SJP Sarawak Journal of Pharmacy

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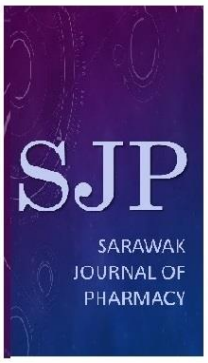

A Review on the Intravenous Oral Antibiotic Conversion Practice in Hospital Kanowit: A Retrospective Study

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ABSTRACT

Introduction: Antimicrobial resistance is one of the most serious public health issues around the globe. Intravenous Oral Switch (IVOS) practice is important in delaying antimicrobial resistance. Hence, information on our IVOS practice helps improve our effort against antimicrobial resistance.

Objective: In this study, we aimed to review current intravenous oral antibiotic conversion practice in Hospital Kanowit.

Methods: We conducted a retrospective observational study in Hospital Kanowit. Patient's information obtained from the medical records unit. All names recorded in the tally card of the intravenous antibiotics between 1st October 2015 and 31st December 2015 screened for possible inclusion. Descriptive analysis was conducted on the mean duration of intravenous antibiotics uses before IVOS. Mann-Whitney test used to compare the length of stay (LOS) between groups based on early IVOS, while one-way ANOVA test used to compare the

duration of intravenous antibiotics use among groups based on results of culture and sensitivity by using the Statistical Package for the Social Sciences (SPSS) version 15.

Results and Discussion: 63 prescriptions identified, screened, and 39 were eligible for early IVOS. Mean age of the patients was 60 years (SD=18.6 years). Mean duration of intravenous antibiotics used before IVOS done was 2.92 days (SD=1.16 days), and the mean LOS was 7.72 days (SD=4.50 days). We found that early IVOS did not reduce the LOS of the patient in hospital significantly (P = 0.906), possibly due to other co-morbidity, logistic and social issues. Results of culture and sensitivity did not significantly affect means duration of antibiotic used before IVOS (P =0.132).

Conclusion: Large array of IV antibiotics was eligible for early IVOS (61.9%), our rate for early IVOS was 76.9%. Local IVOS guideline is necessary, and we have yet to accomplish an ideal intravenous to oral conversion program in our day-to-day clinical practice. Thus continuous effort needed.

Keywords: Intravenous oral switch, antibiotic, practice

INTRODUCTION

Antimicrobial resistance is one of the major health care issues around the globe nowadays. Although different regions have different concerns, due to the prevalence of resistance of major pathogen observed among Asian country, thus Asian countries were pointed out as the epicentres of resistance (1,2). Among community pathogens, penicillin- or macrolide-resistant *Streptococcus pneumoniae*, methicillin-resistant *Staphylococcus aureus* (MRSA), and multidrug-resistant (MDR) enteric pathogens are of major problems in the Asian region (1,3,4). This alarmed us that inappropriate and unnecessary antimicrobial usage and lacking monitoring on the usage leads to an increase in healthcare costs and pathogen resistance (5).

According to guidelines on antimicrobial stewardship program, one of the essential methods to avoid antimicrobial resistance suggested was to convert intravenous (IV) antibiotics to oral treatment rationally or known as Intravenous Oral Switch (IVOS) (6,7). World Health Organization (WHO) reported the irrational use of injection medicines, when oral medication is more appropriate, is one of the major problem worldwide (8). So what is the ideal route of administration for medication? The ideal situation is medications able to have sufficient serum concentrations to produce the desired effect at the same time, it does not produce any undesired effects (6). Therefore, ways to reduce irrational use of antibiotic is IVOS of the injection antibiotic when there is an appropriate oral formulation form of antibiotic available.

So when should we do IVOS for antibiotics? Definitely, this is the main issues that all medical officer concern about when we try to switch from IV administration to oral (PO). Generally, all the research shows that short IV course of therapy for 48-72 hours followed oral switch of the medication therapy is beneficial to many patients (9). However, this is not applicable in special indications in which high dose IV therapy required. such as endocarditis and meningitis, conditions of serious/life-threatening infections, in critically ill patients, or in the presence of contraindications to oral administration as in case of nothing per os (NPO) or comatose patients (2,9).

