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Impact of covid-19 vaccines in chilean healthcare professionals: a pharmacovigilance and monitoring program at guillermo grant benavente hospital

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Resumen

Contexto: La pandemia del COVID-19 es aun una emergencia de salud pública mundial sin una clara resolución. Aunque no hay medicamentos regularmente aprobados por las agencias regulatorias como FDA, o EMA, se dispone de un numero acotado de opciones de inmunización aprobadas para un uso de emergencia. En este sentido, la Agencia Chilena de Medicamentos: Instituto de Salud Pública de Chile (ISP-Ch) aprobó entre diciembre 2020 y marzo 2021, las vacunas de Pfizer-BioNTech, Sinovac, Cansino, y Oxford-AstraZeneca parauso de emergencia, comenzando con un calendario de inmunizacióin que utilizó como criterios de inclusión los grupos de riesgo y las poblaciones altamente expuestas, bajo esta estrategia, el personal de salud, se constituyo en una prioridad de este plan nacional de inmunización.

Metodo: Una muestra de 6617 profesionales de la salud fueron vacunados y monitorizados por el programa de farmacovigilancia del Hospital Regional Guillermo Grant Benavente de la Cuidad de Concepción, durante 3 meses (diciembre 2020- Marzo 2021). 5944 fueron inmunizados con Coronovac™ (Sinovac) y 673 con Comirnaty™ (Pfizer BioNTech). Una aplicación para telefonos inteligentes fue desarrollada por el Servicio de tecnologia de la informacion del Hospital (TICs), donde cada profesional de la salud pudo registrar todos los síntomas experimentados después de la inoculación de la primera y segunda dosis. Una vez realizado el reporte una alerta por email se enviaba automaticamente al programa de farmacovigilancia que evaluaba el reporte y tomaba la decisión de derivar o no al paciente a una atención medica de acuerdo con la severidad de la reacción adversa reportada (moderada o severa). Todos los casos que requirieron asistencia médica, fueron derivados a la equipo de enfermería vía email para el soporte medico

Summary

Background: The COVID-19 pandemic is still a worldwide public health emergency. Although there are no final FDA-approved treatments for Covid-19, a small number of options have been approved for emergency use. The Chilean Agency for Drugs (ISPCh) has approved the vaccines from Pfizer-BioNTech, Sinovac, Cansino, and Oxford-AstraZeneca for emergency use, and the immunization process began in December 2020 following a calendar schedule that outlined criteria for the vaccination of high risk groups and exposed populations. Using this strategy, healthcare professionals were a priority to be vaccinated.

Methods: A sample of 6617 healthcare professionals were vaccinated during a three-month period (December 2020-March 2021); 5944 of them with Coronovac™ (Sinovac) and 673 with Comirnaty™ (Pfizer BioNTech). A smartphone app was developed by the Hospital Information Technology and Communications (TICs) team allowing each professional to register all symptoms that appeared after immunization (first and second doses). When a report was made by a healthcare professional, an email automatically arrived to the Pharmacovigilance team that was evaluated and the decision was made to provide medical support according to the severity of the adverse reaction reported (moderate and severe). All these cases were informed to the Nursing team by an email that also arrived automatically when medical assistance was required, and an appointment was scheduled with a doctor. All reports that involved medical care or assistance were notified to the regulatory authority (Instituto de Salud Publica de Chile). Each case was closed after the determination was made by the pharmacovigilance team and medical staff that the adverse reaction had ended.

correspondiente y fueron reportados a la Autoridad Sanitaria y Regulatoria (ISP-Ch). Cada caso fue cerrado y el paciente dado de alta posterior a la evaluación del equipo médico y de farmacovigilancia.

