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"PERCEIVE THE PRACTICE OF INTRAVENOUS-TO-ORAL CONVERSION OF ANTIBIOTICS AND TO SCRUTINIZE ITS INFLUENCE ON THE LENGTH OF HOSPITAL STAY: A PROSPECTIVE OBSERVATIONAL STUDY"

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ABSTRACT

Background: Development of antibiotic resistance is an increasing global concern, for which several authorities have developed some programs. Antimicrobial stewardship program is developed to limit the unnecessary use of antibiotics which helps reducing antibiotic resistance. To do so, AMSP have developed several strategies. One such strategy is called intravenous-to-oral conversion of antibiotics.Objectives: The study was aimed to determine different IV-to-PO conversion methods, in accordance with antimicrobial stewardship program, and to find the influence of conversion on the length of hospital stay. Also to compare the cost of intravenous and oral antibiotics, identifying which one is economical and more convenient for the patient.Approach:A prospective observational study was conducted for 200 patients at a secondary care hospital in Surat from October 2021 to march 2022.Patients who were hospitalized for >= 24 hrs and administered with IV antibiotics were included the study.Results: Out of 200 patients,161 (80.5%) were converted from IV-to-PO, and 39 (19.5%) were not converted. It was found that 82 (41%) patients were prescribed antibiotics as prophylaxis therapy, 26 (13%) were given empirical therapy, and 92 (46%) had documented infections. A total of 470 antibiotics were prescribed during the study, in which most prescribed antibiotics were cephalosporins 231 (49.14%).LOHS for patients not converted from IV-to-PO was 1.43 days longer than that of the converted cases. The LOHS for patient converted from IV-to-PO was significantly shorter ($p<0.05$) than those who were not converted. After conversion from IV-to-PO, average cost saved for single therapy was INR 125.62 (47.54%).Conclusion: Along with reducing the development of antibiotic resistance, timely and appropriate switching of antibiotics from IV-to-PO route could reduce the length of hospitalization and economic burden of the patient. It will also eliminate IV line infections. So this strategy should be promoted and implemented. Future research is recommended.

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INTRODUCTION

Patients who are prescribed with antibiotics needlessly are at risk for severe side effects with no benefit. Antibiotic overuse has also contributed to antibiotic resistance, a serious global public health problem, which is endangering the efficacy of antibiotics. [1,2] The Centres for Disease Control and Prevention (CDC) has identified a number of bacteria as posing urgent, serious, and alarming dangers, and many of which are already putting a significant clinical and financial strain on Indian healthcare system, patients, and their families.[3] Unfortunately, practically all antibiotics that have been produced have eventually developed resistance (FIGURE 1).

