IMPROVING APPROPRIATENESS OF INJECTABLE ANTIBIOTICS DILUTION AND ADMINISTRATION IN THE MULTIDISCIPLINARY WARDS IN TANJUNG KARANG HOSPITAL

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Abstract

Injectable antibiotics with rapid delivery to infection sites are preferable in hospital settings, particularly in treating patients with moderate to severe infections. Therefore, inappropriate dilution and administration of injectable antibiotics can cause antimicrobial resistance, thrombophlebitis and mortality. A verification study conducted from August to September 2018 in Tanjung Karang Hospital (HTK) demonstrated that only 14.2% of injectable antibiotics had appropriate dilution and administration out of 148 samples. Subsequently, a cross-sectional study was undertaken from August 2018 to February 2019 to improve the dilution and administration of injectable antibiotics among nurses in the HTK. This was followed by the intervention phase (October to December 2018) and post-intervention evaluation (January to February 2019). The indicator measured was the percentage of appropriate injectable antibiotics dilution and administration out of the total injectable antibiotics. The standard was set at 100%. Observations of the six aspects of the appropriateness of injectable antibiotics dilution and administration were carried out. A data collection form was used to document the observations in this study. Results showed that the least appropriate aspects were administration duration and reconstitution concentration. Pareto chart analysis identified the major factors contributing to inappropriate dilution and administration of injectable antibiotics as being unaware of uncommon procedures, unavailability of local protocols, inadequate references and reminders, insufficient knowledge or experience, and a lack of monitoring. Therefore, strategies introduced were the “SWeFT” approach, improving ward pharmacists’ roles in monitoring dilution and administration of injectable antibiotics and antimicrobial stewardship. The percentage of appropriate injectable antibiotics dilution and administration successfully improved to 49.3% after interventions. Among the six aspects assessed, reconstitution concentration and administration duration revealed marked improvements. The rates for uncommon antibiotics also substantially improved by up to 100%. Strategies introduced, especially the “SWeFT” approach, were shown to be effective and hence should be enhanced to include other medications and disciplines.

KEYWORDS: Antibiotics, Dilution, Administration, Error

Problem

Injection is one of the most common routes of medication administration in healthcare. It comprises intravenous (IV), intramuscular (IM) and subcutaneous (SC) routes. IV antibiotics are administered directly into the vein, allowing rapid delivery to the infection sites to achieve rapid clinical response. Hence, they are preferable in inpatient care, where patients are often moderately to severely ill (1-4). One of the key aspects of IV antibiotics is the appropriateness of their dilution and administration. They are crucial to ensure optimal antibiotic efficacy and further prevent the possibility of antibiotic resistance.

Tanjung Karang Hospital (HTK) is a non-specialist government hospital located in Tanjung Karang, Selangor, Malaysia. This district hospital was built in 1966 with 114 beds, encompassing one paediatric ward, one obstetrics and gynaecology ward and two multidisciplinary adult wards, namely Ward 1 (male) and Ward 2 (female). Ward 1 accommodates a maximum of 45 male patients, while Ward 2 has a maximum of 35 female patients. The healthcare staff assigned to each multidisciplinary adult ward consists of an average of three medical officers, one nursing supervisor, 11 nurses and one clinical pharmacist.

Visiting specialists from various disciplines in Sungai Buloh Hospital will attend to patients in HTK on scheduled days every week. It is often observed that visiting specialists tend to prescribe antibiotics uncommon to the HTK setting in many complex and complicated cases. As a result, there is a higher likelihood of making medication errors for nurses who are unfamiliar with the method of diluting and administering these antibiotics.

A verification study in HTK revealed that the percentage of appropriate injectable antibiotic dilution and administration was only 14.2%. This low magnitude was the focus of our study. Several initiatives were planned, with the hope of reducing these errors and achieving 100% appropriate antibiotic dilution and administration across the multidisciplinary wards of HTK within three months.

Background

Medication errors are one of the major clinical issues affecting patient outcomes (5). It is defined as any preventable event that can contribute to inappropriate medication use or patient harm. Medication errors can happen at any stage, including prescribing, transcribing, preparing, administering and monitoring (6).

In the United States of America (USA) alone, medication errors lead to at least one death daily and injure about 1.3 million people annually (7). In France, 10 to 21% of the medication errors that occurred were severe and life-threatening (8,9). In Vietnam, 23.5% of the errors had a moderate impact, with 3.5% being potentially serious (10). According to Malaysia's e-Incident Reporting (e-IR) Report before 2017, 5,689 medication errors were reported, of which 366 reports came from Selangor, Malaysia. About 30% of the reported medication errors in Selangor had resulted in severe harm to the patients (11). A study demonstrated that medication errors related to antibiotics were observed to be more common among nurses (78%) compared to doctors (22%) (12).