Here are some of the benefits of early IVOS (6):

- Reduced risk of cannula-related infections:
- No risk of thrombophlebitis in case of oral administration
- Less expensive than IV therapy
- Reduction in the hidden costs: Hidden costs mainly refer to cost of diluents, equipment for administration, needles, syringes, and nursing time.
- Possible earlier discharge

According to a study done by McLaughlin et al. (2005), a third of inpatients prescribed IV antibiotics for an extended duration of therapy are eligible for the switch to an oral equivalent. The criteria to switch always depends on the particular own facilities policy and protocol (2). Patient selection criteria for IV to oral switch over therapy adopted is as follows (8):

Table 1 Inclusion and exclusion criteria for IV to oral switch

Inclusion criteria	Exclusion criteria
Patient is able to eat their regular or modified diet or receiving enteral nutrition by oral, gastric or other appropriate enteral route	Patients with unreliable response to oral medications (severe nausea or vomiting)
Patient receives other scheduled oral medications	Unable to swallow or unconscious
For patients who receive antibiotics, signs and symptoms of infection resolved or improving (WBC decreasing toward normal range, improving chest X-ray findings, temperature less than 100°F for at least 24-48 hours and respiratory rate <20 breaths/min.)	Strict (nothing per oral) for a procedure
	GI obstruction, malabsorption, active GI bleeding, paralytic ileus or severe diarrhea
	Unresponsive to previous oral therapy
	Patients with grade 3 or 4 mucocytosis
Patient has functional gastrointestinal tract (tolerating at least 1 liter/day of oral fluids or 40 ml/hour of enteral nutrition)	Patients whose disease state that does not support oral therapy (meningitis, infective endocarditis, infection of a prosthetic device, osteomyelitis, sepsis, severe cellulitis, bronchiectasis, pneumonia with AIDS)
An appropriate oral dosage form of prescribed drug is available	
Absorption and bioavailability of oral counterpart is almost comparable to that of parenteral form	Documented pseudomonal infection and/or on IV antibiotic for <24 hours
	Candidemia treated less than 7 days
	Seizure and risk of aspiration
	Hypotension or shock
	Patient refuses oral medication as mentioned in charts
	Immunocompromized patients (febrile neutropenia, on cancer chemotherapy, posttransplant, functional asplenia)

Note: If the patient has one or more symptoms listed under exclusion criteria, then not suitable for switch over from IV to oral medications. WBC=White blood cells, NPO=Nothing per oral, AIDS=Acquired immunodeficiency syndrome

There are three types of IV to PO conversion therapy: sequential, switch and step-down therapies. A sequential therapy consists of converting from IV to oral agents with the same compound; a switch therapy is a conversion with an identical potency, and a step-down therapy is a conversion with a reduced potency (6,8,9).

In Malaysia, a significant 16% of increment in annual antimicrobial consumption reported from 2009 to 2010. Furthermore, systemic use of antibacterial remained the highest-ranked therapeutic group in our healthcare expenditure (10,14). Zooming in to the state of Sarawak, several studies had been carried out, even though is just local isolated studies, but both of them indicates there is irrational use of antibiotics (2, 12). Therefore, the aim of the study was to review the practice of switching from IV to oral antibiotics based on predefined eligibility criteria and the duration of IV antibiotic therapy for respective antibiotics used and LOS. At the same time to correlate between the durations of IV antibiotic used with the LOS and availability of culture and sensitivity. Lastly, we wish to identify the most common type of conversion therapy in Hospital Kanowit.

METHODS

Study design

This is a retrospective observational study conducted in Hospital Kanowit. Patient's information obtained from the medical records unit throughout the study period from 1st January 2015 till 31st December 2015. Universal sampling methods employed where all patients hospitalised for more than 24 hours during the study period of time screened for possible inclusion.

Study population

Adult patient (> 12 years old who admitted to male, female and maternity wards) who started with IV antibiotic included in this study. Only antibiotic which are available in our hospital included in this study are IV Augmentin, IV Unasyn, IV ceftriaxone, IV Ceftazidime, IV cefuroxime, IV Cefoperazone, IV Ciprofloxacin, IV Metronidazole, IV Cloxacillin, and IV penicillin G. IV Gentamicin and IV ampicillin excluded as both of the antibiotics mainly used in paediatric patients.

All paediatric patients, patients who started on antibiotic and referred to other hospitals, patients who referred from other hospitals for continuation of antibiotic, patients who were not eligible for oral formulation based on a permanent physiological condition (e.g.

malabsorption syndrome, partial or total removal of stomach, or short bowel syndrome), those who received IV prophylactic antibiotics, or if a prolonged course of IV antibiotics required as in case of osteomyelitis, endocarditis, and melioidosis excluded from this study (refer to the exclusion list mentioned above).

If the patient was given two or more IV antibiotics, it would be recorded twice or more according to the antibiotic uses. If the patient switch from IV antibiotic to another IV antibiotic, it will be excluded from this study. Same goes to the patient which switch from oral to IV antibiotic the data will be excluded, however when they change to IV antibiotic, we will consider the following date of the change to oral medications if the patients fit the criteria of IVOS mentioned above.