Resultados: desde Diciembre 2020 a marzo 2021, 13234 vacunas fueron administradas a 6617 profesionales de la salud. Considerando todas las dosis adminsitradas, solo el 2.95% de las persona inmunizadas reportaron alguna reacción adversa (n=380) después de la primera o segunda dosis (2.13% con Coronavac (n= 281) y 0.75% con Pfizer-BioNTech (n= 99)). El grupo etario de mayor incidencia fue entre 20-40 años de edad (n=68 y n=222 inmunnizados con Comirnaty y Coronavac, respectivamente); mientras que profesionales de la salud de mayor edad mostraron una mejor tolerancia a ambos tipos de vacunas usadas. Finalmente, los datos revelan que hubo una menor incidencia de reacciones adversas con la segunda dosis de Coronavac respecto de la primera, mientras que con la vacuna de Pfizer-BioNTech hubo mayor incidencia en la segunda dosis que en la primera. No se registraron casos fatales ni casos severos que involucrasen alteraciones sistémicas irreversibles.

Conclusiones: El Esfuerzo cientifico para luchar contra el COVID-19 ha proveído a la población mundial de un importante numero de alternativas aprobadas para uso de emergencia, dos de las cuales han sido usadas masivamente en la población chilena, alcanzando porcentajes de inmunización superiores al 90% de las poblaciónes objetivo; en primera instancia grupos de riesgo y poblaciones especiales altamente expuestas. Usando un programa de farmacovigilancia desarrollado por el Hospital Regional Guillermo Grant Benavente y la Universidad de Concepción, se ha demostrado que las dos formulaciones monitorizadas en este estudio, demostraron ser seguras, bien toleradas, con una baja incidencia de efectos secundarios, sin embargo los datos de eficacia, deberán ser estudiados en un estudio de largo plazo; sin embargo los indidcadores de la pandemia en Chile, sufrieron una importante caída, y se ha iniciado la tercera dosis o dosis de refuerzo que determinará el fortalecimiento del plan de inmunización desarrollado por la autoridad sanitaria chilena.

Palabras clave

Vacunas COVID-19, COVID-19, SARSCoV-2, Coronavirus, farmacovigilancia.

Conflicto de intereses

Este artículo no presenta conflicto de interés.

Results: From December 2020 to March 2021, 13234 vaccine doses were administered to 6617 healthcare professionals. Considering all doses administered, only 2.95% of immunized healthcare professionals reported some adverse reaction (n=380) after the 1st or 2nd doses (2.13% with the Coronavac (n= 281) and 0.75% with the Pfizer-BioNTech vaccine (n= 99)). The more prevalent age group that reported adverse reactions were younger professionals between 20-40 years old (n=68 and n=222 immunized with Comirnaty and Coronavac, respectively); while older professionals demonstrated a higher tolerance to both types of vaccines used. Finally, the data revealed that there was a low incidence for an adverse reaction to the second dose with the Coronavac vaccine, whereas the Pfizer-BioNTech vaccine had a higher incidence for adverse reactions with the second dose. No fatalities, severe cases, or irreversible systemic alterations were reported in the period studied.

Conclusion: The scientific effort to fight COVID-19 has provided the world with four recent approved vaccines to use under emergency use, and two of them have been massively applied to the Chilean population; in the first instance to healthcare professionals and then to high risk groups like elderly people. Using the pharmacovigilance program developed by the Hospital Guillermo Grant Benavente in collaboration with the Universidad de Concepcion, it has been demonstrated that these two vaccines are safe, well tolerated, and have a low incidence of adverse reactions, mainly mild to moderate. Data about efficacy and reinforcing doses need to be evaluated in future studies.

Key words

COVID-19 vaccines; COVID-19; SARSCoV-2; Coronavirus; Pharmacovigilance.

Conflict of interests

This article does not present a conflict of interest.

RESEARCH IN CONTEXT

Evidence before this study

The COVID-19 pandemic is still in progress and vaccine studies continue to be conducted, thus information about the impact of vaccination programs are still being collected. Partial reports are continuously released to check the efficacy and safety of the different vaccine types, but little is known about the adverse reaction (AR) of the general population to the vaccines being used in the national immunization programs. All related data has been provided by clinical trials with controlled populations. We developed a pharmacovigilance program to monitor the incidence of AR in healthcare professionals to evaluate the impact of two vaccines in the general population.

