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Evaluation of Intravenous to Oral Antibiotic Switch Therapy

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ABSTRACT

Antimicrobials use depends on the selection of an agent capable to target the presumed organism at the site of infection with an acceptable safety profile. Hospitalized patients on intravenous therapy can be switched to oral medications once clinical stability is met. Clinical condition decides the necessity of switch. The aim is to study the antibiotic switch between intravenous and oral formulations. This was an observational study conducted in a tertiary care hospital over six months where patients prescribed intravenous antibiotics were included. The study comprises 323 patients where 46.44% were found to be switched while the remaining 53.56% were non-switched. The three types of switching done from intravenous to oral route include a sequential, switch, and step-down therapy. Among them, step-down therapy (42.46%) was the commonly observed type of switch. The mean duration of intravenous to oral switch was found to be 5.253±2.54 days. Similar percentages of switching were observed in both empirical and definitive therapy. The decision to switch was purely from a clinical point of view. This study emphasizes the need for appropriate guidelines and the concept of switching not only reduces the duration of intravenous therapy but also prevents resistance thereby promoting the rational use of antibiotics.

INTRODUCTION:

The discovery of antibiotics has revolutionized medicine in many aspects and innumerable lives have been saved over the century. However, antibiotics use has drastically increased over the past years. The majority of the patients are initially prescribed intravenous antibiotics upon hospitalization, but the most convenient and safest method of medication administration is achieved by the oral route.[1]However, when the antibiotics are used in the wrong way it can lead to little benefits and more side effects. [2]

One of the strategies by which the rational use of antibiotics could be improved is by switching it at the correct time. [3,-5]Switch therapy can be described as an early transition from parenteral to non-parenteral therapy. In our study, we focus on the switch from parenteral to oral therapy. Antibiotics may be switched over from intravenous to the oral route as soon as the patients are clinically stable. The type of this conversion may be a "Sequential therapy", "Switch therapy" or "Step-down therapy". Sequential therapy is the conversion from an intravenous to an oral agent with the same compound; for example, conversion of intravenous Metronidazole to oral Metronidazole. Switch therapy is the conversion to an oral agent with identical potency; for example intravenous Ceftriaxone to oral cefixime. Step-down therapy is the conversion to an oral agent in another class; for example, conversion of intravenous cefotaxime to oral Ciprofloxacin. The choice of the type of switch depends on the antibiotics class and the availability of an oral equivalent. [3,5,6] Antibiotics such as Penicillins(amoxicillin), Macrolides (clindamycin), Tetracycline (doxycycline), Fluoroquinolones (Ciprofloxacin, levofloxacin), cephalosporins (Cefixime, Cefuroxime), Oxazolidinone (linezolid) and metronidazole have both intravenous and oral formulations. [3,7]

In most situations where the patient has developed some infection, antibiotic therapy must be initiated before determining the precise bacterial etiology of the infection. The choice of the antibiotic in such conditions is made empirically. The factors concerning the choice of the antibiotic include the site of infection, the wide range of possible pathogens, rising incidences of resistance, toxicity, and existing antibiotic policies. It is usually necessary to administer the antibiotic intravenously in seriously ill patients. Once the bacteriological etiology has been determined definitive antibiotic therapy can be continued either intravenously or if the patient's condition is stable then can be switched over to the oral route.

A switch from intravenous to oral therapy requires clinical judgment and is likely to depend on the individual patient.[1]While switching to oral therapy certain criteria are to be considered. There should be evidence of clinical improvement, afebrile nature (>24hours), normal pulse and respiratory rate, normal WBC counts, improvement in signs and symptoms and should be able to tolerate oral medications (no GI absorption problem). [8,9]

The timely transition from intravenous to oral therapy is necessary. Most candidates on intravenous therapy are eligible to switch to an oral antibiotic within 2-3 days of therapy. However, in conditions where the patient displays no signs of improvement, not able to tolerate oral therapy, or when a prolonged course of intravenous therapy is essential, then the clinicians have to continue the intravenous course of the therapy as necessary. [5] Hence there also lie certain exceptions in the switching of antibiotics from the clinical point of view.

In this era of no new antibiotics, it is necessary to protect the existing antibiotics and one way to prevent its misuse to avoid overuse is by switching over at the appropriate time. The aim is to study the type of antibiotic switch therapy between intravenous and oral formulations and to evaluate the duration and definitive use of antibiotics between intravenous and oral switch therapy.

