Analysis of cephalosporins available in India: A pharmacoeconomic perspective

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ABSTRACT

Background: Bacterial infections are one of the most common causes of morbidity and mortality in community and hospital settings. The acceptance of the treatment imposes heavy economic burden on the patients. Due to improper drug policy, different costly preparations of the same brand are ordered and tendered, which pose a sheer wastage of money, ultimately causing burden on tax payers. **Aims and Objectives:** The present study was planned to evaluate and compare the costs of different brands of various generations of cephalosporin which may be generic or commercial in nature. **Materials and Methods:** We selected commonly used drugs from different generations of cephalosporins. Cost of drugs (may be generic or commercial or of different formulations) was obtained from latest periodic manuals of Indian Drug Review (INR) and drug today and was analyzed for cost ratio, cost range, and percentage difference among brands from different pharmaceutical companies for oral and parental forms. Correlation among price variations between them was observed by data comparison. **Results:** Cephalosporins were analyzed for the differences in prices. We not only found wide variation between the cost of generic and commercial preparations but also very wide price range and ratio among the same products from reputed to medium companies. **Conclusions:** Our study has indicated about the wide differences in the cost of different cephalosporins which are the most commonly prescribed group of antimicrobials. If hospitals across India adopt uniform policy of prescribing cost-effective preparations (brands/generic) only, then the unnecessary economic burden can be significantly reduced.

Key words: Antimicrobial; Cost effectiveness; Drug resistance; Economic burdens; Pharmaceutical industry

INTRODUCTION

The incidence of bacterial infection is very high in reference to developing world like India, where Gram-positive and negative bacteria are rampant and associated with high morbidity and mortality in community and hospital settings with diseases such as bronchopneumonia, urinary tract infections, and gastrointestinal category. Cephalosporins are one of the main stakes of drugs for above variety of infections. High cost of above drugs particularly in post-COVID epidemic era and difficulty in import of parent cephalosporin's Active Principle Ingredients from manufacturing countries like china has paid attention to think and rethink for revising our drug policy to obtain cheapest variety of above drugs.[1,2]

Rational use of antibiotics not only involves prescribing a medicine to completely eradicate the infection, it involves intelligent use to keep vision on drug sensitivity, proper duration of therapy to prevent resistance, and also at an affordable cost since acceptance of the treatment by patients depends completely on its cost. Improvement on acceptance can reduce the total health-care cost involved in the management of a particular infection.[3] At present, 30–50% of the total bills of the patients in hospitals owe to cost of medicines. Maximum retail price (MRP) is much more as compared to the real cost (going to chemist stores)

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and hospitals and physicians are wrongly blamed for the same.[4,5] Therefore, pharmacoeconomics play an important role and help to compare costs and thus helping in proper utilization of drugs in a long term to save public and country economy in a nutshell.[6]

In a country like India, there are various cephalosporin antibiotics from various companies with different brand names which are available.[7,8] This creates a problem for the physician to make choice for the individual patient. Similarly, few studies are done to determine the bioequivalence of various brands with same parent compound. Many companies may be obtaining the manufacturing licenses from different state agencies without stringent laws. Hence, there are high chances of inadequate quantity too.[9-11]

With this background to address the financial burden due to use of different cephalosporins, we planned to compare the same and keeping it mind that it could help in the drug policy making.

Aims and objectives

The aim of this study was to compare the cost of cephalosporins available in India.

MATERIALS AND METHODS

The cost of different products of same chemical entity, comparable strength, and formulations was obtained on MRP basis and was compared for their price differences, price ratio, and number of companies manufacturing the same product. Before the initiation of the study, formal approval was taken from the Institutional Ethics Committee. The information was obtained from promotional literatures and latest issues of periodically published handbooks such as Indian Drug Review (INR) (January 21) and drug today (January 21),[7,8] for example, – cost of cephalexin (first generation cephalosporin oral drug) whether manufactured by one or multiple companies. Similarly, it was not considered whether belonging to generic or commercial divisions of the company. We mainly compared the oral and parental formulations, excluding the local and topical preparations. We have also included above drugs with suitable combinations (like with other antibiotics ex. ofloxacin, ornidazole, cloxacillin, with lactobacillus and also with beta-lactamase inhibitors such as clavulinic acid, sulbactam and tazobactam) while avoiding irrational drugs such as azithromycin.[12] Nowadays, due to drug resistance instead of using alone, the combination of oral cefixime and cefpodoxime (with clavulinic acid) while parenteral injection of ceftriaxone and cefperazone (with sulbactam or tazobactam) are preferred.