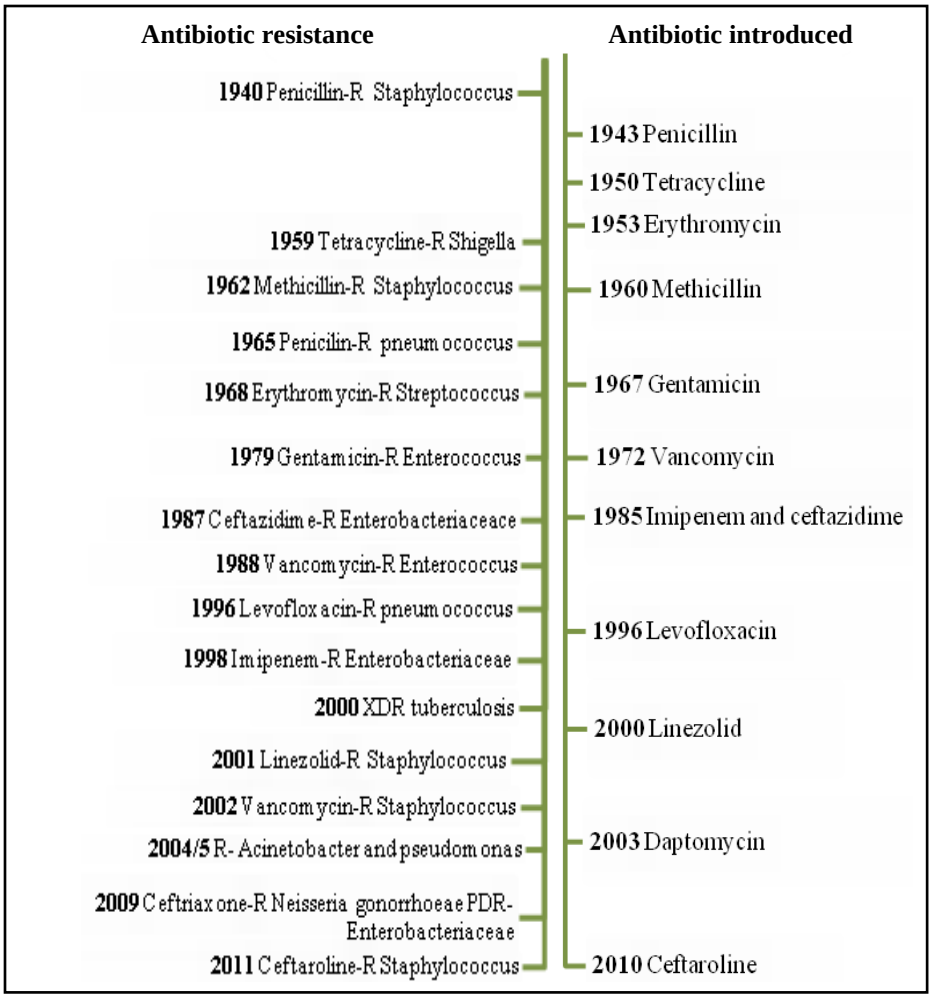

Figure 1: Developing antibiotic resistance [3]

Therefore, to improve drug use and prevent the drug resistance one way is to encourage the individual to complete the course of antibiotic treatment even after they have seen an improvement in symptoms and implementing the conversion of intravenous to oral medication is another way. The concept of early conversion from IV-to-PO medication is a strategy of antimicrobial stewardship program (AMSP) and is not widely used in India, despite its popularity in Western countries.[4](FIGURE 2) The reported extensive misuse and overuse of antibiotics, bacterial resistance, and costs, necessitate the adoption of a few programs to enhance antibiotic usage in hospitals, particularly in low-resource nations.[5] There are three ways in which IV-to-PO conversion can be performed:

1. Sequential therapy: It refers to the act of replacing a parenteral version of medication with its oral counterpart of the same compound.
2. Switch therapy: It describes the conversion of an IV medication to a PO equivalent; within the same class and has the same level of potency, but of a different compound.
3. Step down therapy: It refers to the conversion of an injectable medication to an oral agent in another class or to a different medication within the same class where the frequency, dose, and the spectrum of activity may not be exactly the same.

The best route of administration of any medicine is one that results in a serum concentration high enough to deliver the intended effect while minimizing unwanted effects. So, IV route is most commonly prescribed as it is having very high bioavailability. But with advantages, come several drawbacks like the placement of IV catheter restricts the movement of the patient Further, IV lines form a portal for various bacterial and fungal infections. This leads to secondary infections such as catheter-induced infections and sepsis that require additional antibiotic therapy.Also thrombophlebitis and treatment failure, which may prolong the length of hospital stay and in a small number of cases, death.

The hidden expenses may increase such as the cost of IV sets and pump, laboratory tests, nursing and pharmacy charges. Whereas, the oral route eliminates all these IV line complications, also it is cheaper, easy to administer, and easily available. As a result, choosing the best route of administration is a critical part of ensuring that medications are administered correctly. [6] The assumption that the bioavailability of IV medications is always greater than that of their oral counterpart is true but there are several oral medications that have equivalent bioavailability like levofloxacin have 98% bioavailability in both forms, linezolides also have high bioavailability in oral form. When a large number of IV formulation of medications are administered in oral formulations of the same medication, the quantity of drugs in the blood is roughly the same.[7]A patient should fulfil certain criteria for being able to convert from IV-to-PO drug formulation. (FIGURE 3) By early IV to oral conversion, the length of stay (LOS) in hospital and the cost can be reduced without compromising on the safety and efficacy of the drug. Hence the study was conducted to find the additional benefit of IV-to-PO conversion strategy and was specifically aimed to check the influence of IV-to-PO conversion on the length of hospital stay of the patient.