Added value of this study

This study provides the first evidence about the incidence and severity of AR in healthcare professionals from a Chilean hospital. We characterized the sample population, examined AR after the first and second doses, and made a general evaluation about tolerance to the Comirnaty and Coronavac vaccines. The current study provides important information about the impact of the vaccines on the general population and provides medical support teams with a better understanding of the immunization process and how to manage AR that arise in the vaccinated population.

Implication of all available evidence

Several vaccination programs throughout the world have described the incidence of serious adverse effects related to the use of some vaccines. The impact of the vaccines for use in Latin America has not been thoroughly evaluated, thus a systematic approach to examine the vaccination process and the efficacy of the formulation of those vaccines need to be analyzed and communicated to the authorities and general population in order to confer confidence in the vaccination process. Therefore, the aim of this study was to provide data about the vaccination process in healthcare professionals from Guillermo Grant Benavente Hospital in Concepcion, Chile, in order to provide adequate information to make informed decisions about vaccine use and safety measures in a Latin American population.

INTRODUCTION

The COVID-19 pandemic is still a worldwide public health emergency caused by Coronavirus 2 (SARS-CoV-2) that produces a severe, acute respiratory syndrome. This syndrome causes pneumonia, respiratory failure, and encephalopathy thereby making it lethal. Coronaviruses cross the blood-brain barrier with a significant risk to the CNS [1,2] All these clinical manifestations represent a substantial mortality rate, especially for risk groups that have preexisting health conditions, older adults, and healthcare professionals and front line workers who are highly exposed to COVID-19. Thus, global efforts are focused on developing safe and effective vaccines as a real alternative to fight the pandemic. Throughout history, vaccines have played an important role in disease control and improving public health, for instance, the discovery of the smallpox vaccine by Edward Jenner in 1796, and later when Louis Pasteur showed that disease could be prevented by infecting humans with weakened rabies germs [3]. Since then, vaccines have been effective in reducing the incidence rate of several infections. There has been a rapid development in COVID-19 vaccines during the pandemic to protect the health of millions of people around the world. Although there are no final FDA-approved treatments for Covid-19, a small number of options have been approved for emergency use. The Chilean Agency for Drugs (ISPCh) has approved the vaccines from Pfizer-BioNTech, Sinovac, Cansino, and Oxford-AstraZeneca for emergency use. The immunization process began in December 2020 following a calendar schedule that outlined criteria for the vaccination of high-risk groups and exposed populations. Using this strategy, healthcare professionals were a priority to be vaccinated. We followed the recommendation by PAHO (Pan American Health Organization) for Passive surveillance of Adverse Events Following Immunization (AEFI) which constitutes a fundamental pillar to identify and investigate events subsequent to the introduction of new vaccines.

The pharmacovigilance program is the most important tool to evaluate the global exposure of the general population to vaccines and provides important data for decision making regarding protocols and evaluating the incorporation of new population groups into the immunization program (e.g. pregnant and lactating women, adolescents <18, and children). A strong and active pharmacovigilance program at Guillermo Grant Benavente Hospital in Concepcion, Chile (the largest hospital in the south of Chile) followed and monitored all events associated to the immunization of healthcare professionals that included physicians, nurses, pharmacists, biochemists, and technicians. Adverse reactions (AR) were documented using an informatics system and subsequent clinical actions were implemented according to the severity of the adverse reaction reported.