Injectable antibiotics, especially via the IV route, can be safe and effective only when reconstitution, dilution, and administration are appropriate. It entails various risks of errors, which have been documented globally and locally. For instance, about 60% of reported life-threatening medication errors in the USA and the UK involved injectable drugs (5,13). A study conducted in a government tertiary care hospital in Selangor showed that errors during the administration phase were higher than those in the preparation phase, at 88.6% and 32.8%, respectively (14).

Focusing on IV antibiotics, medication errors similarly may occur at any stage, from reconstitution to the

administration phase (1,4,14,15). There is also a higher chance of errors as most injectable antibiotics are not designed for use readily and require reconstituting and/or further dilution before administration. The most frequent error was administering IV antibiotics within an inappropriate duration (usually too rapidly), while the second was reconstituting or diluting the IV antibiotics with inappropriate diluents (16). According to a multicentre audit on IV-related medication errors, errors in duration or rate of administration in UK and German centres were 49% and 21%, respectively (16). Besides that, the usage of inappropriate diluents was 49% in Germany and 18% in France (16).

Medication errors need to be tackled and prevented, as they reduce treatment efficacy and may conversely harm the patients. For example, any inappropriate diluents used for reconstitution can cause reduced solubility of antibiotics powder, inactivation, and eventually, administration of precipitates to the patients (16,17). The high incidence of inappropriate injectable antibiotic dilution and administration errors may also cause inadvertent complications such as antimicrobial resistance, thrombophlebitis, morbidity and even mortality (5,8-10,11,13,14,18-21). Antibiotic resistance, for instance, can develop when concentration-dependent antibiotics such as aminoglycosides are diluted less than the recommended optimal concentration (12).

Some of the possible factors leading to these medication errors include inadequate knowledge and skills, heavy workload, ambiguous manufacture leaflets on dilution methods, poor communication between healthcare practitioners, distractions, personal problems and equipment errors (1,4,5,20,22-24). These factors can be further classified into personal, contextual, and knowledge-based factors (22). In personal causes, for example, an individual might feel stressed and tired during work, while some may be confused about the prescriber's prescription. Contextual and knowledge-based factors, on the other hand, include inadequately skilled staff, heavy and long working hours, crowded wards and insufficient knowledge and experience (22).

According to a study in the Czech Republic that assessed nursing students in infusing and administering drugs, it was shown that those with master's degrees had the most extensive knowledge compared to those with bachelor's (24). It also highlighted those delegating responsibilities to less qualified healthcare practitioners for medication management were risky, especially if the facility had limited human resources (24). These factors may result in a wrong mixture or incorrect administration duration.

Most inappropriate drug preparation and administration are preventable with proper measures. Adopting correct guidelines and training, increased roles of clinical pharmacists and involvement of multidisciplinary teams can help increase awareness, knowledge, and abilities among nurses and other healthcare practitioners (14,25). Implementation of value-added clinical practices also has an important role. For instance, a study has shown that using an IV-drug compatibility-alert card and permanent supervision by clinical pharmacists can help in a better quality of IV medication preparations and administrations (25).

Measurement

The Patient Safety Goals Guideline highlights avoidable medication errors that can occur at various points of patient care (26). Realising the problems and challenges in HTK, our study focused on the preparation and administration of injectable antibiotics while adapting to the guidelines. The clinical indicator measured was the percentage of appropriate injectable antibiotics dilution and administration. The appropriateness was explored for six aspects - correct reconstitution concentration, dilution concentration, diluents for reconstitution, diluents for dilution, routes, and duration

of administration. The percentage of appropriateness was calculated using the formula below:

$$\text{Percentage of appropriate injectable antibiotics dilution and administration} = \frac{\text{Appropriate injectable antibiotics dilution and administration observed}}{\text{Total number of injectable antibiotics dilution and administration observed}} X\ 100\%$$

In the reconstitution process, a drug manufactured as a dry powder ingredient is mixed with a liquid known as a diluent to produce a particular concentration of drug solution. Dilution, conversely, is a procedure of making the specific concentration of the drug solution more dilute. These aspects were identified from the critical steps highlighted in the Model of Good Care (Table 1). It was only considered appropriate when all these aspects were performed correctly. A data collection form was used to document observations in this study. Since all the observed injectable antibiotics were freshly prepared, the means of storage were not observed in this study. The standard set was 100% in accordance with the Patient Safety Goals 2013 (26).