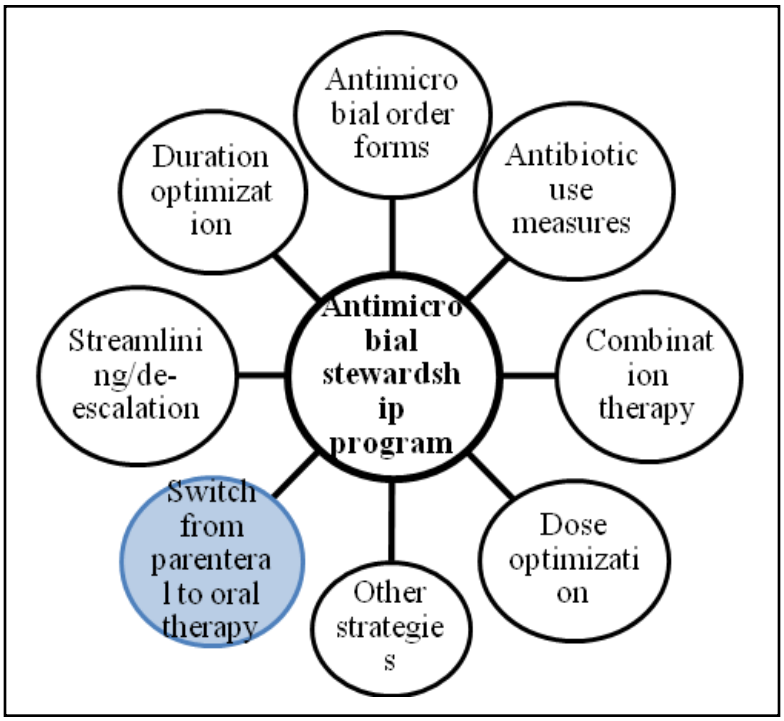

Figure 2: Strategies of antimicrobial stewardship program. [8]

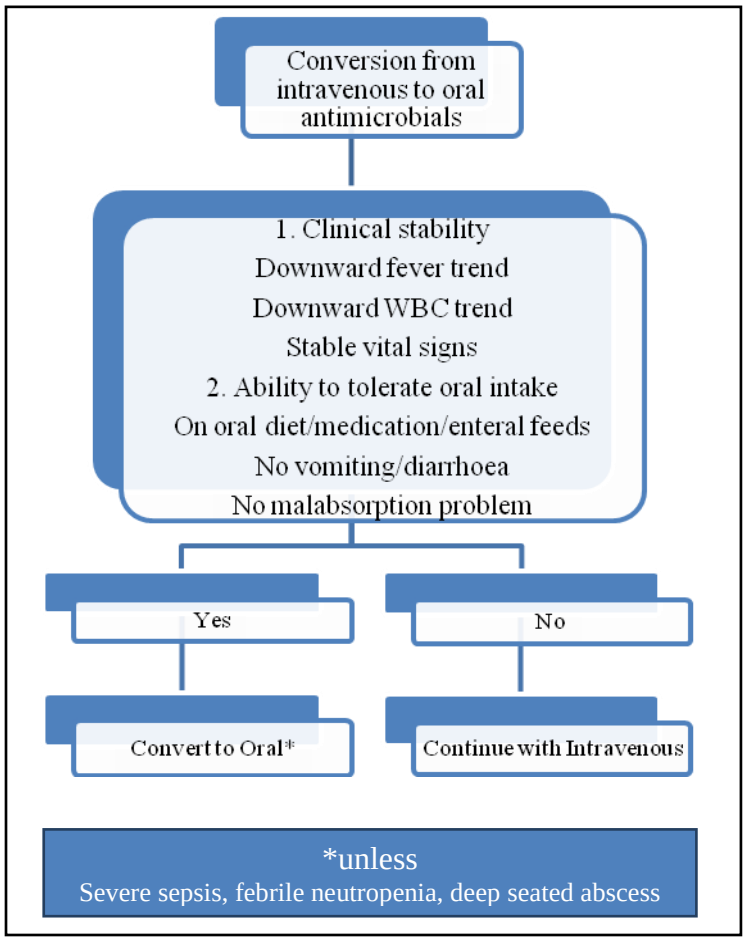

Figure 3: A systemic plan for IV to PO conversion of antimicrobials which is in accordance to AMSP, which when performed if the patient's condition allows, can decrease length of hospital stay and health care costs. [8]

MATERIALS AND METHODS

STUDY DESIGN

This was a Prospective, Observational study.

STUDY DURATION

The total duration for the study was 6 months (1 month for planning, 3 months for data collection and 2 months for data analysis and compilation).

THE NUMBER OF PATIENTS AND STUDY SITES

- The total number of patients enrolled in the study was 200.
- This study was a single-site study in which patients from a secondary care hospital were included.

STUDY PARTICIPATION DURATION OF EACH PATIENT

The interaction between patient depended upon their length of hospital stay and it was different for each individual who was enrolled in the study.

METHODOLOGY

The study was conducted in accordance with the ICH-GCP guidelines. The important documents such as protocol, data collection forms, ICF, CRF was presented to the ethics committee for their approval. The study proceeded after the permission had been granted.

This study was designed as prospective and observational. This was a single-site study which was conducted at secondary care hospital in Surat for inpatients who were administered intravenous antibiotics during hospitalization over a period of three months i.e. from November 2021 to February 2022. The main aim was to determine the influence of different types of intravenous to oral conversion methods for antibiotics on the length of stay in a hospital.

The primary criteria for patient selection was that all patients should be administered intravenous antibiotics for greater than or equal to 24 hours.

