Int J Pharma Res Health Sci. 2017; 5 (6): 1954-61
DOI:10.21276/ijprhs.2017.06.11
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CODEN (USA)-IJPRUR, e-ISSN: 2348-6465

PHS Scientific House
PHARMAHEALTHSCIENCES

International Journal of Pharma Research and Health Sciences

Available online at www.pharmahealthsciences.net

Original Article

To Compare Cost and Effectiveness of Emperically Treated Antibiotic Magnex Forte and Cepez-SB in the Treatment of Acute Gastroenteritis

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ARTICLE INFO

Received: 09 Nov 2017
Accepted: 22 Nov 2017

ABSTRACT

Background: Health systems have multiple goals, but the fundamental reason they exist is to improve health. Cost And Effectiveness Analysis (CEA) is one tool decision-makers can use to asses and potentially improve the performance of the health systems. Cost effectiveness analysis (CEA) is a form of economic analysis that compares the relative costs and outcomes (effects) of different courses of action. **Objective:** The purpose of the study is to asses which intervention provides the highest value for the money and helps to choose the intervention which maximize health outcome in gastroenteritis patients treated with generic (Cepez-SB) and brand (Magnex Forte) formulation. **Methods:** A comparative observational study was conducted in 80 inpatients admitted with gastroenteritis in gastroenterology department in Global Hospital, Hyderabad for a period of six months and data was analyzed using paired T-test. **Results:** In this study a total 80 patients were enrolled out of which 40 patients received brand form (MF) and 40 patients received generic form (Cepez-SB). For brand formulation majority were in the age group of 40-60 and for generic formulation majority were in the age group of 50-60. The average cost of drug per patients in Cepez-SB arm is lower i.e., INR 4455.00/- and for MF arm is INR 4944.00/-. The average number of days symptoms subsided for Magnex Forte group is lower i.e., 3.98 days and for the Cepez-SB group was 4.93 days. The average length of hospitalization for MF is lower i.e., 4.375 days and for Cepez-SB is 4.975 days. The average total hospitalization cost for MF is lower i.e., INR 28474.53/- and for Cepez-SB is INR 29362.95/- .
Conclusion: We provided a detailed description of costs and effects of both brand and generic forms of cefoperazone - sulbactam in gastroenteritis patients. Results demonstrated that Magnex Forte (brand form) was superior to the Cepez-SB (generic form) used in the study in all aspects and that it also had a better safety profile. We concluded the use of generic drugs could be related with an increased days of disease or might lead to a therapeutic failure; on the other hand, a higher drug concentration might expose patients to an increased risk of dose-dependent side-effects. Overall, it is advisable to well evaluate the effects of generic formulations during the therapeutic treatment.

Key words: Gastroenteritis, Cepez-SB, Magnex Forte, cefoperazone-sulbactam, side-effects.

1. INTRODUCTION

Gastroenteritis (GE) is one of the most common acute illness but is rarely life threatening in present population. In developing nations, Gastroenteritis is frequently result of poor sanitation, the lack of safe drinking water or

