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Antibiotics Transition from Intravenous to Oral Use and Their Bioavailability in Teritary Care Hospital

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ABSTRACT

Introduction: Several studies have demonstrated the efficacy and safety of switching from intravenous to oral antibiotics in clinically stable patients. An early switch from Intravenous (IV) to Per Oral (PO) could be one of the factors that influence the Length of Hospital Stay (LOHS).

Aim: To evaluate the practice of switching from intravenous to oral antibiotics and its impact on the LOHS at a tertiary care hospital.

Materials and Methods: A Retrospective study. The practice of conversion from IV to Oral antibiotic therapy was assessed according to predefined criteria for clinical stability. Clinical endpoints such as the day of IV to Oral switch, LOHS, and duration of antibiotic therapy were assessed.

Results: Results reveal that 43.68% of antibiotics were converted from IV to oral formulation while 56.32% of antibiotic courses were not converted from IV to oral. Out of all IV-to-oral conversions, sequential therapy was more commonly used than switch and step-down therapy. LOHS for patients had significantly ($p<0.05$)decreased following IV to oral conversion of antibiotics in comparison to LOHS for patients with the non-conversion of antibiotics from IV to an oral formulation. The day of conversion was more delayed in switch therapy than two other modes of conversion

Keywords: Intravenous to oral switch, Sequential therapy, Step-down therapy

I. INTRODUCTION:

Infectious diseases are more likely to affect the population all over the world. Hence, antibiotic therapy has become crucial in the effective management of infectious diseases. Antibiotic therapy yields good results when they are administered by IV route. At times, one has to consider the concept of IV to PO conversion of antibiotic therapy. Antibiotics are considered suitable for IV to oral conversion if they have an appropriate spectrum, a high degree of activity against the presumed or known pathogen, and good bioavailability. Many patients remain on expensive IV medications, even after they become able to take bioequivalent oral alternatives. Several studies have demonstrated the efficacy and safety of switching from IV to oral antibiotics in clinically stable patients [1,2]. One way of optimizing antibiotic use is to switch earlier from IV to oral therapy, with the following advantages: i) benefits to the patient; ii) lower costs, and; iii) reduced workload, e.g., reduced incidence of catheter-related infections, a shorter LOHS, a reduction in costs and an associated reduction in workload without sacrificing patient safety [3,4]. The multidisciplinary medical team shall consider three important factors proper patient selection, an appropriate therapeutic approach, and patient health education for the successful conversion of IV to oral antimicrobial agents [2,5]. Infectious disease specialists shall evaluate the patient and explore the suitability of the patient for IV to oral switch. This eventually may lead to early discharge and reduce the cost burden on the patient [6] The IV conversion to PO therapy can reduce the length of hospital stay, healthcare costs, and risk of complications related to IV access [8,9]. This conversion may be a “switch therapy”, “sequential therapy” or “step-down” therapy. IV to PO switch programs are highly appropriate and more applicable to antibiotics such as fluoroquinolones (levofloxacin, moxifloxacin), tetracyclines (doxycycline, minocycline), macrolides (clindamycin), co-trimoxazole (sulfamethoxazole-trimethoprim), chloramphenicol, linezolid, metronidazole and antifungal drugs such as fluconazole, itraconazole and voriconazole [10]. According to some authorities, approximately 40% of patients starting on IV antibiotics are candidates for a switch to oral antibiotics after 2-3 days of therapy. There are very few studies on the practice of IV to-oral switch in clinical settings of the Indian population [11]. Hence, the present study aimed to evaluate the practice of IV to oral conversion of antibiotics and its impact on the length of stay in a tertiary care hospital

ADVANTAGES OF ORAL OVER IV ROUTE:

Early switch over from IV to oral therapy has the following major advantages:

