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Review

Gender difference in COVID-19 vaccination; recent concepts

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Abstract

Recently, a few different vaccines have been developed to help end the COVID-19 pandemic. These vaccines have made significant progress toward controlling the disease. Multiple factors contribute to the immunity level that these vaccines can stimulate, including sex. The effect of gender on other vaccines' efficacy has been studied before. The results of these studies are mentioned below. Genetic and hormonal differences between men and women are among the mechanisms suggested for the difference in vaccine efficacy in men and women. Sex hormones play various roles in stimulating or suppressing the immune system. As a result, they are responsible for the intensity and speed at which the vaccine establishes the immune response. In this narrative review study, we discuss the differences in COVID-19 vaccine efficacy and safety between the two genders and the reasons for these differences.

Keywords: Gender differences, COVID-19 vaccines, Safety, Efficacy

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Introduction

There have been different vaccines developed to help end the COVID-19 pandemic. These vaccines have contributed to considerable progress toward controlling the COVID-19 pandemic (1). The level of immunity established by the vaccine depends on a variety of factors, including gender. Gender is a substantial factor regarding the level of the immune response, efficacy, and complications of the vaccine. Before the COVID-19 pandemic, there have been different studies addressing the differences in the efficacy of some vaccines like the measles, mumps, and rubella (MMR) vaccine and tetanus, diphtheria, and pertussis (DTP) vaccine between the two genders (2). In this study, we discourse the gender-related differences on the efficacy of COVID-19 vaccines and their causes.

Method of search

We searched accessible international databases, including PubMed and Google Scholar, and extracted the relevant information from their published articles.

Gender disaggregated data for COVID-19 vaccine's efficacy

There is a myriad of studies on the subject of gender differences in efficacy and immune response of available COVID-19 vaccines, and yet they hold inconsistent results. In the study of Pellini et al (3) on 248 subjects, 158 females and 90 males, with a median age of 47 years, the antibody production level, seven days after the injection of the second dose of BNT162b2 (Pfizer) vaccine was assessed. They found antibody response in the female subjects was significantly higher than males.

In the study by Vassilaki et al (4) on 1643 subjects without the history of COVID-19 prior the vaccination with 553 males and 1110 females, and a median age of 49 years; showed, the titration of anti-SARS-Cov-II IgG, 20 to 30 days after the injection of the second dose of BNT162b2 (Pfizer) vaccine were higher significantly in women.

Going through the results of third-phase clinical trial studies of COVID-19 vaccines that had a high number of participants, as stated in the study of Jensen et al (1), no significant difference in the efficacy of Moderna, Pfizer, and Johnson and Johnson vaccines between the men and women was detected.

Accordingly, the study of Baden et al (5) conducted on 28207 subjects (47.4% female and 52.6% male) to examine the efficacy of the Moderna vaccine, showed the efficacy level was 95.4% and 93.1% for men and women, respectively, since their difference was not statistically significant. Likewise, the study conducted by Polack et al (6) on 37706 subjects regarding the efficacy of the Pfizer vaccine showed, vaccine efficacy was not significantly

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Implication for health policy/practice/research/medical education

Sex hormones play various roles in stimulating or suppressing the immune system. Recent studies show that the immune response to vaccines is more potent in women than in men. However, the studies so far on the gender effect on the efficacy of COVID-19 vaccines have inconsistent results. Some of these studies show no significant difference between the two genders regarding vaccine efficacy, while others report a higher immune response in female subjects. Therefore, we need more detailed studies with bigger sample sizes to be conducted.

different between the age, gender, race, ethnicity, and body mass index. Polack et al (6) reported that the vaccine efficacy was 93.7% and 96.4% for women and men, respectively, which is not different among them. Additionally, in similar studies to determine the efficacy of Janssen (Ad26. COV.S) and AstraZeneca (AZD1222) vaccines, their authors did not report a significant difference between the two genders (7, 8).

