Quality of Pharmaceuticals in Kenya — An Overview

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Over the past years Kenya has been treated to press reports about poor quality pharmaceuticals in the market and problems with the same in public institutions. This paper reviews mechanism in place in Kenya to minimise availability of poor quality pharmaceuticals and information available.

Key Words: Review, pharmaceuticals, quality, surveillance, Kenya

INTRODUCTION

The supply of good quality essential drugs was recommended in the Alma-Ata declaration of 1978 as one of the prerequisites for the delivery of health care. When the concept of essential drugs lists (EDL) was introduced by World Health Organization (WHO), some governments embraced it, Kenya included. They developed EDLs[1] on which they based their procurements in terms of maximum quantity at minimum cost. The drugs procured from both local and international suppliers are assumed to be of good quality. This however, seems to have resulted in "cheap" drugs which in some occasions are of questionable quality. The WHO Certification Scheme on the quality of Pharmaceutical products moving in International Commerce has not achived the desired results. The reasons for this are many and varied. They nevertheless revolve around the tenets of WHO pronouncements which usually assume that an adopting or implementing country has the will and implementing mechanisms to achieve the objectives. Nevertheless, a quality drug is the most critical armamentarium in the treatment or management of some disease states.

Drug registration constitutes the first line activity in ensuring that a product on the market is efficacious, safe and of good quality. Thus most countries require that drugs must be evaluated and registered before they are allowed to be freely sold within their jurisdiction. In some countries drug registration exercises are complemented by a Drug Quality Control Laboratory which monitor quality of drug products on the market. In some cases the laboratory carries out an analysis in order to finalise an application for registration of a drug.

Drug registration

The importance attached to having a quality drug on the market is best seen in a decision by the Kenya government in 1982 to initiate registration of drugs before they are freely available in the country. Drugs are vetted by a Commitee on Drug Registration, which is a committee of experts of the Pharmacy and Poisons Board (PPB) and certified before being available on the market. The vetting exercise is primarily confined to scrutiny of documentation supporting the drug in terms of efficacy, safety and quality. In addition the packaging and aesthetics of the product are also considered. When documentation is considered inadequate, the applicant is requested to supply additional information.

Efficacy and safety of a drug

These aspects establish that a drug product when administered would elicit claimed effect(s) and that it has no deleterious effects on the human or animal. The level of documentation depends on whether the drug is a new molecule or a generic. For generic drugs, extensive use in various parts of the world over a number of years result in reviews and inclusion in authoritative reference works. Further, post-market surveillance data could already have identified any problems. Consequently the amount of data required is not demanding.

The information supporting a new drug product must be detailed enough and validated to support the following:

a) Pharmacology of the product in both laboratory animals and clinical use

b) Safety in respect of toxic effects such as teratogenicity, carcinogenicity, interactions with other drugs etc. For veterinary drugs, residue levels in animal products is crucial because of consumption by humans.

c) Effective dose levels and regimens in humans or target animal species.

Quality

A new product so termed "the innovator brand" sets the bench mark on quality of the drug molecule. The pharmaceutical development of a dosage form and use of the same in clinical trials will establish quality parameters such as, quantity of active ingredient, allowable levels of degradation products and related substances, dissolution, disintegration etc. Other quality indicating parameters must conform to compendia requirements for the type of dosage form. Any generic formulations that may be developed later on must of neccessity be equal to or better than the brand product in terms of quality.

The quality of generics is an area that requires critical scrutiny during the vetting of documents. While the drug molecule is well known in terms of safety and efficacy, pharmaceutical formulations can not be the same. The pharmaceutical formula, quality specifications of the active and non-active ingredients of

generics are therefore of interest to reviewers. The performance of the dosage form during a claimed shelf-life and comparison to the innovator product is sometimes demanded. Lately, samples of products are selected at random and sent to the National Quality Control Laboratory (NQCL) for evaluation of quality before registration.

Once a drug has been registered and placed on the market, the regulatory authority has to constantly monitor it for compliance with both product specification and international standards. In practice, this rarely happens, due partly to the fact that the NQCL is understaffed. That all drugs in the market are not of quality is an accepted fact. Governments which are able, have tried to strengthen control by setting up national drug quality control laboratories to further monitor whether drugs registered and available on local commerce continues to conform to declared and pharmacopoeial requirements. Leading countries in the region are Zimbabwe which hosts the WHO regional quality control laboratory and Kenya whose NQCL was started with financial aid from GTZ.

Drug quality control laboratories give opinions, as regards quality, based on a grouping of testing parameters performed terminally and may detect batch failures (defects) or indeed indeterminate errors in manufacturing. Testing therefore does not improve quality. The latter must be built into a product. Consequently, since the mid 1 970s quality assurance of pharmaceutical products has shifted the emphasis from analysis of finished products to good manufacturing practices (GMP). Attention has also focused on packaging which protect a drug form light, air, moisture, etc. A poor quality product is therefore indicative of problems with GMP in the plant.

