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RESEARCH ARTICLE

Impact of antimicrobial stewardship program on prescribing pattern of cephalosporins in the department of surgery

Urvi Patel[1], Anuradha Sujai Joshi[2], Jaishree Ganjiwale[3], Barna Ganguly[2]

[1]Senior Drug Safety Physician, APCER Life Sciences, Ahmedabad, Gujarat, India, [2]Department of Pharmacology, Pramukhswami Medical College, Karamsad, Gujarat, India, [3]Department of Central Research Services, Pramukhswami Medical College, Karamsad, Gujarat, India

Correspondence to: Anuradha Sujai Joshi, E-mail: annuradhaj7@gmail.com

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ABSTRACT

Background: Cephalosporins are one of the widely prescribed antibiotics in clinical settings. Despite several years of its use, little is known about their prescribing pattern, especially in reference to antimicrobial stewardship program (ASP). **Aims and Objectives:** Evaluation of cephalosporin prescribing pattern, prior to and after implementation of ASP. **Materials and Methods:** This was an observational study on both prospective and retrospective data from surgery wards at a tertiary care teaching hospital. Data were collected from surgery case files and analyzed for demographic details, cephalosporin prescribing pattern, and its appropriateness in relation to ASP. **Results:** Data were selected from a total of 300 surgery case files (n = 150 each of year 2012 and 2014). Overall, there were 68% of male and 32% of female patients. Cephalosporins were prescribed, generation wise, i.e., the 1st generation in 34.7%, the 2nd in 1.3%, the 3rd in 63.3%, and the 4th in 0.7%, in 2012, while in 2014, they were prescribed as follows: 55.3% (1st), 0.7% (2nd), 44% (3rd), and 0.0% (4th). In 2012, various types of treatments were advocated consisting of cephalosporins, i.e., 73.3% (prophylactic), 26.7% (empirical), while none were rendered definitive treatment. In 2014, 91.3% of patients were treated prophylactically, 6.7% were treated empirically, and 2.0% were on definitive therapy. About 77.3% of patients were switched over from parental to oral in 2012 while 78% in 2014. The data revealed significant impact of ASP ($P < 0.05$), in terms of appropriate prescribing of cephalosporin's, i.e., 13.3% in 2014 and 6.7% in 2012, respectively. **Conclusion:** Successful implementation of ASP can improve antibiotic prescribing in clinical practice.

KEY WORDS: Cephalosporins; Antimicrobial Stewardship Program; Surgery

INTRODUCTION

Antibiotics are one of the most commonly prescribed medications both in community and hospital settings. Overuse, misuse, and inappropriate prescribing of antibiotics have resulted in emergence of drug-resistant strains which represent a major public health problem.[1] Antimicrobial resistance is a grave global public health concern and has escalated in recent past.[2] In context to this, there has been an acceleration in resistance to one of highly efficacious and frequently used antibiotic, i.e., cephalosporins.[3,4] Wide availability of various formulations of cephalosporins and its generations with their expanded indications has a major impact on prescribing patterns in hospital and community practice.[3] Various studies demonstrate an association between inappropriate cephalosporin's use and emergence of multiple antibiotic resistant organism, for example, *Klebsiella*, *Escherichia coli,* and *Proteus mirabilis*.[5-8]

Studies on prescribing pattern of antibiotics reveal that treatment should be scrutinized at international, national,

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regional, and institutional levels. Efforts should be undertaken to implement antimicrobial stewardship program (ASP) in hospital settings.[9] ASP deals with systematic approach to optimize use of antimicrobials in terms of dose, route, and duration of antimicrobial drugs and streamlining of antibiotic policies.[9]

There seems to be abundant and growing body of evidence demonstrating that ASPs decrease the quantity and improve the quality of antimicrobial prescriptions in both academic and community hospitals, but somehow the measurement of their impact on patient outcomes and antimicrobial resistance has been difficult to find.[10] There are lot of studies on the use of cephalosporins by clinicians, but little is known about its prescription pattern and rational use, especially in context to ASP.[11] This study is an effort to find the prescribing pattern of cephalosporins and also to evaluate the impact of ASP in patients admitted to surgical wards.