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- ✓ Reduced risk of cannula-related infections: For the administration of IV medications, one is required to insert a cannula, which remains in place for some days and eventually can result in secondary infections caused by bacteria and fungi. This may ultimately lead to the need for additional antibiotics and subsequently financial burden to the patient[1]
- ✓ Risk of thrombophlebitis: No risk of thrombophlebitis in case of oral administration[1,3,11]
- ✓ Less expensive than IV therapy: Most of the oral medications available on the market are less expensive as the parenteral medications must be sterile and isotonic, consequently leading to cost savings for the patient[1,15,16]
- ✓ Reduction in the hidden costs: Hidden costs mainly refer to the cost of diluents, types of equipment for administration, needles, syringes, and nursing time. Needles, syringes, diluents, and other types of equipment are unavoidable requisites for parenteral administration. Above all, an experienced professional must be there to administer the injection. As a result, it may cause a financial burden for the patient and take away valuable nursing time for patient care [1,15,16]
- ✓ Earlier discharge: Injections are usually administered in a hospital setting as it requires an experienced professional to administer the medication, especially IV infusions. Hence the patient's stay at the hospital is prolonged. Early switch over to oral medications can help to overcome this barrier and may result in early discharge of the patient.[1]

TYPES OF IV TO ORAL CONVERSIONS

There are mainly three types of IV to PO conversions.

Sequential therapy: Refers to the act of replacing a parenteral version of a medication with its oral counterpart of the same compound. For instance, conversion of injection. pantoprazole 40 mg OD (once daily) to tab. pantoprazole 40 mg OD[16]

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. For example, switch over from inj. ceftriaxone 1 g BD (bis in die) to tab. cefixime 200 mg BD,[17] switch over from inj. pantoprazole 40 mg BD to tab. rabeprazole 20 mg BD

Step-down therapy: It refers to the conversion from an injectable medication to an oral agent in another class or to a different medication within the same class where the frequency, dose, and spectrum of activity (in the case of antibiotics) may not be the same. For example, conversion of inj. cefotaxim 1 g to tab. ciprofloxacin 500 mg, switch over from inj. heparin to tab. warfarin.

PRACTICAL APPROACHES FOR CONVERSION OF A PATIENT FROM IV TO ORAL THERAPY:

The establishment of an IV-to-oral switch program at a hospital is the stepping stone toward the successful conversion of a patient from IV to oral therapy. It is the sole responsibility of a clinical pharmacist to establish such a guideline with the approval of the Pharmacy and Therapeutics committee of the hospital and ensure that the conversion is done in tune with the guideline.[1,2,18]

- First, a clinical pharmacist should identify patients who receive IV medications and also recognize the need for IV medication in those patients, and check for the indication
- Second, regular follow-up is needed to check whether the patient's clinical status (WBC [white blood cells], vitals, culture report, patient's physical and mental condition, etc.) is improving or not. If the patient is eligible for conversion. check whether the conversion was done
- Inform the physician about the patients who are eligible for conversion but have not converted within the appropriate time
- Make suitable recommendations for the selection of an oral medication for conversion
- Review the feedback of the physicians
- Monitor the patient's clinical progress after the switchover and convert the patient back to parenteral medication, if required
- It is always advisable to verify the knowledge and beliefs of physicians regarding the guideline for the switch over from IV to oral therapy. A data collection tool like questionnaires can be used for the same.

INCLUSION CRITERIA

i) Adult in-patients receiving an IV antibiotic for more than 24 hours; ii) the patients able to sufficiently absorb oral medications via oral, nasogastric, or feeding tube route; iii) patients in whom signs and symptoms of infection resolving or improving; iv) patients who were improving clinically and stable (negative blood cultures for ≥48 hours; White Blood Cell (WBC) count

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stable/normalizing; A febrile: temperature 24 hours)

EXCLUSION CRITERIA

Patients younger than 18 years of age; patients who were not eligible for oral formulation based on a permanent physiologic condition (e.g., malabsorption syndrome); patients with active gastrointestinal bleeding; a patient who refused oral medication; patients whose disease severity met the following criteria [ICU vasopressor dependent or hemodynamically unstable, decreased consciousness, seizures, immunocompromised status {neutropenia, Absolute Neutrophil Count (ANC)}].