PROCEDURE

Inform consent form was obtained from the patient who were enrolled in the study to initiate it. After obtaining the consent, the antibiotic prescription and treatment chart of the patient were diligently reviewed, the selected patients were receiving intravenous antibiotics for >= 24 hours. The study objective was to observe the conversion of antibiotics from IV to the oral route and comprehend the influence of this conversion on the length of hospital stay. This was done by meticulously observing the patient treatment sheet till the patient got discharged. Data was collected using a data collection form, which consists of four parts. The first part includes patient's demographic details (age, gender, allergies, hospital ward admitted in, diagnosis, medical history, and surgical history). The second part consists of treatment information of patients (indication for antibiotic therapy, microbiological reports, administered antibiotic with class, day of conversion, the route converted to, the converted antibiotic with class, type of conversion and the length of hospital stay). The third part includes clinical data and vitals. The fourth part consists of not converted drug details (name, class, route of administration, duration of therapy, and the length of hospital stay).Statistical analysis was carried out by finding the mean and determining the percentage. T-test and chi-square was used to find the correlation between LOHS and conversion from IV-to-PO. The result of the study revealed the most beneficial type of intravenous-to-oral conversion methods for antibiotics which reduced the length of stay in the hospital. On the basis of the analysis, a final conclusion was made that explained whether conversion of IV-to-PO route is beneficial or not.

STUDY CRITERIA

Inclusion criteria

- Patient receiving>24 h of ordered IV antibiotics
- Both male and female patient of any age groups
- Patient who can tolerate oral formulations

Exclusion criteria

- Pregnant and lactating women
- Patient not eligible for oral formulations upon certain conditions like malabsorption syndrome, patient with active gastrointestinal bleeding.
- Patient require prolong IV therapy like those suffering from critically ill diseases(CNS infection)

RESULTS

GENDER WISE DISTRIBUTION OF PATIENTS

A total of 200 patients were enrolled in the study, out of which 112 (56%) were male and 88 (44%) were female.

Table 1. Gender wise distribution.

Gender	Frequency	Percentage
Male	112	56%
Female	88	44%
Total	200	100%

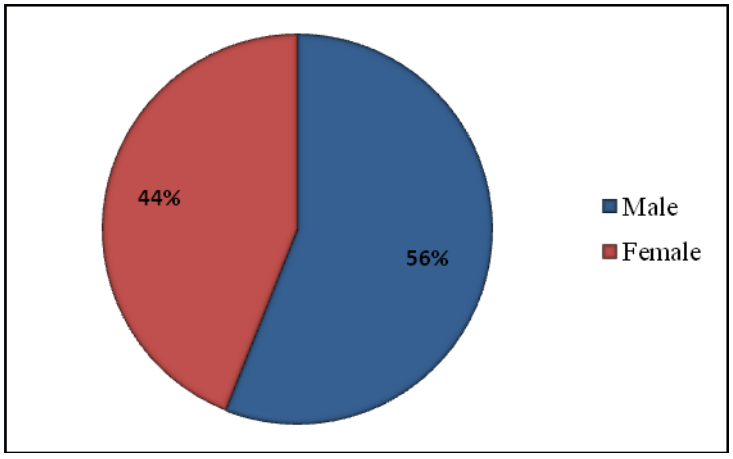

Figure 4. Gender wise distribution.

AGE-WISE DISTRIBUTION

The result showed that there were 31 (15.5%) patients in the age range below 18 years, 125 (62.5%) patients in the age range 18-65 years, and 44 (22%) patients in the age range above 65.

Table 3. Age wise distribution.

Age Category (Years)	Frequency	Percentage
Below 18	31	15.5%
18-65	125	62.5%
Above 65	44	22%
Total	200	100%

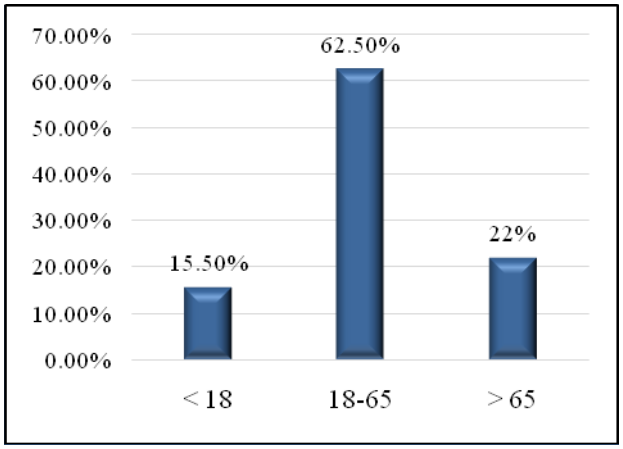

Figure 5. Age-wise distribution.

WARD WISE DISTRIBUTION

In the study, we included patients from four different wards. Out of which 86 (43%) were from the general ward, 82 (41%) were from the surgical ward, 22 (11%) were from the paediatric ward, and 10 (5%) were from MICU.

