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COVID-19 Vaccination in Patients under Medical Conditions, Immunogenicity and Safety: A Systematic Review and Meta-Analysis

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Abstract

A comprehensive search was carried out in mainstream bibliographic databases or Medical Subject Headings, including ScienDirect, PubMed, Scopus, and ISI Web of Science. The search was applied to the articles that were published between January 2020 and early 2023 With strict literature search and screening processes, it yielded 14 articles from 373 articles of initial literature database. Among 14 study results, there was acceptable for immunogenicity, both humoral and cellular immune responses in 11 studies (78.57 %), whereas acceptable potent immunogenicity was found in patients aged more than 40 years with chronic diseases, particularly, chronic respiratory diseases and coronary artery diseases. Only potent T-cell response was identified in one study. No significant difference in vaccine safety compared with healthy subjects and effective neutralizing antibodies (two doses completion) against SARS-CoV-2 (COVID-19) in patients older than 60 years with diabetes and/or hypertension were demonstrated after completion of COVID-19 vaccination. Immunogenicity and safety in aged people and individuals living with various chronic diseases (both infectious and non-infectious) is highlighted in this study. In conclusion, specified local and systemic AEs and unsolicited AEs, AESI, and SAEs after each vaccination and after the second dose should be monitored. Recording the adverse events of special interest (AESI) and serious adverse events (SAEs) throughout the patients' vaccination course should be performed and can decrease COVID-19 vaccination hesitancy in these persons.

Keywords: adverse reactions; COVID-19; immunogenicity; neutralizing antibody; safety; vaccine

Abbreviations

AEs: adverse events, AESI: adverse events of special interest, AIDS: acquired immunodeficiency syndrome, BNT: Pfizer vaccine (BNT162b1, BNT162b2), ChAd: AstraZeneca vaccine (AZD1222 or ChAdOx-nCov19), CI: confidential interval, COVID-19: coronavirus disease 2019, DAIDS: Division of AIDS, ELISA: enzyme-linked immunosorbent assay, GMR: geometric mean ratio, HIV: human immunodeficiency virus, IMIDs: immune-mediated inflammatory diseases, GMT: geometric mean titer, MNA: microneedle assay, NIH: National Institute of Health, PLWH: people living with human immunodeficiency virus, SAEs: serious adverse events, VLA: Valneva (VLA2001) vaccine.

Objective of the Study

To identify immunogenicity and safety profiles of COVID-19 vaccination (two or three doses) among patients with various medical conditions, such as hypertension, diabetes, endocrine diseases/disorders, neurological diseases/disorders, malignancies, organ transplantation, solid-organ transplantation, etc.

Introduction

Several COVID-19 vaccines were developed to limit its ability to spread [1]. Currently, several studies support immunogenicity and safety of a third-dose-COVID-19 vaccination in healthy persons, patients with hematological malignancies, and solid-organ-transplant recipients, but are still questionable in patients with immune-mediated inflammatory diseases (IMIDs) [2-18].

Methods of the Study

Search Strategy and Inclusion Criteria

A comprehensive search was carried out in mainstream bibliographic databases or Medical Subject Headings, including ScienDirect, PubMed, Scopus, and ISI Web of Science, following the PRISMA guidelines. The search was applied to the articles that were published between January 2020 and early 2023 [Figure 1]. Our first involved performing searches of article abstract/keywords/title using strings of [“COVID-19” or “SARS-CoV-2”, “severe-acute-respiratory-syndrome-coronavirus-2”, “coronavirus-disease 2019”, “nCoV 2019”, “SARS-CoV-2 vaccines”, “COVID-19 vaccines”, SARS-CoV-2 vaccination”, “COVID-19 vaccination”, “efficacy”, “immunogenicity”, “safety”, “medical conditions”, “metabolic”, “immunocompromised”, “organ transplant”, “solid-organ transplant”, “malignant or cancer”, “pulmonary” or “lung”, “renal” or “nephrological”, “endocrinological”, “diabetic”, “hypertension”, “hypertensive”, “obese”, “obesity”]. After a first approach of search, published articles focusing on medical conditions or diseases or disorders that related to SARS-CoV-2 or COVID-19 vaccine immunogenicity and safety were retained and the information on COVID-19-related medical conditions or diseases or disorders was extracted for having a crude knowledge involving their themes. Another round of publication search was conducted for adding the missing published articles that were not identified by the first round.