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contaminated food. In developed nations, bacterial gastroenteritis may result from contaminated water supplies, improperly processed foods, or person to person contact in places such as child care centers. The modern food production system potentially exposes millions of people to disease causing bacteria through its intensive production and distribution methods. Gastroenteritis is the inflammation of the digestive tract particularly stomach, large and small intestine. GE is caused by the ingestion of viruses, certain bacteria and parasites[1,2]. The symptoms include nausea, vomiting, watery diarrhea, abdominal pain and cramps. These symptoms are sometimes accompanied by bloating, low fever, chills, headache and overall weakness or tiredness. It is a self-limiting illness that will resolve by itself. Medications such as antibiotics, analgesics, ant emetic's, ant diarrheal and rehydration therapy should be used sparingly for the relief of symptoms. Cefoperazone-Sulbactam is used as an empirical therapy in the treatment of acute GE due to its broad spectrum antibiotic activity and lesser side effects than other antibiotics. Here, the purpose of the study is to compare the cost and effectiveness of brand form (Magnex Forte) and generic form (Cepez-SB) of Cefoperazone-Sulbactam[3,4]. Cost-effectiveness analysis (CEA) is a form of economic analysis that compares the relative costs and outcomes (effects) of different courses of action. CEA of a health care intervention or program requires a comparison of that intervention with alternative methods of dealing with the patients in a given health state[5]. The alternative method may be some other treatment or no treatment at all. For example, the use of a drug such as captopril might be compared with another antihypertensive mediation such as a beta-blocker[6]. In this study we are comparing brand versus generic formulation of same drug (cefoperazone+sulbatam) in order to reduce the medication prices and reduce the economic burden on national health systems. A generic drug is a pharmaceutics drug that is equivalent to brand name product in dosage, strength, route of administration, quality performance and intended use[7]. This article reviews the papers published about cost and effectiveness of different antibiotics used in gastroenteritis in the indexed literature for the last 10 years, analyzing the methods used in improving the patients care and economic burden in health care system[8].

Pharmacoeconomics:

Pharmacoeconomics is the field of study that evaluates the cost and efficacy of a pharmaceutical product. It refers to the scientific discipline that compares the value of one pharmaceutical drug or drug therapy to another. Pharmacoeconomics identifies, measures, and compares the costs and consequences of drug therapy to healthcare systems and society. It mainly focuses on the cost (inputs) and consequences (outcomes) of the drug. In addition to it, it addresses the clinical, economic, and humanistic aspect of health care interventions, in the prevention, diagnosis, treatment, and management of disease. It is a collection of descriptive and analytic techniques for evaluating pharmaceutical interventions, spanning individual patients to the health care system as a whole[9,10].

Cost Effectiveness Analysis:

A cost effectiveness analysis (CEA) is used to simultaneously compare the costs and outcomes of different interventions. In CEA a single clinical outcome is used to measure effectiveness, such as cure or remission, or avoidance of an event. Ex: Hospitalization. The cost effectiveness of a therapeutic or preventive intervention is the ratio of the cost of the intervention to a relevant measure of its effect .the measure of effect depend on the intervention being considered. Example include the no. of people cured of a disease, the mmHg reduction in diastolic blood pressure and the no. of symptom free days experienced by a patient[11]. The selection of the appropriate effect measure should be based on clinical judgment in the context of the intervention being considered.

The term cost effectiveness is often used loosely to refer to the whole of economic evaluation, but should properly refer to a particular type of evaluation, in which the health benefit can be defined and measured in natural units (e.g. years of life saved or quality adjusted life years, ulcers healed) and the costs are measured in money. It therefore compares therapies with qualitatively similar outcomes in a particular therapeutic area. For instance, in severe reflux esophagitis, we could consider the costs per patient relieved of symptoms using a proton pump inhibitor compared to those using H_2 blockers. CEA is the most commonly applied form of economic analysis in the literature, and especially in drug therapy. It does not allow comparisons to be made between two totally different areas of medicine with different outcomes[12].

- Measurement of outcome (health benefits): health benefits across therapies are measured in similar natural units.
- Synthesis of cost and benefit: cost per life year gained, cost per patient cured, cost per life saved etc.

Cost effectiveness is typically expressed as an incremental cost effectiveness ratio (ICER), the ratio of change in cost to the change in effect.

Why Cost Effectiveness Analysis is Important?

Health systems have multiple goals, but the fundamental reason they exist is to improve health. Yet health systems with very similar levels of health expenditure per capita show wide variations in population health outcomes. Part of the difference can be explained by variation in non-health system factors, such as the level of education of the population. But part can also be

explained by the fact that some systems devote resources to expensive interventions with small effects on population health, while at the same time low cost interventions with potentially greater benefits are not fully implemented. CEA analysis is one tool decision makers can use to asses and potentially improve the performance of health systems[13]. It indicates which interventions provide the highest "value for money" and helps them choose the interventions and programs which maximize health for the available resources.

