Journal of Pharmaceutical Health Services Research, 2021, Vol 12, 591–593
doi:10.1093/jphsr/rmab016
Short Communication
Advance Access publication 12 April 2021

JPHSR Journal of Pharmaceutical Health Services Research

OXFORD

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Pharmacovigilance of COVID-19 vaccines in the context of Nepal: an assessment based on early adverse drug reaction reports

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Received December 24, 2020; Accepted March 20, 2021.

Abstract

Objective The objective of this study was to assess the ongoing pharmacovigilance of coronavirus disease-19 (COVID-19) vaccines in the Nepalese context based on the available preliminary adverse drug reaction (ADR) reports and suggest approaches for strengthening pharmacovigilance mechanisms.

Methods Currently, many COVID-19 vaccines are under advanced development and some have begun to be administered. In Nepal, the vaccination programme was initiated with Oxford/AstraZeneca COVID-19 AZD1222 (Covishield) vaccine on January 27th targeting frontline healthcare professionals, sanitary staff and security workers. Newspaper reports and ADR reports received at a regional pharmacovigilance centre in Nepal were analysed. Nepal initiated a national pharmacovigilance programme 15 years back and has 14 functioning regional pharmacovigilance centres. The authors examine the strengths and challenges facing the current pharmacovigilance system in ensuring the safety of COVID-19 vaccines.

Key findings The news coverage has not mentioned any deaths till date with COVID-19 vaccination. Some patients reported vomiting, urticaria and sudden increase in blood pressure. Few people suffered from headache, fever and myalgia after being vaccinated. A vaccine, approved in an accelerated manner may have safety concerns. The vaccine may cause several types of reactions, but serious reactions have not been reported. Occurrence of adverse effects due to the vaccine is being studied.

Conclusions Involving key stake holders, training health professionals and strengthening existing reporting procedures are important. Developing a system of reporting and analysing ADRs daily can help generate actionable intelligence to improve the safety of the vaccination programme. Establishing functioning communication channels between regulatory authorities and other stakeholders is crucial.

Keywords: COVID-19; Nepal; pharmacovigilance; vaccine

Introduction

The COVID-19 pandemic has adversely affected the world with certain sectors like travel, tourism and hospitality being hit the hardest. COVID-19 vaccines are expected to strengthen the immune system of the vaccinated individuals offering protection and a more permanent solution.[1] A COVID-19 vaccine is being administered in the United Kingdom and in other countries.[2]

Currently, many vaccines are under various phases of clinical trial,[3] and every country should ensure these newly developed vaccines are used within the framework of functioning, robust pharmacovigilance systems. Since these vaccines have undergone accelerated development and clinical trial, post-marketing surveillance studies are mandatory. But, as these vaccines are being used among large populations within a short time, detailed post-marketing studies may not be viable and hence safety largely depends on the country's existing pharmacovigilance system. The authors examine the challenges and opportunities associated with pharmacovigilance of COVID-19 vaccine/s in Nepal.

Nepal established its national pharmacovigilance programme in 2004 and was recognized as a full member for WHO Programme for International Drug Monitoring in July 2006.[4] The reporting of adverse drug reactions (ADRs) is not mandatory. The 14 regional centres report ADRs to the national centre for further assessment and forwarding to the Uppsala Monitoring Centre, the international centre for pharmacovigilance.

On 27 January 2021, the first phase of vaccination started in Nepal. Soon there may be more than one vaccine available creating challenges for ADR monitoring. The viral strains used to make the vaccine can be different possibly leading to different types of ADRs. Adjuvants used may also cause ADRs and may be different among different vaccines. Due to the severity of the pandemic the clinical trial duration has been shortened. For Nepal, challenges can also arise while distributing the vaccines, and maintaining the cold chain for assuring the vaccine quality. Recent reports suggest the vaccines require maintenance of a strict cold chain for their effectiveness.[5]

During preliminary trials, there were ADR reports with the vaccines. In a COVID-19 vaccine trial, at least one ADR was noticed in more than 75% of recipients within the first 7 days of administration. The commonest ADR was injection site pain (58%) and fever (46%).[6] In another study, injection site pain was noticed in 58% recipients and fever in 50%.[7] These preliminary reports suggest a high incidence of ADRs which further mandates the importance of a functioning pharmacovigilance programme at the country level.

Methods

Nepal is using Oxford/AstraZeneca COVID-19 AZD1222 (Covishield) vaccine. The first phase targeted frontline healthcare professionals, sanitary and security workers. These individuals had to provide their identification for getting vaccinated. ADRs reported to a regional centre following the first phase of vaccination were analysed for causality and severity using the widely accepted Naranjo algorithm and Modified Hartwig and Siegel scales, respectively. Authors also examine possible reporting approaches to obtain actionable ADR data quickly to improve the safety of the COVID-19 vaccine.

Results

Preliminary evaluation of ADRs reported to regional pharmacovigilance centre

Five ADRs were reported (Table 1) to a regional pharmacovigilance centre located at KIST Medical College.

Fever, myalgia, urticaria, diarrhoea and sudden rise in blood pressure were among ADRs reported with the vaccine. There are many ongoing studies of ADRs caused by the vaccines in Nepal.