All keywords combinations from medical conditions or disease types and SARS-CoV-2 (COVID-19) vaccine efficacy (immunogenicity and safety) variables to bind the population of cases under consideration. Search string for disease groups include [“SARS-CoV-2 vaccines (vaccination)” or “COVID-19 vaccines (vaccination)” or “medical conditions” or “medical diseases” or “immunocompromised” or “organ transplant” or “solid-organ transplant” or “malignant or cancer” or “pulmonary” or “lung” or “endocrinological” or “diabetic” or “renal” or “nephrological” or “hypertension” or “hypertensive” or “obese” or “obesity”]. The initial literature databases were further manually screened with the following rules: 1) non-SARS-CoV-2 (COVID-19)-related articles were excluded; 2) articles that did not report immunogenicity and safety related to SARS-CoV-2 (COVID-19) vaccines (vaccination) were not considered, such as commentary articles, or editorial; 3) non-peer reviewed articles were not considered to be of a scholarly trustworthy validity; and 4) duplicated and non-English articles were removed. The articles were carefully selected to guarantee the literature quality, which is a trade-off for quantity [Figure 1].

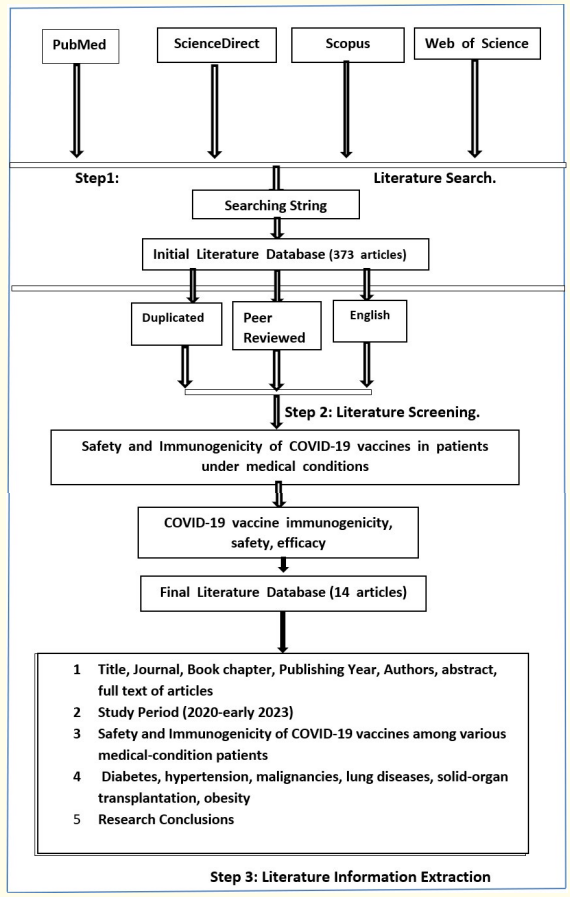

Figure 1: Literature Search and Screening Flow.

With strict literature search and screening processes, it yielded 14 articles (Table 1) from 373 articles of initial literature database. Needed article information was extracted from each article by : 1) direct information including journal, title, authors, abstract, full text documents of candidate studies, publishing year; 2) place name of the study area; 3) study period; 4) research method used; 5) type of variables studied; 6) types of SARS-CoV-2 (COVID-19)-immunogenicity- and-safety-efficacy-related medical conditions or diseases or disorders studied; and 7) the conclusions made about the impacts of SARS-CoV-2 (COVID-19)-immunogenicity-and-safety-efficacy-related medical conditions or medical diseases or medical disorders on human health.

