SJIF Impact Factor: 5.464

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

ISSN: 2457-0400
Volume: 6.
Issue: 5
Page N. 197-202
Year: 2022

Review Article www.wjahr.com

A REVIEW ON SWITCH OVER OF ANTIBIOTICS FROM INTRAVENOUS TO ORAL ROUTE OF ADMINISTRATION IN CLINICAL PRACTICE

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Received date: 20 March 2022 **Revised date:** 10 April 2022 **Accepted date:** 30 April 2022

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ABSTRACT

Switching from Intravenous to oral therapy as soon as patients are clinically stable can reduce the length of hospitalization and lower associated costs. Intravenous medications are more bioavailable and have greater effects, some oral drugs produce serum levels comparable to those of the parenteral form. Medications involved in switch therapy include antibiotics, analgesics, antipsychotics, and anti virals. Fluoroquinolones and macrolides were the most commonly converted antibiotics. Among the various routes of administration of medications, oral administration is considered to be the most acceptable and economical method of administration. The main drawback of intravenous to oral conversion is the belief that oral medications do not achieve the same bioavailability as that of intravenous medications and that the same agent must be used both intravenously and orally. Even though intravenous to oral therapy conversion is inappropriate for a patient who is critically ill or who has inability to absorb oral medications, every hospital will have a certain number of patients who are eligible for switch over from intravenous to oral therapy. A substantial number of patients starting on iv antibiotics were candidates for an early iv to oral therapy. The antibiotics are well accepted by the physicians and reduce the cost of the antibiotics and help to lower the medication errors in the community.

KEYWORDS: Hospitalization, intravenous, oral, medications, antibiotics.

INTRODUCTION

The ideal route of administration of any medication is the one that achieves serum concentrations sufficient to produce the desired effect without producing any untoward effects. Safest and convenient way of medication administration is achieved by oral route. If the given oral medication achieves tissue and blood concentration to the same extent as that of the intravenous (IV) medication, then there is little therapeutic difference between IV and oral medications. The available oral formulations in the market are easier to administer, safe and achieve desired therapeutic concentrations, thus making the per oral (PO) route an ideal choice.

World Health Organization (WHO) reports that the irrational use of medicines is a major problem worldwide. The over-use of injections, when oral formulations would be more appropriate, is one of the key factors for the irrational use of medicines. Hence IV to oral switch over within an appropriate time is one of the major aspects to improve the rational use of injections. Moreover, once the culture and sensitivity reports are available, IV to oral switch over enables one to select a cheaper or older antibiotic, which is as effective as the IV antibiotic. In the Indian scenario, the concept of early switch over from IV to oral therapy is not common even though it is popular in Western countries. Previous research study results of Palanisamy and colleagues explained that in the general medicine department of a 450 bedded tertiary care hospital in south India for a period of 6 months showed that the average cost of antibiotics and the length of stay of patients could be reduced due to early switch over from parenteral to oral therapy. A new approach to carry out the IV to oral switch over is to establish a computerized intervention. Patient's data along with details of medications received are entered into a computer and on every day at midnight, the computer compiles a list of patients who are matching with selection criteria for switch over. Pharmacist takes the print out of the list and

discusses with the physician for switch over according to the clinical status of the patient.[1-7]

Pharmacist-facilitated antimicrobial stewardship initiatives can aid to IV to PO switches. Recent studies in 2014 have underscored the cost savings and effectiveness of IV to oral switch therapy. Previous research studies showed that for low risk variants of Staphylococcus aureus bloodstream infection can be switched from IV to PO rapidly. Even IV treatment of methicillin-resistant Staphylococcus aureus involving the skin can be shifted to PO therapy in many patients. Early switching of intravenous to oral antibiotics is possible, and positive outcomes have been reported in medical wards.In addition, a meta-analysis study found that early switching of intravenous to oral antibiotics is possible in moderate to severe community-acquired pneumonia (CAP). In particular, quinolones can be switched effectively and rapidly from intravenous to oral formulations when patients can tolerate medications orally.

Advantages of oral over IV route

1. 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.
2. Risk of thrombophlebitis: No risk of thrombophlebitis in case of oral administration.
3. Less expensive than IV therapy: Most of the oral medications available at the market are less expensive as the parenteral medications must be sterile and isotonic, consequently leading to cost savings by the patient.
4. Reduction in the hidden costs: Hidden costs mainly refer to cost of diluents, equipment's for administration, needles, syringes, and nursing time. Needles, syringes, diluents, and other equipment's are the unavoidable requisites for the parenteral administration. Above all, an experienced professional must be there to administer the Injections. As a result, it may cause a financial burden for the patient and take away valuable nursing time for patient-care.
5. 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 stay at the hospital is prolonged.