RESULTS

Between December 2020 and March 2021, a total of 6617 healthcare professionals from Guillermo Grant Benavente Hospital were immunized with two doses of the two vaccines approved by the Chilean regulatory authority (Instituto de Salud Publica de Chile) of which 5944 (89.8%) were immunized with Coronavac (CV, Sinovac Laboratories) and 673 (10.2%) with Pfizer BioNTech (PB). Of the total population vaccinated with PB (n=673), the gender distribution was 40.8% (n=275) male and 59.1% (n=398) female; whereas the gender population for the CV vaccination was 32.9% (n=1961) male and 67.1% (n=3983) female. For both vaccination groups, females made up the largest percentage (Figure 1A). To evaluate the impact of the vaccination process on healthcare professionals, adverse reaction (AR) was voluntarily reported to the pharmacovigilance team through a smartphone app and analyzed according to the criteria used in the literature for local and systemic events [4]. From the total doses administered (n=13234), the number of reports for AR after administration of the first or second doses were 380 which represented 2.87% of the total doses administered (Figure 1B). These reports represented any AR described by the vaccinated subjects. From these total events reported, 0.75% (n=99) were associated to the PB group, while 2.12% (n=281) were related to the CV group (Figure 1C); representing 7.4 % and 2.4 % of the total AR, respectively, in relation to the total doses administered (Figure 1D).

Figure 1. General data of immunized healthcare professionals. (A) Participation of subjects disaggregated by gender (men and women) and by type of vaccine PB (n=673, white bars) and CV (n=5944, black bars). (B) Total percentage of AR observed from both vaccinated groups. (C) Total AR reports for the group vaccinated with PB (n=99, white bar) and CV (n=281, black bar). (D) Percentage of AR reported in C, in relation to total doses administered by type of vaccine PB (n=7.4%, white bar) and CV (n=2.4%, black bar).