MATERIALS AND METHODS:

Study Design and Study Population:

This is a prospective observational study carried out for six months in PSG Hospitals. The patient's information was collected from the case files after obtaining informed consent. All hospitalized patients receiving intravenous antibiotics were screened for this study. The study was approved by the Institutional Ethics Committee (IHEC-PSG IMST 19/004).

Inclusion Criteria:

Both male and female patients above 12 years, all patients prescribed intravenous antibiotics were included in the study.

Exclusion Criteria:

Patients receiving other routes of antibiotic except intravenous and oralandthose who are not willing to participate in the study were excluded from the study.

Outcome:

The primary outcome is to identify the type of switch used in the antibiotic class when a switch was made. The secondary outcome is to evaluate the duration and the definitive use of antibiotics between intravenous and oral switch therapy.

Study Procedure:

The study was conducted in two wards at PSG Hospitals. Patients were included in the study based on the inclusion and exclusion criteria. A data collection form was prepared and data was collected during the ward rounds by analyzing the case files. The data collected include age, sex, date of admission and date of discharge, diagnosis, prescribed antibiotics, duration of antibiotic therapy, intravenous site infection, and vital signs. Following the data collected, the type of switch, the duration of intravenous therapy, and the empirical/definitive therapy were assessed. The documentation and analysis of data were done by us.

Statistical Analysis:

Statistical analysis was performed using the Statistical Package for the Social Science software (SPSS version 20.0). Simple descriptive statistics including percentages, frequencies for categorical variables, and mean± standard deviation for continuous variables were used.

The 2 groups of patients (i.e. switched and non-switched) were compared for statistically significant differences using the chi-square test for empirical/definitive therapy. A P-value of ≤0.005 was considered statistically significant.

RESULTS AND DISCUSSION:

RESULTS:

The study was performed for over six months. A total of 323 patients who were prescribed intravenous antibiotics upon hospital administration were included in the study. An overall gender distribution shows 66.56% (n=215) males and 33.44% (n=108) females of which 44.18% (n=95) of males were switched and 50% (n=54) of females were switched.Age distribution shows 0.6% (n=2) of pediatric population, 79.2% (n=256) of adult population and 20.1% (n=65) of geriatric population. 47.2% (n=121) patients of the adult population were switched and 43% (n=28) patients of the geriatric population were switched.

The antibiotic classes that were prescribed include cephalosporin 43.5%, penicillin 16.3%, carbapenems9.1%, fluoroquinolones7.6%, macrolides 6.1%, lincosamides 4.6%, glycopeptides 1.6%, aminoglycosides 1.4%, oxalidinones0.6%, tetracyclines0.2% and metronidazole 8.4%. One way ANOVA was performed for antibiotic class with switch and more number of switches occurred in the antibiotic class cephalosporin followed by Penicillin ($p<0.05$).

Out of the total 323 patients, 46.44% (n=149) patients were found to be switched, while remaining 53.56% (n=174) were non-switched. The 149 switched patients received 179 intravenous antibiotics and of the switches done sequential, switch & stepdown therapy accounted for 34.07% (n=61), 23.46% (n=42) & 42.46% (n=76) respectively.

The most commonly observed type of switch over was step down therapy. The most switched antibiotic in sequential therapy was metronidazole (37.7%), in switch therapy was cephalosporins (92.8%) and in step-down therapy was cephalosporins (50%).

The combined use of intravenous and oral therapy:

Of the 323 patients receiving intravenous antibiotics, a total of 149 patients were switched and 174 patients were not switched. However, 97 of the patients had received oral therapy along with intravenous antibiotics. The ability to tolerate oral medicines was one of the criteria in switching, yet 97 (30.03%) patients received intravenous along with oral therapy, which proves there is no presence of gastro-intestinal absorption problem in those patients. Of these 97 patients, only 27.83% (n=27) were switched and the rest 72.13% (n=70) were non-switched.

Duration of Antibiotic:

The total mean duration of intravenous antibiotics for switched and non-switched patients was 5.69±2.99 days. Student t-test was performed and results showed there is no statistically significant difference between switched and non-switched groups concerning the duration of intravenous antibiotics. Thus switching happened in less than no days and the switched group has a lesser duration of intravenous therapy than the non-switched group.

The mean duration for the antibiotic switch was found to be 5.253±2.54 days. The mean duration of intravenous therapy was 5.253 days after which it was switched to an oral route and the mean duration of the oral therapy was 5.471 days. Maximum numbers of switches

from intravenous to oral antibiotics were done on day 3 and the switch occurred to a maximum of day 10.