CEA requires information on:

- The extent to which current and potential interventions improves population health i.e., effectiveness.
- The resources required to implement the interventions i.e., costs.

The impact of interventions on population health is vital. But it is also important to determine the role of interventions in contributing to other socially desirable goals, such as reducing health inequalities, and being responsive to the legitimate expectations of the populations.

2. MATERIALS AND METHODS

Study Protocol

It is a comparative observational study conducted for the period of six months and patient who met the study criteria where included in the study. The required data were collected from the patient case sheets by using suitable patient profile form and the obtained data were evaluated in relation to drug use.

Study Design

A comparative observational study

Study Criteria

Inclusion Criteria:

- Male and female patients diagnosed with acute gastroenteritis admitted to the hospital.
- Patients of age 10-80 years.

Exclusion Criteria:

- Patients less than 18 years of age and more than 60 years of age.
- Patients having UTI, RTI and Bed Sores.
- Patients with hospital acquired infection.
- Immunocompromised patients.

Source of data:

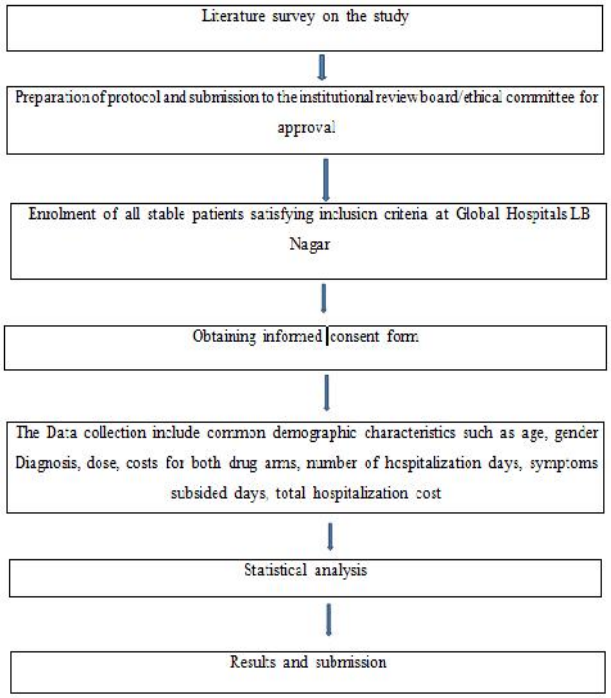
- All relevant and necessary data will be collected from
- Patient case notes
- Laboratory data
- Billing department
- Any other relevant sources

All collected data was documented in a suitably designed data collection form developed for the study.

Designing of data collection form:

A suitable data collection form was designed to collect, document and analyze the data. Data collection form includes the provision for collection of important information like patients socio-demographics details like age, sex, name, case notes, laboratory data, drug costs, number of hospitalization days, total hospitalization cost, symptoms subsided number of days, social history.

Method of study (Plan of work)

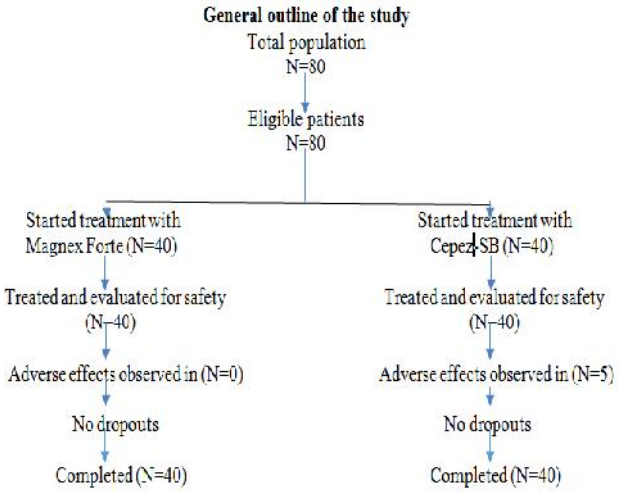


Study Procedure

- The study team will be visiting the study sites every day on regular basis. Patients meeting the inclusion and exclusion criteria will be selected for the study.
- The data collection form contains relevant information about patient's demographics, billing details, effectiveness of study drug.
- All the relevant patient data will be collected from case sheets in a suitably pre designed data proforma on daily basis.
- Billing data was collected from I.P. billing department.
- Consecutive follow-ups were done.
- All collected data will be analysed using relevant statistical methods.

