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Short Report

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Posted Date: December 29th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-1210542/v1>

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SAFETY AND IMMUNOGENICITY OF COMBINATION OF VACCINES - COVISHIELD AND COVAXIN – A PILOT STUDY

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Keywords: COVID-19, Covaxin, Covishield

Conflict of Interest: None

Abstract:

This single-center prospective observational study was conducted to assess the safety and immunogenicity of combination vaccines AstraZeneca's ChAdOx1-nCov-19 (Covishield in India) and inactivated whole virion BBV152 (Covaxin). A total of 330 unvaccinated healthy volunteers were screened for SARS-COV2 seropositivity. RT PCR tests were conducted for seronegative volunteers (n =44). They were randomly assigned to four groups and given either same or mixed vaccines at an interval of 4 weeks between the two doses. Mix and match of vaccines did not evoke any adverse events. Combination of vaccines elicited similar immune responses in 4 groups. In Conclusion, Combination vaccines are safe and immunogenic.

INTRODUCTION:

Vaccination has been shown to be protective against severe COVID-19 disease by various studies^{1,2,3,4}. However, the vaccine efficacy was demonstrated to be less effective against the emerging variants of SARS-CoV-2⁵. Recent studies by Kant R et al.,⁶ Com- COV study⁷, Combi Vacs trial⁸, ChAdOx1 nCoV-19, and BNT162b2⁹ have all demonstrated greater immunogenic response and increased protective efficacy with combination of vaccines. All these studies mainly focussed on Pfizer (BNT162b2), Moderna (mRNA-1273) and AstraZeneca (ChAdOx1-nCov-19). We aimed to assess the safety and immunogenicity of combination of AstraZeneca's ChAdOx1-nCov-19 (Covishield in India) and inactivated whole virion BBV152 (Covaxin) with 4 weeks' interval. This study was conducted to reduce various difficulties in vaccinating populations across the world specially to mitigate vaccine deficit.

Materials and Methods:

This is a single-centre prospective observational study conducted at AIG Hospitals, Hyderabad, India. The study protocol was approved by the Institutional ethics committee (AIG/IEC-CT 51/08.2021-01). We recruited 330 healthy volunteers and screened for seronegativity for SARS-CoV-2 antibodies (IgM and IgG by chemiluminiscence; Roche Cobas e 601) and SARS-CoV2 negative report by RT-PCR. 3 ml of blood was drawn for screening SARS-COV2 antibodies. Nasopharyngeal swabs were collected from individuals who were seronegative (n=44) for SARS-CoV RT-PCR employing Taq path kits (Thermoscientific, USA). All the volunteers have provided written informed consent. Eligible participants (n=44) were divided randomly into four groups. (**Figure 1**). Group1- Covishield –Covishield group (homologous), Group 2 Covaxin –Covaxin group (homologous), Group 3 – Covishield –Covaxin group (heterologous), Group 4 –Covaxin –Covishield group (heterologous). Healthy volunteers were given 1st dose of Covishield (0.5 ml of intramuscular in deltoid) in group 1 and group 3 while volunteers in group 2 and group 4 received Covaxin (0.5 ml of intramuscular in deltoid) as 1st dose. After 4 weeks of 1st dose, groups 1 and 4 received Covishield as 2nd dose while groups 2 and 3 received Covaxin as 2nd dose respectively. Their SARS-COV2 neutralizing antibodies titers (S-spike protein by chemiluminiscence employing automated Diasorin Liaison XL commercial kits and Roche Cobas e 601 for RBD- Receptor Binding Domain) were assessed at 28 days after the 1st dose and 14 days after second dose (45 days of first dose) of vaccination. They were carefully monitored for any adverse effects of combination of vaccines for 60 days.

The data including demographics and neutralizing antibody titers adverse effects were entered in MS-excel and analyzed using SPSS version 23. Categorical variables were expressed in percentages (frequency distribution) and continuous variables as mean and standard deviation (SD). Chi-square tests and ANOVA tests were used appropriately.