MATERIALS AND METHODS

The study protocol was approved by the Institutional Ethics Committee (Ref no. HMPCMCE: HREC/UGPG/23/Session 1/9) before conducting the study and written, informed consent was obtained from patients in their vernacular language. They were explained about the purpose and nature of research study. This was an observational study on both prospective and retrospective data from surgery wards.

A total of 300 case files of patients admitted in surgery wards were included in the study. Out of these, 150 case files were from 2012 to 2014 each, i.e., before and after implementation of ASP (which was in 2013). Hospital numbers of admitted patients who were prescribed "cephalosporin's" during the years 2012 and 2014 in surgery wards were retrieved from "system" department month wise and from each month. Retrospective data were retrieved from the case files of patients admitted in the year 2012 available in medical record section of the hospital; prospective data were collected from the case files of patients admitted in the year 2014. All the case files which were collected, fulfilled the inclusion criteria i.e. all patients who were prescribed, cephalosporin's as one of the first line antibiotic therapy during their hospitalization period in surgery wards. Case files of patients were evaluated for various details as follows: Demographic details, disease conditions, comorbidities, culture sensitivity tests, types of surgery and surgical wounds, details of cephalosporin prescribing in terms of choice of individual drug, dose, frequency and duration, type/s of treatment (prophylactic, empirical, and definitive), escalation and de-escalation of drugs, switchover from parenteral to oral cephalosporin's with their regimen, other concomitant antimicrobial drugs prescribed, and total duration of hospitalization.

All mentioned data from 2012 were compared to that of 2014 with reference to ASP for their appropriateness and change in prescribing pattern. Data were entered into Microsoft Excel 2007, and analysis was done. Descriptive statistics in terms of frequency and percentages were used for variables such as demographic profile, disease conditions, and cephalosporin's prescribing patterns and Chi-square test was applied to compare the prescribing pattern of various cephalosporin drugs and its generations and appropriateness of treatment, pre- and post-implementation of ASP in terms of choice of individual drug, dose, frequency, and duration, type/s of treatment (prophylactic, empirical, and definitive), and switchover from parenteral to oral cephalosporin's with their regimen. Results were considered as significant if $P < 0.05$.

RESULTS

As depicted in demographic profile in Table 1, patients were divided into three age groups as follows: 0–18 years, 19–50 years, and >50 years, respectively. Overall, there were 68% of male and 32% of female patients in both the years. The details of the given parameters are mentioned in Table 1. In the given study, in both the years, majority of the patients, i.e., 65 (43.3%) patients were suffering from gastrointestinal (GI) disease conditions such as appendicitis, gastric perforation, intestinal obstruction, and cholecystitis, 39 (26%) from trauma, and infections 4 (2.7%) in 2012, while in 2014, the indices showed that 34 (22.7%) of the patients suffered from GI conditions, 59 (39.3%) from trauma, and 7 (4.7%) patients were suffering from infections, respectively [Figure 1]. Distribution of the types of surgeries performed and various types of surgical wounds are given in Figure 2.

Overall, distribution of prescribing pattern of cephalosporin's in terms of its generations in 2012 was as follows: The 1st generation in 52 (34.7%), the 2nd in 2 (1.3%), the 3rd in 95 (63.3%), and the 4th generation in 1 (0.7%), while the distribution of cephalosporin's, according to its generation, in 2014, was as follows: 83 (55.3%) in the 1st generation, 1 (0.7%) in the 2nd, and 66 (44%) in the 3rd generation [Figure 3]. On comparative analysis in between both the years, it was found that there was a rise in cefazolin prescriptions from 32.7% to 53.3% while there was a drop in ceftriaxone prescriptions from 60% to 39.3% in 2012–2014.