Statistical Analysis

Descriptive statistics were performed by using Microsoft excel to analyze the following data according to: Data were expressed as proportions for age wise, cost wise, symptoms subsided (success rate of brand and generic) wise, total cost wise. Data was analyzed using paired T-test and presented as percentage mean +/_ S.D for gender comparison, cost comparison, and total cost comparison.



3. RESULTS

➢ Age Distribution:

Table 1: Age distribution for Magnex Forte

Age (years)	Number of patients	Percentage
10-19	00	0%
20-29	04	10%
30-39	03	7.5%
40-49	06	15%
50-59	10	25%
60-69	10	25%
70-79	07	17.5%

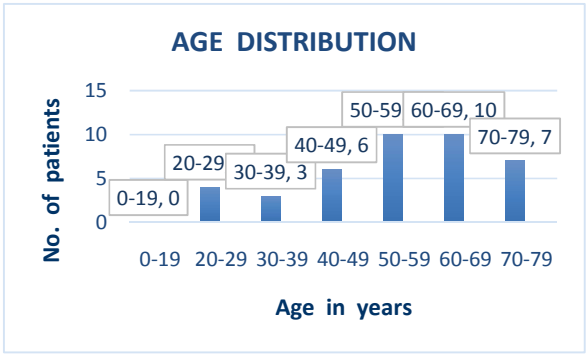


Fig 1: The higher number of patients were reported under age group 50-69 i.e., 50% of patients have been included here. Lowest number of patients were reported under age group 30-39 i.e., 7.5%

Table 2: Age distribution for Cepez–SB

Age in years	No. of patients	Percentage
10-19	01	2.5%
20-29	06	15%
30-39	07	17.5%
40-49	04	10%
50-59	09	22.5%
50-69	06	15%
70-79	07	17.5%

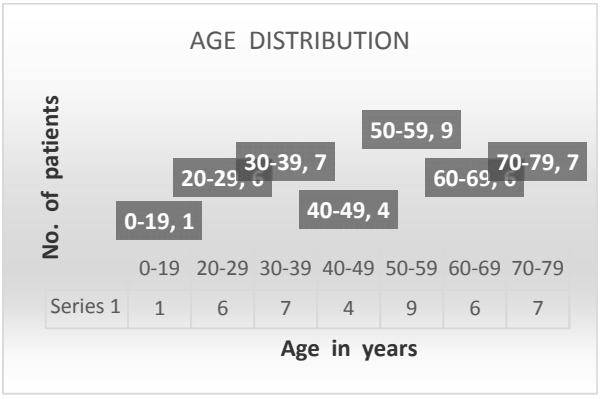


Fig 2: The highest number of patients receiving Cepez-SB have been reported under the age group of 50-59yrs i.e., 22.5% and lowest number of patients were reported under the age group 0-19yrs i.e., 2.5%