Types of IV to oral conversions

There are mainly three types of IV to PO conversions.

1. Sequential therapy: It refers to the act of replacing a parenteral version of a medication with its oral counterpart of the same compound. For instance, conversion of inj. pantoprazole 40mg OD (once daily) to tab. pantoprazole 40mg OD.
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. For example, switch over from inj. ceftriaxone 1g BD to tab. cefixime 200mg BD, switch over from inj. pantoprazole 40 mg BD to tab. rabeprazole 20mg BD.
3. 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 the spectrum of activity (in the case of antibiotics) may not be exactly the same. For example, conversion of inj. cefotaxim 1g to tab. ciprofloxacin 500 mg, switch over from inj. heparin to tab. Warfarin.[8-10]

Practical approaches for conversion of a patient from IV to oral therapy

1. 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.
2. 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.
3. Inform the physician about the patients who are eligible for conversion but not converted within the appropriate time
4. Review the feedback of the physicians.
5. Monitor the patient's clinical progress after the switch over and convert the patient back to parenteral medication, if required.
6. It is always advisable to verify the knowledge and beliefs of physicians regarding the guideline for switch over from IV to oral therapy.
7. Bioavailability of medications included in IV to oral conversion

Bioavailability

Usually 100% bioavailability is assured only for IV medications and not for other routes like intramuscular or subcutaneous route. When a medication is administered intravenously it can directly reach the blood circulation and thereby assure 100% bioavailability. The oral antibiotics must achieve serum bactericidal activity almost comparable to that of its IV counterpart.[11-15]

Therapeutic application of IV to oral switch over Special focus on some common disease conditions

1. Infectious diarrhea/typhoid (enteric) fever
2. Acute watery diarrhea is mainly caused by the pathogens Escherichia coli, campylobacter, salmonella or vibrio species. The preferred therapy is a quinolone IV or PO for 5 days. Both IV and oral formulations of quinolones have same bio-availability.

Main use of these switch from IV to Oral are

1. Community-acquired pneumonia

One of the most common uses of intravenous-to-oral (IV-to-PO) switch therapy is in the treatment of CAP.

CAP is most commonly caused by Streptococcus pneumoniae infection. The natural history of CAP is beyond the scope of this article; see Pneumonia, Community-Acquired for more information. In terms of switch therapy, approximately 40-50% of patients admitted for intravenous antibiotics can be switched to oral antibiotics within 2-3 days.

2. Bacterial peritonitis, pyelonephritis, adult septic arthritis

Other uses of switch therapy can include the treatment of spontaneous bacterial peritonitis. A more cost-effective switch therapy in the treatment of spontaneous bacterial peritonitis in patients with cirrhosis who are not receiving prophylaxis with quinolones involves the use of a cephalosporin rather than intravenous ceftazidime.

3. Antibiotics

Switch therapy is possible with various oral antibiotics. Antibiotics ideal for intravenous-to-oral (IV-to-PO) switch programs include chloramphenicol, clindamycin, metronidazole, trimethoprim-sulfamethoxazole, fluconazole, itraconazole, voriconazole, doxycycline, minocycline, levofloxacin, moxifloxacin, and linezolid.

Fluoroquinolones

Fluoroquinolones are suitable for switch therapy.

Levofloxacin and ofloxacin

The intravenous and oral formulations of levofloxacin have same-dose bioequivalence, allowing for switch or step-down therapy from parenteral to oral formulations of the same agent at the same dose. Levofloxacin provides almost complete(≥99%) oral bioavailability, suggesting that oral administration may provide exposure that is comparable to that of the intravenous regimen.

Levofloxacin has activity against pneumococci, including penicillin-resistant isolates, and activity against aerobic gram-negative rods but not Pseudomonas. It can be used to treat CAP. The adult dose is 500 mg PO qd for 7-14 d. It is not recommended for children. Levofloxacin is a pregnancy category C medication.[16-20]

Ofloxacin penetrates the prostate well and is effective against Chlamydia trachomatis. It is derived from pyridine carboxylic acid and has broad-spectrum bactericidal effect. It is specifically used to treat prostatitis and UTI. In adults, the dosing for prostatitis is 400 mg PO once, while dosing for chronic prostatitis is 200-400 mg PO q12h.

