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Lessons learned from a cluster of immunization errors in newborns

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Abstract

Background: Vaccines are safe and effective, but adverse reactions can occur. Immunization errors (IEs) are one of the types of adverse events following immunization. The Moroccan Pharmacovigilance Centre (MPC) received a cluster of IEs from a maternity university hospital (MUH) regarding six newborns who were inadvertently administered rocuronium instead of hepatitis B (HepB) vaccine. The newborns experienced respiratory distress and one had a fatal outcome.

Objectives: The study aimed to describe the investigation findings, the underlying causes, and contributing factors of the IEs cluster, and proposed risk minimization actions.

Design: We carried out a descriptive analysis of the cluster of IEs related to the HepB vaccine reported to the MPC.

Methods: An investigation was conducted by the Ministry of Health according to the World Health Organization guidance. The root cause analysis was performed to identify underlying causes and contributing factors that lead to IE occurrence.

Results: The cluster analysis showed that the main contributing factors were the look-alike rocuronium and HepB vaccine packaging, the first-time running HepB vaccination for newborns in the MUH, the lack of a full-time pharmacist, and the unsafe storage of rocuronium and vaccines. The administration of Sugammadex to the newborns followed by their transfer to the neonatal care unit resulted in the recovery of five of the six newborns. Proposed recommendations included (1) raising awareness of healthcare professionals to the risk related to look-alike medications, (2) training nurses to ensure vaccination to implement procedures related to immunization practices, (3) nomination of a full-time pharmacist, (4) reassessment of the safety of drug storage and dispensing at the hospital pharmacy, particularly for high-alert medications.

Conclusion: Reporting IEs, particularly serious ones, allows us to identify causes and contributing factors that led to their occurrence. Lessons learned from errors are key to take risk minimization actions to improve vaccine safety worldwide.

Keywords: immunization error, pharmacovigilance, preventability, risk minimization action, root cause analysis, vaccine safety

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Introduction

Immunization plays a major role in saving lives by protecting individuals from the burden of infectious diseases. Vaccines are widely recognized as one of the world's most successful and cost-effective health interventions. According to the World Health Organization (WHO), immunization currently prevents 4–5 million deaths every year,[1] among which, 2.5 million are children.[2]

Vaccines are safe and effective. Yet, immunization errors (IEs) can occur due to adverse events

following immunization (AEFIs) in patients.[3] They often constitute the greatest proportion of AEFIs.[4]

European Medicines Agency included IEs in the definition of medication errors as unintended failures in the drug treatment process to lead to, or have the potential to lead to, harm to the patient.[5] According to the WHO, IE-related reactions refer to an AEFI caused by the inappropriate handling, prescribing, or administrating of a vaccine.[6]

One of the situations causing IEs is the administration of a drug or diluent, instead of the actual vaccine, such as insulin, oxytocin, and neuromuscular blocking agents (NBAs). NBAs are high-alert medications (HAMs), with a well-documented history of leading to injuries, even death, when used in error.[7] Indeed, the Institute for Safe Medication Practices National Medication Errors Reporting Program received over 100 reports of errors involving NBAs.[8] These drugs were inadvertently administered to patients who were not receiving proper ventilatory assistance.

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other drug-related problem including vaccines.[9] When AEFIs occur in Morocco, they are reported to the Moroccan Pharmacovigilance Centre (MPC), an agency within the country's Ministry of Health. The MPC is responsible for collecting, analyzing, and evaluating adverse event reports related to health products. Identifying signals of adverse reactions are reviewed for the MPC to implement risk minimization measures and health strategies for greater medication safety in the kingdom.

In Morocco, in 1999, the hepatitis B (HepB) vaccine was included in the routine schedule of the National Immunization Program (NIP). In 2009, the WHO recommended the introduction of the HepB vaccine birth dose, within 24 h after a child is born.[10] This recommendation was implemented, in 2011, in Morocco. However, the HepB immunization was only administered in primary healthcare settings in the country. In 2017, the HepB vaccine was recommended to be administered at maternity university hospitals (MUHs), those belonging to the public health sector. They are specialized in caring for women during pregnancy and childbirth and serve as a venue for clinical education and training in obstetrics and midwifery.