Drug ratio, cost variation, and cost variation percentage were derived from following formulas.[13]

$$\text{Drug ratio} = \frac{\text{Highest rate of one company}}{\text{Lowest rate for the same product}}$$

$$\text{Range} = \text{Maximum price} - \text{Minimum price}$$

$$\text{Percentage cost variation} = \frac{\text{Maximum cost} - \text{Minimum cost}}{\text{Minimum price}} \times 100$$

RESULTS

The cost of 20 cephalosporins (parent compounds and few of recommended combinations as mentioned above in various formulations whether injectables, dispersible tablets, syrups, and regular tablets) was taken from indexed periodicals and variability in the cost on daily dose basis was compared. Out of above formulations studied, percentage cost variation was more than 150% in every, out of which 3–4 had this variation more than (maximum seen in cefuroxamine brands) 1200% with the exception of cefazolin in adult doses (where only two companies manufacturing it with the same cost).

We have also tried to compare the most commonly used strengths for common public such as 250 and 500 mg. The formulations with greater strength such as 500 mg and 1000 mg, was cheaper as compared to 125 and 250 mg regular tabs while injectable formulations are always costly as compared to oral. However, comparing charts of cefotaxime, ceftriaxone, and cefoperazone, large difference in costs was observed (Table 1), which shall help the patients in long-term on the daily doses basis as well the small quantity (as per body weight) which is frequently used for pediatric patients. Similarly, in syrups and dispersible tabs, cost ratio was also very high and 6–8 drug formulations had this cost ratio more than 2 (Table 2).

Tablet cefuroxime 250–500 mg and 1–2 g had maximum cost range (14.5–190) and cost ratio of 13. Injection cephazolin and cefdinir had minimum cost variation and low cost ratio, where only few (two) companies are manufacturing it while combinations are always high such as with clavulinic acid, sulbactam, and tazobactam. There are huge number of formulations available for different category of drugs that are sold under the umbrella of various brand names.[13] General public instead of consulting physicians directly purchase cephadroxil or other oral drugs

Table 1: Variation among different brands of cephalosporins on cost/day basis (adult doses)						
Drugs	Formulations	Dose/day	Manufacturing companies	Cost range (INR)/day	Cost ratio	Cost variation ratio (%)
First generation						
Cephalexin	125–500	500 mg q.i.d	18	14.5–69.6	4.8	406
Cephadroxil	125–500	500 q.i.d	19	4–21	5.2	425
Cephazolin	Inj 0.5–1.5 g	0.5–1.5 g 6 h	2	150/day	1	0
Second generation						
Cefaclor	250–500 and 600 mg	in b/d	6	76.5–208	2.72	550
Cefuroxime	250–500	250 b.d	43	14.8–190	13	1182
Cefuroxime combinations	Same base as above	Do	7	29.2–280	6.9	858.9
Cefoxitin	NA	-	-	-	-	-
Cefprozil	250–500 mg	500 mg 0d	4	30–100	3.33	233.3
Cefotitan	NA	-	-	-	-	
Third generation						
Cefotaxime	1–2 g	1–2 tds	7	112–324	2.89	189.26
Cefotax+sulbactam	1–2 g	Do	5	696–917	1.31	32.89
Ceftriaxone	1–2 g	1–2 gms in d/d doses	78	78–220	2.82	214.28
Cetrax+sulbactam	1–2 g	Same	....	81–223	2.75	175
Cetrax+tazobactam	1–2 g	same	....	100–175	1.75	75
Cefdinir	300, 600	600 mg d/d	9	61–250	4.09	316.66
Cefperazone	250–1 g vial	2–4 gm/d	7	468–885	1.89	89
Cefperazone+sulbactam	Do	Do	11	187.5–795	4.24	324
Cefixime	200, 400 mg	200 bd	9	17–45	2.64	164
Cefixime+clavulinate	Do	Do	5	696–917	4.14	31.75
Ceftazidime	Inj 250–1 g	1 g tds	25	689–1462	2.12	112.3
Cefpodoxime	200, 400 mg	200 bd	110	24–106	4.46	341.66
Cefpodoxime+clavulinate	200–400	Do	11	30–75	2.5	150
Ceftibuten	400 mg	400 od	1	222	-	-
Fourth generation						
Cefepime	Inj 1, 2 g	1–2 g d/d	18	214—468	2.18	118.69
Cefpirome	1–2 g	1–2 g bd	12	486–1180	2.26	142.79
5th gene						
Ceftaroline						

