

Branded versus Generic (*Branded-Generic*) Medicines-For Whose Benefit?

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ABSTRACT

Introduction: Cost of medicines is a major concern today. Generic drugs provide major saving opportunity in healthcare expenditure since they usually have lower price. However, physicians and patients are apprehensive regarding their quality, although they are bio-equivalents of the innovator products. The present study therefore compares the price structure and antibacterial activity of the branded products and their *branded-generic* counterparts. **Methodology:** Commonly used branded and *branded-generic* versions of three oral cephalosporins available in the pharmacy were studied. Health cost was compared by comparing Maximum retail price (MRP) and price-to-retailers (PTR) and trade margins. The antibacterial activity of the pairs was assessed by "Kirby Bauer" disk diffusion method, by comparing the zones of inhibition. **Results:** The retailer margin for the three branded medicines was in the range of 17-25% but for their *branded-generic* versions, it was huge, in the range of 73-130%. By switching over to branded generic medicines cost benefit to pharmacist ranged from 270% to 422% but for patients it was only 5%-48.3%. There was no difference in the zones of inhibition obtained for the branded generic and the corresponding branded drugs, indicating equal effectiveness. **Conclusion:** Branded generic cephalosporins, equi-effective as the branded versions, with lesser cost to the

patient, can be used clinically. However, cost benefit to the patients, being hyped in the media, is very meager compared to the profit margins for the retailers. Steps are needed to ensure that the cost benefit with the use of generics reaches the patients in appropriate amounts.

Key words: Branded-branded generics, cost of medicines, antimicrobial activity

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INTRODUCTION

India is the 4th largest producer and 10th largest exporter of drugs in the world. In spite of Government provision for health care budget, major proportion Indian population does not have access to even essential medicines.^[1] With the sky-rocketing healthcare costs, the interest in generic drugs has increased all over the world, amongst rich or poor. Generic drugs enable major savings in healthcare expenditure since they are usually substantially lower in price than the innovator brands.

^[2] In India, in view of poor accessibility and affordability of people, it is absolutely essential that the generic drugs should be made available to minimize the cost of treatment. Reported production and use of generic drugs had jumped from 49% of the global drug market in 2000 to 78% in 2010.^[3] In India, many pharmaceutical companies manufacture a product under both types, i.e., the branded product which they advertise and push through doctors and *branded-generics* which they expect to be sold over the counter by retailers. Generic drugs in simple terms are the copy of the branded ones having same ingredients, same dosage, same indications and exactly same pharmacological effects, as the manufacturing companies use the same active ingredients in both type of formulations. However, physicians are apprehensive regarding the quality of generic drugs.^[4] Consumer awareness for the generics, variety of trade names available in the market, and price variation is also very limited. Though in certain parts of India, government authorities recommend prescribing drugs by their generic names, drugs continue to be prescribed by the brand names and Doctors as well as patients do not want pharmacists to change the trade name written by doctor, despite the possible cost benefit. The present study was therefore undertaken to compare the price structure and antibacterial activity of the branded products and their *branded-generic* counterparts after the institutional ethical clearance. The same study had also been selected for ICMR-STs 2016-17.

Objectives

1. To compare the Price-to-patient (MRP - Maximum Retail Price) and Price-to retailers (PTR) and Trade margin of "branded" and "*branded-generic*" equivalents of some commonly used oral cephalosporins available in the tertiary care hospital pharmacy.

2. To compare the antibacterial activity of these formulations of cephalosporins.

METHODOLOGY

Three commonly used oral cephalosporins available as branded and *branded-generic* versions were selected. Basic information of the brands used was recorded from the formulation packs [Table 1].

