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Review Article

The road of generic medicines towards improving the accessibility of essential medicines

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ABSTRACT

The skyrocket rising of the prices of medicines is one of the problems for people to access medicines essential for the maintenance of their health; generic medicines seem to be the savior and way out of this burden. Apart from stimulating domestic production of pharmaceuticals, generic medicines has increased availability and affordability of essential medicines especially in low and mid income countries. Promoting the use, strict regulation and improving the standards of production of generic medicines especially in developing countries will reduce the doubts and skepticisms people are having on generic medicines thus increasing the use of generics therefore improving the accessibility of essential medicines.

Keywords: Generic medicines; essential medicines; accessibility; affordability

INTRODUCTION

In 1984, the Hatch-Waxman act was passed in the US, which allowed the FDA to approve the use of generic medicine basing on bioequivalence studies (Shrank *et al*., 2011). Generic medicines are copies of their brand name counterparts which are both pharmaceutically equivalent and bioequivalent to their brand name twins. The aim of this act was to avoid the unnecessary duplications of tests thus reducing the production costs and eventually lowering the drug prices. Furthermore the act allowed competition between brand drugs and generic drugs and among the generic companies in giving the medicines consumer best prices which will lead to increase affordability and accessibility of medicines. Since then generic medicines have been at the center of government policy in containing pharmaceutical costs in developed countries, on the other hand in developing countries generic medicines has increased, though not to the satisfactory level, the availability, affordability and accessibility of essential medicines since most of generic medicines if not all are cheaper and therefore affordable.

Medicines are part and parcel in ameliorating and boosting people's health. High prices of essential medicines have been a roadblock to better access and proper health care especially in high income countries, where it is not the availability of medicines that matters but the containment of pharmaceutical costs is a major concern (Igbinovia, 2007). In developing countries the headache is the unavailability and the high cost of essential medicines which renders most people unable to purchase them. Apart from the high prices, the inadequate availability of essential medicines in low and mid income countries, both in public and private sectors seems to be far away from meeting the demands. This means that millions of poor people especially in low income countries can't get the medicines they require for their health needs as are neither available nor accessible to a large fraction of the population and hundreds and thousands of people dies of preventable and treatable diseases.

Access to low priced essential medicines, not only is one part of the right to health but is also one part of millennium development goals (WHO, 2011; UN, 2012). According to the World Health Organization (2011), about 30% of the world population does not have access to life-saving medicines. In some countries in Asia and Africa, the situation is even worse (Bate, 2008). Ideally, people should be capable of getting the right medicine, in the right dose and at the right time and regardless of their income, everyone should be able to meet his/her medical needs; whether through public or private outlets (WHO, 2003) The world health organization (2006) and Hossein (2011) estimated that between 10-30% of medicines in many developing countries are counterfeit. Apart from other reasons such as poverty, a huge burden of infectious diseases, insufficient regulatory structure; High prices of real medicines are the major motive for the counterfeiters. In some places it may take a several month wages to buy an innovator drug of an expensive antibiotic or a

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two weeks wages to buy a generic medicine (WHO, 2008). The morbidity and mortality, leaving alone the contribution to drug resistance strains of diseases caused by these counterfeit medicines are increasing every day. It is believed that by improving the availability and accessibility of essential medicines by making sure that high quality, low price medicines are available to the public, will help to combat the problem of counterfeit medicines (Newton *et al.*, 2010). Generic medicines can be a means, not only to reduce pharmaceutical costs but also to increase affordability and availability of essential medicines especially in low and mid income countries.

Physical and geographical availability

Unlike in the high income countries, in the low and mid income countries the availability of medicines does not match the demand. Up to date, still there is a large gap between delivery and demand in most of these countries (WHO, 2003). After the introduction of generic medicines, most of the higher income countries introduced generic medicines into their supply chain systems followed by enforcing the substitution of brand medicines by generic medicines whenever possible. For instance, in the US, the percentage of prescribed generic medicines increased every year reaching 69% in 2008 of all the medicines prescribed in that year (Frank, 2007). This means that, generic medicines not only made medicines available in the US but also affordable and accessible; thus filling both the delivery and the need gaps.

In most of the public hospital, in low and mid income countries, medicines are more or less free but low availability of essential medicines make accessibility of essential medicines through public sectors difficult (Cameroon *et al*., 2008). The WHO report on the global medicines situation of 2011 showed that the availability of essential medicines was 38.1% and 63.3% in public and private sector respectively (Kaplana *et al*.,2012;Dorlo *et al*.,2012), however the medicines in most of private sectors are inaccessible to the poor due to high prices (WHO, 2003). Since brand name medicines are high priced, therefore, they are out of reach in most of low and mid income countries especially in the rural areas. In spite of generic medicines increasing access to essential medicines regardless of technological and manufacturing capacity and reducing the monopoly and oligopoly of the brand manufacturing companies, it seems that they are not cheap and many enough to guarantee a universal accessibility of essential medicines (Cameroon *et al*., 2008).