FIGURE 1

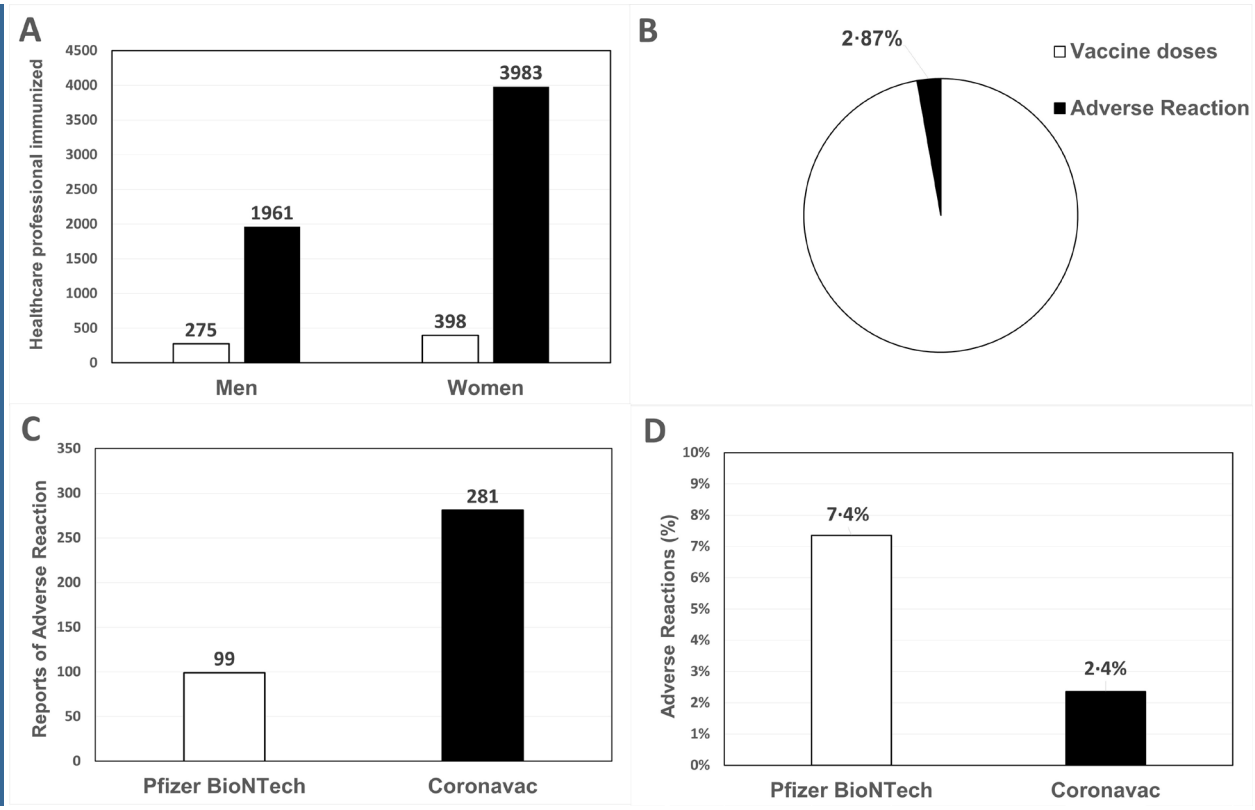


Figure 2. Incidence of AR according to gender. (A) Disaggregation of AR reports according to the gender of participants immunized with PB (n=99, white bar) or CV (n=281, black bar). (B) Percentage of AR from the total reports disaggregated by gender (men and women) and vaccine PB (white bar) or CV (black bar), respectively.

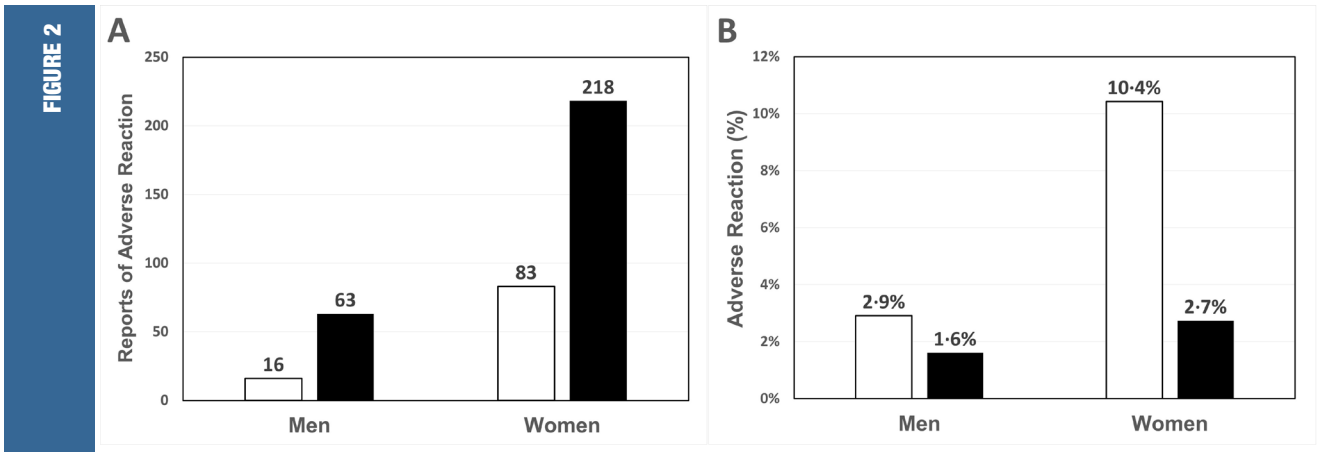
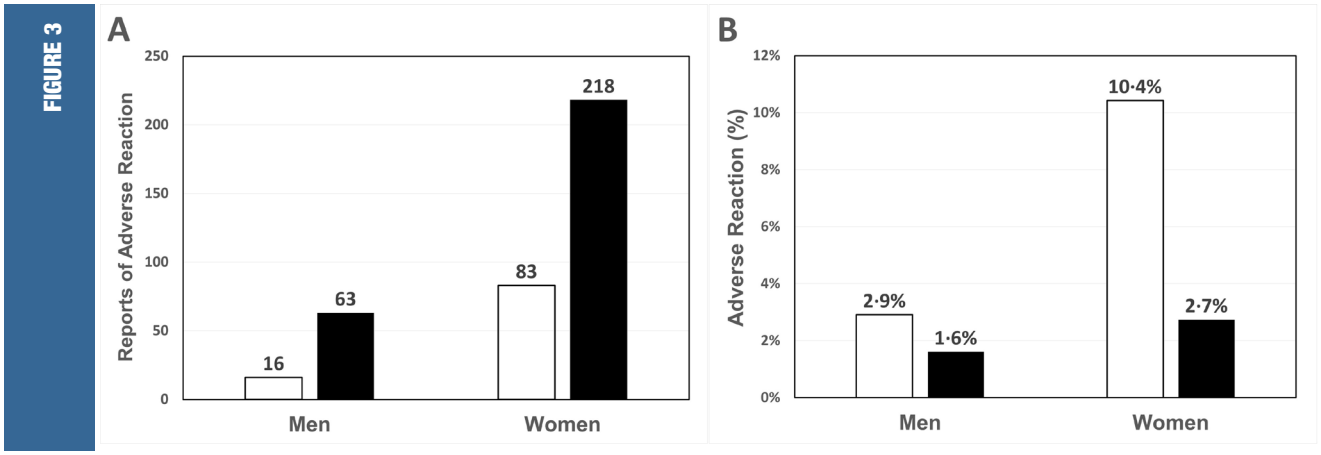