BIOAVAILABILITY OF MEDICATIONS INCLUDED IN IV TO ORAL CONVERSION

Usually, 100% bioavailability is assured only for IV medications and not for other routes like intramuscular or subcutaneous routes. When a medication is administered intravenously it can directly reach the blood circulation and thereby assure 100% bioavailability. To be effective, oral antibiotics must achieve serum bactericidal activity almost comparable to that of their IV counterparts.[1,9] Table 1 explains the examples of IV to oral switchover for medications with >90% bioavailability. Examples of drugs with good bioavailability (60-90%) eligible[19,20] for IV to oral switchover are given in Table 2.

Oralantimicrobials**equallypotent**totheIVformulation		
ParenteralTherapy	**OralTherapy**	**OralBioavailability**
Ciprofloxacin200mgIVq12hCiprofloxacin400 mgIVq12h	Ciprofloxacin 250 mg PO BIDCiprofloxacin 500 to 750 mg POBID **NOTE**:spaceoraldosetwo hours before or six hours aftercalcium, magnesium, and iron.Holdenteral feeds onehourbeforeandafter the dose(donotuse oralsuspensioninfeedingtu besdueto clogging)	70%
Clindamycin600mgIVq8h	Clindamycin450mg PO TID	90%
FluconazoleIVoncedaily(dailydosesamefor bothIVandPO administration)	Fluconazolepooncedaily(d ailydosesameforbothIV andPO administration)	90%
Levofloxacin750mgIVq24hLevofloxacin500 mgIVq24h	Levofloxacin750mgPOdai lyLevofloxacin500mgPOd aily	99%
Metronidazole500mgIVq8h Metronidazole500mgIVq12h	Metronidazole500mgPO TID Metronidazole500mgPO BID	100%
Moxifloxacin400mgIVoncedaily	Moxifloxacin 400 mg PO oncedaily	90%
Sulfamethoxazole–trimethoprim(co-trimoxazole) 800/160 mg IVq8h	Sulfamethoxazole–trimethoprim(co-trimoxazole) 1 DS tab POBID	85%

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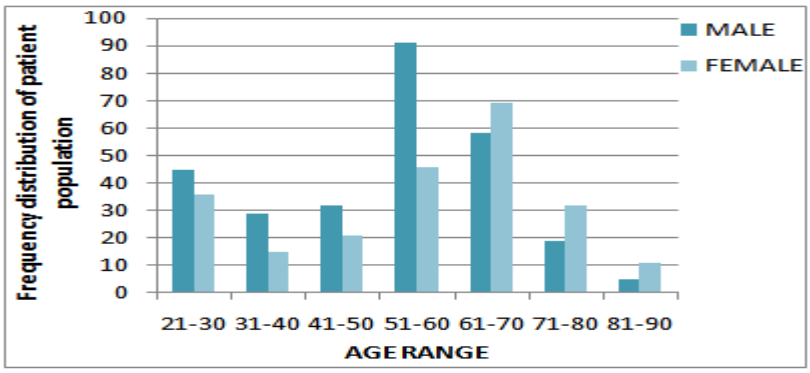
Voriconazole400mgIVq12hx2doses then200mgIVq12h	Voriconazole 400 mg PO BID x 2doses then200mgPOBID	96%

Oralantimicrobials are lesspotentthanIVformulations. Step-downtoalesspotentoralagentrequiresindividualpatientassessment		
ParenteralTherapy	**OralTherapy*** **	**Oral Bioavailability**
Azithromycin 500 mg IVoncedailyx3days(5daysifsuspectedlegionella)	Azithromycin500mgPO x1then250mgPOoncedailyx 4days Or Azithromycin500mgPOdaily x3days	37%*
Cefazolin1gIVq8h	Cephalexin***500 mgPOQID	90%
Cefuroxime750mgIVq8hCefuroxime1.5gIVq8h	Cefuroxime500mgPOBIDwithfood	50%
Cloxacillin1to2gIVq6h	Cloxacillin500mgPOQIDonehourbeforeortwohours aftermeals **or**Cephalexin500mgpoQID	50%
PenicillinG1to2millionunitsIV q6h	PenicillinV300 mg POQID **or**Amoxicillin500 mgPO TID	60-73% Amoxi=80%
Acyclovir#5mg/kgIVq8h	Acyclovir#400mgPOTID **or**Valacyclovir#1gPO BID	Acyclovir=10 –20% Valacyclovir=54%

NOTE:Theabovedosesshouldbeadjustedfortheindication,patient'sage,weight,andrenalfunctionwhen necessary.

lowbioavailabilitybutrapidlymovesinto tissuesresultinginlowserumconcentrationsbuthighandpersistent tissue concentrations(note500mgoral dose =loadingdose)If a pathogen has been identified ensure the organism is susceptible. Note: cephalothin istherepresentingagentinmicrobiologytestingforcephalexin.