Difference in cost

Medicines are available to patients at the MRP mentioned on the package of medicine. PTR is the price at which wholesaler (distributor) sells the product to the retailer and was noted from the purchase rate vouchers. Price-to-patient and price-to-retailers was analyzed for all the "pairs" of cephalosporins and Trade Margin for the retailer was calculated by using the formula:

$$\frac{100 \times (\text{MRP} - \text{PTR})}{\text{PTR}}$$

We also calculated the percentage increase in trade margin for the retailer and % cost benefit to the patient on switching to generic products.

Antibacterial activity

The antibacterial activity of all the selected formulations of the 3 cephalosporins against *Escherichia coli* and *Staph aureus* species isolated from different clinical samples was tested by "Kirby Bauer" disk diffusion method according to the 'Clinical and Laboratory Standards Institute' (CLSI) guidelines.^[5]

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The present study was performed with 30 µg Cephalosporin containing discs. The 3 Cephalosporins were coded as 1, 2, 3 with suffix B for branded and BG for branded generic drug in each pair. The 30 µg Cephalosporin discs of different brands were prepared by serial dilution using phosphate buffer 6 or 7 for the available strength of tablets or capsules. The discs were soaked for 24 hours and refrigerated. Antibacterial activity was tested the next day. Zones of inhibition was measured in mm after 24 hours of incubation by CLSI / Eucast reference for Disk diffusion (Kirby-Bauer) method.^[6,7]

Data analysis

Cost aspect was analyzed by comparing the PTR, MRP, Trade margin and percentage difference in trade margin for the retailer and cost benefit to the patient on switching to the generic brand. For measurement of antibacterial activity, zone of inhibition was measured in millimeter (mm).

Observations and results

The samples of the 6 formulations obtained were stored according to the manufacturer's packaging instructions and kept there until testing. The microbiologist who conducted the study was kept blinded. The description of the codes for all the brands and the details of drug products selected for this study are given in Tables 1 and 2.

The above table shows the basic details of the procured branded and branded generic cephalosporins. All the drugs studied during May-June 2016 were manufactured in 2015 and had expiry in 2017.

Assessment of cost benefit

Table 2 shows the cost benefit to pharmacist (Trade margin) and patients with the use of selected branded generic drugs. It is seen that the trade margin which is 25% with branded cephalixin increased to 130.5% with branded generic cephalixin—effectively increasing the profit to the pharmacist by 422%. With the difference in the MRPs of the two products, cost benefit to the patients is 42.6% which is just 10% of the benefit to the retailer. Thus, the study reveals that there are huge mark-ups for retailers on *branded-generic* medicines because of significantly lower PTR. The retailer margin for three *branded* medicines studied was in the range of 17-25%, but for their *branded-generics* version, it was in the range of 73-130% [Table 2]. By switching over to branded generic medicines cost benefit to pharmacist increased from 270% to 422%. Patient benefit depends on the difference in MRP. For the three drugs studied, patient benefit was only 5%-48.3%.

Assessment of antibacterial activity

We have compared the antibacterial activity of branded and branded generic formulations of 3 oral cephalosporins using disk diffusion method (Kirby-Bauer method). Each tablet in the respective pair

had the same strength [Table 1]. The results of the study in terms of diameters of zones of inhibition produced by the different brands of cephalosporin tablets against the tested bacterial strains are given in Table 3. Photographs of the plates with the zones of inhibition are given in Figure 1. According to Table 3, amongst the three pairs of oral cephalosporins, the zones of inhibition did not differ between the branded and branded generic formulations. In fact, the zones of inhibition for the branded generics were slightly larger than those for the corresponding branded formulations.

DISCUSSION

The Original concept of Generics distinguishes these products from the 'patented' or 'innovator' products marketed by a company who has invested a lot of time, money and effort on the research. Once out of patent, the drug can be manufactured by other companies who have not invested in it at the research level and hence their brands can be available at a lesser cost to the patients. In low and middle income countries, originator brand medicines generally cost substantially more than their generic equivalents. Generic drugs provide the opportunity for major savings in healthcare expenditure.^[2] In India the concept has a completely different connotation. Branded does not mean innovator patented products, but brands on which the company spends a lot for marketing, against the generics which are sold by giving huge incentive to the retailers.