Figure 3. Age related reports of AR. (A) Total report of vaccinated subjects disaggregated by age range and vaccine type: PB (n=99, white bar) or CV (n=281, black bar), respectively. (B) Total reports of AR disaggregated by degree of severity (mild to moderate).

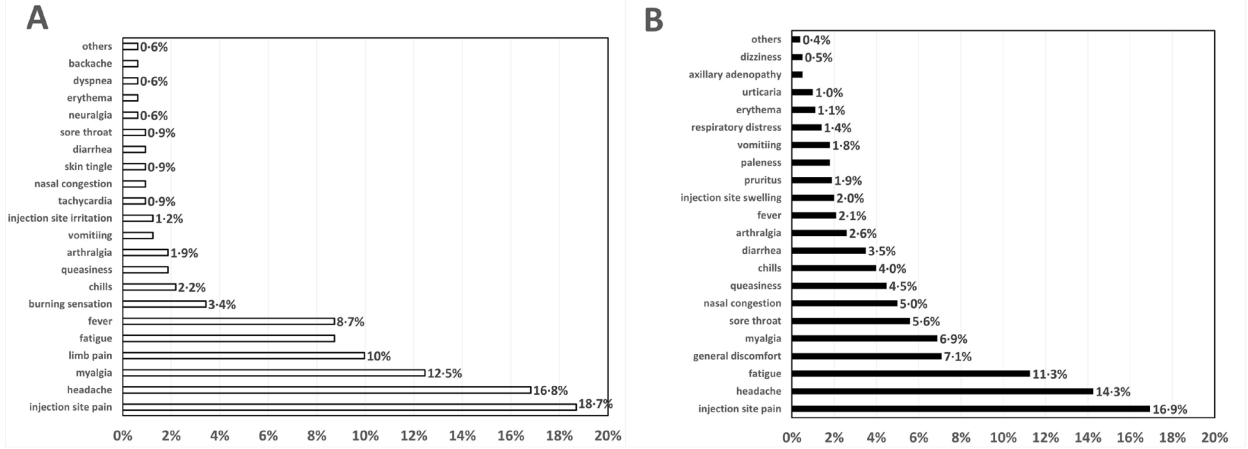


In order to identify the incidence of AR according to population gender, a disaggregation of all the data showed that the higher prevalence of AR was in women, with 0.62% (n=83) and 1.64% (n=218) for PB and CV vaccines, respectively (Figure 2A). On the other hand, the prevalence of AR in men was only 0.12% (n=16) and 0.47% (n=63) for PB and CV vaccines, respectively (Figure 2A). Comparatively, the incidence of AR from the total number reported was higher in the PB group as compared to the CV group, and women had a higher incidence of AR in both vaccine groups (10.4% and 2.7% for PB and CV, respectively (Figure 2B).