Table 4. Ward wise distribution.

Wards	Frequency	Percentage (%)
General	86	43
Surgical	82	41
Paediatric	22	11
MICU	10	5
Total	200	100

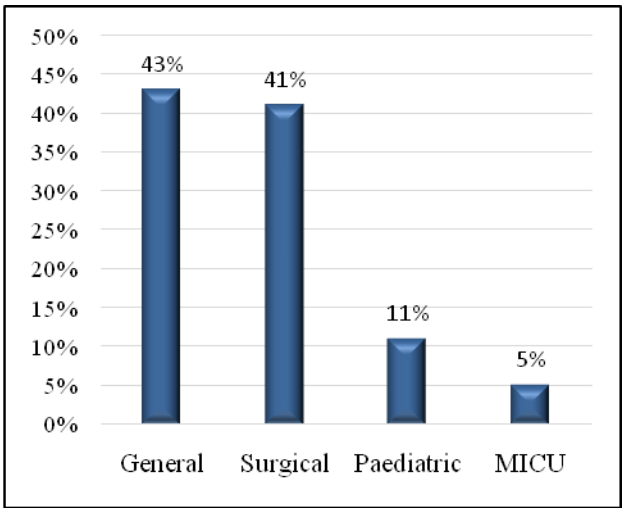

Figure 6. Ward wise distribution .

ANTIBIOTIC INDICATION IN PATIENTS

Out of 200 patients that were enrolled in the study, 82 (41%) patients were prescribed antibiotic as prophylaxis therapy, 26 (13%) were given empirical therapy for not documented infection and 92 (46%) were documented infections.

Table 5. Indication of antibiotics in patients.

Indication	Frequency	Percentage (%)
Prophylaxis	82	41
Empirical	26	13
Documented infection	92	46
Total	200	100

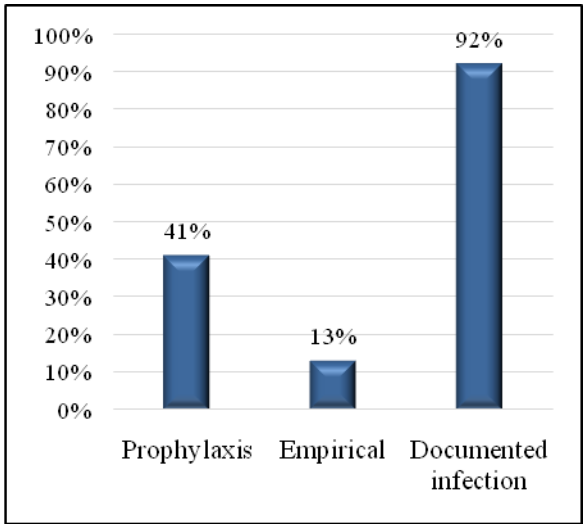

Figure 7. Indication of antibiotics.

TYPES OF CONVERSION

The most common type of conversion method used in the hospital was switch therapy with 86 patients (41.34%), which was followed by step-down with 61 patients (29.32%) and last was sequential with 22 patients (10.57%). Number of patients who were not converted was found to be 39 (18.75%).

Table 6. Types of conversion.

Type of conversion	Frequency	Percentage (%)
Sequential	22	10.57
Switch	86	41.34
Step-down	61	29.32
Not converted	39	18.75

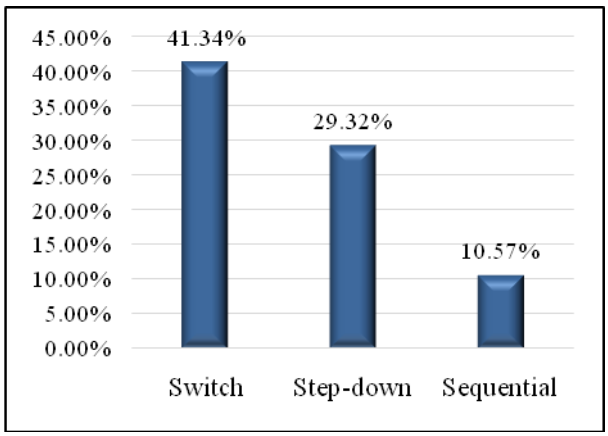

Figure 8. Types of conversion.

NUMBER OF CASES CONVERTED FROM IV-TO-PO & NOT CONVERTED

Among 200 cases, 161 (80.5%) were converted and 39 (19.5%) were not converted.

Table 7. Frequency of converted and not converted cases.