Table 1: Details of demographic profile of admitted patients

Demographic details	Number of patients (%)	
	Year 2012	Year 2014
Age distribution (years)		
0–18	15 (10)	18 (12)
19–50	84 (56)	95 (63.3)
>50	51 (34)	37 (24.7)
Number of male/female	102 (68)/48 (32)	102 (68)/48 (32)

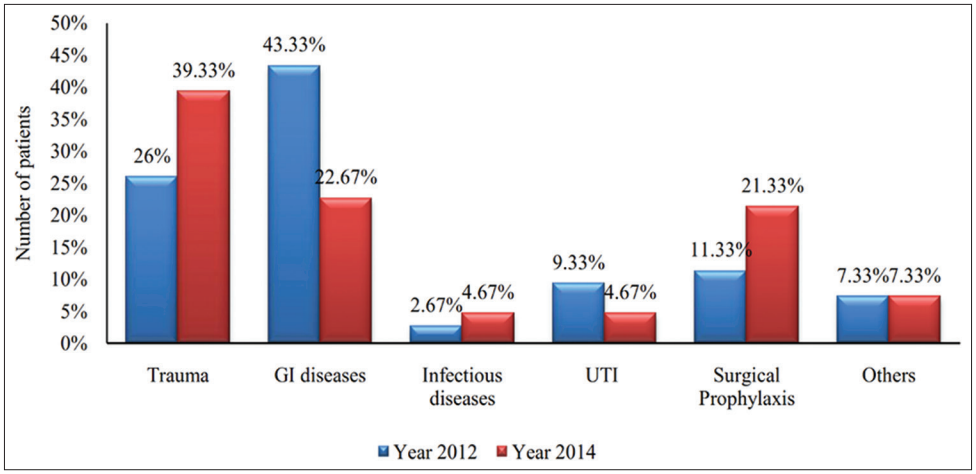

Figure 1: Distribution of disease conditions for which patients were admitted in the surgery department in 2012 and 2014

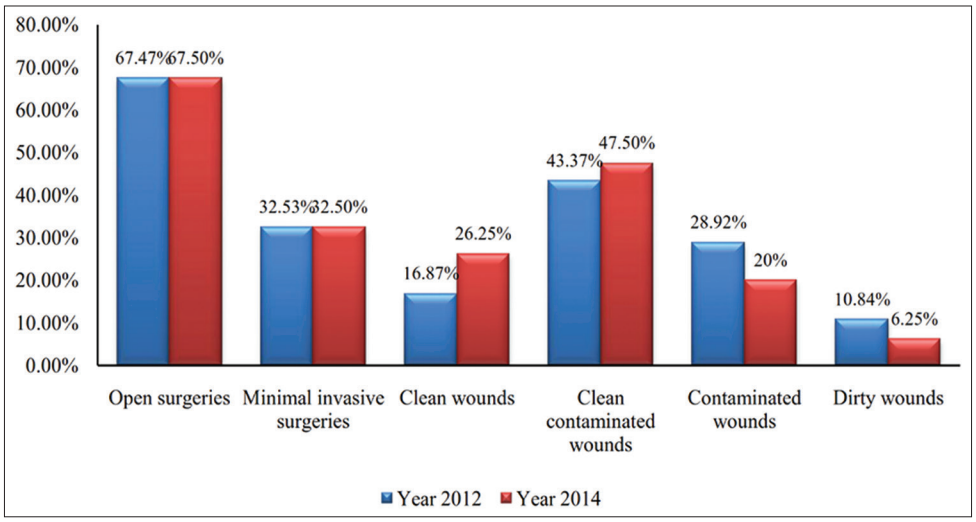

Figure 2: Distribution of various types of surgeries performed and types of surgical wounds