Pharmaceutical production needs a large capital, technology and stuffs with the required technical expertise. These three factors are obstacles for low and mid income countries and many other countries to produce brand medicines. But after the introduction of generic medicines, a lot of countries including many developing countries have started to produce pharmaceuticals because the production of generic medicines does not need heavy investment as producing innovator medicines (Kaplan, 2005). In Africa, for example, about eighty percent of the countries have some medicines producing capacity at the tertiary and secondary level and local producers supply 25-30% of local demand. Domestic production of generic medicines has been one of a way of enhancing the availability and accessibility of high quality and affordable essential medicines especially in lower income countries (UNIDO, 2005). Though it is impossible for local manufacturers to satisfy the pharmaceutical needs of a country, yet some of the eastern Mediterranean countries have increased their manufacturing capacity of medicines to between 60% to 95% of their essential medicine needs (WHO, 2011). Local production has made it easier for essential medicines to be available in rural areas both in public and private sectors and at more or less affordable prices. In low and mid income countries, up to 40-60% uses local drug sellers as primary sources of medicines, some of which are located deep in the rural and underserved areas. Through these sellers generic medicines most of them locally produced reach most of the underserved population, because in these areas not only you will never find a brand medicine but also many of the people will not afford it. No tariffs and taxes on locally produced drugs therefore local producers are expected to sell their products at a low price compared to the imported ones (UNIDO, 2005). Local production of generic medicines not only save the foreign currency and stimulate exports but also it provide the country with a cheaper and reliable source of essential medicines. Last but not least local production can improve geographical accessibility of essential medicines by improving the distribution of medicines especially in rural areas and also by improving the production of medicines for neglected diseases (Kaplan & Laing, 2005).

Local productions of generic medicines have not only helped the domestic countries as witnessed in Brazil success in treating people living with HIV/AIDS (Arzeno *et al*., 2005) but also other countries as well. The low and mid income countries for a long time of period has been relying on China and India for both raw materials and affordable generics and the role of the latter countries is so critical to public health needs in the former countries (WHO, 2011). For example, 80%of all donor funded annual purchase of ARVs in 2008 was supplied by India and about 75% of the API produced in china and India are exported (Bumpas *et al*., 2009; Waning *et al*., 2010). Although the World Trade Organization Agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS) and the Doha Declaration on TRIPS and Public Health provide flexibilities that developing nations could utilize in order to supplement and potentially substitute imported medicines with products that are either manufactured in-country or within neighboring states, TRIPS seem to be a threat to generic medicines effort to improve medicines accessibility

(Grace, 2004). Apart from the delay of the introduction of generic medicines because of TRIPS, this change of laws and industry can affect the position of India and China as the sustainable suppliers of pharmaceuticals to low and mid income countries (Chaudhuri *et al*., 2010).

Affordability

Affordability is the association between the price of medicines and the ability of either the government or an individual to pay for it. Access to medicine is not about the availability of medicines but also include the individuals especially the poor being able to afford them. It is also about filling the need gap and not only the coverage gap (WHO, 2003)

Generic medicines are usually 20%-90% less expensive than the brand medicines, together with the market competition brought by generic medicines; generic medicines can produce much savings to patients (European Generic Medicines Association, 2002). In the US generic medicines account for two third of all filled prescriptions but yet accounts for 20% of the spending in pharmaceuticals (Aaron *et al*., 2011). By using generic medicines instead of brand medicines, the US had saved about $734 billion between 1999 and 2008 in health care savings (Generic Pharmaceuticals Association, 2009) and $1.07 trillion between 2002 and 2011 with $192.8 billion saved in 2011 alone [US Generic drug savings, 2012]. In UK about two third of the medicines dispensed by the National Health service are generics and still cost only 29% of the NHS drug bill, saving about €10 billion in England and Wales alone (British generic manufacturing association). Whereby in japan the use of generic medicines has reduced the total drug cost by about 1.3 trillion JPY (Kobayashia *et al*., 2011). This means that utilization of generic medicines can improve the affordability hence accessibility of essential medicines (Karim *et al*., 1996; 25-Caroll, 1995) and with their lower prices, generic medicines cause competition which can reduce both the average prices of medicines (Franck *et al*., 1997) and the prices of the innovator medicines (Caves *et al*., 1991).