II. RESULTS



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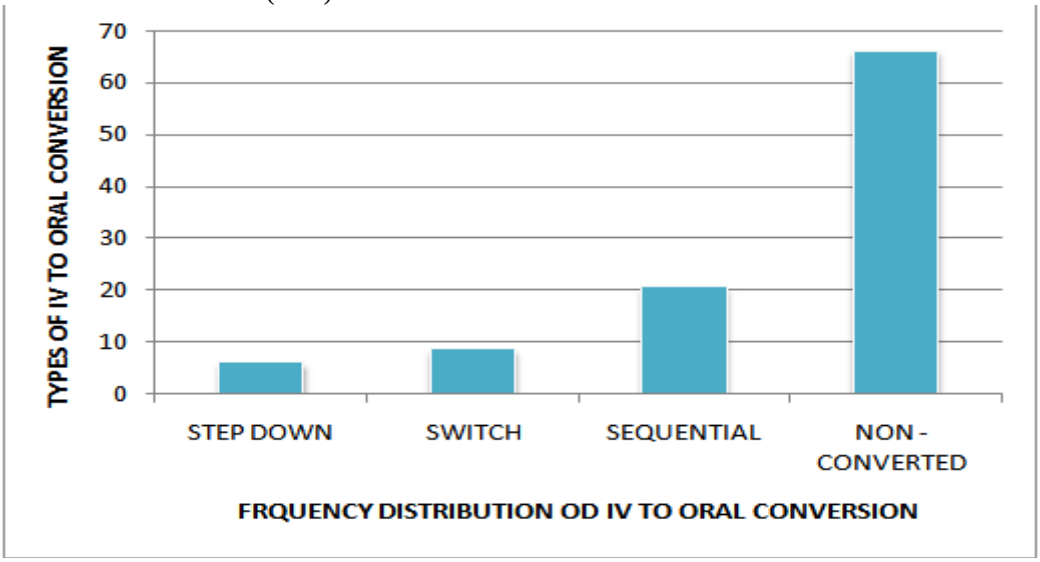
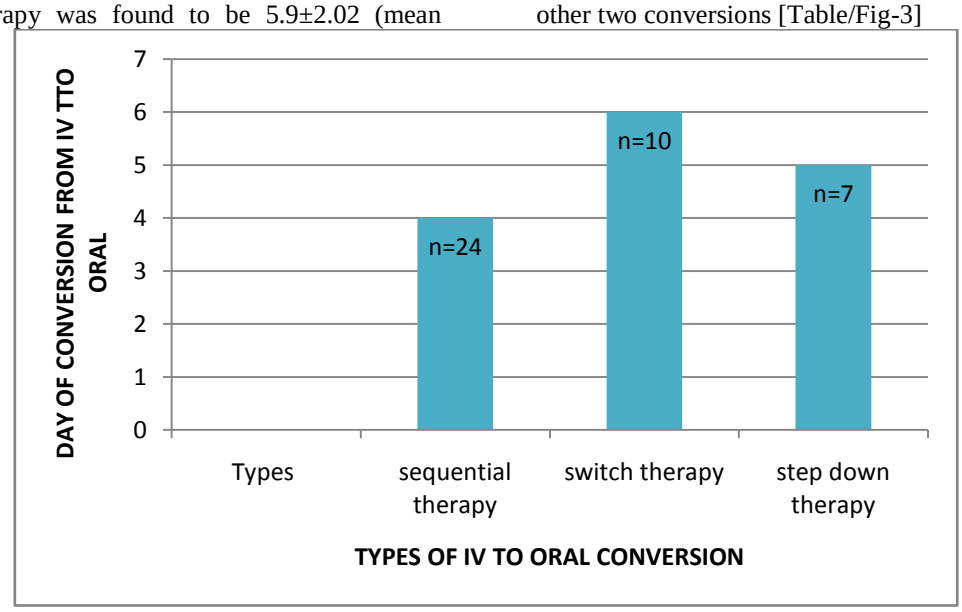
In the eligible patient population, the higher frequencies of male patients were in the age range of 51-60 while female patients were in the age group of 61-70 years [Table/Fig-1].