The MUH notified the MPC after a cluster of six newborns experienced serious adverse events just a few minutes after the administration of the HepB vaccine. One of the newborns had a fatal outcome. The preliminary investigation by the medical team revealed that the newborns were inadvertently administered rocuronium intramuscularly, instead of the HepB vaccine. An official investigation was then initiated by the Ministry of Health on the day following the incident.

The objective of this paper is to describe the findings of the investigation, the underlying causes, and contributing factors of the preventable AEFI reports, as well as proposed risk minimization actions to avoid similar IEs.

Methods

Study design

We carried out a descriptive study of the cluster of IEs related to the HepB vaccine reported to the MPC.

Data source

The reports of the IEs cluster were extracted from VigiFlow, a web-based individual case safety reports management system. VigiFlow is available for use by national pharmacovigilance centers of the WHO Program for International Drug Monitoring. The data entered are available in VigiBase, the WHO international database.

Investigation is mandatory for IEs when the following two situations arise, according to recommendations by the WHO.[3] They are (i) the reported IEs led to serious events and (ii) the reported IEs belong to a cluster. The Ministry of Health initiated an investigation involving a multidisciplinary team to include the Inspection Division, the NIP, the Hospital and Ambulatory Care Department, and the MPC. The investigation was conducted the day after the IEs occurred.

The WHO investigation form was used to collect data about the patient, the event, the suspected vaccine administered, the immunization practices

at the vaccination site, and the patient's parents and relatives.[3]

Data analysis

AEFI causality assessment

The AEFI causality assessment is a systematic review of data about an AEFI case. The aim is to determine the likelihood of a causal association between the event and the vaccine received. The WHO causality assessment will classify AEFIs as (A) consistent causal association to immunization, (B) indeterminate, and (C) inconsistent causal association to immunization.[11]

Root cause analysis

The root cause analysis (RCA) of the error was performed by the investigation team. The RCA is, indeed, a systematic investigation technique to identify underlying causes and contributing factors that lead to the making of errors. The RCA consists of four steps[12]:

- describing in detail the event and activities leading up to the error while using medical records and interviewing key participants in the patient's care;
- identifying the proximate cause(s) that explain why the event occurred;
- identifying the contributing factors that permit errors to occur. The Ishikawa diagram was used for this purpose;
- developing an action plan to establish risk minimization actions that can be implemented and tested.

Results

AEFI causality assessment

Investigations showed that reported AEFIs have a consistent causal association with immunization and were classified as IE-related reactions.

Root cause analysis

The following are the results of the RCA:

Step 1: Event description. This step was performed during the investigation procedure in the vaccination location at the MUH. The cluster of six newborns occurred on the same day; they were four females and two males, between 1 and 3 days old. They were supposed to receive the HepB vaccine. They all experienced bradycardia, three of whom developed cyanosis and apnea; and, two, of those three, convulsed. They received emergency resuscitation at the MUH.

The medical staff then detected the IE: the rocuronium was administered instead of the HepB vaccine. The Sugammadex, the reversal agent of NBA, was then administered to the newborns. One of them had a fatal outcome while the other five were transferred to a neonatal care unit in the pediatric university hospital. The outcome was favorable for four while one had sequela.

Concerning immunization practices, the nurse involved in the error occurrence received an immunization training session 1 week before running the first session of administering the HepB vaccine in the MUH. As for the vaccine storage, the cold chain was respected, although the HepB vaccine was stored in the same cold room as the other drugs available in the pharmacy.

Step 2: Proximal causes. The staff member at the pharmacy selected the rocuronium, instead of the HepB vaccine, because the packages for both medications looked alike. The two drugs were stored next to each other in the cold room. Their packaging design had similar colors (white and blue). In addition, the number of vials per box and the volume contained therein were numerically identical for both the rocuronium and the HepB vaccine (solution for injection, 10 mg/ml in 5 ml vials, 10 vials).