(OTC basis) from direct chemical stores. This should be strictly avoided, as incomplete knowledge, inadequate therapy, and unknown microbiology in particular infection can be always problematic when given on empirical basis.[14]

DISCUSSION

Our study has revealed about the wide differences in the cost of various generations of cephalosporins manufactured and supplied by different companies. The same single drug formula manufactured by various companies also highly varies in the MRP.

Major indication for injectable drugs arises in serious conditions such as lower respiratory pneumonia, bronchitis, S.T.D (gonorrhea), typhoid, hospital infections (like septicemia, post-operative cases, traumatic cases and burns) which carry high risk and morbidity. Here, third generation parenterals such as ceftriaxone, ceftazidime and cefperazone are drug of choice. The high cost of above drugs put the patients on tremendous economic burden.

In the present scenario, much emphasis is given to rational drug therapy. As stated by the WHO, rational use of drug requires that patients receive medication appropriate to their clinical needs, in doses that meet their own individual requirements for an adequate period and at the lowest cost to them and their community.[15] One of the high costs of the medicines is prescription of commercial preparations and too highly influenced by promotional schemes, other incentives, etc. For some medicines, the cost between generic and commercial preparations carries a ratio of 5-fold–13-fold. Lack of information about the high difference on the part of health-care providers makes it very difficult for them to prescribe the most economical brand of such cephalosporins which should be an important part of rationale drug prescription.

Physicians and surgeons are highly dependent on the promotional literature and information provided by medical representatives regarding the cost of medications. A multiple study has also indicated about the same ignorance of clinical staff.[15] Hence, above cost analysis (pharmacoeconomics) of various formulations not only

Table 2: Variation among different brands of cephalosporins on cost/day basis (pediatric doses)

Drugs	Formulations	Dose/day	Manufacturing companies	Cost range (INR)/day	Cost ratio	Cost variation ratio (%)
First generation						
Cephalexin	125–500	250 qid	11	5.5–30	5.45	445
Cephadroxil	125–250	30 mg/kg 2–4.9	6	2.62–4.9	1.87	87.02
Cephazolin	125–250 mg	25–50 mg/kg in 2–4 d/d doses	6	22.90–84.40	3.68	268.55
Second generation						
Cefaclor	125–250	50–80/kg in d/d	10	36.44–54	1.48	48.18
Cefuroxime	125–250 mg	125 b.d	30	16.5–104	6.5	530.30
Cefuroxime combinations	Same base as above	Do	3	38–95	2.3	150
Cefoxitin	NA	-NA	-NA	-NA	-NA	- NA
Cefprozil	125–250 mg	125–250 0.d	4			
Cefotitan	NA	-NA	NA-	NA-	NA-	NA
Third generation						
Cefotaxime	125–500 mg/vial	50–70 mg/kg tds	20	117–322	2.70	175.25
Cefotax+sulbactam	Do	Do	5	696–917	1.31	31.75
Ceftriaxone	125–250 mg/vial	30–50 mg/kg bds	20	44–168	3.88	281.81
Cetrax+sulbactam	Same	Same	28	35–70	2	100
Cetrax+tazobactam	Same	Same	20	126–390	3.09	209.52
Cefdinir	300—600	14mg/kg od	2	42–54	1.27	28.57
Cefperazone	250–500 mg vials	30–200 mg/kg in d/d	35	250–722	2.9	188.8
Cefperazone+ sulbactam	500 mg, 1–2 g vials	Aver 100 mg/kg (ref 20 kg)	25	296–1160	3.91	291.89
Cefixime	100–200 mg	8 mg/kg/day	21 (ped formulations)	7.2–44	5.45	511.11
Cefixime+clavulinate	50–100 mg/5 ml syrup	Do	6	12–39	3.25	225
Ceftazidime	125 mg, 500 mg, 1, 2 g	80 mg/kg av 1g bd for 20 kg	22	306–654	2.10	113.72
Cefpodoxime	50, 100 mg tabs	10 mg/kg in d/d doses	13	20.55–64.13	3.10	212.06
Cefpodoxime+ clavulinate	Tab 50, 100 mg and syrup 50 mg/ml	Do	34	30–70	2.3	133
Ceftibuten	NA	NA	NA	NA.	NA	NA
Fourth generation						
Cefepime, cefpirome, and ceftaroline not recommended for pediatric	Inj					