➢ Unit Cost of The Drug and Drug Cost Per Day

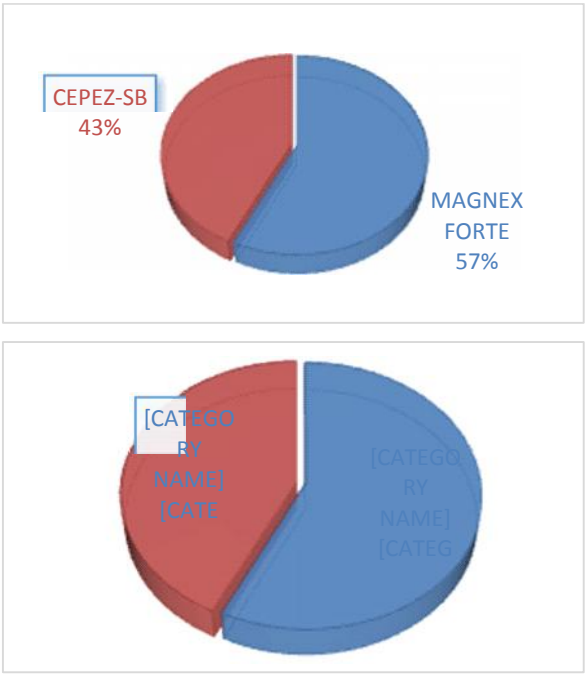


Fig 3: The unit cost of the drug for Magnex Forte is INR 603.00/- and for Cepez-SB is INR 450.00/- and the drug cost per day for Magnex Forte is INR 1206.00/- and for Cepez-SB is INR 900.00/-

Table 3: Distribution table based on total hospitalization days for Magnex Forte and Cepez-SB

Total no. of hospitalization days	Magnex Forte	Cepez-SB
2	5	3
3	10	12
4	7	5
5	7	2
6	7	7
7	2	4
8	2	6
9	0	1

Table 4: Comparision of Magnex Forte and Cepez-SB based on number of days drug given

Drug given	No. of patients	Mean no. of days drug given	Standard deviation
Magnex Forte	40	4.1	1.533
Cepez-SB	40	4.95	2.099

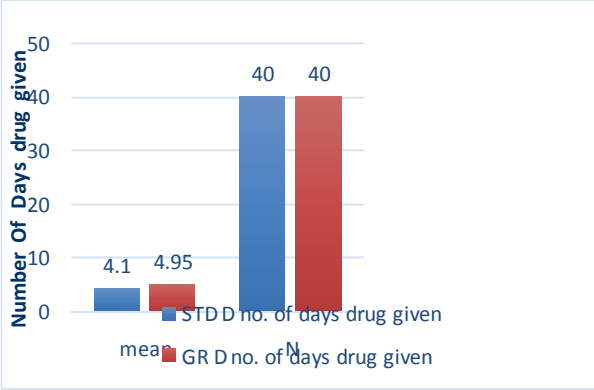


Fig 4: The mean number of days drug given for Magnex Forte is 4.1 days and for Cepez-SB is 4.95 days, there was a difference of approx. one day for both arms i.e., generic drug was prescribed a day higher than the branded drug

Table 4: Comparison of Magnex Forte and Cepez-SB based on total cost of the drug

Drug given	No. of patients	Mean total cost of drug	Standard deviation
Magnex Forte	40	4944.6	1848.259
Cepez-SB	40	4455	1889.505

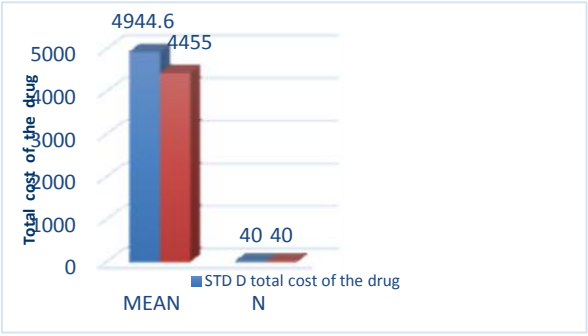


Fig 5: The total cost of drugs Magnex Forte and Cepez-SB is having difference approx. Rs 500/- that is INR 4944.6/- for MF and INR 4455.00/- for Cepez-SB

Table 5: Comparison of Magnex Forte and Cepez-SB based on based on symptoms subsided

Drug given	No. of patients	Mean	Standard deviation
Magnex Forte	40	3.98	1.441
Cepez SB	40	4.93	2.068

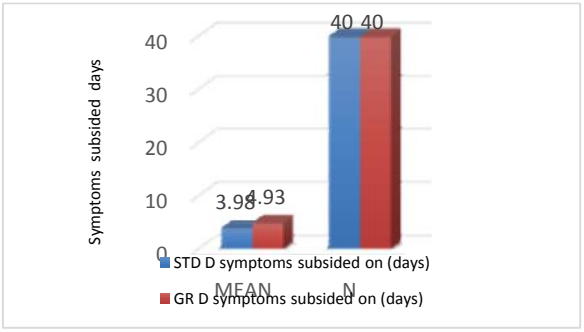


Fig 6: The average no. of days symptoms subsided between the Magnex Forte (brand) (3.98 days) and Cepez-SB (generic) (4.93 days) and is having difference of approx 1 day