Step 3: Contributing factors. The Ishikawa diagram was used to identify the factors contributing to this cluster of IEs (Figure 1). The following cause categories were identified:

Working conditions. The shortage of human resources at the hospital pharmacy contributed to the IE occurrence. The pharmacist responsible was a part-time employee. The pharmacy was understaffed for its daily duties. This led to cumulative tasks and an additional workload for available workers. On the day of the incident, both the pharmacist and main pharmacist technician were on sick leave. The nurse who accidentally selected the rocuronium, instead of the HepB vaccine, was not familiar with the dispensing procedures.

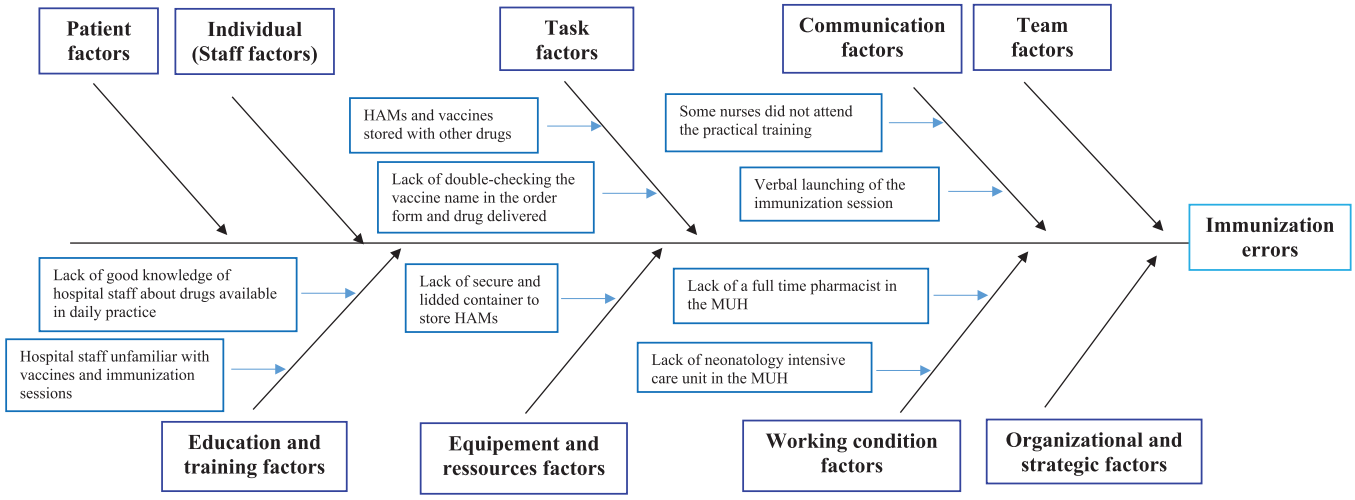

Figure 1. The Ishikawa diagram with identified contributing factors to the immunization errors occurring.
HAMs, high-alert medications; MUH, maternity university hospital.

In addition, a neonatology intensive care unit was lacking. The newborns were admitted to the adult intensive care unit in the maternity ward, and, afterward, they were transferred to the pediatric university hospital.

Education and training. The investigation revealed that the hospital staff did not have adequate knowledge about the International Non-proprietary Names (INN) and brand names of drugs used in daily practice. In fact, the nurse who launched the immunization session checked the brand name of the drug delivered by the pharmacy. She thought it was the proper name of the HepB vaccine. In addition, she omitted to check the INN of the delivered drug, which was rocuronium, known as a HAM.

The hospital staff was also unfamiliar with vaccines and immunization sessions. Even though the nursing staff was trained on the workflow of an immunization session prior to the launching of the HepB vaccination, some safeguards were not carried out during the first session initiated in the MUH.

Equipment and resources. NBAs are HAMs to require particular storage conditions. It is well known that such medications should be stored in secure and lidded containers. In the MUH, such equipment was not available in the pharmacy. The rocuronium was stored in a tray without any label precautions to highlight the importance of wariness when administering the medication.