The mean duration for the antibiotic switch was found to be 4.983±2.25 days for sequential therapy, 4.7±2.03 days for switch therapy, and 5.78±2.92 days for step-down therapy. A one-way ANOVA test was done and results revealed that there is no statistical difference between the three types of the switch concerning the duration for the switch.

Table No. 1: Mean duration of switch over taking place for the different types of switch

Type of switch	Mean duration of therapy (Days)
Sequential	4.98
Switch	4.7
Stepdown	5.78

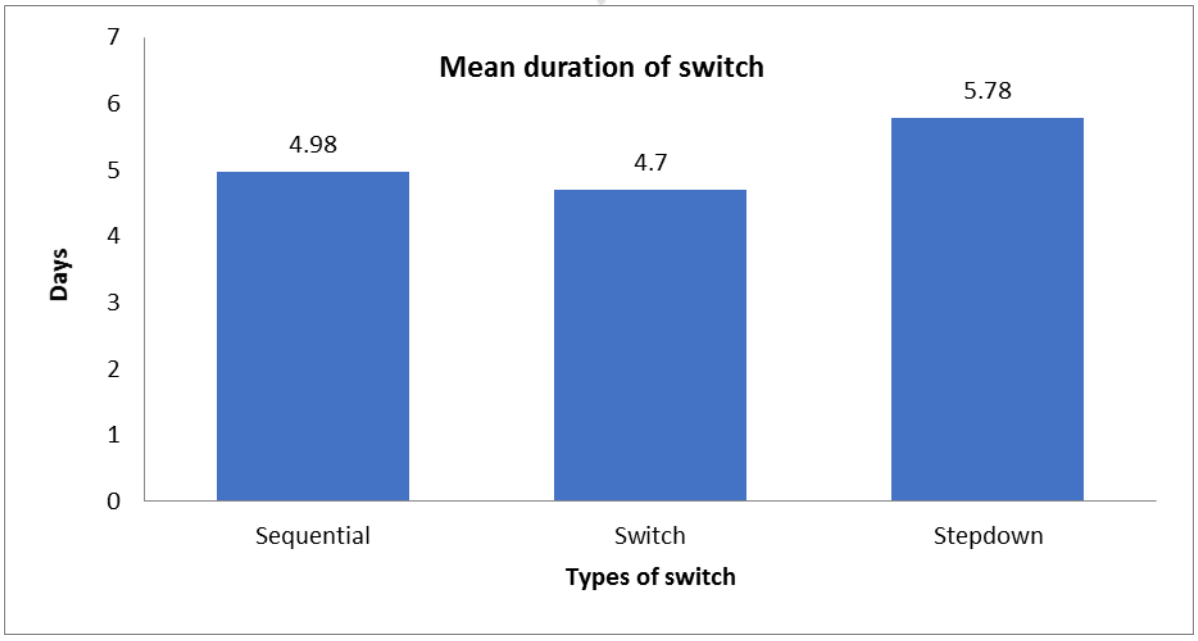

Figure No. 1: Mean duration of a switch for sequential, switch, and step-down therapy

Definitive Therapy:

In our study, a total of 108 patients had positive culture and were given definitive therapy whereas the remaining 215 patients were continued on empirical therapy.47.20% of the definitive therapy was switched and 46% of the empirical therapy was switched.

Chi-square test was performed and showed that there is a statistically significant association ($p<0.005$) between empirical and definitive therapy concerning the frequency of switch from intravenous to oral antibiotics. Thus definitive therapy has more number switches than empirical therapy.