	Frequency	Percentage (%)
Converted	161	80.5
Not converted	39	19.5
Total	200	100

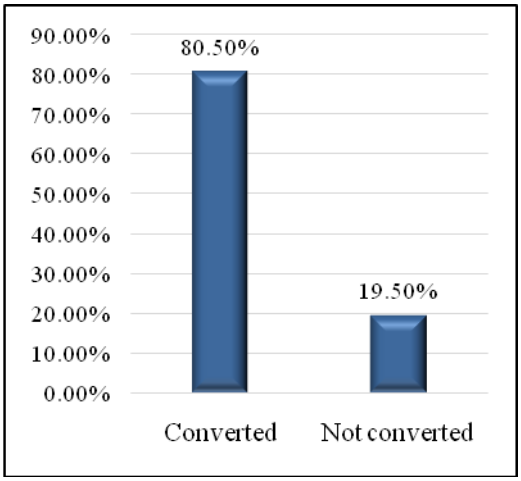

Figure 9. Frequency of conversion.

LENGTH OF HOSPITAL STAY

The length of hospital stay (LOHS) and day of conversion for IV to PO converted and non-converted cases was calculated as: Mean LOHS for IV to PO converted cases was 4.31 days and LOHS for not converted cases was 5.74 days. LOHS for patient who were converted using sequential therapy was 4.42 days, switch therapy was 4.43 days and step-down was 4.13 days.

Table 8. LOHS.

Type of conversion	LOHS (days)
Converted from IV to PO	4.31
• Sequential	4.42
• Switch	4.43
• Step-down	4.13
Not converted	5.74

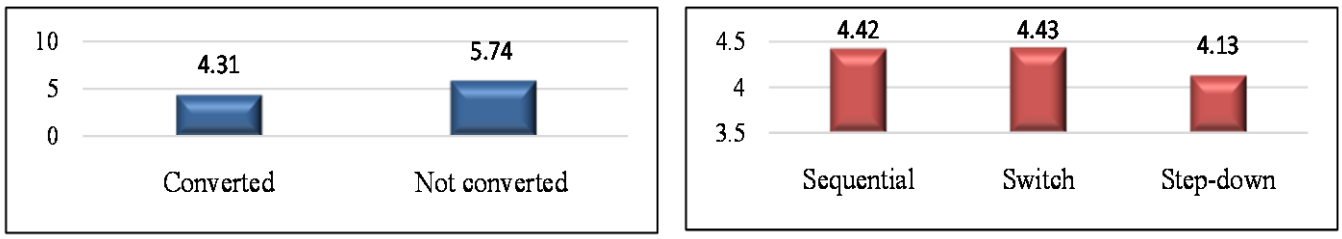

Figure 10. LOHS.

DURATION OF IV THERAPY

Average duration of IV therapy for converted cases was found to be 3.96 days. Average duration of IV administration for sequential therapy was 3.95 days, switch therapy was 4.27 days, and step-down therapy was 3.52 days.

Table 9. Duration of IV therapy.

Type of conversion	Average duration of IV therapy
Sequential	3.95
Switch	4.27
Step-down	3.52

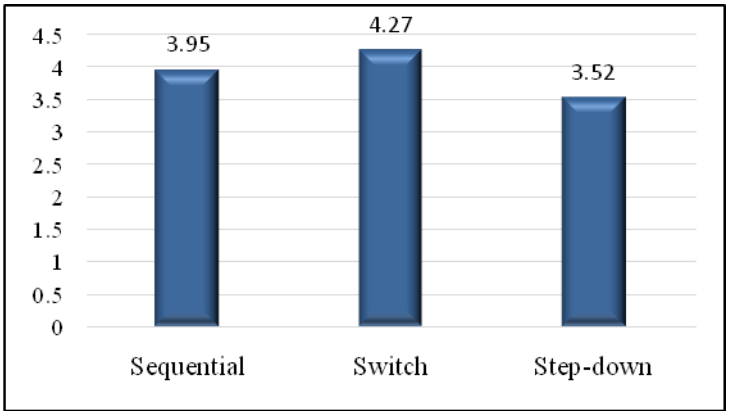

Figure 11. Duration of IV therapy.

CLASS OF ANTIBIOTIC PRESCRIBED

In the study, total of 470 antibiotics were prescribed. In which mostly prescribed antibiotics were cephalosporins - 231 (49.14%), which were followed by combination - 73 (15.53%), penicillin - 57 (12.12%), fluoroquinolones - 43 (9.14%), imidazole - 34 (7.23%), macrolide - 14 (2.97%), aminoglycosides - 8 (1.70%), tetracycline - 5 (1.06%), carbapenem - 4 (0.85%) and glycopeptide - 1 (0.21%).

Table 10. Class of antibiotic prescribed.