In the recent study by Abu Jabal et al (9) on 514 subjects (193 men and 321 women), they measured the anti-spike IgG SARS-Cov-II levels 21 days after the injection of the first dose of the Pfizer vaccine. This study also reported no significant difference between the immune response of men and women. Furthermore, another study showed that the immune response is similar in age and gender subgroups, whereas, in subjects with multiple coexisting conditions, the immune response was lower (10).

Gender differences for COVID-19 vaccine safety

Former studies on the gender-related factors affecting the efficacy of vaccines other than the COVID-19 vaccine show that women would have higher immune responses. Additionally, women suffer from more complications (2). Women account for 83% of all the post-vaccination anaphylactic shock cases between 1990 and 2016 in people between the age of 19 and 49 (11). Thus, according to these pieces of information, it is reasonable to hypothesize the same outcome for COVID-19 vaccines. According to the Centers for Disease Control and Prevention (CDC), out of 13.7 million Pfizer vaccine recipients who received two vaccine shots, 61.2% were women, while 79.1% of post-vaccination complications occurred in women (12). Another study in Switzerland showed that out of 2.8 million people vaccinated by Moderna and Pfizer vaccines, 1953 subjects experienced adverse effects, and these subjects were 69.2% female and 27.8% male (1)

Pathophysiology

There are different mechanisms proposed for the difference in vaccine efficacy between men and women. The innate and acquired immune responses in women are more rapid and more powerful, making them more susceptible to autoimmune diseases and also more prone to experiencing post-vaccination adverse effects than men (2,13).

Another mechanism is the genetic and hormonal differences between the two genders (14). Testosterone and estrogen, two sex hormones, play various roles in establishing an immune response (15). Higher levels of estrogen in women are related to having higher immune responses, and higher levels of testosterone in men correlate with a weaker immune response to vaccines (14). Additionally, progesterone and androgens will oppose the activity of the immune system through estrogen-related pathways (16).

Progesterone boosts interleukin 4 (IL-4), suppresses the type 1 T-helper responses, lowers the T-cell-dependent antibody responses, and reduces the proliferation rate of T-cells (17).

Further, the number of genes associated with immunity is 10-fold higher in the X chromosome than the Y chromosome (CON 14). Following having two X chromosomes, women will produce more immune-related proteins than men (18, 19).

Conclusion

As mentioned before, there has been a multitude of studies on the subject, focusing on other vaccines other than COVID-19. These studies show that the immune response to vaccines is more potent in women than in men. However, the studies so far on the gender effect on the efficacy of COVID-19 vaccines have inconsistent results. Some of these studies show no significant difference between the two genders regarding vaccine efficacy, while others report a higher immune response in female subjects. Therefore, we need more detailed studies with bigger sample sizes to be conducted.

Authors' contribution

Conceptualization, validation, investigation, resources, data curation, visualization, supervision, project administration, funding acquisition, writing—original draft preparation: PS and SY; Writing—review and editing: HRJ, PS and SY.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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References

1. Jensen A, Stromme M, Moyassari S, Chadha AS, Tartaglia MC, Szoeke C, et al. COVID-19 vaccines: Considering sex differences in efficacy and safety. Contemp Clin Trials. 2022;115:106700. doi: 10.1016/j.cct.2022.106700.
2. Fischinger S, Boudreau CM, Butler AL, Streeck H, Alter G. Sex differences in vaccine-induced humoral immunity. Semin Immunopathol. 2019;41:239-249. doi: 10.1007/s00281-018-0726-5.
3. Pellini R, Venuti A, Pimpinelli F, Abril E, Blandino G, Campo F, et al. Initial observations on age, gender, BMI and