Ciprofloxacin

Ciprofloxacin also has a role in IV-to-PO switch therapy. Giamarellou and colleagues demonstrated that high-dose ciprofloxacin administered intravenously for at least 3 days and then orally is therapeutically equivalent to the routine regimen of intravenous ceftazidime plus amikacin, even in febrile patients with severe neutropenia (ie, polymorphonuclear leukocyte count,<100/µL). Ciprofloxacin (Cipro) is a fluoroquinolone with activity against pseudomonads and most gram-negative organisms but no activity against anaerobes. It inhibits bacterial DNA synthesis and, consequently, growth. Continue treatment for at least 2 d (7-14 d typical) after signs and symptoms have disappeared. The adult dose is 250-500 mg PO bid for 7-14 d. It is not indicated in children. Ciprofloxacin is a pregnancy category C medication.

Cephalosporins

Similar switches can be effective with cephalosporins. Validated treatment algorithms, such as the Classification of Community-Acquired Pneumonia (CoCAP), now enable decisions concerning which patients with CAP require hospitalization and which patients will benefit from early switch therapy. Generally, unstable patients with CAP are suitable candidates for early switch therapy, which consists of rapid initiation of 1-2 days of intravenous therapy followed by 5 days of oral therapy, with early hospital discharge after the administration of 1-2 doses of oral antibiotic.

Cefuroxime, cefuroxime axetil, and cefetametpivoxil

Previous research studies of intravenous cefuroxime followed by oral cefuroxime axetilsuggested this regimen is both effective and well-tolerated as rapid switch therapy and has the potential to reduce overall health care costs and improve patient satisfaction. Specifically, Van den Brande and colleagues noted that intravenous cefuroxime twice daily followed by oral cefuroxime axetil is a simple and effective sequential therapy regimen for the treatment of CAP.

Cefuroxime is a second-generation cephalosporin that maintains gram-positive activity of first-generation cephalosporins and adds activity against Proteus mirabilis, Haemophilusinfluenzae, Escherichia coli, Klebsiella Pneumonia, and Moraxella catarrhalis. The condition of the patient, severity of the infection, and susceptibility of the microorganism determine proper dose and route of administration. The adult dose is 500 mg PO bid for 20 d or, alternatively, 750-1500 mg IV/IM q8h, not to exceed 6 g/d. In children, dosing is 250 mg PO bid for 20 d. Use the adult dose for adolescents. Cefuroxime is a pregnancy category C medication.

Cefixime has activity against aerobic gram-negative rods. It arrests bacterial cell-wall synthesis and inhibits bacterial growth by binding to one or more of the penicillin-binding proteins. Cefixime is a pregnancy category B medication.

Macrolides

Macrolides are used for switch therapy include azithromycin and clarithromycin.

Azithromycin
The macrolide azithromycin appears to be superior to the cephalosporin cefuroxime in intravenous therapy and a subsequent switch to oral therapy. This was shown in a cost-effectiveness analysis of IV-to-PO switch regimens of azithromycin versus cefuroxime with or without erythromycin in the treatment of patients hospitalized with CAP.

Azithromycin (Zithromax) is active against gram-positive bacteria and organisms responsible for atypical pneumonia but resistant to erythromycin-resistant pneumococci. It inhibits bacterial growth, possibly by blocking dissociation of peptidyl tRNA from ribosomes, causing RNA-dependent protein synthesis to arrest. It is used to treat mild-to-moderate microbial infections**.** Azithromycin is a pregnancy category B medication.

Other antibiotics
Other antibiotics that can be used for switch therapy include clindamycin, ertapenem, linezolid, metronidazole, and trimethoprim-sulfamethoxazole.

Antifungals
Anti fungals are used for switch therapy include itraconazole andfluconazole.

Antidepressants
Citalopram can be used as switch therapy.

Analgesics
Acetaminophen Promptly switching intravenous acetaminophen to oral acetaminophen is possible in patients with severe pain.

