Implementation of adverse event reporting for medical devices, India

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Abstract

A well-structured vigilance system is the backbone of a robust regulatory framework to ensure the quality and promote the safe use of medical devices. The regulation of medical devices, however, is a complex and evolving area that is often complicated by legal technicalities. For example, legal terminologies are sometimes non-uniform even within the same regulatory system. Regulations may differ from one country to another. Here we report our experiences with the design of a system to monitor the safety of medical devices in India.

Introduction

Rapid growth in the use of medical devices in health-care settings has been enabled by technological advancements, such as drug–device combination products, automation and wireless technology, and advanced clinical application of devices.1 The estimation of the global market for medical devices increased from 260 billion United States dollars (US$) in 2006 to over US$ 380 billion in 2016.2 The quality of devices, however, can vary and even the best-designed products can fail in clinical practice. Post-market surveillance is therefore essential to ensure the quality and evaluate the safety and performance of medical devices. Despite the importance placed on surveillance of drug safety, the need for better monitoring of medical device-associated adverse events receives less attention.

A well-structured vigilance system is the backbone of a robust regulatory framework to ensure the quality and promote the safe use of medical devices. The regulation of medical devices, however, is a complex and evolving area that is often complicated by legal technicalities. For example, legal terminologies are sometimes non-uniform even within the same regulatory system. Regulations may differ from one country to another. Here we report our experiences with the design of a system to monitor the safety of medical devices in India.

Local setting

Earlier, medical devices were regulated under the Indian Drugs and Cosmetics Act and no systematic structure was in place to collate adverse events associated with medical devices. Several reports3 of deaths and hospitalization due to faulty hip implants, cardiac stents and poor-quality devices prompted the health ministry to launch the materiovigilance programme.

Relevant changes

From July 2015 to October 2019, the commission received 1931 adverse event reports, mostly from marketing authorization holders; 1277 were serious events. Reporting increased markedly after 2017. Cardiac stents were the most reported device (926 events; 47.95%). To encourage a culture of reporting, the commission has raised awareness about the programme among stakeholders, developed user-friendly reporting tools and guidelines, and conducted training for hospital personnel on medical device adverse event reporting.

Lessons learnt

Regular training to stakeholders develops a sense of responsibility towards reporting medical device adverse events and ensures quality data reporting. Reporters must be assured that reporting adverse events does not have any legal implications for them and given acknowledgement of their role in high-quality device associated adverse event reporting.

Reference

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of the manufacturing, import, labelling, sale and distribution of medical devices, including in-vitro diagnostics, and the conduct of clinical trials. The organization drew up an initial priority list of medical devices to be regulated under the Medical Devices Rules 2017 (Box 1) and will add other devices to the list over time.

After the launch of the programme, the Indian Pharmacopoeia Commission started developing user-friendly reporting tools, technical documents and manuals, and conducting district- and zone-level training for stakeholders on the importance of reporting medical device adverse events, and use of the tools available. The reporting tools include forms for event reporting and recall or field safety corrective action and, more recently, an online reporting form that can be filled electronically. A toll-free telephone number was also made available for patients and users to report events. Patient follow-up or any further information may also be shared through these tools. The commission started building a network of monitoring centres across the country and recruiting subject expert groups.

At regional level, the materiovigilance framework is organized around health-care facilities, manufacturers and their legal representatives, and any individual aware of an incident incurring risk for themselves or others. The commission receives reports of medical device adverse events from throughout the country, including from notified medical device adverse event monitoring centres, adverse drugs reaction monitoring centres and marketing authorization holders. The commission has two partner organizations; the Sree Chitra Tirunal Institute for Medical Sciences and Technology provides the research and development facility to test medical devices and the National Health System Resource Centre assists with developing standard operating procedures and guidance manuals and in identifying monitoring centres.

At present, the materiovigilance programme has 26 dedicated medical device adverse event monitoring centres across India, which report events spontaneously on a voluntary basis. In addition, more than 270 adverse drugs reaction monitoring centres established under the pharmacovigilance programme have also been requested to report adverse events on medical devices. Once the commission enrol a medical institute or hospital as a monitoring centre, a research associate at the monitoring centre starts collating and sending medical device adverse events to the commission. Research associates liaise between the commission and the patient or user, record and validate any reported incident, recommend precautionary measures as appropriate, report incidents to the commission and also inform the medical device manufacturer. Any suspected serious adverse events and action taken, including recall of devices, must be reported to the commission and the Central Drugs Standard Control Organization within 15 calendar days of the event becoming apparent. The commission also receives voluntary reports of non-serious incidents from any person.