In lower and mid income countries, the prices of medicines vary across the country, sometimes being higher than the reference prices mainly caused by the add on costs on the supply chain (Cameroon *et al*., 2009). The costs of treatment of chronic diseases are unbearable due to their going on nature and the need for combination therapy. In this situation, the use of brand medicines in lower income countries will just push more people further down the poverty line (Niëns *et al*., 2010). In higher income countries, about 60% of the pharmaceutical costs are covered by the insurance and social security funds, whereby in developing countries up to 90% of the payments are out of pocket (WHO, 2004). Not only that the prescription medication expenditure are increasing (IMS Health reports, 2009) but also more people avoid filling prescriptions due to cost or skip doses to make prescriptions last longer (Safran *et al*., 2002; Steinman *et al*., 2001;Mojtabai *et al*.,2003). There is a clear financial motive to use generic medicines, especially for those using more drugs; use of generics might be more helpful for them to save money (Simoens *et al*., 2006).

Despite the fact that generic medicines are the heart of affordability and accessibility of essential medicines especially in low and mid income countries, nonetheless to some people is still not that cheap to buy. Low procurement prices of generic medicines does not always translate into lower drug prices in the outlets, patients usually pay high prices especially in the private sector where the mark ups are higher sometimes up to more than 500% in retail markets (Cameron *et al*., 2008). Treatment of some chronic diseases like coronary heart disease, diabetes and asthma can cost up to more than one day wages when using cheaper generic medicines in some of the low and mid income countries. In these countries, some generic medicines cost about eight times or more than its international reference price (Mendis *et al*., 2007). Adjusting medicine prices (Lee *et al*., 2006), introducing mandatory generic substitution policy (Engström *et al*.,2006; Andersson *et al*., 2007) and introducing more generic medicines of different classes may reduce the pharmaceutical costs, because generic medicines provide affordable medicines which are equivalent to their innovator medicine counterparts (Peters *et al*., 2009)

Acceptability

The negative attitude and perception of consumers and health professionals towards generic medicines is one of the obstacles towards achieving universal accessibility of essential medicines through the use of generic medicines. Criticism of generic medicines mainly base on the approve process which is less rigorous than the brands (Blier, 2007). Though many people might agree that generic medicines are less expensive, does not cause more side effects and are as effective as brands, still very few will prefer generic medicines to brands. The beliefs that brand medicines are safer, of higher quality and even more effective than the generic medicines, is one of the concerns of many of patients' about generic medicines (Babara, 2011). Sometimes health professionals might have a positive attitude towards generic medicines, but the patient's unattended skepticism and doubts about the quality and effectiveness of generic medicines may hinder the use of generic medicines. On the other hand, physicians also seem to be sailing in the same boat of incredulity, especially when they have to choose medicines for themselves; they prefer brand to generic medicines (Hamann *et al*., 2012). The fear of experiencing a new effect or new or increased side effects (Håkonsen *et al*., 2011) and the association of low price equals low quality (Himmel *et al*., 2005 ; 46- Waber *et al*., 2008) are among the reasons to why the acceptance of generic medicines sometimes depends on the disease

condition (Figueiras, 2008; Ganther, 2000). In spite of generic medicines being less expensive than their brand counterparts, paradoxically patients with low income (Håkonsen *et al*., 2012) and older patients (Shrank *et al*., 2009) who usually use more medicines are less receptive of generic medicines. Sometimes generic medicines can be an additional factor for poor adherence to medicines (Roman, 2009; Håkonsen *et al*., 2011) especially for chronic drug users. The possibility that every time a patient might buy a different generic medicine probably with different colors or shapes or both might be confusing. However some studies have shown that the use of generics can improve adherence to treatment (Shrank, 2006; Bello, 2012), especially when patients are well counseled and given all the required information about generic medicines.

Despite the negative attitude and perceptions, promotion of the use of generic medicines is still one of the ways to increase accessibility of essential medicines. Through introducing more generic medicines in the market, the competition between brand and generic and between generics will increase which will lead to higher savings thus attracting more patients to use generic medicines (Jennifer, 2000). Educating the public is another way of promoting the use of generic medicines (Hassali, 2009; Thomas *et al*., 2009); people should know what generic medicines are and be capable of differentiating generic medicines from counterfeit drugs (Håkonsen et *al*., 2011). Negative attitude and perception have shown to be associated with insufficient information about generic medicines (Kobayashia *et al*., 2011; Babara, 2011)and better understanding of generic medicines was associated with the increase use of generic medicines (Palagyi *et al*., 2008;Shrank *et al*.,2009). Medical professionals can play a substantial part in encouraging patients to use generic medicines as some people will use generic medicine simply because it was the recommendation of a medical professional (Toverud, 2010).