Early conversion defined as IVOS done less than or equals to 72 hours or three days doses. Definition of IVOS criteria adopted from (9), if the patient fulfils the criteria, they will be classified as eligible for IVOS:

- Able to tolerate oral therapy; no vomiting or diarrhoea or NPO
- Patient afebrile temp >36 and <38 ℃ for at least 24 hours or patient temperature are showing a reducing trend.
- **Not more than one of the following:**
    1. Patient TWBC is < 4 or > 12 (if in a trend toward the normal range and without neutropenia is acceptable)
    2. BP unstable (BP have to be stable; Systolic blood pressure > 90 mmHg)
    3. RR > 20 breaths/min
    4. HR > 90 beats/min at rest (HR <100 BPM)

Data collection

Name and identification number of all patients who received IV antibiotics recorded in the tally cards for respective antibiotics. We traced the name recorded in the tally cards for their medical records. Then we screened the candidate recorded for antibiotic use according to the inclusion and exclusion criteria. The necessary data retrieved from the

medical records recorded in a structured data collection form by the principal investigator without any interference on results.

Instruments

Our data collection form developed based on a questionnaire from similar research done by Zeina M Shrayteh (2014). The data collection form included demographic characteristics of patients, co-morbidities, allergies, primary diagnosis or presumed indication for antibiotic therapy, microbiological results if available, antibiotics administered, specifying the duration of IV therapy, and LOS, lastly whether they are illegible for IVOS. Pre-testing was done for the data collection form to assure the reliability and validity of the data collection form.

Statistical analysis:

Percentage of early and non-early conversion of IV antibiotic to an oral antibiotic and mean length of IV antibiotic use analysed by using the Statistical Package for the Social Sciences (SPSS) version 15. For the association of the early conversion of IV antibiotic to the oral antibiotic with DDD and LOS will be analysed with Independent T-test and simple linear regression with a value of $P < 0.05$ is considered statistically significant.

Ethical consideration:

The study conducted in compliance with ethical principles outlined in the Declaration of Helsinki and Malaysian Good Clinical Practice Guideline. The study was approved by the Medical Research Ethics Committee (MREC) with NMRR ID NMRR-15-2041-27788.

RESULT

Sixty-three inpatients' prescriptions were identified given IV antibiotics of interests from 1st October 2015 till 31st December 2015. Thirty-nine of all prescriptions screened were eligible for early IVOS.

Table 1: Patients demographic data (n=39)

Variables	Frequency (n)	Mean (SD)
Age (Year)		60.00 (18.60)
Gender		
Male	20	
Female	19	
Duration IV Antibiotic Use before IVOS (Day)		2.92 (1.16)
Length of stay (Day)		7.72 (4.50)
Early IVOS		
No	11	
Yes	28	
Culture Isolation		
Not available	7	
Negative	21	
Positive	11	

We included 39 prescriptions (of 39 patients) which were eligible for early IVOS in this study. Mean age of the patients was 60 years (SD=18.6 years). Duration of IV antibiotic use before IVOS was 3.54 days (SD=1.30 days) and days based on doses was 2.92 days (SD=1.16 days). Mean LOS was 7.72 days (SD=4.50 days). Early IVOS was done for 28 patients. Culture and sensitivity were not available for seven patients, 21 showed no growth and 11 showed positive growth.

Table 2: Prevalence of the type of intravenous oral switch practice

Type of IVOS	Frequency (n)
Sequential therapy (*same compound*)	32
Switch therapy (*same class, similar effect*)	1
Step-down therapy (*different class, similar effect*)	6

Sequential therapy was the most common IVOS practice in Hospital Kanowit, followed by a step-down therapy and switch therapy. Table 3 shows the mean duration of IV antibiotic used before IVOS done for the respective antibiotics.

Table 3: Mean duration of IV antibiotics used before IVOS done (based on the dose of the days)

Variables	Mean (SD), day
IV Amoxycillin Clavulanic acid	2.90 (0.80)
IV Ampicillin Sulbactam	2.22 (1.35)
IV ceftriaxone	3.17 (1.33)
IV cefuroxime	3.45 (1.72)
IV Metronidazole	1 (0.47)
IV Cloxacillin	3.25 (0.43)

Table 4: Comparing the length of stay between groups of patients with or without early IVOS done

Variable	Early IVOS Yes n=28 Median (IQR)	Early IVOS No n=11 Median (IQR)	Z Statistic[a]	*P* - Value[a]
Length of stay (LOS)	7 (4) [b]	6 (10) [b]	-0.520	0.603

[a]Mann-Whitney test [b]Skewed to the right

We found that in Hospital Kanowit early IVOS did not reduce the LOS of a patient in hospital significantly (P =0.603).

