

Quest for good quality medicines in hospitals: a structured approach**Jayant Kumar Kairi***

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ABSTRACT

Patients use medicines to gain speedy recovery from illness or to maintain wellbeing under the care of their physicians. For chronic illnesses, the pharmacotherapy may continue for the entire lifetime. Significant expenditure is incurred in sustaining this pharmacotherapy. Quite expectedly, the patients are concerned about the quality of medicines that they receive and consume. In recent times, the quality concerns have increased phenomenally due to media hype and overexposure all around. Ensuring quality of medicines in developing countries is not easy. Multi-pronged approaches are needed to ensure procurement of good quality medicines by institutional buyers. However, ensuring the procurement of good quality medicines is not enough. The quality of medicines has to be maintained till their consumption by patients and a rational, scientific method has to be adopted to ensure this goal. A structured approach in ensuring good quality medicines for optimum pharmacotherapy is being presented in this review.

Keywords: Counterfeit, Compliance-aids, Medicines, Quality**INTRODUCTION**

There is a demand for quality in every product humans consume, and medicines are no exception. Oxford Dictionary defines quality as “the standard of something as measured against other things of a similar kind; the degree of excellence of something.” In the context of medicines, the US FDA has mentioned the following about quality of medicines:

“Every pharmaceutical product has established identity, strength, purity, and other quality characteristics designed to ensure the required levels of safety and effectiveness. For the purposes of this guidance document, the phrase achieving quality means achieving these characteristics for a product”.¹

Generally, quality issues in the context of medicines arise when there is more than one manufacturer of the medicines. The question is asked, whether the new manufacturer’s drug affects the patient the same way as the original one? A new molecule brought in the market by a company under a brand name is protected by a patent and usually sold as a branded product. Since patents stay for a fairly long time, the medicine becomes synonymous with the brand. On expiry of the patent, any manufacturer is free to manufacture and market the medicine, as long as it conforms to the standards set by pharmacopeias. This means that the quality parameters of the medicines have been standardised by the pharmacopoeias and in India, the Drug Controller General of India (DCGI) is the final authority to ensure that all medicines manufactured under the licence issued on his behalf will adhere to these standards. Additionally, all manufactures are expected to

conform to Good Manufacturing Practice (GMP) guidelines issued by the World Health Organisation (WHO).

Some terms need a bit of illustration and understanding. What we know colloquially as medicine, i.e. tablets, capsules, ampoules, are actually the formulations of the Active Pharmaceutical Ingredient (API), also known as bulk drug. When a bulk drug is mixed with stabilizing agents, excipients and preservatives, the formulation is made. Bringing in a new bulk drug in market is enormously difficult and expensive. The cost of drug research is very high and only very large organisations can afford it.² Bringing in a formulation of a recently patent expired drug is relatively easy and hence sought after very much. To do so, what needs to be proved is that the new formulation is as effective and safe as the original brand. Limited laboratory and clinical data are required to be submitted to the drug regulator.³ The profitability involved in launching a generic version of highly successful brand attracts a lot of manufacturers and therefore, concerns regarding safety and equivalence in the minds of consumers go up. There are reasons for getting concerned and worried in our country. Even in highly developed countries, there are several instances on record where medicines have been recalled due to being substandard.^{4,5} In a news release on 28 Nov 2017, the WHO has reported that 1 in 10 medical products in developing countries is substandard or falsified and urged the governments to take action.

Why ensuring good quality medicines is difficult?

There are numerous hurdles in ensuring quality. In the context of medicines procurement by large organisations in India like Armed Forces Medical Services (AFMS), Central Government Health Scheme (CGHS), Employees State Insurance Corporation (ESIC) etc, providing large scale institutional and outpatient care, the problem is twofold because the supply is usually from two sources. Centrally procured drugs through rate contracts (RCs), are evaluated extensively but they have a large number of participants in the bidding. If the bidder who qualifies, produces the necessary certification by the competent authority regarding quality, then there is little ground to disqualify them on the basis of perception, novelty or unfamiliarity. At the time of writing this article, the number of approved laboratories in India, authorised to issue such certificates is 264.⁶

