 1 (E4-ORF1). Blocking E4-ORF1 with siRNA prevents the effects of Ad36, and transfection of lentivirus with E4-ORF1 reproduces the Ad36 effects. Increased adiposity is caused by stimulation of at least three pathways by Ad36. Cell membrane glucose receptors are increased via the Ras pathway, leading to increased intracellular glucose [26;27]. Fatty acid synthase is increased, which converts the glucose to fatty acids. Finally, peroxisome proliferator-activated receptor-γ is increased, resulting in differentiation of adult stem cells into adipocytes. In addition, it has been reported that there is association between human adenovirus 36 (Ad36) infection and increased adiposity in humans, mice, chickens and monkeys [26-28]. Ad36 infection in animals is associated with increased body weight,

epididymal fats, visceral fats and inguinal fats. Moreover, Ad36 infection induces inflammation in fat tissues through inflammatory cytokines and infiltrated immune cells [29,30].

Conclusion

The Sputnik V COVID-19 vaccine in this study was safe and was capable of significantly inducing weight gain in mice (p value <0.00001).

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