hypertension in antibody responses to SARS-CoV-2 BNT162b2 vaccine. EClinicalMedicine. 2021;36:100928. doi: 10.1016/j.eclinm.2021.100928.
4. Vassilaki N, Gargalionis AN, Bletsa A, Papamichalopoulos N, Kontou E, Gkika M, et al. Impact of Age and Sex on Antibody Response Following the Second Dose of COVID-19 BNT162b2 mRNA Vaccine in Greek Healthcare Workers. Microorganisms. 2021;9:1725. doi: 10.3390/microorganisms9081725.
5. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al; COVE Study Group. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. N Engl J Med. 2021;384:403-16. doi: 10.1056/NEJMoa2035389.
6. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al; C4591001 Clinical Trial Group. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med. 2020;383:2603-15. doi: 10.1056/NEJMoa2034577.
7. Sadoff J, Le Gars M, Shukarev G, Heerwegh D, Truyers C, de Groot AM, et al. Interim Results of a Phase 1-2a Trial of Ad26.COV2.S Covid-19 Vaccine. N Engl J Med. 2021;384:1824-35. doi: 10.1056/NEJMoa2034201.
8. Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al; Oxford COVID Vaccine Trial Group. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet. 2021;397:99-111. doi: 10.1016/S0140-6736(20)32661-1.
9. Abu Jabal K, Ben-Amram H, Beiruti K, Batheesh Y, Sussan C, Zarka S, et al. Impact of age, ethnicity, sex and prior infection status on immunogenicity following a single dose of the BNT162b2 mRNA COVID-19 vaccine: real-world evidence from healthcare workers, Israel, December 2020 to January 2021. Euro Surveill. 2021;26:2100096. doi: 10.2807/1560-7917.ES.2021.26.6.2100096.
10. Dagan N, Barda N, Kepten E, Miron O, Perchik S, Katz MA, et al. BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting. N Engl J Med. 2021;384:1412-23. doi: 10.1056/NEJMoa2101765.
11. Su JR, Moro PL, Ng CS, Lewis PW, Said MA, Cano MV. Anaphylaxis after vaccination reported to the Vaccine Adverse Event Reporting System, 1990-2016. J Allergy Clin Immunol. 2019;143:1465-73. doi: 10.1016/j.jaci.2018.12.1003.
12. Gee J, Marquez P, Su J, Calvert GM, Liu R, Myers T, et al. First Month of COVID-19 Vaccine Safety Monitoring - United States, December 14, 2020-January 13, 2021. MMWR Morb Mortal Wkly Rep. 2021;70:283-288. doi: 10.15585/mmwr.mm7008e3.
13. Flanagan KL, Klein SL, Skakkebaek NE, Marriott I, Marchant A, Selin L, et al. Sex differences in the vaccine-specific and non-targeted effects of vaccines. Vaccine. 2011;29:2349-54. doi: 10.1016/j.vaccine.2011.01.071.
14. Trigunaite A, Dimo J, Jørgensen TN. Suppressive effects of androgens on the immune system. Cell Immunol. 2015;294:87-94. doi: 10.1016/j.cellimm.2015.02.004.
15. Klein SL, Marriott I, Fish EN. Sex-based differences in immune function and responses to vaccination. Trans R Soc Trop Med Hyg. 2015;109:9-15. doi: 10.1093/trstmh/tru167.
16. Moulton VR. Sex Hormones in Acquired Immunity and Autoimmune Disease. Front Immunol. 2018 Oct 4;9:2279. doi: 10.3389/fimmu.2018.02279.
17. Ortona E, Pierdominici M, Rider V. Editorial: Sex Hormones and Gender Differences in Immune Responses. Front Immunol. 2019 May 9;10:1076. doi: 10.3389/fimmu.2019.01076.
18. Ciarambino T, Barbagelata E, Corbi G, Ambrosino I, Politi C, Lavalle F, et al. Gender differences in vaccine therapy: where are we in COVID-19 pandemic? Monaldi Arch Chest Dis. 2021;91. doi: 10.4081/monaldi.2021.1669.
19. Ruggieri A, Anticoli S, D'Ambrosio A, Giordani L, Viora M. The influence of sex and gender on immunity, infection and vaccination. Ann Ist Super Sanita. 2016;52:198-204. doi: 10.4415/ANN_16_02_11.