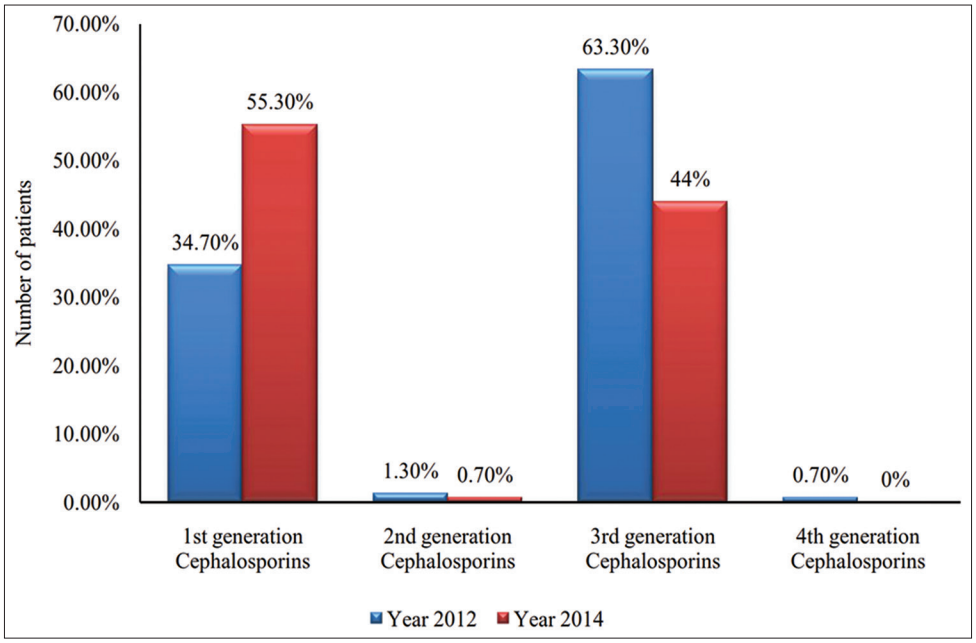

Figure 3: Generation wise distribution of cephalosporins and other details of drugs

In both the years, 145 (96.7%) cephalosporins were prescribed by generic name and only 5 (3.3%) cephalosporins were prescribed by brand name. Regarding to the route of administration, most of cephalosporins were administered

by intravenous route. In 2012, 145 (96.7%) patients were prescribed intravenous cephalosporin's and 5 (3.3%) patients were on oral cephalosporin's while in 2014, 147 (98%) patients were on intravenous cephalosporin's and only 3 (2%) patients were on oral cephalosporin's.

Overall treatment was categorized into three main groups, i.e., prophylactic, empirical, and definitive, respectively. On comparison in between the 2 years, the data revealed that, in 2012, 110 (73.3%) patients were advocated prophylactic treatment, 40 (26.7%) patients were managed with empirical treatment, while none were on definitive treatment while in 2014, 137 (91.3%) patients were on prophylactic treatment, 10 (6.7%) patients were managed by empirical therapy, whereas 3 (2%) patients were managed by definitive therapy.

In regard to appropriateness of prophylactic and empirical treatment in terms of choice, dose, frequency, duration, and overall use, the data highlight that there were significant changes in appropriateness of prophylactic treatment, as shown in Tables 2 and 3.

Switchover from parenteral to oral cephalosporin's was initiated in 116 (77.3%) cases in 2012 while in 2014, switchover was done in 117 (78%) cases. In context to this, in both the years, among oral cephalosporins, cefixime was maximally prescribed, i.e., 74 (63.8%) in 2012 and 59 (50.4%) in 2014, cefadroxil 36 (31%) in 2012, and 58 (49.6%) in 2014, and cefuroxime axetil 6 (5.2%) in 2012, and none in 2014. Regarding appropriateness of oral cephalosporins in 2012, 102 (87.9%) drugs were choice wise appropriate while in 2014, 110 (94%) drugs were choice wise appropriate. Whereas in terms of regimen in 2012, 37 (31.9%) drugs were appropriate while in 2014, 30 (25.6%) drugs were appropriately prescribed. It was observed that 10 (6.7%) patients were treated appropriately in 2012, while 20 (13.3%) patients were treated appropriately in 2014 ($P = 0.042$). Mean hospitalization stay of patients was 6.20 days in 2012 while 5.47 days in 2014.

Table 2: Prophylactic treatment and their appropriateness in terms of various parameters mentioned in table. All the parameters were compared with the antimicrobial stewardship program guidelines of our hospital

Variables	Appropriate drugs (%)		*P* value
	Year 2012 (*n*=110 [73.3])	Year 2014 (*n*=137 [91.3])	
Choice	97 (88.2)	125 (91.2)	0.428
Dose	107 (97.2)	135 (98.5)	0.475
Frequency	110 (100)	130 (94.9)	0.016*
Duration	44 (40)	33 (24.1)	0.007*
Overall	40 (36.4)	20 (14.6)	<0.0001*

**P* value statistically significant

Table 3: Empirical treatment and their appropriateness in terms of various parameters mentioned in table. All the parameters were compared with the antimicrobial stewardship program guidelines of our hospital

Variables	Appropriate drugs		*P* value
	Year 2012 (*n*=40 [26.7%])	Year 2014 (*n*=10 [6.7%])	
Choice	37	10	0.372
Dose	39	10	0.614
Frequency	40	10	-
Duration	11	1	0.246
Overall	9	1	0.377