Sr. No.	Class of antibiotic	Frequency	Percentage (%)
1.	Cephalosporins	231	49.14
2.	Penicillin	57	12.12
3.	Fluoroquinolones	43	9.14
4.	Imidazole	34	7.23
5.	Macrolide	14	2.97
6.	Aminoglycoside	8	1.70
7.	Tetracycline	5	1.06
8.	Carbapenem	4	0.85
9.	Glycopeptide	1	0.21
10.	Combination	73	15.53

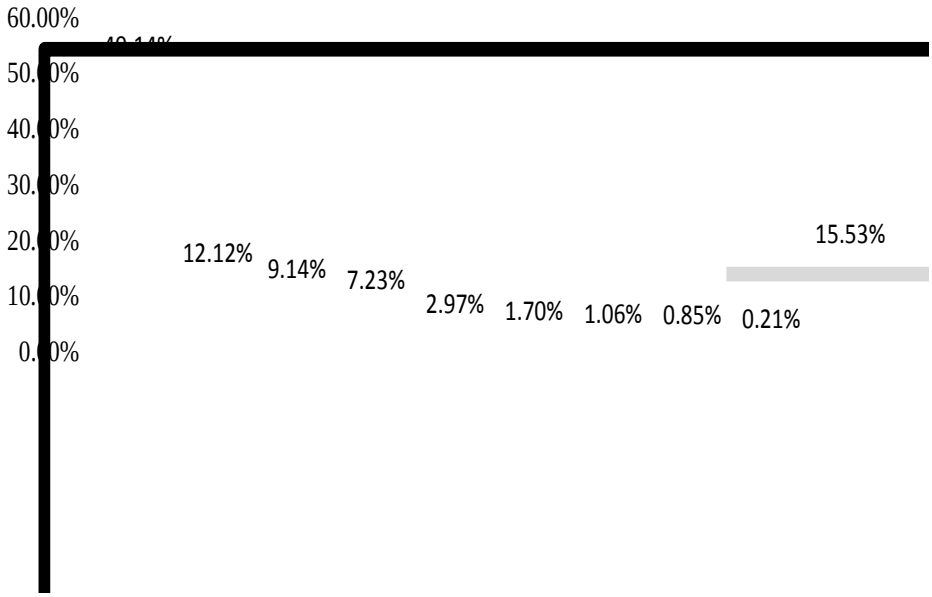

Figure 12. Class of antibiotic prescribed.

COST ANALYSIS OF IV & PO

Total cost of IV therapy was found to be Rs. 46,784 and total cost of PO was found to be Rs. 11,895. Total of Rs. 34,889 amount was reduced on conversion from IV to PO of antibiotics. Average cost of IV therapy was Rs. 194.93 (73.77%) and that of PO was found to be Rs. 69.31(26.22%). Average cost saved for single therapy was Rs. 125.62 (47.54%).

Table 11. Cost analysis of IV & PO.

Route of administration	Total Cost (Rs.)	Average cost (Rs.)	Percentage (%)
IV	46,784	194.93	73.77
PO	11,895	69.31	26.22
Cost reduced	34,889	125.62	47.54

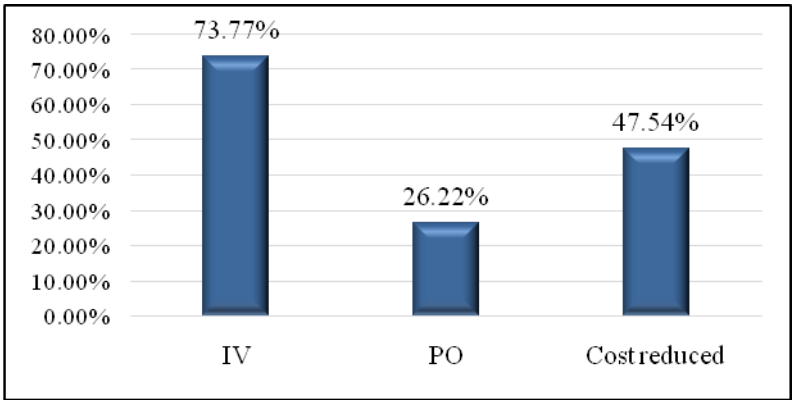

Figure 13. Cost analysis of IV & PO.