During the interview of the pharmacy staff, they pointed out that the cold room in the hospital pharmacy was poorly lit. This contributed to mixing up the look-alike packaging of the HepB vaccine and the rocuronium.

Tasks. Two contributing factors have been identified. Regarding medicine storage, the pharmacy staff should have stored rocuronium separately from other drugs. A label to read, 'high-alert medication', should have been placed on the shelves and containers where these medications were stored. In addition, vaccines should be kept apart from the other drugs in storage.

The second factor is related to the management of an immunization session. In the past, HepB immunization was administered at primary healthcare settings in Morocco. Following the WHO recommendations to give infants the first dose of the HepB vaccine within 24 h after birth, the HepB vaccine began to be administered at MUHs. The standard operating procedures for vaccination were not available in these hospitals as they were from the NIP. In fact, the MUH was the location for the current cluster of first-time HepB immunization for newborns. The immunization session was conducted by a nurse when it should have been supervised by a medical team as stated in the immunization procedures.

Another contributing factor was the lack of double-checking the vaccine name before delivery

and administration. The member staff at the pharmacy omitted to make a second review of the order form to ensure the right drug was delivered. Moreover, since she was managing the session alone, the nurse, launching the immunization session, was unable to apply this important step for the safe application of the vaccine.

Communication. Communication issues were also detected in the investigation of IEs. The line manager at the maternity ward was not aware that some nurses had not attended the practical training course prior to launching the HepB immunization. The nurse who carried out the first immunization session was among them. She was not aware of the name of the HepB vaccine available in the maternity ward. Furthermore, the order form and delivery note had both mentioned, 'HepB vaccine', but not the brand name. Consequently, the nurse thought that rocuronium was the brand name of the HepB vaccine.

The verbal launching of the first HepB vaccine immunization session in the MUH was an additional contributing factor. The launching should have followed administrative procedures to inform the hospital staff and to include the involvement of a medical team.

Step 4: Risk minimization actions. The investigation team proposed risk minimization actions to prevent such situations from happening. Among them is the designation of a full-time pharmacist at the MUH. Together with a staff, he should reassess the safety of drugs, vaccines' storage, and dispensing with special attention to HAMs. IEs are to be avoided among nurses, involved in immunization sessions, when they are aware of the importance of implementing procedures, related to immunization practices.

Raising awareness among all healthcare professionals, about the risks due to look-alike and sound-alike medications, is key to preventing the recurrence of similar errors. They should also be aware of the lists of HAMs and preventive strategies for safe usage. The risk minimization actions also highlight the importance of reporting medication errors, including IEs, to learn from past errors. The proposed measures drew attention to the need for Sugammadex availability in all healthcare facilities with NBAs. The investigation team also proposed that pharmaceutical companies, marketing NBAs, should place warning labels to read: 'Warning: paralyzing agent – causes respiratory arrest'.

Discussion

This paper conveys the steps and findings of the investigation and the RCA carried out on the IEs reported to the MPC. Based on the first and crucial step of reporting the IEs, related to the HepB vaccine, the pharmacovigilance center of the RCA was part of the investigation. The RCA is primarily focused on the failures of systems and processes, rather than errors committed by individuals. The RCA revealed several causes and factors of system frailty to contribute to the IEs. Identified factors were the shortage of human resources, a lack of knowledge by the hospital staff regarding drugs and vaccine names used in their daily practices, and training issues to carry out immunization sessions. The lack of equipment to handle HAMs and vaccines was also detected, as well as non-compliance with procedures and tasks. The identified factors belong to medication safety risk factors, as described in the WHO guideline, regarding reporting and learning systems for medication errors.[13]