Deterioration of pharmaceutical products during storage and distribution is common, particularly under the tropical conditions of high ambient temperature and humidity. Cases are known where pharmaceutical products remain in bonded warehouses in Mombasa, at high temperature and humidity, for months while the importers try to sort out problems of import documentation. In the rural health facilities, drugs are rarely stored according to the recommended conditions. For a few products, deterioration may be manifested as a change in physical characteristics such as change in colour, precipitation in case of solutions, etc. Deteriorations of drugs could also occur after dispensing. Patients often fail to complete the prescribed course of treatment and the remnants are kept for months before use again.

Market surveillance

There has been low key drug market surveillance in Kenya since 1981. Although documentary information was considered adequate and the product registered, market surveillance has shown problems with Carbamazepine tablets in-vitro [2] and in bioavailability studies [3]. Comparative biovailability of generic Chlorpropamide tablets to innovator brand showed equivalence [4].The extent of problems with quality of drugs has been documented for the Kenyan Market in a series of articles on the work of the Drug Analysis and Research Unit of Nairobi University. It indicates problems at about 22 - 25% of all samples analyzed [5-8]. This trend has been noted in recent work from the same unit, but not yet published. There appears to be no difference in failure rate amongst local and imported products. Latter data indeed show less failure rate amongst local products compared to imports. Data from Zimbabwe could be different. It is however, worrying when one thinks of situations in the neighbouring countries which have yet to have laboratories to monitor their local markets. Establishment of a national quality control laboratory serves as a deterrance since manufacturers know there is a possibility of sub-standard products being detected.

Observable and possible problems

As mentioned above, terminal testing of pharmaceuticals provide only statistics on quality performance but can not improve on the quality of the products. Good manufacturing practices are the core to building a quality product that meets national and international standards. To achieve this, pharmaceutical manufacturing requires clearly defined and documented pathways of measurements and procedures that are also traceable.

When the observed results of quality are considered two contributing problems are discernable.

The first is an absence of or unwillingness to strictly use standard operating procedures and secondly inadequate quality control laboratory facilities to monitor the quality of final products. These problems can best be considered under the following three sub-headings.

i) Lack or insufficient validation of manufacturing processes.

During the development of a product, all steps of manufacture are validated and documented. This include, mixing times, drying times, moisture content etc. The validated steps or procedures allow the manufacturer to consistently produce a product with the same quality. Such data normally forms the basis for specific standard operating procedures. Equally important is the stability of technical staff. Frequent turnover of staff in a manufacturing plant lead to loss of continuity and also consistency.

ii) General Standard Operating Procedure (GSOP)

Such procedures detail how manufacturing personnel approach the production of a drug product. They give an overview of steps to take in preparation of materials, equipment, handling bulk to avoid contamination or mix-up. In a study of 8 steroidal topical preparations, 50% had different active principle from that which was declared [9].

This presented a serious case of product inequivalence and gross negligence of good manufacturing practices. An investigation of phenoxymelthyl penicillin dry suspension found one product to contain about 33% of labelled dose [10].

iii) Specific Standard Operating Procedure (SSOPs)

Specific SOPs are intended to facilitate replicate manufacturing. The quality or lack of it in products should therefore be consistent in the majority of samples. Factory visits and results of analysis show this not to be the case. It is more evident that some manufacturers follow rule of the thump. Inconsistent production procedures have been observed for some metronidazole tablets [11].

That some of the above are the problems and that the local industry has been slow in moving into the mainstream of current GMP has indeed been pointed out [12,13]. Considering that imports fare equally badly, the same problems must be prevailing in other countries.

A study of various generics have been documented. In 1988, aspirin products on the market [14] had a 50% failure in specifications. Tetracycline raw materials and finished products of imported and local origin were found to be of good quality [15]. Problems have been observed with diazepan injections. One product with glycerol as a vehicle was under performing [16]. Intravenous infusions from 4 local manufacturers had sterility breakthroughs of between 10.5 - 28.6% and failure rate for chemical content 13.3% to an alarming 66% amongst manufactures [17]. A study of Co-trimoxazole preparations [18] showed failure rates of 69% for imported and 78% for local tablets. 50% imported and 89% local suspension products also did not meet all compendial requirements.

CONCLUSION

The statistics quoted in this review article goes to emphasize that there are both good quality and poor quality products in Kenya. The magnitude of poor quality products remain to be determined. This would require well thought out market surveillance programmes by both NQCL, DARU and any other similar laboratories. Such programmes should be funded by the Pharmacy and Poisons Board as one of their objectives of ensuring quality drugs in the Kenyan market.

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