Out of 117 patients, "non-converted from IV to PO" accounted for 76 (65%) while "converted from IV to PO" accounted for 41 (35%). Out of 41 (100%) of converted, sequential, switch, and step-down therapy contributed 24 (58.53%), 10 (24.39%), and 7 (17.07%) respectively. The most frequent type of conversion observed in this study was the sequential conversion therapy [Table/Fig-2]



The mean number of days of IV to PO conversion was found to be 3.95±1.73 (mean duration of IV therapy: 3.95 days and mean duration of PO therapy: 2.25 days) in the case of sequential conversion whereas the mean number of days of IV to PO conversion in switch and step-down therapy was found to be 5.9±2.02 (mean duration of IV therapy: 5.9 days and mean duration of PO therapy: 2.4 days) and 4.8±2.43 (mean duration of IV therapy: 4.8 days and mean duration of PO therapy: 2.2 days) respectively. Results implied that the day of the conversion of switch therapy was significantly high in comparison to the other two conversions [Table/Fig-3]



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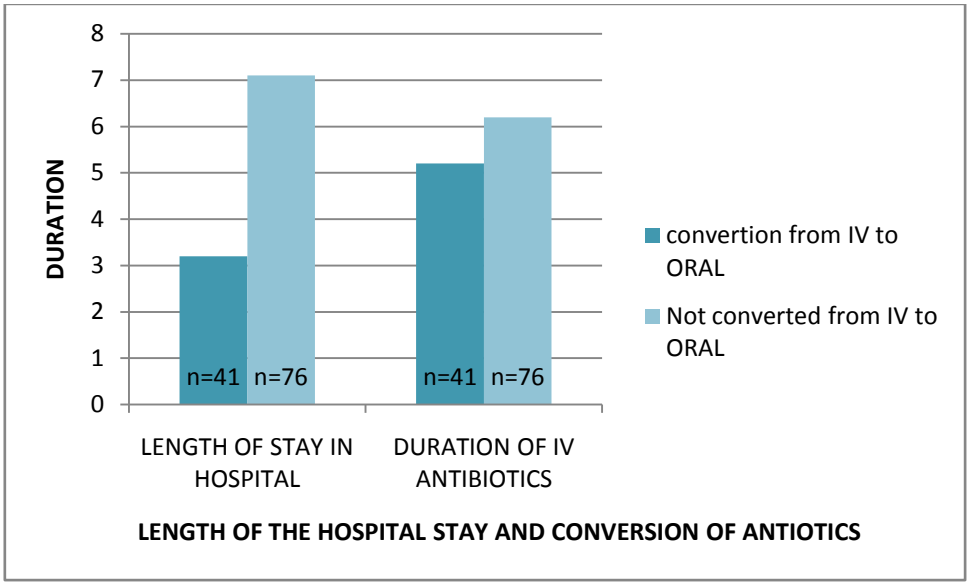
In IV to PO conversion therapy, the mean period of LOHS of patients was 6.84 days (mean duration of IV therapy: 4.48 days and mean duration of PO therapy: 2.36 days) whereas, in the case of non-converted therapy, the mean period of LOHS of patients was 8.71 days (mean duration of IV therapy: 5.86 days). The two-way ANOVA analysis results revealed that there was a statistically significant ($p<0.05$) decrease in LOHS between the converted group and non-converted group while there is no statistically significant difference between the converted group and non-converted group concerning the duration of IV antibiotic therapy [Table/Fig-4].



III. CONCLUSION:

Timely and appropriate switching of antibiotics from IV to oral therapy could reduce the length of hospitalization of patients.

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