beneficial to patients (save time and money) but also to health system, in the form of awareness and some knowledge to the prescriber about the cost of different cephalosporins in the specific sensitive infections. Generic drugs are lower in cost as compared to commercial preparations and health-care cost can be reduced to large extent if they are replaced by generic antibiotics. They are, by enlarge believed to have good bio-equivalence (if local companies are avoided), from generic divisions of reputed companies that are included in the national drug policy. If local companies also prove their equally good efficacious and good bio-equivalence data, those cephalosporins will gain physician confidence regarding prescription to their patients.[16]

Pharmacoeconomics plays a very important role while prescription of medicines by the physicians and subsequent cost of therapy, in which an individual or a family has to bear for his treatment. Pharmacoeconomics compare the costs to help the patients and health system in a long-term and in turn saving the foreign exchange to stabilize our economy. Similarly, it describes the economic relationship between drug research, manufacture, logistics, and ultimately use by the patients.

In our country, drug price is controlled according to the drug price control order 2013 (DPCO). National pharmaceutical pricing authority, government of India fixes the ceiling price of drugs in accordance with DPCO 2013. Drugs price is revised every year according to the wholesale price index. Results of this study indicate that there is an urgent need of controlling cost variation among different brands of available antibacterial drugs.[17,18]

Sometimes, clinicians are concerned about the quality of generic medicines and this might be a reason for avoiding them. Although they are manufactured in accordance with good manufacturing practices, these are wrongly considered as inferior to branded preparations.[19] If any doubts arise, they can shift to reputed brands in case of life-threatening diseases such as pneumonia, meningitis, or endocarditis.[20]

Thus, factors that have impeded access to affordable generic and essential medicines in India include (i) wrong notions among policymakers, prescribers, and patients about branded drugs and generic drugs and (ii) high prices of medicines due to progressive dismantling of the system regulating medicine prices.

There is a need of incorporating the topic of pharmacoeconomics in the medical curriculum so that students are also aware of the cost and economic burden due to their slight accurate prescriptions. The study also revealed about the flexibility in cost in relation to the open policy of government, no of companies manufacturing the same product. Open competition generally brings down the cost of particular antibiotic. In government drug policy, physicians can be given a list of particular brands, which can only be prescribed in a particular condition and assurance of availability of particular generic form of cephalosporins. A systematic review of 38 randomized controlled trials of generic and brand-named cardiovascular drugs concluded that they were clinically equivalent.[20]

The Government of India has recently started generic drug stores all over the country, where tablets are available at cheaper rates. The quality of cephalosporins available in these stores at cheaper rates should be checked periodically as compared to commercial preparations as a confidence building measure among the pharmacists, prescribers, and consumers for promoting the use of generic drugs.[21,22] Pharmaceutical manufacturers cite the high cost of research and development as a reason for the excessive pricing of drugs. However, considerable money is spent on product promotion and overhead cost.[23] Results of this study indicate that there is an urgent need of controlling cost variation among different brands of available antibacterial drugs.

Limitations of the study

This study is based on the data extracted from the drug books published by different publications and is time bound as the data under reference is regularly updated depending upon the price revision of the formulation by the pharmaceutical companies.

CONCLUSIONS

Generic antibiotics and their suitable combinations shall save a tremendous amount of budget allocation in purchase of cephalosporin antibiotics, if limited numbers of antibiotics as essential drugs are incorporated in individual state and national drug policies. By avoiding costly medicines which may be high in cost due to simply being a product of international and reputed fame, our government can reallocate funds for a number of positive things such as infrastructure and other diagnostics. In terms of patient savings, also they can help a developing country like India.

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