Generics are supposed to be marketed and prescribed by the generic name of the drug. However, physicians are apprehensive regarding the quality of generic drugs.^[4] That has led to the emergence of the so called 'branded generics', wherein the same reputed companies started manufacturing a product under both types, i.e., the branded product which they advertise and push through doctors and *branded-generics* which they expect to be pushed over the counter by retailers.

This is one of the first studies in India conducted systematically to compare difference in health care cost and antimicrobial efficacy of three oral cephalosporins available as branded and branded generic products. Efforts were made to procure these products having close manufacturing and expiry dates [Table 1].

Findings of the study revealed that though these branded generics are available to the patients at a somewhat lower cost than the corresponding branded formulations, this cost benefit is negligible as compared to the tremendously higher trade margins they offer to the retailers, who therefore willingly promote the sale of such (branded generic) products.

Other studies in India comparing different generic medicines to their branded counterparts also show that price-to-patient for the *branded-generic* version was not much less than to its *branded* counterpart; the price difference being only 71-100% of the branded formulation.^[8,9]

Table 1: Details of the drug products selected for comparative analysis

Cephalosporin	Code	Batch No	Mfg date	Expiry Date	Brand Name & Manufacturer
Cephalexin	B1	2706924	6/2015	2/2017	Sporidex 250 Sun pharma
	BG1	B651155	11/2015	6/2017	Cephadex 250 Cipla
Cefuroxime Axetil	B2	5133176	12/2015	11/2017	Zocef 500 Alkem
	BG2	WBT-5240B	10/2015	9/2017	Bullcef 500 Ultra-Drugs Pvt. Ltd.
Cefixime	B3	EI 51546	11/2015	10/2017	Ziprax-200 DT Cipla
	BG3	TX-7718	05/2015	4/2017	Cefixar-200 DT Legen healthcare

B1, B2, B3 - Branded products, BG1, BG2, BG3-Branded Generic products

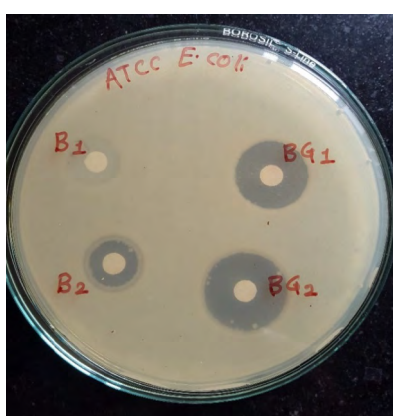
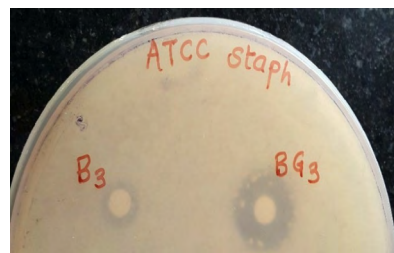
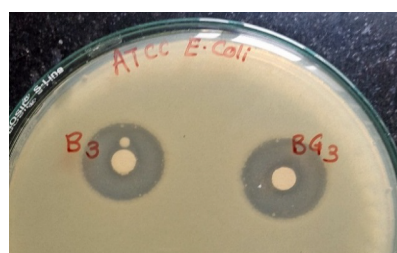
Table 2: Cost benefit to pharmacist and patient

Pair Sr. No	Drug Name	PTR	MRP	Trade Margin %	Increase in trade margin	On switching to branded generics		
						% increase in trade margin	Cost benefit to the patient	% Cost benefit to Patient
1	Cephalexin (B1)	84.8	106	25				
	Cephalexin (BG1)	26.40	60.8	130.5	105.5	422%	45.2	42.6%
2	Cefuroxime Axetil (B2)	460	557	21.08				
	Cefuroxime Axetil (BG2)	160	288	80	58.92	270%	269	48.3%
3	Cefixime DT (B3)	81	95	17.28				
	Cefixime DT (BG3)	52	90	73.07	55.79	322%	5	5%