For drugs procured locally also, more or less, the difficulties are similar to those of central purchase, especially in large hospitals. All expenditure though public grants from government necessarily have to follow the directions and purchase procedures as notified from time to time. Audit requirements, preferential purchase policies, price agreements etc. may put additional hurdles in ensuring quality or a perception of good quality medicines in the minds of the consumers. Research has proven that consumers assess quality on the basis of two parameters,

brand name and price.⁷ While purchasing in government hospitals, purchase of medicines occur by generic name and the lowest cost (amongst those who fulfil the quality requirements technically). Hence, the patients with chronic ailments who know their medicines well, sometimes raise concerns about the quality of medicines issued to them if it is of an unfamiliar brand or much lesser in price in comparison to any well known brand of that medicine. Patient education and bringing a change in perception is a significant hurdle as speaking and explaining to the patient on this matter in a busy hospital with crowded out patient departments is difficult.

How can consumers ensure good quality of medicines?

It can ensure quality by systematic planning and approach. Action for the goal of good quality medicine needs to be undertaken at three stages.

- At the time of procurement
- While stocking in the medical stores
- After issue to the patients

Ensuring quality of medicines before procurement

One of the proven approaches in improving quality of medicines is to have reduced inventories.⁸ Lesser the number of drugs to be procured, lesser is the risk of exposure to poor quality medicines. Drug and therapeutics committees (DTCs) duly constituted and contributed by multiple specialities select and approve procurement of a limited number of agents amongst many in a particular drug class, thus deciding the hospital formulary based on standard treatment guidelines (STG).⁹ With the implementation of standard treatment guidelines, it is possible to reduce intra-class varieties in most drug classes leading to better inventory control.¹⁰ The end result thus is, reduced inventories, lesser variety in procurement and lesser quality concerns. The DTCs can also function as a collegium or panel of experts that approves list of manufacturers that by experience are consistent in providing good quality medicines and consumables. Members from all specialities and sub-specialities contribute their inputs and such collaborative decisions, to a large extent eliminates bias and allegations of favouritism in selection of vendors. Research supports this methodology of vendor selection by panel of experts in comparison to single person decisions.¹¹ Such actions promote rational prescribing, prevent unnecessary duplication in medicines, reduce wastage, confusion and fixed dose combinations that are asked to be procured in the hospital.¹² Over a period of time, all these methods contribute immensely to promote procurement of better quality medical formulations. Substitution of prescribed medicines with another of the same class in case of non-availability of the prescribed brand, if utilized judiciously and approved by the DTC also contributes to rational prescribing and reduced inventories.^{13,14}

Ensuring quality of medicines during procurement

The medicines procurement in most government hospital settings are regulated by multiple guidelines and orders directed to ensure financial propriety. In case of AFMS, Defence Procurement Manual is one such document. Other bulk consumers of medicines such as CGHS, ESIC etc have also their respective procurement manuals for medicines. All quality concerns have to be fitted or moulded to fit the framework of procurement policies of the organisation. Many quality promoting measures such as pre-registration of vendors, inspection of their facilities, checking of necessary certifications, history of successful and reliable supply with good track record etc are inbuilt in the organisational framework.¹⁵ Some additional measures implemented by some large hospitals making bulk purchases when the value of order exceeds a predetermined amount, is to demand a test report of the supplied drugs from a National Accreditation Board for Testing and Calibration Laboratories (NABL) accredited laboratory regarding the quality of medicine.

The committee constituted for receiving the ordered medicines have a very important and vital role in ensuring quality of medicines. An alert receipt committee in addition to ensuring the compliance with the terms and conditions of supply order, should also employ common sense look out for counterfeit medicines. As per the Department of Essential Drugs and other Medicines, WHO, Geneva, the counterfeit medicine is defined as-

“One which is deliberately and fraudulently mislabelled with respect to identity and/or source. Counterfeiting can apply to both branded and generic products and counterfeit products may include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient active ingredient or with fake packaging.”¹⁶

In studies carried out under the aegis of WHO, there is very alarming data on counterfeits. As per one US FDA report of year 2004, fake drugs comprise approximately 10% of the global medicines market.¹⁷ The incidence of counterfeit drugs in studies carried out in India vary from 0.046 to 3.1%.¹⁸ Some easy safeguards against counterfeit drugs are to:

