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MEDICAL DEVICE SAFETY AND SURVEILLANCE IN INDIA

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ABSTRACT

Serious adverse events (SAEs) reported since 1989 compelled investigators to find the cause and set the pace for development of regulations for medical devices. This also included the incidence where medical device failed to perform positively. Reporting of SAEs has thereafter evolved in many nations and has taken shape as stringent regulatory system in the name of "Pharmacovigilance". This article draws parallel attention to current scene in India and other developed nations in reporting adverse event with respect to medical devices.

KEYWORDS: Medical Device, Safety, Pharmacovigilance, SAEs.

INTRODUCTION

In 1989 there were three reports of sudden death in patients in the USA, who were given barium through barium enema kits. The first patient was a 49 year-old female with a history of atopic dermatitis, allergic rhinitis and asthma who was undergoing a barium enema for occult blood. She suffered an allergic reaction, had increasing dyspnea, then became cyanotic and underwent unsuccessful resuscitation efforts and died.

The second patient was a 41 year-old female who complained of nausea shortly after insertion and inflation of the tip/cuff assembly, went into cardiac arrest within 30 seconds and died.

The third patient was a 72 year-old female who had an immediate reaction after the tip portion of the tip/cuff assembly was inserted even before the administration of the barium contrast agent. She had vascular collapse and died.

As a result of these serious adverse events (SAEs), investigations were intensified to find out the cause of the allergic reactions and death. Literature review showed a potential problem with reactions to devices containing latex. As a result, the manufacturer of the enema tips voluntarily agreed to send out an urgent Medical Alert to approximately 10,000 radiologists that notified them of adverse reactions possibly associated with latex allergy that could occur during barium enema procedures. An FDA Medical Alert which outlined the occurrence of several severe allergic reactions to medical devices containing latex and suggestions of ways to screen and protect allergic patients, was sent to physicians

This event set the pace for the development of regulations for medical devices since it was realized that medical devices too could be responsible for SAEs.

Failure of medical devices is also another real threat to positive outcomes. This is particularly highlighted by the failure of implant where in an error in implantation procedure led to the occurrence of pregnancy in 77% of women. Another area of concern was the question whether the introduction of non-chlorofluorocarbon (CFC) propellants in metered dose inhalers (MDIs) would lead to fresh attacks of asthma or failure to control asthma. This made it vital to institute effective measure to monitor the safety and efficacy of the new propellants (*Sergent F, 2005*) .This can be achieved through a stringent pharmacovigilance (PV) system which contributes to the assessment of the risk-benefit profile of medical device encouraging safe, rational and more effective use. *(Gupta P. et al. 2010).*

In 1992, in order to bring about uniformity among the national medical device regulatory systems and increase the access to safe, effective, and clinically beneficial medical technologies, five countries in membership conceived the Global Harmonization Task Force (GHTF). The five members were: European Union, United States, Australia, Japan, and Canada. The GHTF provides the guidance on mandatory reporting of adverse events for device manufacturers and voluntary reporting for users. *(Gupta P. et al. 2010).* Though PV regulations in India for medical devices have not yet been defined clearly, CDSCO requires medical device manufacturers to report adverse event.

Medical devices

The spectrum of a medical device is incredibly immense which is improbable to describe in a concise definition due to its dynamic nature. However FDA has described Medical device as "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article including any component, part or accessories" which is intended to be used for prevention, diagnoses or treatment of the disease (Table 1) (*Chin R; Medicine and Healthcare Product Regulatory Agency 2013).* There is s disparity in the definition and classification of medical devices in India as compared to the USA (Table 2).