Results

Published Year	*Results*	*Reference*
2023	Supporting the safety and immunogenicity of a third COVID-19 vaccination in IMIDs patients.	[19]
2023	Acceptable safety profile of SII-NVX-CoV2373 vaccine compared to NVX-CoV2373 vaccine.	[20]
2022	Acceptable safety and immunogenicity of COVID-19 vaccines in people living with AIDS.	[21]
2022	Acceptable safety of COVID-19 vaccines in lung-cancer patients receiving immune checkpoint inhibitors.	[22]
2022	At day 146, all three dose levels of all three age cohorts reached 100 % of seroconversion.	[23]
2022	Serum neutralizing antibody in the four groups (diabetes, hypertension, combined diabetes and hypertension, and healthy controls) were 97.3 %, 97.3 %, 100.0 %, 98.7 %, respectively at 28 days after the second vaccination.	[24]
2022	Induced SARS-CoV-2-specific neutralizing antibody and T-cell response had reasonable protection level (vaccine efficacy > 50 %, etc.) against ancestral SARS-CoV-2 strains and up to Omicron variant with dose fractionation of mRNA and protein subunit vaccines.	[25]
2022	At day 14-28 post-first-dose vaccination, there was no significant different neutralizing antibody between the group of chronic diseases with aged > 40 years and healthy controls.	[26]
2022	Immunocompromised patients treated with anti-CD20 medication demonstrated potent T-cell-response preservation.	[27]
2021	COVID-19 vaccine (QazCOvid-in®) was well tolerated and safe in both clinical phase 1 clinical trial (randomized, single-blind, placebo-controlled) and phase 2 clinical trial (open-label).	[28]
2021	The geometric mean ratio (GMR) of SARS-CoV-2 50 % neutralizing antibody titers after two doses of vaccination (BNT162b2) in the group of 12-15 years old related to the group of 16-25 years old was 1.76 (95 % CI: 1.47-2.10).	[29]
2021	COV-BOOST trial: Acceptable immunogenicity (homologous or heterologous) third dose boost (BNT or ChAd vaccine), except VLA vaccine.	[30]
2020	After three doses of inactivated COVID-19 vaccines, no serious adverse reactions were demonstrated. (ChiCTR200034780).	[31]
2020	No severe adverse reactions were noted after three doses of mRNA-based COVID-19 vaccines (BNT162b1 and BNT162b2 vaccines). Acceptable immunogenicity was demonstrated.	[32]

Table 1: Demonstrating the 14 study results.

Discussion

Among 14 study results [19-32], there was acceptable immunogenicity, a key response for the development of a vaccination-induced immunogenicity both humoral and cellular immunity 2 or 3 doses of vaccination [19] and acceptable safety in 11 studies (78.57 %). Acceptable potent immunogenicity was found in patients aged more than 40 years with chronic diseases, particularly, chronic respiratory diseases and coronary artery diseases [26]. Only potent T-cell response was identified in one study [27], and there was no significant difference in vaccine safety compared with healthy subjects [24]. Effective neutralizing antibodies (two doses completion)

against SARS-CoV-2 (COVID-19) in patients older than 60 years with diabetes and/or hypertension [24] were demonstrated after completion of COVID-19 vaccination. After completion of COVID-19 vaccination, females revealed higher immune response than males [24]. SII-NVX-CoV2373-vaccine-related-adverse-events (AEs) incidence was higher, compared to the healthy controls [20]. In India, among adults, SII-NVX-CoV2373 vaccine revealed well tolerated, safe, and immunogenic [20]. Pooled seroconversion rate in people living with HIV (PLWH) after the first and second doses were 67.51 % and 96.65 %, respectively [21]. In lung-cancer patients, number of doses (third dose, etc.) and intervals of mRNA-COVID-19 vaccination are suggested to maintain effective immunity [22]. In young children, after full vaccination with WIBP-CorV, antibody response was characterized up to 180 days [23]. In COVID-19-vaccination safety control, actively monitoring for specified local and systemic AEs and unsolicited AEs for 7 days after each vaccination and for 2 weeks after the second dose, respectively, by using structures diary cards or online-platform cards [20]. Adverse events of special interest (AESI) and serious adverse events (SAEs) should be recorded throughout the patients' vaccination course [20]. All AEs, SAEs, and AESI were graded on a scale of 1-5 with pre-defined criteria following the Division of AIDS (DAIDS) table for severity, corrected version 2.1, July 20, 2017 of the United States National Institute of Health (NIH) [20]. To our knowledge, age, an important factor that has been documented in other COVID-19 vaccines (Corona Vac, BNT162b2 and an adenovirus-vectored COVID-19 vaccine) in influencing vaccine responses [23]. Inducing antibody response was higher in children and adolescent than in adults and aged people [23].

Conclusion

Immunogenicity (both humoral and cellular) and safety in aged people and individuals living with various chronic diseases (both infectious and non-infectious) is highlighted in this study. Specified local and systemic AEs and unsolicited AEs, AESI, and SAEs after each vaccination and after the second dose should be monitored. Recording the adverse events of special interest (AESI) and serious adverse events (SAEs) throughout the patients' vaccination course should be performed and can decrease COVID-19 vaccination hesitancy in these persons.

Authors Contributions

Dr. Attapon Cheepsattayakorn conducted the study framework and wrote the manuscript. Associate Professor Dr. Ruangrong Cheepsattayakorn and Professor Dr. Porntep Siriwanarangsun contributed to scientific content and assistance in manuscript writing. All authors read and approved the final version of the manuscript.

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