- Look for altered expiry date.
- Observe for wide variation of color, shape, thickness or markings on tablet/capsule.
- Observe the product's package for differences in paper texture, size, thickness of labels, gloss and finish on the paper
- Look for differences in fonts, font sizes, print colour or raised print.¹⁹

World over, counterfeit medicines are reported first by the patients. Hence listening to the patients is important. Clinical surveillance for subdued or failed therapeutic actions despite clear cut diagnosis and accurate therapy may be a pointer for substandard or counterfeit medicines. In the event of strong suspicion, lab testing of suspected

drug is advisable through CDSCO approved drug testing laboratory which is hosted on the CDSCO website.⁶ As on date, in addition to the seven drug testing laboratories directly under the control of CDSCO, there are 134 NABL accredited labs where the suspect drug can be tested.

Ensuring quality of medicines during stocking at medical stores

Proper handling and storage is must for preservation of efficacy of all medicines. Storage must be as per the recommendations of the manufacturer. For many medicines, prevention of contact with air or exposure to light and maintenance of appropriate temperature is important.^{8,20} Some examples are:

- Sodium valproate, aspirin, and paracetamol are known to deteriorate due to moisture.
- Atenolol, furosemide, prochlorperazine, thyroxine are known to deteriorate on exposure to light.
- Clozapine is known to be affected by exposure to atmosphere.
- Numerous drugs require to be stored at temperature 2-8 deg Celsius.

During storage, it is advisable to stock the medicines for internal use separate from those for external use only. Look alike and sound alike (LASA) drugs should be stored separately and special care must be taken to prevent medication errors on this account.^{21,22} Confusion and errors are bound to occur if alphabetic stocking is done. Refrigerators for stocking medicines should be separate and exclusive for the purpose. It must be ensured that the medicines that need cooling are not frozen, as they lose their efficacy.²³ Scrupulous care must be ensured to preserve the labels and packaging. Access to the storage area must be restricted. Regular pest control and anti-vermin treatment of storage areas help in preserving the quality of medicines. Special care is must for high risk, narcotic and psychotropic substances and expensive medicines. For intravenous (IV) fluids, care must be taken to protect the product label for correct identification, visual inspection for particulate matter of either black or white colour.²⁴ The IV fluids should be carried in proper trolley or container during transport.

Ensuring quality of medicines after they have been issued to the patients

For many ailments, it is usual for patients to collect and stock medicines for many months at their end. The reason for doing so could be to ensure supply while visiting abroad. Also, many times patients stock up the medicines to avoid a 'not-available' situation in future, at their usual place of collection. Anti-hypertensives, anti-diabetics and medicines for chronic kidney disease are some commonly stocked drugs. Such patients need to understand the necessity to follow the storage instructions scrupulously. Some common reasons for loss of efficacy due to deterioration of the quality of medicines at patient end are:

Non-maintenance of the storage instructions

If medicines meant to be in cool/cold temperature gets frozen, the efficacy may be lost on thawing.

Use of compliance aids

These are simple devices that help in administration of numerous drugs as per the dosing schedule wherein the medicines are rearranged as per their time of administration. These devices also known as multi-compartment compliance aids or dose administration aids. Available through e-commerce websites like Amazon or eBay, they offer attractive solutions for timely administration of correct medicines. Webstercare Cold Seal Flexi-Pak, Pillmate are popular brands of such devices. Dosette box is a simpler version of compliance device. The benefits of such devices are not established by evidence as yet and hence should be used after a careful weighing of pros and cons of using them.²⁵ Since, these devices involve removal of the tablet or capsule from the main pack, medicines that are affected by light, moisture or exposure to atmospheric air are at risk of getting deteriorated or losing efficacy unless due care is employed.

Crushing the tablets

Patients who have a difficulty in swallowing tablets or capsules, especially the elderly, may choose to crush the formulation before mixing it with food or beverage and consuming it. Controlled, delayed or sustained release medicines, enteric sugar or film coated tablets should not be crushed as this may destroy the pharmacokinetic advantage that is in-built in the formulation.²⁶

CONCLUSION

The quality of medicine used affects the therapeutic outcome. It is in everyone's interest to ensure that only the good quality medicines are administered to the patients. Multipronged strategy is required to achieve this goal. The responsibility to ensure this outcome lies with all the stakeholders- doctors, hospital administrators, pharmacists, patient and their caregivers.

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