Table 5: Comparing Mean duration of Intravenous (IV) antibiotic use based on results of culture and sensitivity

Results of Culture and sensitivity	n	Duration of IV antibiotic used (doses) Mean (SD)	F Statistic (df)	P-Value[a]
Not available	7	2.31 (0.78)	2.146 (2;36)	0.132
Negative	21	2.84 (1.17)		
Positive	11	3.44 (1.30)		

Our study revealed the mean duration of antibiotic used before IVOS done not significantly affected by the results of the culture and sensitivity (P =0.132).

DISCUSSION

Generally, 61.9% of the IV antibiotics are eligible for an early IVOS similar result (78.8%) found in the study done by Shrayteh ZM et al. in the year 2014 (6). However, the study shows that only one-third of those eligible for IVOS converted. In contrast, our finding showed that IVOS conversion rate in our hospital was 71.8%. This contrast mainly was due to the sample size taken in our study was not comparable to the study mentioned. Besides, the study mentioned was a multicentre study which could be more generalisable to the population (6).

The most common IVOS practice in our hospital was sequential therapy followed by a step-down therapy, and switch therapy. This is in accordance with the study done by Shrayteh et al. (6). Among the common antibiotics used in our hospital, we found that IV Cefuroxime, IV Ceftriaxone, and IV Cloxacillin did not achieve early IVOS as the mean duration used before IVOS exceeded 3 days (72 hours). IV ceftriaxone mainly used in our hospital for Leptospirosis, severe pneumonia, and cases with infection of unknown origin. Therefore, IVOS implemented with more cautious and mainly depend on patient response to the antibiotic used. So the duration of IV ceftriaxone use would be longer. Moreover, delay in IVOS was also because uncertain and afraid to oral switch too early, which would worsen patient conditions.

IV Cloxacillin indicated for wound infections, which most of the time rely on the wound progress of the patient to determine the need for IVOS. Besides, generally wound infections would need longer IV treatment in order to penetrate to the infection site. Last but not least, IV cefuroxime is mainly for urinary tract infections (UTI). Problems faced in our hospital was the recurrent cases for UTI, especially among patient having uncontrolled Diabetes Mellitus (DM), this leads to the extended use of IV cefuroxime in our hospital. This condition was concerning where we knew IV cefuroxime found to be one of the antibiotics which cause collateral damage contributing to the development of Extended Spectrum Beta-Lactamases (ESBL). This finding alerts us the need to review the use of these IV antibiotics to promote rational use of these IV antibiotics.

On top of that, contradict results found where early IVOS does not reduce the LOS of patient length of stay in hospital significantly. Most studies concluded that one of the benefits of early IVOS was to reduce patient LOS in the hospital which, could prevent nosocomial infections and reduce the medical cost expenses. Patient after early IVOS was not discharged due to there are concomitant chronic diseases (such as Tuberculosis, uncontrolled DM, and chronic wound injuries). Apart from that, logistic issues also contributed to the delay of discharge of patients.

Last but not least, we also found that the availability of the culture and sensitivity did not affect the mean duration of IV antibiotic usage before the oral switch (P=0.132). This finding contradicted the finding of the study done by Shrayteh ZM et al. in the year 2014, where availability of results of culture and sensitivity have better early IVOS rate (6). This was mainly because the medical officer reviewed the patient clinically, when the patients fulfilled and fit for early IVOS, IVOS would be done even without the culture and sensitivity. Hence culture and sensitivity served as the confirmation and reviewing the IVOS practice made.

LIMITATION

Study results were not generalizable to the whole population in Sarawak, as the study were only a single-centred cross-sectional study. A prospective interventional study to improve the IVOS practice highly recommended. The results retrieved from medical records; hence, the results might subject to high chances of incomplete data and misjudgements.

CONCLUSION

Generally, in our study, we found the mean duration of all IV antibiotics used before the oral switch was 2.92 days (SD=1.16 days). We complied with the standard that defined early IVOS was less than 72 hours. Nevertheless, 61.9% of IV antibiotics was eligible for early IVOS, and 71.8% of them switched to oral treatment. Even though there is a room of improvement, especially among these three IV antibiotics which are IV cefuroxime, IV ceftriaxone, and IV Cloxacillin. However, this study gave us a valuable insight into the current practice of IVOS in our hospital in that particular time. At least we knew that our hospital performance was in the right track in order to delay emerging of antibiotic resistance in the district hospital. Lastly, this study also served as point surveillance to evaluate the effectiveness of our antimicrobial stewardship team.

ACKNOWLEDGEMENTS

We would like to show our gratitude to our colleagues from Clinical Research Centre who provided insight and expertise that greatly assisted the research. We are also immensely grateful to all hospital staffs that provide full cooperation in helping to complete this study.

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