Figure 1: Flow chart of the mix –vac study

Results:

A total of 44 participants were eligible for mix and match vaccine study (mix –vac study). Among 44 volunteers, 21 received the homologous vaccines and 23 received the heterologous vaccines. The mean age in Covishield homologous vaccine group was 34.83 ± 7.58 years, and Covaxin homologous vaccine group was 31.33 ± 5.20 years, Covishield followed by Covaxin heterologous group is 31.58 ± 5.32 years and Covaxin followed by Covishield heterologous group was 32.27 ± 5.26 years with no significant difference ($p=0.49$). There is no significant difference in all the four groups in respect to comorbidities like hypertension (**TABLE-1**). The mean antibody titers of S-IgG and RBD IgG at 45 days after 1st dose of vaccine in both Covishield homologous group are 1122.04 ± 1172.69 and 13967.83 ± 12981.67 , both Covaxin homologous groups are 406.29 ± 649.88 and 4294.27 ± 6263.12 , Covishield followed by Covaxin heterologous group are 1729.18 ± 1427.92 and 13260.32 ± 10543.31 and Covaxin followed by Covishield heterologous group are 1807.98 ± 1746.18 and 6463.83 ± 7102.90 respectively. There is no significant difference ($p= 0.08$) in antibody titers at 45 days in all the groups. The volunteers experienced fever, injection site pain, and mild headache in all the groups with no significant difference between the groups (**TABLE-1**). There are no major adverse effects in mixed vaccine groups.

TABLE -1: Demographic and clinical profile of participant's mix-vac study.

	Both Covishield Group -1 N=12	Both Covaxin Group -2 N=9	First Covishield then Covaxin Group -3 N=12	First Covaxin then Covishield Group -4 N=11	P valu e*
Age	34.83±7.58	31.33±5.20	31.58±5.32	32.27±5.26	0.49
28th Day S- IgG Antibodies	930.40±1017. 24	274.08±448.85	1385.84±1506.74	669.74±1212.20	0.17
RBD –IgG Antibodies	5892.63±470 1.03	4162.49±7152. 63	9687.86±9369.48	11033.05±17372. 96	0.43
45th Day S- IgG Antibodies	1122.04±117 2.69	406.29±649.88	1729.18±1427.92	1807.98±1746.18	0.08
RBD IgG Antibodies	13967.83±12 981.67	4294.27±6263. 12	13260.32±10543. 31	6463.83±7102.90	0.08
Smoking (Yes)	2 (16.67%)	1 (11.11%)	1 (8.33%)	2 (18.18%)	0.89
Alcohol intake	2 (16.67%)	3 (33.33%)	2 (16.67%)	5 (45.45%)	0.33
Comorbidities (Hypertension)	2 (16.67%)	4 (44.44%)	2 (16.67%)	6 (54.54%)	0.12
1st Visit dose 1					
Fever (yes)	4 (33.33%)	3 33.33%)	4 (33.33%)	4 (36.36%)	0.99
Headache (yes)	5 (41.67%)	4 (44.44%)	7 (58.33%)	5 (45.45%)	0.85
Pain at site (Yes)	9 (75.00%)	5 (55.55%)	3 (25.00%)	6 (54.54%)	0.10
2nd Visit dose 2					
Fever (Yes)	2 (16.67%)	2 (22.22%)	1 (8.33%)	4 (36.36%)	0.40
Headache (Yes)	8 (66.67%)	4 (44.44%)	8 (66.67%)	5 (45.45%)	0.55
Pain at site (Yes)	5 (41.67%)	5 (55.55%)	6 (50.00%)	4 (36.36%)	0.82

*Chi-square test and One-Way ANOVA were used

Discussion:

Our study is the first Indian prospective pilot study demonstrating the safety and immunogenicity of combination vaccine with Covaxin and Covishield in healthy volunteers. These results are similar to the study done by Kant R et al(n=18)⁶ which included only Covishield first dose followed by Covaxin, but our study included both Covishield followed by Covaxin and Covaxin followed by Covishield groups. The major limitation of the study was the smaller number (n=44). Despite the small number, our study included two groups with two combination of vaccines that are in use in this part of the world. However, these results need to be assessed in larger cohorts. Since the number is small in this study, our results do not interpret the best combination but it helps to answer the apprehensions among the general public about combination vaccine and prevent vaccine hesitancy.

Conclusion:

The combination COVID-19 vaccination (Covishield followed by Covaxin, and Covaxin followed by Covishield) is safe and immunogenic with no major adverse effects.

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