DISCUSSION

Cephalosporins are broad-spectrum antimicrobial agents that are often used empirically to treat suspected bacterial infections and also to treat culture-proven infections due to selected Gram-positive and Gram-negative microorganisms.[12] They differ widely in their spectrum of activity, susceptibility to beta-lactamases, serum half-life, and penetration of the central nervous system. In general, the 1st generation and the 2nd generation agents are most active against staphylococci and streptococci, and the 3rd generation agents are most active against the *Enterobacteriaceae* and *Pseudomonas*. Maintaining expertise in the choice and use of these agents will remain a challenge to physicians as additional investigational cephalosporins continue to be developed and introduced into clinical practice. Since during the past decade, there has been an acceleration in resistance to antibiotics, especially cephalosporins, and various studies demonstrate an association between inappropriate cephalosporins use and emergence of multiple antibiotic-resistant organism.[5,6] ASPs involve systematic approach to optimize the use of antimicrobials in terms of dose, route, and duration of antimicrobial drugs. Cephalosporins are one of the most widely used class of antibiotics in health-care settings.[13,14] In the current study, after evaluating cephalosporin prescribing pattern in details, it was found that there was an increase in appropriateness of treatment from 6% in 2012 to 13.8% in 2014 which is statistically significant ($P < 0.05$). In this study, majority of the patients fell in the age group between 19 and 50 years in both the years, i.e., 56% in 2012 and 63.3% in 2014. This is in line with the study conducted by Shankar *et al*., wherein 50.8% of patients fell between the age groups of 20 and 60 years.[3] Although cephalosporins seem to possess an undoubted popularity in all age groups in our study, the most common reason for majority of patients being prescribed cephalosporins, in 19–50 years age group, was mainly due to majority of patients being admitted for different types of surgeries.

In the current study, the most common disease conditions, for which cephalosporins were prescribed in inpatients, were GI conditions, i.e., 43.3% of cases, trauma in 26% of cases, and infections in 2.7% in 2012 while in 2014, GI conditions in 22.7% of cases, trauma in 39.3% of cases, and infections in 4.7% of cases. Reason is broader spectrum antimicrobial activity of cephalosporins.[15,16] The prescribing pattern of cephalosporins and its generations in 2012 was the 1st generation in 34.7% of cases, the 2nd in 1.3% of cases, the 3rd in 63.3% of cases, and the 4th generation in 0.7% of cases, while, in 2014, the 1st generation in 55.3% of cases, the 2nd in 0.7% of cases, and the 3rd in 44% of cases, respectively. Hence, as evident, here, the 3rd generation cephalosporins were maximally prescribed. Furthermore, a higher prescribing of the 3rd generation cephalosporins 81.56% in urban population was observed in a study conducted by Satravanan and Muthukumar.[17] Furthermore, one of the prospective observational studies on the use of antibiotics at an emergency department in tertiary care hospital conducted by Mamatha *et al*. stated that cephalosporins (54.3%) were one of the most commonly prescribed antibiotics in their hospital.[13] Further, their study also revealed that practice toward polypharmacy and antibiotic prescribing was frequent in the emergency department. Hence, there is a strong need for guidelines and protocol for the use of antibiotics in the emergency departments. Here, in our study, following initiation of ASP interventions in 2013, the use of the 3rd generation cephalosporins declined in subsequent year. Similar finding is supported by a study conducted by Cairns *et al*. found a 10.9% decline in the use of the 3rd and 4th generation cephalosporins after implementation of ASP.[15] The current findings of our study imply that clinicians are gradually abiding with the ASP guidelines.