At the commission, each report received is segregated into initial, follow-up or final and allotted a unique reference number. Regarding initial and follow-up reports, the commission further seeks information from the reporter or patient until the conclusion is reached. Trained professional staff at the commission then assess these reports for quality and completeness of data and, if found valid, they are further evaluated by a group of external subject experts and sent to the core technical committee for further processing.

**Box 1. Medical devices regulated under India’s national regulations**

The following medical devices and in-vitro diagnostics are currently regulated in India: cardiac stents, drug-eluting stents, catheters, heart valves, orthopaedic implants, intraocular lenses, intravenous cannulae, bone cements, ablation devices, internal prosthetic replacements, intrauterine contraceptive devices, condoms, tubal rings, umbilical tapes, blood sera, scalp vein sets, ligatures, sutures, staplers, surgical dressings, disposables syringes, hypodermic needles, perfusion sets and in-vitro diagnostic tests for human immunodeficiency virus, hepatitis B surface antigen and hepatitis C virus.

**Fig. 1. Flowchart of India’s materiovigilance programme**

- Adverse events caused by medical devices are reported by:
  - health-care professionals;
  - recognized medical device adverse event monitoring centres and adverse drugs reaction monitoring centres;
  - marketing authorization holders; or
  - person having direct or indirect knowledge of a medical device adverse event;
  - using either customised reporting form, field safety corrective action form, toll-free helpline number or mobile phone application

- Indian Pharmacopoeia Commission assesses reports of suspected medical device adverse events

- Incomplete and/or incorrect reports

- Complete reports

- External subject experts together with commission staff members assess the reports and provide a consensus on actions needed

- Core technical committee makes recommendations based on inputs from subject experts meeting

- Central Drugs Standard Control Organization discusses the recommendations and takes regulatory action if needed

Note: Indian Pharmacopoeia Commission is the national coordination centre for materiovigilance programme. Central Drugs Standard Control Organization is the national regulatory authority for the manufacturing, import, labelling, sale and distribution of medical devices.
to prepare any necessary recommendations. The recommendations of the core technical committee are forwarded to the Central Drugs Standard Control Organization for further discussion and regulatory action, if any. If the data are incomplete or invalid, reports are relayed back to the relevant monitoring centre or reporter with the query or necessary comments, so that the report can be corrected or completed and returned to the commission for evaluation (Fig. 1).

The commission also receives recall and field safety notices from other regulatory agencies worldwide, such as the United States Food and Drug Administration, the Therapeutic Goods Administration of Australia, Health Canada and the Medicines and Healthcare Products Regulatory Agency, United Kingdom of Great Britain and Northern Ireland. These notices are circulated to all monitoring centres to check whether the same or similar devices are available in their local healthcare organizations.

Medical device adverse event monitoring centres are now obliged to organize advance-level training for hospital personnel in their respective region and continuing medical education training in materiovigilance to increase awareness about the programme. Training programmes for the professionals involved in data collection, processing and analysis are organized periodically to develop competency for assessing the cause and performing root cause analysis for adverse events. The trainings are designed by the commission with the help of partner organizations and delivered by staff from the commission, the Central Drugs Standard Control Organization, partner organizations and industry representatives in one-day (basic level) or two-day (advanced level) courses, depending on stakeholder’s needs.

Relevant changes

From the start of the materiovigilance programme in July 2015 up to October 2019, the Indian Pharmacopoeia Commission has received and analysed more than 1931 medical device adverse events, 1277 (66.1%) of which were serious. Reporting of device-associated adverse events in India increased markedly after 2017, when the Medical Devices Rules came into effect and after the development of various user-friendly reporting procedures (Box 2).

Reported events mostly concerned medium to high-risk category medical devices that were known and procedural errors. Adverse events associated with cardiac stents were the most commonly reported (926 events; 47.95%), followed by intrauterine contraceptive devices and orthopaedic implants. Most of the events (1439; 74.5%) were received from marketing authorization holders.

An example of how the data are used to address safety concerns is expulsion of intrauterine contraceptive devices and genital haemorrhage, which is found to be related to devices. During analysis of adverse event reports from different locations, the commission observed they were from the same faulty batch of devices supplied by the manufacturer. The findings were communicated to the Central Drugs Standard Control Organization to act and to monitoring centres for further surveillance of similar cases.