Table 1: Examples of medical devices

Medical devices	Use
Bone cement	Bone fracture
Insulin pen	Diabetes
Inhaler, nebulizer	Asthma
x-ray machine	Diagnosis
Pregnancy test kits	Diagnosis

Medical device	Use
Dialysis products	Kidney failure
stents	Coronary heart disease
Pacemaker with microchip technology	Coronary heart disease
MRI machines	diagnosis
Hearing aids	Hearing incapacity

Table 2: Differences in medical devices definition and classification between Indian and USA

Parameter	India	USA
Definition of medical device	10-device category regulated as drug	Includes all instruments, materials, machines, appliances, in vitro diagnostic agents, implants, software, accessories, and disinfectants
Medical device classification	No defined classes for devices	3 classes: class I, class II, and class III

The evolution and diversity of medical devices has greatly contributed in the improvement of quality and efficacy of healthcare, playing a crucial role in the diagnosis, prevention, monitoring, and treatment of diseases and have improved the compliance and quality of life of people suffering from disabilities.

Adverse Event (AE) reporting criteria for medical devices *(Gupta P. et al. 2010)*

The reporting regulations for medical devices vary in different countries (Table 3)

The reporting criteria however are common (Table 4)

Table 3: Reporting regulations for medical devices of different countries

Pharmcovigilance aspects	**India**	**US**	**UK**
Post Marketing Surveillance activities	AE reporting For importers: complaint handling, adverse event reporting procedure	Medical device tracking, MDR, MDR event files, records, and written procedures, Complaint handling, Recall procedure and seizures	AE reporting, FSCA and field safety notices, Investigations, Enforcement, Postmarket clinical follow-up, Records
Requires AE reporting by	Manufacturers only	Manufacturers, importers, user facilities, users, distributors, and health professionals	Manufacturers, users, health professionals, authorized representatives, and MHRA
Criteria for reporting	Event has occurred Medical device's association with the event, Event led/might lead to death/serious injury	Death or serious injury, Device malfunctions, User error, Injury/illness requiring medical, intervention	Event has occurred Medical device's association with the event, Event led/might lead to death/serious injury
Reporting time frame	Unanticipated death or serious injury within 10 days, All other reportable events not later than 30 elapsed calendar days	Manufacture: death, serious injury, and malfunctions – 30 calendar days, and events requiring immediate remedial action – 5 working days User facility: death and serious injury – 10 working days Distributors and importers: death, serious injury, and malfunction to manufacturer – 10 working days	Serious public threat – 2 calendar days Death/serious deterioration – 10 elapsed calendar days Other incidents – 30 elapsed calendar days After receiving user reports from MHRA, reporting 3 working days
Recall communication	-	Telephone calls, telegrams, and mailgrams First class letters approved by FDA General public warning Public warning through specialized news media	FSN approved by MHRA as per specified format within 48 hours of FSCA agreement In case of urgency, through telephone, fax, or by a visit

Table 4: Reporting criteria for AE reporting of medical devices

• In case an adverse event has occurred, and the manufacturer becomes aware of the information
• If it is estimated that the manufacturer's device is directly associated with the event based on the current literature evidence
• If the event has led to or might have led to death or serious injury of a patient, user, or other person.
Note: *In addition to the above reporting criteria, a manufacturer in India must also report events that do not require to be reported under regulations, so that trends or patterns of their occurrence can be monitored*

In India, the Federation of Indian Chambers of Commerce and Industry (FICCI) is the focal point for regulations of medical device. It has been working closely with the Central Drug Standard Control Organization (CDSCO) and Indian medical regulators (both importer and native manufacturers) to improve the safe and effective use of medical devices in tandem with global manufacturing procedures and streamlining the regulatory process toward global harmonization.

If the product is being imported to India, the importer has to submit post market surveillance data including protocol and report not exceeding 5 years for the following

1. Procedures for distribution of records
2. Complaint handling
3. Adverse incident reporting
4. Procedure for product recall

The manufacturers have to submit post market surveillance data for a period of 3–5 years. Recently, the CDSCO has issued the guidelines for Adverse Event related to medical devices.