In the present study, individually, drug wise, the most common drug prescribed among cephalosporins was ceftriaxone in both years, i.e., 60% of cases in 2012 while 39.3% of cases in 2014, respectively. This is similar to the study conducted by Salah, wherein 55% ceftriaxone was used.[18] More use of ceftriaxone might be due to its broad spectrum of antimicrobial activity, good pharmacokinetic/pharmacodynamics profile, and efficacy which influences clinicians' preference for the selection of antibiotics.[19]

According to the current study, more parenteral cephalosporins were used in 2014 as compared to 2012. This might be attributed to various advantages of parental cephalosporins as they are faster acting, can be administered in unconscious patients, post-operative, and dysphagic patients. Although ceftriaxone has many advantages over other antimicrobials, its overuse should be discouraged because it is one of the restricted antibiotics and its overuse can be an implication in emergence of multidrug-resistant Gram-positive and Gram-negative microorganisms.[20] Switchover from parenteral to oral cephalosporins was done in 77.3% of cases in 2012 while in 2014, switchover was done in 78% of cases. There was a significant increase in the use of cefadroxil and decrease in the use of cefixime, after switchover, in 2014. Since early switchover from parenteral to oral route in case of antibiotics is one of the key recommendations in ASP and a major determinant in safe antimicrobial prescribing, the findings of our study are an evidence that clinicians are careful in prescribing cephalosporins in terms of switchover of drugs.[9,21]

In this study, majority of patients were treated with prophylactic treatment in both the years, i.e., 73.3% of cases in 2012 while in 2014 in 91.3% of cases. The reason could be prevention of treatment failure, transmission of secondary infections, and longer hospitalization stay. The findings also revealed that choice and dose wise appropriateness of prophylactic treatment improved in 2014 while other parameters did not show any improvement ($P < 0.05$). In context to this, there are certain confounders need to be kept in mind such as patients' immune status, the infecting agent, and nature of surgery performed while optimizing prophylactic treatment for patients. Although we encountered less number of data for definitive treatment 2% in 2014, the findings conclude that there was a gradual improvement in the use of definitive treatment subsequent to implementation of ASP, which shows gradual streamlining of modes of therapy by the clinicians in accordance with ASP guidelines.

In the current study, the impact of ASP on prescribing pattern of cephalosporins was 13.3% in 2014. This is comparable with the Cochrane review conducted by Davey *et al*. found that change in prescribing of antibiotics after 1 year of implementation of ASP ranges from 3.5% to 42.5%.[22]

Furthermore, these findings tally with a study conducted by Borde *et al*. which concluded that an intensified ASP targeting cephalosporin use in the setting of a large academic hospital is an effective intervention[23] and a systemic review conducted by Kaki *et al*. which mentioned that ASP is associated with improved antimicrobial utilization without compromising the short-term clinical outcomes.[24] Finally, in the current study, overall, after evaluation of cephalosporin prescribing pattern in between the 2 years, i.e., 2012 and 2014, it was concluded that there was an increase in appropriateness of treatment from 6% in 2012 to 13.8% in 2014 which is statistically significant ($P < 0.05$).

Strength and Limitations of this Study

- Overall, after evaluation of cephalosporin prescribing pattern, it was concluded that there was a statistically significant increase in appropriateness of treatment from 6% to 13.8% in the 2 years, respectively. These data, in turn, will be useful for updating current ASP guidelines and ensuring successful adherence of ASP by clinicians
- At our hospital, ASP has been found to be one of the several initiatives in the health-care policy programs and has been identified as one of the important strategies to

ensure proper use of antimicrobials. Thus, comprehensive ASPs have demonstrated an overall reduction in antimicrobial use, institutional antimicrobial resistance rates, and hospital pharmacy expenditures associated with health care

- The study was conducted in a tertiary care rural teaching hospital with relatively small number of patients which may allow bias of the given population
- Outdoor patients and ICU patients were excluded from this study. Data regarding total data of cephalosporins purchased in individual departments in 2012 were not available, so, due to feasibility issues defined daily dose of cephalosporins for 2012 as well as 2014 could not be calculated. Limitations as these do not under estimate the importance and the value of key findings of our study
- Long-term and more extensive studies of this type will be helpful in identifying the merits and demerits of ASP for rational use of cephalosporins.

CONCLUSION

The current study has provided a baseline information regarding appropriateness of prescribing pattern of cephalosporins in reference to ASP, in terms of indications and appropriateness. ASP can be a helpful tool for the health-care institutions to reduce inappropriate antimicrobial use, improve patient outcomes in terms of morbidity and mortality, and reduce adverse consequences of antimicrobial use. Health-care professionals, especially clinicians, need to adhere to ASP guidelines for preserving the effectiveness of the current antimicrobials, especially in context to cephalosporins.

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