Table 6: Comparison of Magnex Forte and Cepez-SB based on other costs of the drug

Drug given	No. of patients	Other cost of the drug	Standard deviation
Magnex Forte	40	23530.65	9127.448
Cepez SB	40	24907.95	13295.985

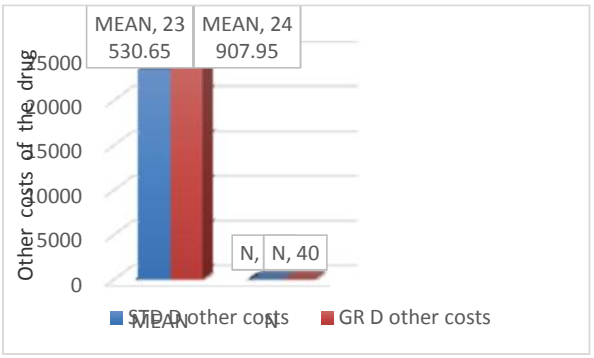


Fig 7: The other costs for Magnex Forte and Cepez-SB is having a difference of 1377.3 rupees difference i.e. 23530.65 for Magnex Forte and 24907.95 for Cepez-SB

Table 7: Comparision of Magnex Forte and Cepez-SB based on total hospital expenditure

Drug given	No. of patients	Mean total hospital expenditure	Standard deviation
Magnex forte	40	28474.53	10373.071
Cepez SB	40	29362.95	14886.503

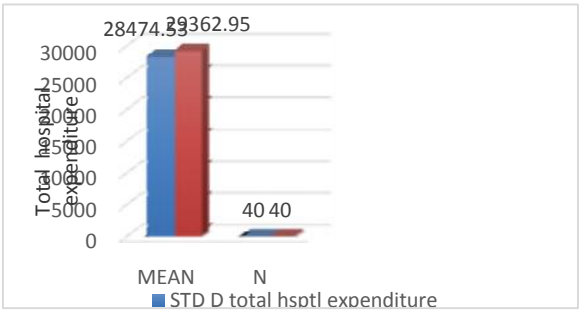


Fig 8: The total hospital expenditure of Magnex Forte and Cepez-SB is having approximately Rs1000/- difference that are INR 28474.53/- for Magnex Forte and INR 29362.95/- for Cepez-SB

Table 8: Side effects observed for both drugs

Drug given	Total no. of patients	Side effects observed	Side effects in no. of patients	Percentage
Magnex Forte	40	Nil	00	0%
Cepez-SB	40	Rashes	05	12.5%

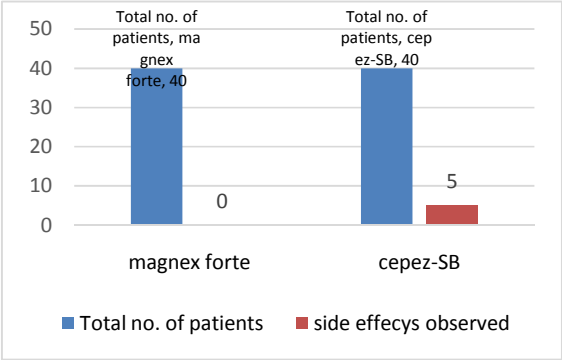


Fig 9: The side effects were reported for only generic drug in 5 random patients receiving Cepez-SB, Magnex Forte has shown nil side effects

4. DISCUSSION

India has one of the world's highest reported rates of bacterial resistance. For cephalosporin's, the most frequently used antimicrobials clinically, the emergence and prevalence of bacterial resistance, especially to the third generation cephalosporin's, has shifted the focus to the combination of β-lactam and β-lactamase inhibitors. The overuse of carbapenems and the subsequent increase in resistance to these drugs also warrants consideration of the role of the β-lactam and β-lactamase inhibitor combination. Cefoperazone/sulbactam is a conventional combination with activity against many pathogens and clinical efficacy in a variety of infections. Therefore, we selected Cefoperazone/sulbactam to consistently illustrate the cost and effectiveness between brand and generic forms.