Table No. 2: Percentage of the switch in empirical and definitive therapy

	Switched(%)	Non-switched(%)
Empirical	46	54
Definitive	47.2	52.8

Significance level, $p<0.005$

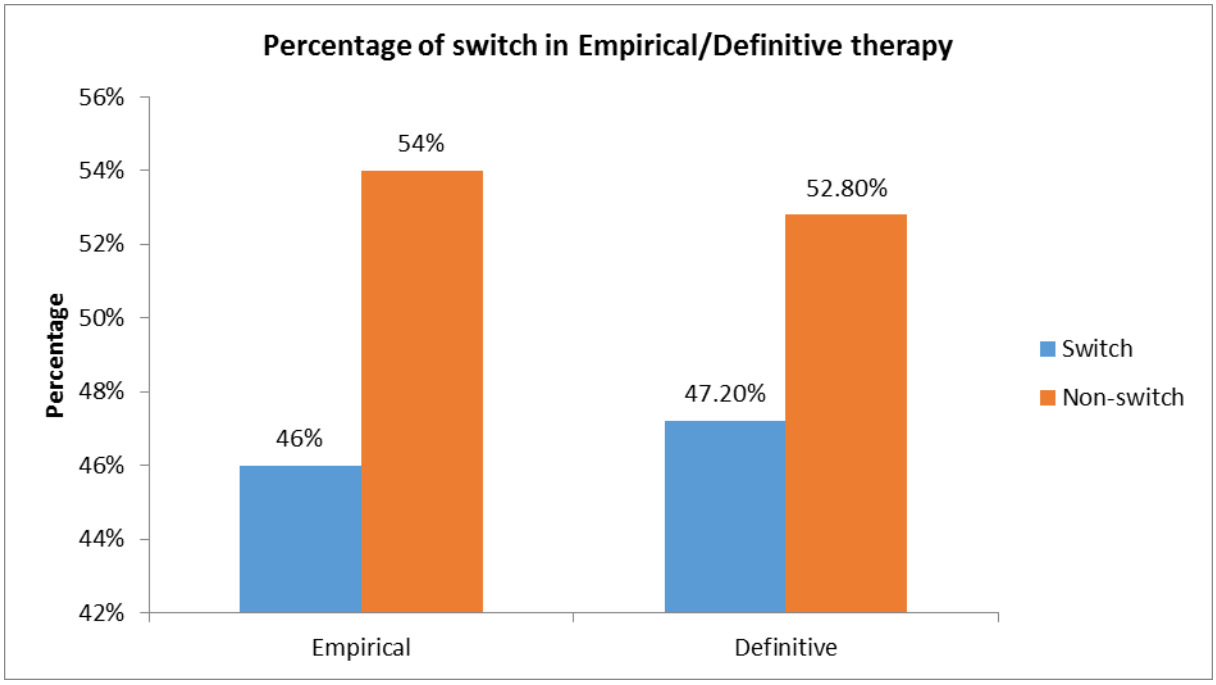

Figure No. 2: Percentage of Switch in Empirical/Definitive Therapy

DISCUSSION:

The study was done to aid in switching from intravenous to oral medications in the hospital set up. The concept of switching is not so common in Indian hospitals [9], and our study is an observational one done to know the practice of switching in a tertiary care hospital.

Patients prescribed intravenous antibiotics were enrolled in the study. The intravenously administered antibiotics were either switched to a suitable oral formulation or continued intravenously. Administered intravenous antibiotics available in the same oral formulation

involved mostly penicillin, cephalosporins, fluoroquinolones, and metronidazole where sequential switch therapy was used. Whereas for antibiotics with no equivalent oral formulations available, switching over was done through switching to a different drug or different class of antibiotic. Ceftriaxone with no oral equivalent, the modification was done through switch therapy (switched to cefuroxime/cefpodoxime) or step down therapy (switched to fluoroquinolones/linezolid/doxycycline). Step-down therapy was the commonly practiced switch over in this study followed by sequential therapy. Whereas in a study done by Tejaswini[3] sequential therapy was the common type of switch.

The percentage of switch therapy and the mean duration of oral therapy were similar to the study of Tejashwini. [3]The mean duration in the present study is 6, similar to that of the Mertz-control phase [4] and close to the study by Bertussa[8] which was 7 days. In this study, the mean duration of intravenous therapy in the switched group was the same as the non-switched group during the hospital stay similar to the study done by Shrayteh, *et al.* [5]

Once the culture reports are available, the intravenous medication can be changed into an oral formulation with potency equal to that of an intravenous drug. [6]The evaluation of empirical and definitive therapy showed that the majority of the patients received empirical therapy and the percentage of the switch were similar in patients receiving both empirical and definitive therapy.

Inappropriate use of intravenous antibiotics can be reduced by the timely switch over therapy. However, our study showed a similar mean duration of intravenous antibiotics in both switched and non-switched groups, despite the majority of the switch done on the third day. This may be due to the increased duration of usage of intravenous antibiotics empirically, a clinical condition requiring intravenous use of antibiotics and not switching over at the appropriate time in some patients.

CONCLUSION:

Large numbers of antibiotics are suitable for switching from Intravenous to oral therapy through various types of switch. Our study is a preliminary level observational study done in two wards where step-down switch therapy was mostly done. The intravenous antibiotic duration was lesser in the switched group. Among the empirical and definitive therapy, the definitive therapy group had more number of switches. Timely switching of antibiotics is

required with appropriate oral equivalent. Thus, further a prospective study involving other wards with a structural guideline is needed.

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