PTR - Price to the retailer; MRP - Maximum retail price; *Branded Generics/Branded* drug products and their trade margins

Table 3: Zones of Inhibition of different brands of oral cephalosporin

Pair Sr. No.	Drug Name	Zone of Inhibition (mm)		Recommended Zones of inhibition (mm)	
		<i>E. coli</i> ATCC	Staph ATCC	<i>E. coli</i>	<i>S. aureus</i>
1	Cephalexin (B1)	18 mm	25 mm	15-21	29-37
	Cephalexin (BG1)	21 mm	33 mm		
2	Cefuroxime Axetil (B2)	15 mm	15 mm	20-26	27-34
	Cefuroxime Axetil (BG2)	20 mm	15 mm		
3	Cefixime DT (B3)	20 mm	10 mm	23-27	
	Cefixime DT (BG3)	21 mm	15 mm		

A) Zone of inhibition against *E. coli*B) Zone of Inhibition against *S. aureus***Figure 1:** Zone of Inhibition of different Pairs of oral cephalosporin

Since there is not a substantial difference in the MRPs of these products, this higher trade margin is possible because of the very low PTR for the branded generics. PTR reflects the manufacturing cost of the product. This naturally leads to a question about the quality of generic drugs, supposedly produced at lower production cost? This justifies the apprehension about their quality in the minds of the clinicians and patients. There exists a widespread belief among people and dispensing chemists that a *branded* product is better in terms of quality and safety than the generic.^[10,11]

Many reports comparing the effectiveness of branded generics and their branded counterparts are available. Many studies are conducted

to test the therapeutic bio-equivalence of generic drugs even prior to marketing and there are number of published studies assuring the safety and efficacy of these generic drugs.^[12-14] There are also many studies reporting that generic antibiotics behave differently from brand products against pathogenic microorganisms.^[15,16] Doubts have also been raised about the efficacy of generic antibiotics, based on complaints from the medical community reported in the literature and at international meetings.^[17] Farzana *et al.* have also reported comparable values of Minimum Inhibitory Concentrations for the local and multinational brands of 1st, 2nd and 3rd generation cephalosporins against clinical isolates of *S. aureus*.^[18] A study carried out in Pakistan,

showed no difference of *in-vitro* antibacterial activity of Ceftriaxone, even for the brand having the lowest MRP.^[19] Another study by Bashir *et al.* reported that the multinational brands of Cephadrine had better zones of inhibition than local Pharmaceutical companies. However, the difference was not statistically significant.^[20]

Our study has shown that the branded and branded generic pairs of the same antibiotic had equal antimicrobial activity when tested *in vitro*. Comparable antimicrobial activity *in vitro* may however, get compromised by inadequate bioavailability of the formulation, resulting in inadequate antimicrobial activity *in vivo*. This aspect of comparison has not been addressed in our study. This limitation of our study needs to be taken care of by further studies. Such robust proof generated about equal effectiveness of these and other such pairs would make these products available at whatever cost benefit they offer to the patients. The other important point highlighted from our study and many others^[18,19] is the tremendous difference in cost benefit to the retailers as compared to that for the patients. This demands that appropriate steps be taken to ensure that the cost benefit with the use of generics reaches the patients in appropriate amounts. Measures like defining the relative MRPs for branded and branded generic formulations of the same drug can be a step in this direction.

CONCLUSION

Our study revealed that the 3 branded and branded generic cephalosporins were equieffective *in vitro*. More elaborate studies would be needed to establish equal efficacy *in vivo*.

Measures are needed to ensure that the cost benefit does not remain restricted to the retailers and is also available to the patients in appropriate proportion.

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