The proximal cause of these IEs is due to the look-alike packaging of the HepB vaccine and rocuronium. This cause was also reported in the inadvertent administration of NBAs, instead of other drugs.[14] In addition, a similar cluster was reported involving the administration of atracurium subcutaneously, instead of the HepB vaccine, to seven infants. The similar appearance of atracurium and HepB vaccine vials was identified as a major contributing factor to IE occurrence.[15] Furthermore, a study regarding fatal outcomes following IEs reported to the EudraVigilance described two cases in relation to HepB vaccines that were confused with insulin and rocuronium. In both cases, the wrong drug was accidentally administered, due to confusion in packaging similar to the HepB vaccine. This study highlights the importance of measures to improve visually distinguishing features of vaccines and medicines.[16] In the European Union, clear guidelines are in place to limit similarity in packaging.[17] The WHO has released recommendations to limit confusion between vaccines and medicines by, for example, separate storage places for these products. This recommendation was included in our proposed risk minimization actions.

In our cluster, the type of reported IEs is a wrong-drug administration error. A 2009 analysis of 154 events over a 5-year period showed that an NBA was not the intended drug in 37% of all wrong drug errors.[18] Moreover, rocuronium is a HAM belonging to the list of medications used in acute care settings, as established by the Institute for Safe Medication Practices.[19] HAMs are medications that bear a heightened risk of causing significant patient harm when used in error. The consequences of an error in the administration of HAMs are especially devastating to patients.[20] For that purpose, such medications require strengthened vigilance throughout the medication use process to prevent errors from occurring.

Pharmaceutical companies are also key actors in the safe use of HAMs. Globally, they should commit themselves to introduce mandatory warning statements for labels of medicines containing NBA to minimize the risk of look-alike packaging errors.[21–23] To differentiate NBAs from other drug classes, patient safety organizations recommended a red cap and a red ferrule for NBA vials with white lettering to read: 'Warning: paralyzing agent'.[24,25] Thereby, IEs, related to NBAs, should not happen when evidence is available of their past occurrence. They are preventable to the extent that non-occurrence is expected.

Several preventive actions are needed before running the immunization session, especially when the staff is unfamiliar with such procedures. In fact, multiple actions and best practices are proposed by international organizations for preventing IEs, in general, and vaccine administration errors, in particular.[26,27] These actions include writing the brand name and vaccine name on all orders. The vaccines should be stored in bins or containers separate from other drugs. Preventive actions suggest supervisors and staff members triple-check their work. They should recruit a colleague to oversee their administration of a vaccine to a patient. Training is key for safer immunization procedures, especially when new vaccines are used in a healthcare facility.

Conclusion

The safe use of vaccines is of paramount importance to maintain people's confidence in the healthcare delivery system of immunization programs. However, IE-related reactions are known to happen. Such events are preventable when established, efficient preventive actions are implemented during immunization sessions to avert harm to vaccine recipients. When they occur, IEs should be immediately reported, particularly serious ones, to determine how they happened. This will allow appropriate risk minimization actions to prevent IEs from recurring in the future. Pharmacovigilance centers are contributing greatly to vaccine safety by collecting IEs, implementing proactive and reactive actions, and sharing lessons learned from these errors at both national and international levels.

Declarations

Ethics approval and consent to participate

This is a non-interventional study. The Moroccan Pharmacovigilance Centre has confirmed that no ethical approval is needed for the collection, analysis, and publication of spontaneous adverse events reported to the Moroccan Pharmacovigilance Centre. The data were analyzed anonymously.

Consent for publication

Not applicable.

Author contributions

Loubna Alj: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Visualization; Writing – original draft; Writing – review & editing.

Amina Tebaa: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Visualization; Writing – review & editing.

Ismail Talibi: Methodology; Writing – review & editing.

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Mohammed Benazzouz: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Writing – review & editing.

Rachida Soulaymani Bencheikh: Conceptualization; Methodology; Visualization; Writing – review & editing.

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Competing interests
The authors declare that there is no conflict of interest.

Availability of data and materials
The datasets for this study are available in VigiBase, the World Health Organization international database of individual case safety reports. The datasets are not publicly available because of the Uppsala Monitoring Center data protection policy. Requests to access the datasets should be directed to the corresponding author.

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