Data on the age distribution within the studied population demonstrated that AR events occurred more often in younger people than older ones (Figure 3A). The graph in figure 3A shows that healthcare professionals between 20-40 years old represented 1.68% (n= 222) and 0.51% (n= 68) for the CV and PB vaccines, respectively, whereas only 4 subjects over 60 years of age reported AR with the CV vaccine. The high tolerance of older subjects is quite interesting and this should be studied further since it could be indicative of more tolerability, or less capacity of the immunological system to generate any response to the vaccine and will need to be correlated with a study on antibody levels. The notification of AR between the first dose (n= 31) of PB and the second dose (n= 68) showed a marked increase, as well as in the degree of severity of the events from mild to moderate (Figure 3B). According to the literature [4-6], the population that was immunized with the CV vaccine had a decrease in AR reports between the first dose (n= 197) and the second dose (n= 86).

Figure 4. Global report of AR. Percentage of several AR reported to Pharmacovigilance for the PB vaccine (A) and the CV vaccine (B).

FIGURE 4



In order to know the type of AR reported by the healthcare professionals, the report form included most frequent types of AR reported in the literature to be chosen by the subjects according to their personal experience in the vaccination process. For both population groups vaccinated with CV and PB, the most frequent AR reported were injection site pain and headache (16.9% and 14.3% for CV, and 18.7% and 16.8% for PB respectively); while less frequent AR were dyspnea and neuralgia in the PB group, and urticaria and dizziness in the CV group (Figure 4A,B). Other AR mentioned were: swelling, lipothymia, dysphonia, cellulitis, hypotension, hypertension, drowsiness, cough, asthenia, polydipsia, sweating, facial edema, erythema, vertigo, facial paralysis, facial tingling, loss of taste, chest pain, conjunctivitis, photophobia, earache, gait disorder, and petechiae.

DISCUSSION

The global scientific effort to fight COVID-19 has provided the world with four recent approved vaccines to use under emergency use, and two of them have been massively applied to the Chilean population; in the first instance to healthcare professionals and then to high-risk groups like elderly people. Using the pharmacovigilance program developed by the Hospital Guillermo Grant Benavente in collaboration with the Universidad de Concepcion, it has been demonstrated that these two vaccines are safe, well tolerated, and have a low incidence of AR, mainly in the mild to moderate levels. We found that the most prevalent systemic AR including headache and fatigue also agreed with other reports from countries like UK, where one of the vaccines analyzed here was also used (PB) [7]. Although AR were more prevalent in women than in men, older people were more tolerant, and the second doses were tolerated better than the first. Although other studies have examined COVID-19 vaccine effects in the general population, this is the first study that evaluates the effects of two vaccines in Chilean healthcare professionals, the main risk-population that fight against the virus. Our data demonstrate that short-term AR for both vaccines used are low in frequency, mild in severity, and short-lived. Younger, professional women had a higher frequency of AR according with clinical trials and epidemiologic reports published in the last months [7], and a lower frequency for the second dose as compared to data reported by Monin et al. [8]. Data about long term efficacy and reinforcing doses need to be evaluated in future studies. In the context of the global pandemic that we are experiencing, vaccines represent an important tool to fight against SARCoV-2. Furthermore, the main dilemma about the use of these vaccines related with their safety has not been a critical point, and all local and systemic AR have been events that can be managed with simple clinical approaches and safe drugs like NSAIDs. Our findings, is the first evidence that demonstrate that the PB and CV vaccines approved in Chile to be used under emergency criteria are safe, and the incidence of AR in healthcare professionals exposed to these two vaccines is very low, according to global reports from clinical trials. In summary, the exposure of first line workers to vaccine immunization appears to be safe and has a low rate of AR. Additionally, having a strong pharmacovigilance program with the main objective to monitor the immunization process and supervise the care of health personnel is of utmost importance.

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