Antivirals
Acyclovir (Zovirax) inhibits activity of both HSV-1 and HSV-2. It has affinity for viral thymidine kinase and, once phosphorylated, causes DNA chain termination when acted on by DNA polymerase. Patients experience less pain and faster resolution of cutaneous lesions when used within 48 h of rash onset. It may also prevent recurrent outbreaks. Early initiation of therapy is imperative. Approximately 40% of patients started with iv antibiotics in the wards studied were candidates for an early switch. During the first phase of the study, before implementation of switch guidelines, only 54% of patients who could have been switched were actually switched to oral treatment, after a median of 6 days of iv therapy. After implementation of the antibiotics, this percentage rose to 83%, and therapy was also switched earlier, after a median of 4 days of therapy. In the analysis of reasons for not switching when the criteria were met, no consistent or compelling reasons for not switching were apparent. During the 6 weeks following completion of the oral course, recurrence of infections, or readmissions due to reinfection did not occur. The percentage of patients treated with antibiotics, the length of hospitalization of these patients, the number of courses per patient, the length of the courses, and the indications for therapy were comparable for the two periods, as was the percentage of patients treated orally during the entire course, and the percentage of patients starting on iv treatment who met the criteria for iv- oral switch. Hence, the patient groups and a number of indicators of the physicians' antibiotic policy were comparable for the two periods.With an early switch considerable savings can be achieved: when we extrapolate theresults of the study periods, over dfl.100,000 per year, that is c.US$50,000, can be saved for the wards studied. In a number of comparative, randomized studies, savings reached per patient with an early iv- oral switch ranged from £220 to US$5600. These savings were achieved by lower purchase costs for oral antibiotics, but also by a shortened period of hospitalization. The estimated annual reduction for an average hospital in purchase and administration costs of antibiotics ranged from US$30,000 to US$80,000. The present study was not designed to prove in a double-blind fashion that an early switch to oral therapy has the same efficacy as a full IV course.

In accordance with a number of recent reviews and a consensus statement of the American Thoracic Society concerning the management of community-acquired pneumonia, we believe that the available studies provide sufficient evidence to switch to oral treatment if the condition of the patient has improved after a few days. Since there is a compelling reason to change the current prescribing practices, an important question is how to alter these practices. Patient Education alone is usually not effective. Intervention programmes that are successful usually provide immediate feedback, directed to the physician-in-charge, about a specific patient, and consisting of clear, unambiguous advice.[21]

Scope of switch from IV to Oral are
IV-to-PO switch therapy can be used with many kinds of medications, but particularly useful in antibiotics. Many studies have shown that IV-to-PO switch therapy is a viable option in infectious diseases.

- Antibiotic IV-to-PO switch therapy has been effectively used in conditions such as:
- Community-acquired pneumonia (CAP): Pneumonia that is contracted from the general population outside the hospital. CAP is most commonly caused by Streptococcus pneumoniae, but also by a few other bacteria and viruses.
- Spontaneous bacterial peritonitis: Bacterial infection of the abdominal membrane (peritoneum) common with fluid collection (ascites) from liver cirrhosis.
- Pyelonephritis: Kidney inflammation from bacterial infection. Adult septic arthritis: Joint inflammation caused by bacterial infection.
- Typically, intravenous antibiotics can be switched to oral medication in two or three days, provided the patient's condition is stable.

- The important factors that influence switch to oral therapy include:
- Absence of suppurative (pus-forming) infection.
- Ability for oral food intake.
- No positive blood culture test results.
- Respiratory rate.
- Heart rate and blood pressure.
- Absence of fever.
- Oxygen saturation Patient's mental status
- To implement a safe and effective IV-to-PO switch therapy in community-acquired pneumonia following criteria are essential:
- Improvement in cough and respiratory distress.
- Absence of fever for at least eight hours.
- White blood cell count within the normal range.
- Ability for oral intake of food and medications.

For successful implementation of IV-to-PO therapy, it is important for hospitals to establish a protocol to

- Identify the patients on IV medication suitable for switch therapy.
- Check if the patient's condition is stable for switch therapy.
- Implement the switch in consultation with the physician.
- Monitor the patient's progress after the IV-to-PO switch.
- A computerized program where the pharmacist, physician and infectious disease specialist coordinate the switch can streamline the process.

CONCLUSION

More number of medications are suitable for conversion from IV to oral therapy and various types of IV to oral conversions are possible. There are various guidelines available in this regard and each hospital should implement such a guideline at the initiation of a clinical pharmacist in order to accomplish an ideal IV to PO conversion therapy.[22] The clinical pharmacist should thoroughly review the medical records and identify patients who are eligible for parenteral to oral therapy conversion. In the Indian scenario, we have yet to accomplish an ideal IV to PO conversion program in our day-to-day clinical practice. The swtichover therapy has shown tremendous results. Before implementation of switch over guidelines 54% of patients who could have been switched were actually switched to oral treatment, after a median of 6days of iv therapy. After implementation of guidelines, the percentage rise to 83% therapy was also switched earlier, after a median of 4 days.

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