DISCUSSION

An ideal route of drug administration is one that achieves serum concentration sufficient to produce desired effect without producing undesired effect. IV route is widely used but can lead to several complications like IV line reactions, requires more personnel time and added cost as well as higher the length of hospital stay.In the study of 200 participants, majority were males compared to female which is similar to study conducted by Zeina M. Shrayteh et al. [9] It was found that in age group 18-65 years the frequency of prescribing antibiotics was higher, which was followed by above 65 years of age group and the least prescribed antibiotics was in age group below 18 years.Four different wards were included, out of which the ratio of antibiotic prescription was higher in general ward, which was followed by surgical ward and then for paediatric ward and the ratio was least in ICU ward. A similar study was conducted by Tamilselvan T et al, which showed that higher proportion of antibiotic was used in general ward. [10]Mostly the antibiotic were prescribed for documented infection, which was followed by prophylaxis and then for empirical therapy which was almost same as to the study conducted by Asuman et al. [11]

Among all the converted cases, the type of conversion more frequently used was switch therapy, which was followed by step-down and then sequential therapy, when compared to a study conducted by Yannamani Satya Tejaswini et al in which sequential therapy was more frequently used, which was followed by switch and then step-down therapy. [12]The study included wards in which IV therapy was administered and were converted to PO therapy. Out of 200 most of the cases got converted i.e. 161 were converted and rest 39 were not converted.In the study, mean LOHS for cases converted from IV to PO was shorter compared to not converted cases. The mean LOHS for converted cases was 4.32 days and that for not converted cases was 5.74 days. According to type of conversion the average LOHS for switch therapy was found to be longest with 4.43 days, which was followed by sequential therapy with 4.42 days and then step-down with 4.13 days. The mean duration of IV therapy for converted cases was found to be 3.96 days, similar outcomes were seen in a study conducted by Mouwen AMA et al. [13]The most commonly prescribed antibiotic in the hospital were cephalosporins, penicillin and fluoroquinolones. The frequency of antibiotic prescription in the hospital for cephalosporins was 49.14%, which was followed by penicillin 12.12% and then fluoroquinolones 9.14%. In the study conducted by Ozkurt et al, the first line antibiotics were cephalosporins – beta lactamase inhibitors and penicillin – beta lactamase inhibitors.[14]It was found that the mean cost for not converted cases were higher in comparison to converted cases. The average cost of IV therapy was 194.93 and average cost of PO therapy was 69.31. Average cost saved for single therapy was ₹ 125.62.It was found that there was significant reduction in the LOHS of converted cases as compared to not converted cases, using T-test.For correlating LOHS of different conversion types, chi-square was used and it was concluded that there was no significant correlation between different type of conversion methods and their LOHS. Therefore any type of conversion method will give beneficial effects.

CONCLUSION

To conclude this research, it was found that most of the cases included in the study were converted from IV-to-PO therapy but the conversion was initiated during discharge. Rational use of antibiotic appears to be better for healthy society and that will influence the outcome of a patient in a fruitful way. According to ICMR guidelines the ideal day of conversion for a patient was on the 2nd day which was similar to the findings of the study i.e. on the 3rd day. Out of 161 patients converted which were included in the study, there was unnecessary delay in conversion for around 6.5% of eligible patients. For addressing this missed opportunity for conversion, implementation of IV-to-PO conversion program must be initiated. It was also found that, changing the route of administration from IV-to-PO results in direct cost reduction (medication cost, supply cost, IV antibiotic therapy cost and other hidden expenses). Personnel time preparing and administering doses is greatly reduced. Proactive conversion to oral formulation reduces the length of hospital stay and save medication/supply cost and total hospital cost.

In effect of preliminary findings of the research, further improvement for practicing conversion of IV-to-PO and reduction of barriers for the effective implementation of this program, is required. Clinical pharmacist and Physician should come together to work hand-in-hand to improve the practice of conversion from IV-to-PO. As the impact of IV therapy, the incidence of IV infections, rate of relapse, LOHS and cost issues were all assessed in this conversion program. Furthermore, the computerized methods for the appropriate conversion from IV-to-PO should be implemented so that opportunity for conversion wouldn't be missed by regular reminders. Addressing all this issues has the potential to reduce inappropriate antibiotic use and resistance. Timely and appropriate switching of antibiotics from IV-to-PO therapy could reduce the length of hospitalization of the patients. Future research is recommended considering other approaches to reduce the antibiotic resistance and the length of hospital stay.

LIMITATIONS

The major drawback of this method was that univariate analysis may not account for all of the confounding variables associated with LOHS. Other than IV-to-PO conversion, multivariate logistic regression analysis might be a better way to find other confounding variables that are linked to outcomes like LOHS and antibiotic duration. Furthermore, the trial did not include pharmacist intervention. Another study with a bigger sample size will be required to address these gaps.

ABBREVIATIONS

LOHS - Length of hospital stay;
AMSP - Antimicrobial stewardship program;
ICMR - Indian counsel of medical research;
IV -Intravenous;
PO - Oral;
ICU - Intensive care unit;
NICU - Neonatal intensive care unit.

AUTHOR'S CONTRIBUTION

Honey, Khushi, Shivani and Prit for designing and conducting study, analysing data, interpretation of results and drafting manuscript.

Dr. Merin Sara Philip and Dr. Gaurav Raiyani were involved in supervision.

Final approval of the version to be published is given by all the authors.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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