Lessons learnt

Setting up a medical device vigilance system in a low-middle income country of more than 1.36 billion people involves several challenges. Over the past 4 years, the Indian Pharmacopoeia Commission has gained considerable knowledge about how to develop the necessary tools and reporting culture for medical device surveillance. In the early implementation phase, stakeholders were largely unaware of the materiovigilance programme and its requirements and procedures. Therefore, the commission needed to start providing formal training under the programme to stakeholders through its network of partner organizations (Box 3). Since there are many different stakeholders in the programme with a need for and interest in materiovigilance, training had to be designed at different levels, with different content and for different time periods. At the regional level, regular training to health-care professionals was needed to foster a sense of responsibility and generate awareness on what, how and where to report medical device adverse events. To counter any reluctance to report adverse events, health-care professionals need to be assured that submitting a report does not have any legal implications for them and be given acknowledgement of their role in high-quality reporting by the regulatory authority.

Box 2. Medical device adverse events reported to the Indian Pharmacopoeia Commission

A total of 1931 adverse events were reported from July 2015 to October 2019:

- 40 events in 2015; 53 in 2016; 254 in 2017; 687 in 2018; and 897 in 2019 (till October 2019).
- 1277 events were classified as serious and 654 as non-serious.*
- 936 events were associated with cardiac stents; 226 with intrauterine contraceptive devices; 179 with orthopaedic implants; 75 with intravenous cannulae; 76 with catheters; and 449 with other types of device.
- 1439 events were reported by marketing authorization holders; 419 by medical device adverse event monitoring centres; 70 by adverse drug reaction monitoring centres and 3 by consumers.

* Criteria for seriousness of events are defined in the Indian Medical Devices Rules 2017.

Box 3. Summary of main lessons learnt

- Identification of monitoring centres and proactive on-site assessment and capacity-building through regular basic and advanced level training expands the reach of the programme and ensures quality data reporting.
- Regular training to health-care professionals about the materiovigilance programme develops a sense of responsibility and raises awareness on what, how and where to report medical device adverse events.
- Reporters of medical device adverse events must be assured that reporting does not have any legal implications for them and be given acknowledgement of their role in high-quality reporting by the regulatory authority.
Next steps

The online medical device adverse events reporting form is currently in English language only. To enhance participation from regional patients and users, the commission is working towards providing the form in other languages commonly used in India (Hindi, Punjabi, Bengali, Tamil, Telugu, Malayalam, Gujarati and Marathi). A mobile phone application for reporting device associated events is also under development that will enhance access to the materi vigilance programme.

Unlike for drugs, there is no database for medical device adverse events in India. Developing a national database for analysing and management of adverse event reports will facilitate the coding of medical device adverse event terminology. This database should include the statistical tools to support calculation of proportional reporting ratios and the information component for signal detection. Engaging consumer societies and patient-based organizations for reporting adverse events may also be considered. At the national level, provisions related to post-market surveillance of medical devices are a prerequisite. Reporting events to the regulatory authority should be mandatory for marketing authorization holders, especially concerning serious adverse events and recalls, while being voluntary for patients and users. Introduction of education on vigilance of medical products at undergraduate and postgraduate levels in academic institutions for health-care professionals is recommended.

To further enhance the reporting culture in India, the commission is identifying new monitoring centres and strengthening its staff in public and private hospitals and research centres across the country. Since the data provided by monitoring centres will contribute to regulatory decisions, the commission is planning to implement inspections or audits of monitoring centres to ensure the quality of reported cases. The commission, along with the Central Drugs Standard Control Organization, is continuing to make it mandatory to submit periodic safety usage reports on medical devices to the commission and the Central Drugs Standard Control Organization to monitor the quality and safety aspects of medical devices used in India.

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Mise en œuvre d’un système de signalement des événements indésirables pour les dispositifs médicaux en Inde

Résumé

La croissance rapide de l’utilisation des dispositifs médicaux a attiré l’attention sur les lacunes dans le suivi systématique des événements indésirables associés aux dispositifs médicaux en Inde. Une réglementation nationale sur les dispositifs médicaux a été mise en place en janvier 2018. Soutenue par un réseau national de centres de surveillance, la Commission de la Pharmacopée indienne coordonne les signalements d’événements indésirables effectués par les fabricants, les représentants légaux et les patients ou les utilisateurs. La Commission assure un suivi et une évaluation des signalements avec des groupes d’experts et adresse à l’autorité réglementaire nationale des recommandations sur les mesures nécessaires.