Table 1 ADRs reported following COVID-19 vaccination

S. No	ADR manifestations	Onset of ADR	Causality assessment	Severity assessment	Management of ADR
1	Diarrhoea, pain in abdomen	29th January (after 2 days of vaccination)	Probable	Moderate Level 3*	Pantoprazole, Ketorolac and Buscopan along with oral rehydration solution
2	Sudden rise in blood pressure (180/120)	27th January, after the vaccination	Probable	Moderate Level 3*	Amlodipine and labetalol, and additionally alprazolam
3	Headache and Vomiting	After 6 h of vaccine administration	Probable	Moderate Level 3*	Paracetamol and normal saline (0.9%NaCl)
4	Fever, chills, headache, myalgia, malaise, flu like symptoms.	24 h after getting the vaccine	Probable	Moderate Level 3*	Paracetamol tablet
5	Generalized rashes and urticaria	Seen immediately after vaccination	Probable	Moderate Level 3*	Fexofenadine

*The ADR requires that the suspected drug be withheld, discontinued otherwise changed, and/or on antidote or other treatment is required. There is no increase in length of stay.

The authors examine possible ADR reporting approaches for a newly launched COVID-19 vaccine (Figure 1). The suggested programme should encourage ADR reporting from all stakeholders either directly to the national centre or preferably through the regional pharmacovigilance centres.

Discussion

Establishment of a new ADR reporting form highlighting vaccine type, distributor details, details of the professional administering the vaccine, history of COVID-19 diagnosis, COVID-19 symptoms at the time of vaccination among others has to be developed, involvement of all regional centres to establish reporting procedures, resource allocation and obtaining extra manpower (pharmacists/pharmacologists) for facilitating ADR reporting is necessary. The core staff at these centres must be trained on early detection and reporting of ADRs. The regional centres can create awareness, conduct training programmes and collect ADRs. Knowing the vaccine safety profile from manufacturers can help to be vigilant for similar ADRs among the vaccinated population. The Uppsala Monitoring Centre can share safety information on the newly launched vaccines.

Currently, ADRs are being reported for vaccines used for national immunization programmes. There is a standard procedure for reporting using the adverse effects following immunization (AEFI) system. ADRs are reported, assessed, categorized and data stored as per national and global guidelines. The AEFI investigational committee was established as per the 'Immunization act 2072 BS in Nepal'.[8]

Adverse effects due to vaccine administration have been reported in newspaper articles including reactions similar to those mentioned in Table 1.[9, 10] ADRs are being reported and collected at individual centres and by interested researchers. However, a system whereby data can be collated and analysed at the national level to provide an integrated picture and actionable intelligence about vaccine ADRs is not yet functioning. Due to the rapid roll-out of vaccination, such a system with reports being generated daily can help strengthen the safety of COVID-19 vaccination. Problems noted can be addressed. Data can also be analysed at state, ethnic, regional and other levels. Nepal has great ethnic and genetic diversity which can influence ADRs to the vaccines. Greater integration between the AEFI system and the national pharmacovigilance programme may be required. Due to the ongoing studies, we expect more information about vaccine ADRs will be available soon. Consumers can be educated about ADR reporting through various mass media and using different social networking sites.

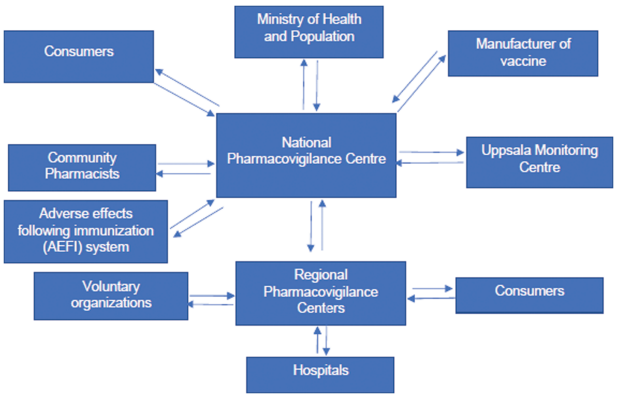

Figure 1 A proposed pharmacovigilance system for COVID-19 vaccines in Nepal.

Conclusions

ADRs can be reported through the vertical immunization programme and also via horizontal reporting programmes. A system whereby ADRs are collated and analysed in real-time nationally can strengthen vaccine safety. An effective pharmacovigilance system is vital for safe use of COVID-19 vaccines and hence the pandemic can serve as a wakeup call for developing countries to strengthen pharmacovigilance systems. The approaches examined here may be relevant to other countries with developing pharmacovigilance programmes.

Acknowledgement

The authors would like to acknowledge Dr. Trishna Shrestha, Department of Family Medicine, KIST Medical College, for reporting ADRs to the regional pharmacovigilance centre.

Author contributions

Concept and design (P.R.S., S.P., and N.J.); acquisition of data (N.J.); analysis and interpretation of data (S.P., N.J.); drafting of the manuscript (P.R.S., S.P., N.J., and G.D.), revising the manuscript for critical intellectual inputs (all authors). All authors have read and approved the final submitted version of the manuscript.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of Interest

The authors report no conflicts of interest in this work.

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