Quality

Bioequivalence refers to the equivalent rate and extent of delivery of a drug active ingredient at the site of action as that of the reference drug. The fact that the safety and effectiveness of the reference drug are known, bioequivalent generic drug is expected to have the same safety and effectiveness profiles as the reference drug. As mentioned above, the objective is to avoid the unnecessary repetition of tests which in turn will reduce the costs of production and therefore the price to the end user. On top of being bioequivalent to its brand counterpart, the manufacture of generic medicines should observe all international standards in such a way that generic medicines will always have the same risks and benefits as those of their reference product [Peters *et al*., 2009]. Whilst generic and its reference medicine have to be pharmaceutically equivalent, generic companies are not forced to use the same excipients as those used in the reference drug. However there should be plausible evidence especially when a different excipient is used that the kind and the amount of excipients used will not change the safety and the efficacy of the product (FDA Code of Federal Regulations). Although there is a possibility of excipients to influence the pharmacokinetics of a drug; some negatively (Wandel *et al*., 2003; Talia *et al*., 2007) and some positively (Cornairea *et al*., 2004) - still there is no clear evidence that the differences between the generic and its reference medicine in excipients has got clinical advantage (Kesselheim *et al*., 2007). In large part, the widespread substandard and poor quality generics (Adegbolagun *et al*., 2007) is mainly contributed by the shortcomings of medicines regulatory authorities, especially in the low and mid income countries (Ratanawijitrasin *et al*.,2002), and not the excipients differences as some anecdotal reports want us to believe. The regulatory authorities should make sure that low price generic medicines are of the required quality and produced in acceptable standards in order to protect the populace from substandard generic medicines which are not bioequivalent to their brand counterparts (Peters *et al*., 2009). Insufficient domestic drug regulation and law application together with inadequate abidance of domestic pharmaceutical industries to GMP, results into a large number of poor quality medicines in most of low and middle income countries. It was found in Thailand that companies adhering to GMP guidelines seem to produce reliable products as compared to factories which do not comply with GMP guidelines (Wangboonskul *et al*., 1996) .So strengthening regulatory bodies and improving quality of the production of medicines might reduce the high rates of substandard and will facilitate the availability and accessibility of high quality and relatively cheap medicines.

For a long time, generic medicines have been associated with the increase of substandard medicines all over the world, especially in the low and mid income countries. A medicinal product may turn to be substandard because of manufacturing problems; Products having slightly high or low active ingredient is an indication of bad manufacturing .Things like drug products lacking active ingredients (Dorlo *et al*., 2012; Shakoor *et al*., 2003) are caused by inadequate drug regulation and poor pharmaceutical industries compliance with WHO GMP guidelines. These guidelines require every pharmaceutical industry to have a quality control department to make sure that a drug product will never enter the market unless is of acceptable quality. Ongoagchai et al (2011) found that man, machines, materials and method can cause drug quality problems thus rendering the drug products substandard. The use of active ingredients of inferior quality not only may make the drug product substandard but also may lead to increased side effects and unwanted clinical effects. Inadequate packaging can cause degradation of the drug product which has shown to be one of the main

reasons for medicines' poor quality especially when exposed in adverse conditions of high temperature and humidity of the tropical countries (Shakoor et al., 2003; Risha et al., 2003). Poor manufacturing, distribution and storage practice by the workers can easily affect the quality, safety and effectiveness of a drug product (Arya, 1995). Adequate quality control systems in the pharmaceutical industry and strict drug regulation should be capable of detecting these potential problems to secure the effectiveness and safety of generic drugs. On top of all that, the pharmaceutical market seems to be characterized by multiple standards (Caudron *et al*., 2008), whereby the quality of medicinal products depends on the level of income (Newton *et al*., 2010) and strictness of drug regulation in the country of destination (Nishtar , 2012). This might explain the high possibility of finding and procuring a low quality drug product in poor resource countries as compared to developed countries. Low technology, lack of the necessary expertise and capital can explain the huge number of substandard drug products manufactured by smaller generic companies found in most of developing countries compared to those manufactured by large generic companies (Bate *et al*., 2012). Therefore focusing only on generic medicines minimizes scope of the problem of substandard medicines where as the main concern should be improving the quality of drug products produced and available in low and mid income countries. This will need capacity building, technology transfer to these countries, help them to improve regulation of drug products and medicines supplied to these countries should be of high quality as those sold in the high income countries.

CONCLUSION

In spite of all the negative attitudes and perceptions people are having on generic medicines, still generic medicines have shown to be undeniable means of containing pharmaceutical costs and improving accessibility of essential medicines. By provoking local production in low and mid income countries, generic medicines have improved to some extent the geographical availability of essential medicines. Through making sure that the low procurement prices of generic medicines results into low prices of medicines in retail outlets, more people especially the poor will be able to access essential medicines and fulfill their medical needs.

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