La Commission a reçu 1931 signalements d’événements indésirables, principalement de la part de titulaires d’autorisation de mise sur le marché; 1277 étaient des événements graves. Le nombre de signalements a nettement augmenté à partir de 2017. Les stents cardiaques étaient le dispositif faisant l’objet du plus grand nombre de signalements (926 événements; 47,95%). Pour encourager une culture du signalement, la Commission a mené des actions de sensibilisation sur le programme auprès des parties prenantes, a élaboré des outils conviviaux et des directives de déclaration et a formé le personnel hospitalier au signalement des événements indésirables associés aux dispositifs médicaux.

La formation régulière des parties prenantes développe un sens des responsabilités vis-à-vis du signalement des événements indésirables associés aux dispositifs médicaux et garantit la déclaration de données de qualité. Les déclarants doivent avoir l’assurance que le signalement d’événements indésirables n’a aucune répercussion juridique pour eux et leur rôle dans la qualité des signalements des événements indésirables associés aux dispositifs médicaux doit être reconnu.

Mise en œuvre d’un système de signalement des événements indésirables pour les dispositifs médicaux en Inde

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Environnement local Avant 2015, il n’existait aucune structure systématique pour compiler les événements indésirables associés aux dispositifs médicaux. Plusieurs signalements de décès et d’hospitalisation causés par des prothèses de hanche défectueuses, des stents cardiaques et des dispositifs de mauvaise qualité ont poussé le ministère de la Santé à lancer le programme de matériovigilance.

Changements significatifs Entre juillet 2015 et octobre 2019, la Commission a reçu 1931 signalements d’événements indésirables, principalement de la part de titulaires d’autorisation de mise sur le marché; 1277 étaient des événements graves. Le nombre de signalements a nettement augmenté à partir de 2017. Les stents cardiaques étaient le dispositif faisant l’objet du plus grand nombre de signalements (926 événements; 47,95%). Pour encourager une culture du signalement, la Commission a mené des actions de sensibilisation sur le programme auprès des parties prenantes, a élaboré des outils conviviaux et des directives de déclaration et a formé le personnel hospitalier au signalement des événements indésirables associés aux dispositifs médicaux.

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Leçons tirées La formation régulière des parties prenantes développe un sens des responsabilités vis-à-vis du signalement des événements indésirables associés aux dispositifs médicaux et garantit la déclaration de données de qualité. Les déclarants doivent avoir l’assurance que le signalement d’événements indésirables n’a aucune répercussion juridique pour eux et leur rôle dans la qualité des signalements des événements indésirables associés aux dispositifs médicaux doit être reconnu.

Vénédiction et des dispositifs médicaux en Inde
Resumen

Implementación de la notificación de eventos adversos para dispositivos médicos, India

Situación El crecimiento acelerado en el uso de dispositivos médicos ha llamado la atención sobre los vacíos en el seguimiento sistemático de los eventos adversos asociados a los dispositivos médicos en la India.

Enfoque La implementación de la normativa nacional sobre los dispositivos médicos comenzó en enero de 2018. Con el apoyo de una red nacional de centros de seguimiento, la Comisión de Farmacopea de la India coordina las notificaciones de los eventos adversos presentadas por los fabricantes, los representantes legales y los pacientes o usuarios. La Comisión realiza el seguimiento y la revisión de las notificaciones con los grupos de expertos y envía recomendaciones sobre las medidas necesarias a la autoridad reguladora nacional.

Marco regional Antes de 2015, no existía una estructura sistemática para recopilar los eventos adversos asociados con los dispositivos médicos. Varias notificaciones de muertes y hospitalizaciones por implantes de cadera defectuosos, stents cardíacos y dispositivos de mala calidad llevaron al Ministerio de Salud a poner en marcha el programa de tecnovigilancia (materiovigilance programme).

Cambios importantes Entre julio de 2015 y octubre de 2019, la Comisión recibió 1931 notificaciones de eventos adversos, la mayoría de ellas de titulares de la autorización de comercialización; 1277 fueron eventos graves. Las notificaciones aumentaron notablemente después de 2017. El dispositivo más notificado fue el stent cardíaco (926 eventos; 47,95 %). Para fomentar una cultura de notificación, la Comisión ha sensibilizado a las partes interesadas sobre el programa, ha desarrollado herramientas y directrices de fácil uso para la notificación y ha impartido formación al personal hospitalario sobre la notificación de los eventos adversos de los dispositivos médicos.

Lecciones aprendidas La formación regular a las partes interesadas desarrolla un sentido de responsabilidad hacia la notificación de eventos adversos de los dispositivos médicos y garantiza la calidad de la notificación de los datos. Quienes notifiquen eventos adversos deben saber que la notificación de los mismos no tiene implicaciones legales para ellos y que se les reconoce su participación en la notificación de eventos adversos asociados a los dispositivos de alta calidad.

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