Not-reportable incidents or events

The definition of not reportable AE as defined by regulated countries and India, are similar with few exceptions. The following events are exempted from reporting in all countries

• If the deficiency of a device is reported by the user before its use and therefore no serious injury has occurred

• If the chief cause of the adverse event is estimated to be the patient's pre-existing condition

• If the patient used the device after expiry of its shelf life

• If the design feature for protection against malfunction complied with the relevant standards and operated correctly

• If the deficiency was associated with a negligible chance of causing death or an SAE and had been established and documented as acceptable after risk assessment

• If the side effects are expected, clinically well-known and foreseeable and documented in the device master record and in the manufacturer's labelling , are clinically well known, with an appropriate risk assessment.

• If the adverse event was caused by errors of use and abnormal use

According to the recent amendments directed by the CDSCO, the manufacturer is liable to report unanticipated death or serious injury or a serious public health threat within 10 days of becoming aware of the event, and all other reportable events not later than 30 elapsed calendar days. Because of the uncertainty of the reportable events, the manufacturer must report within the expected time frame.

The Clinical Impact of Medical Device Adverse Event Reporting Strength *(FDA, 1996)*

The data obtained from clinical trials cannot assure that the device will not have any risk or problem when used by patients. So the safety system in allows the continuous surveillance of all patients in their real life. In addition it also has following benefits;

i. AE reporting is relatively cost-effective mean to discover serious adverse event not recognised during the clinical trial.
ii. The data gained through AE reporting by manufacturers and consumer helps to assess the causality relationship between the medical device and adverse event.
iii. Involvement of health care professional in AE reporting has been demonstrated as the most effective source of new AE reports that led to changes in labelling which ensures the complete and in depth reporting of AE.

Limitation *(FDA, 1996)*

In addition to the advantages, the AE reporting system for medical devices has a number of drawbacks as listed below

i. In case of voluntary reporting system by patients, the spontaneous reporting form is often subjective and imprecise which can an approach to a conclusion about the relationship between exposure to a medical device and the occurrence of an adverse event.
ii. Another major concern with AE reporting is underreporting of adverse event which represent only a small portion of the number that have actually occurred.

iii. Unlike clinical trial where in all data are obtained under strictly controlled condition, in AE reporting it is uncontrolled and hence there is possibility of influence of a number of biases that can affect reporting. These biases include the length of time a product has been on the market, country, reporting environment, detailing time and quality of the data.

iv. Further the interpretation of the data is crucially dependent on the quality of information submitted by health care professionals in their reports. It was observed that analysts read fewer than one-third of adverse event reports for the first time within 30 days and less than half within 60 days in every year from 2003 to 2007.

End note

The AE reporting regulation of each country differs from one another to some extent. As mentioned above according to UK regulation, only manufacturers are considered for the reporting of adverse event related to medical device where as in US it is addressed not only to the manufacturer but also to device facilities user. FDA also undertakes the reporting of problems associated with the medical device or its malfunction or error use problems, the same is not considered in UK.

The voluntary reporting of any adverse event has been facilitated in both the country by the consumer to report the actual experiences of patients during ambulatory use of medical devices. This voluntary reporting serves as mean for patients to notify the regulatory bodies about adverse event due to medical devices.

The efficacy of the AE reporting system can be increased by implementation of a protocol for reviewing adverse event reports by regulatory bodies of medical devices. The regulatory bodies should follow up and address manufacturers who routinely submit late report or with incomplete data or those with a history of noncompliance with adverse event submission requirements.

To improve the reporting quality by consumer of products, the medical device regulatory body should consider the implementation of strategies which will train and educate consumer regarding AE reporting and promote the effective AE reporting.

The latest news in Economic Times India, reported that 4-month old baby was burnt alive in an incubator in a private nursing home in Allahabad and many more such incident over a period of year highlights the alarming need to draw line in regulating device market. A stringent Medical Device Safety Surveillance protocol must be implemented as an essential

part of safety monitoring in the real life setting and in the research setting to efficiently evaluate any adverse event occurring due to medical device. This will ensure the safe and effective use of medical devices & improve the overall standard of health care.

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