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Research Article

Mixing of Sputnik V and AstraZeneca COVID-19 vaccines

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Abstract

Background and Aim: The coronavirus disease 2019 (COVID-19) vaccine helps to develop immunity to SARS-CoV-2, the virus that causes COVID-19, in most cases preventing the disease. Although various brands of vaccines work in different modes, all COVID-19 vaccines prompt an immune reaction to make the body remembers how to protect from the virus in the future. The present study aims to evaluate the safety and the immune response for mixing of Sputnik V and AstraZeneca COVID-19 vaccines on mice.

Materials and Methods: Our experimental study was performed on mice weighing on average of 20 g, selected by random allocation. The mice were divided into four groups of 12. Group one received a single dose of 0.5 ml Sputnik V COVID-19 vaccine**,** group two received two doses of 0.5 ml AstraZeneca COVID-19 vaccine, group three received two doses of 0.5 ml Sputnik V together with 0.5 ml AstraZeneca COVID-19 vaccine and group four received two doses of 0.5 ml of 0.9 % NaCl.

Results: Our study shows that mixing of Sputnik V and AstraZeneca COVID-19 vaccines is safe and induces good immunity for mice.

Conclusion: Mixing of Sputnik V and AstraZeneca COVID-19 vaccines creates no problems and provides good immunity to mice and may be an interesting technique to help to overcome shortcomings of one or the other vaccine. Further toxicity studies are required to assess potential hazards for humans to evaluate the histopathological characteristics.

Keywords: sputnik V COVID-19 vaccine; astra zeneca COVID-19 vaccine; mice; coronavirus disease (COVID-19); RNA; Pfizer-BioNTech; SARS-CoV-2; Libya; cross-priming; spike

Introduction

Coronavirus Disease 2019 (COVID-19) pandemic causes the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). The plague has affected almost every side of human life and will persist to do so until most of the population is vaccinated. SARS-CoV-2 infection starts with the attachment of the trimeric ‘‘spike’’ glycoprotein to the virion surface binding to angiotensin-converting enzyme 2, allowing viral entrance and starting of viral replication [1, 2]. Several vaccine platforms were developed to generate a rapid emergency response. The main types of COVID-19 vaccines currently available are: messenger RNA (mRNA) vaccine (Pfizer-BioNTech) [3], vector vaccine (AstraZeneca and the University of Oxford, Sputnik V) [4], Protein subunit vaccine (Novavax) and inactivated virus (Sinovac Biotech) [5]. Most authorized vaccines need two doses administered at three or even months separation time. Several European countries and Canada are now recommending a different vaccine as the second dose for some patients and they found such approach could be beneficial. In addition, in three recent studies, researchers have established that following one dose of the vaccine made by AstraZeneca with a dose of the Pfizer-BioNTech vaccine produces powerful immune responses, as measured by blood tests [6]. Two of the studies even recommend mixed vaccine application which was at least as

protective as two doses of the Pfizer-BioNTech product [6]. Due to short supplies of Sputnik V COVID-19 vaccine component II to Libya the study was required to investigate the possibility of having a different vaccine for the second dose.

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 the Institutional Animal Ethics Committee of University of Tripoli.

Clinical and necropsy Observations

This study represents one arm of the safety evaluation program for the two vaccines and was designed to assess local tolerance to acute toxicity. The aim was to evaluate these parameters following the administration of the proposed human vaccine dose. The mice were divided into four groups of 12. Group one received single dose of 0.5 ml Sputnik V COVID-19 vaccine**,** Group two received two doses of 0.5 ml AstraZeneca COVID-19 vaccine and the second dose was given after 21 days, group three received two doses of 0.5 ml (human dose) Sputnik V and 0.5 ml (human dose) AstraZeneca COVID-19 vaccines after 21 days and group four (control) received two doses of 0.5 ml of 0.9 % NaCl. Mice were examined every day for 40 days. Any signs of ill health were recorded daily. Blood samples for IgM and IgG were taken from animals in day 14 and day 35 after first dosing. At necropsy a full macroscopic examination was performed on each animal. Organs macroscopically examined were spleen, lungs, liver, kidney, heart, brain, testes, and ovaries.

Statistical analysis

The difference among various treated groups and the 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 42 days post-immunization observation for the four groups. At the necropsies no macroscopic treatment related changes were observed. Antibody binding the SARS-CoV-2 spike protein was induced by vaccination, and, as expected, the temporal induction of anti-spike IgM was faster than that of IgG.

The potential vaccine combinations of Sputnik V and AstraZeneca COVID-19 vaccines have been tested on mice. This primary result of mixing vaccines proves safety and effectiveness and could speed the effort to protect people. This is consistent with the implications by Cristóbal Belda-Iniesta, a clinical research consultant at the Carlos III Health Institute. Governments might instantaneously distribute new doses without worrying about setting aside second shots of explicit vaccines to provide people weeks or months later. In addition, Europe and Canada have an added incentive [6]. Millions of people there received an initial dose of the AstraZeneca vaccine before governments recommended younger aged groups to avoid it because of the risk of a rare clotting disorder. They were left wondering what to do next: get a second dose or switch to a different vaccine like Sputnik V which may help sorting the issue.

The capability to mix and match vaccines might make vaccination programs more flexible and may speed up the process and reduce the impact of any supply-chain disruptions [7]. AstraZeneca is conducting a similar study of combining its COVID-19 vaccine with the Russian coronavirus vaccine. Sputnik V, uses harmless viruses to carry components of the coronavirus into cells. Sputnik V, which has greater than 90% efficacy against COVID-19, is a heterologous prime–boost vaccine, consisting of different viral components in the first and second doses [8].

Our study is a trial of combining two vaccines which could strengthen immune responses by connecting the best features of each. This appears chiefly beneficial since vaccine developers are combating coronavirus variants that seem to be partly resistant to certain immune responses. Different reactions to two different vaccines could be more procreative compared to what either vaccine can accomplish on its own. These possibilities remain to be proven experimentally on human for COVID-19.

AstraZeneca and Sputnik produce DNA vaccines based on similar mechanisms and consist of delivering genes or fragments of it, encoding immunogenic antigens, to the host cells by using DNA plasmids as a vector. This approach induces both humoral and cell-mediated immune responses efficiently [9]. The formulation of both vaccines is made such that the genetic material is translocated to the host cell nucleus. Once it reaches there, the mammalian promoter present in its vector structure is activated, triggering the transcription of the gene used for the vaccine throughout the host's cellular machinery. The antigen-presenting cells (APCs) are the major target cells to receive the genetic material. In addition, myocytes are reported to play a vital role. After translation of the translocated gene into a protein or protein fragment, it is processed into peptides which bind to major histocompatibility complexes (MHC) class I or II. Cells other than APC, such as the myocytes, use MHC-I for antigen presentation, and APC, such as dendritic cells (DCs), can use MHC-II, resulting in cross-priming and presentation of antigens to both CD4+ and CD8+ T cells [10,11].

Conclusion

Our study shows that AstraZeneca vaccine given as second dose to mice after Sputnik V COVID-19 vaccination–produces an immune response with no side-effects.

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