Results demonstrated that Magnex Forte was superior to the Cepez-SB used in the study in all aspects and that it also had a better safety profile. In addition to its clinical advantage in treating acute gastroenteritis, also found that average drug cost per patient for the successfully treated population was lower in the Cepez-SB group, although there was no significant difference between the two treatment arms. The average number of days required for symptoms to subside is was one day longer for Cepez-SB but this is not very significant. Additionally, the study also found that the average cost of treatment per patient overall, was lower in the Magnex forte group than the Cepez-SB (but no significant difference was found in any of these cases). One of the limitations of the phamacoeconomic evaluation in the present study was the lack of inclusion of costs of alternative therapy in event of failure of study medication. In this study, we observed rashes in 5 patients who are on Cepez-SB (generic drug). Additionally, the ICER results showed that the cost of treating a patient with Magnex Forte was over INR 935.17/- less per additional successfully treated patient.

In year 2016, a study was conducted by koomanachai P, Tongsai S, Thamlikitkul V, on Effectiveness and Safety of Generic Formulation of Cefoperazone/Sulbactam (Bacticep) in Treatment of Infections at Siriraj Hospital. In this article two hundred twenty nine hospitalized patients who had infections and received original or generic cefoperazone sulbactam were included. Baseline characteristics and clinical features of infections in both groups were comparable. Favorable outcomes (72.9% vs. 72.2%) and infection-related deaths (4.7% vs. 11.1%) between generic cefoperazone/sulbactam group and original cefoperazone/sulbactam group, respectively, were not significantly different. No significant differences in adverse events were observed between groups. This article conclude that the Generic cefoperazone/sulbactam (Bacticep) was found to be non-inferior to original cefoperazone/sulbactam for therapy of infections in hospitalized patients at Siriraj Hospital. Similarly, in our current study results demonstrated that brand drug was superior to generic drug in all aspects and has better safety profile but, there is no much significant difference between the two drug arms.

In India, where the current health-care system requires patients to "self-pay" for their treatments, and therefore prescribers are sensitive to prices, it is important for a treatment to show a pharmacoeconomic advantage. Magnex forte (brand form) had more effective therapy and a lower overall average cost of treatment per patient when compared to the Cepez-SB (generic form). Though this difference was not significant, it reflects a trend in costs. With emerging privatized health care in India, the results will have considerable impact on how hospital groups may decide to purchase medications for patients. It will be important to consider not only the drug acquisition costs when making a treatment decision, but to consider the lower overall treatment cost when treating patients with acute Gastroenteritis.

5. CONCLUSION

In this study, at baseline, 80 patients were randomized to treatment in the study with 80 patients in the Magnex forte arm and 40 patients in the Cepez-SB arm. Results demonstrated that Magnex forte (brand form) was superior to the Cepez-SB (generic form) used in the study in all aspects and that it also had a better safety profile. In conclusion, the use of generic drugs could be related with an increased days of disease or might lead to a therapeutic failure; on the other hand, a higher drug concentration might expose

patients to an increased risk of dose-dependent side-effects. Overall, it is advisable to well evaluate the effects of generic formulations during the therapeutic treatment. As the science is still in its nascent stage, more pharmacoeconomic work will be necessary to establish sound methodologies in the Indian health-care context.

6. ACKNOWLEDGEMENT

The authors wish to thank the management of School of Pharmacy, Anurag Group of Institutions, Venkatapur, Ghatkesar, Telangana, India and Global Hospital, Hyderabad, Telangana, India for providing necessary equipment for research, constant encouragement, facilities and support.

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Conflict of Interest: None

Source of Funding: Nil