This quality improvement study was undertaken in the two adult multidisciplinary wards, Ward 1 (W1) and Ward 2 (W2), from August 2018 to February 2019. Our study was conducted in three phases, namely the verification phase, the intervention phase and the post-intervention phase. The study included injectable antibiotics prescribed in W1 or W2 during the study period. Exclusion criteria were adult patients with end-stage renal failure, fluid restriction, and critically ill patients, as these patients have their specific dilution guidelines. A sample size of 148 was calculated using the Raosoft Sample Size Calculator and was selected via convenient sampling in each pre-intervention and post-intervention phase. Patients who met the criteria were selected by a ward pharmacist (observer). The observer would go on any day or shift to observe staff nurses preparing and administering injectable antibiotics to the patients.

During the verification phase, a direct observation method was used to verify the percentage of appropriate injectable antibiotic dilution and administration from August to September 2018. This observational method, established by Barker and Mac Connell, was chosen over self-reporting or questionnaire survey methods, as it has been shown to provide the most reliable data (14,27-30). Consent was obtained prior to observation. During observation, any improper antibiotic dilution and administration likely to cause imminent harm to the patient was verbally intervened in the usual manner. Nevertheless, it was still included as an error in the data collection form.

In order to further explore the underlying factors that may contribute to the failure of the aspects to meet their standards, a focus group discussion was conducted. It was conducted in a non-intimidating environment among two pharmacists (moderator and assistant moderator) and eight staff nurses with similar backgrounds and experiences. All the information obtained through the focus group discussion was manually recorded and kept confidential.

Subsequently, a self-administered questionnaire consisting of the possible factors was designed and distributed to 42 staff nurses from W1 and W2 to collect their opinions about the factors that most likely contributed to the inappropriate injectable antibiotic dilution and administration. The data collected were then converted into a Pareto chart to determine the major contributing factors.

The results of this study were analysed using the Statistical Package for the Social Sciences (SPSS) software for Windows Version 22 (SPSS Inc., Chicago, IL, USA). Descriptive statistics was employed, whereby categorical data were presented as percentages. The verification phase revealed that the percentage of appropriate injectable antibiotics dilution and administration by nurses in the adult multidisciplinary wards was only 14.2% (n=21) out of 148 observations.

Table 1: Model of Good Care (MOGC) in improving appropriateness of injectable antibiotics dilution and administration

No	Process	Criteria	Standard	Verification	Post-Intervention
1	Check and verify injectable antibiotics order	• Screening for 5R by pharmacists			
		a) Right patient	100%	100%	100%
		b) Right drug (i.e., injectable antibiotics)	100%	100%	100%
		c) Right dose	100%	100%	100%
		d) Right route	100%	100%	100%
		e) Right time (frequency and duration)	100%	100%	100%
2	Countercheck injectable antibiotics order	• Countercheck all drugs filled (i.e., injectable antibiotics) against the medication order	100%	100%	100%
		• Detect and correct any filling errors	100%	100%	100%
		• Supply reminder on uncommon drug administration procedures (i.e., Injectable antibiotics)	100%	**10%**	100%
3	Prepare injectable antibiotics	• Apply aseptic method	100%	100%	100%
		• Correctly prepare drug (i.e., injectable antibiotics) by staff nurses or doctors			
		a) The right drug is chosen (i.e., injectable antibiotics)	100%	100%	100%
		b) Appropriate reconstitution (concentration)*	100%	33.8%	93.8%
		c) Appropriate dilution (concentration)*	100%	100%	100%
		d) Appropriate diluents (reconstitution)*	100%	74.4%	75.2%
		e) Appropriate diluents (dilution)*	100%	100%	100%
4	Administer injectable antibiotics	• Correctly identify patient	100%	100%	100%
		• Assess administration site	100%	95%	98%
		• Correctly administer the drug (i.e., Injectable antibiotics) by staff nurses or doctors:			
		a) Appropriate route of administration*	100%	100%	100%
		b) Appropriate duration of administration (rate)*	100%	18.9%	52.7%
5	Monitoring	• Monitor drug reconstitution, dilution and administration (i.e., Injectable antibiotics)	100%	**10%**	50%
		• Detect and correct any errors	100%	100%	100%

** indicates six aspects identified used to measure appropriateness*

Initial Assessment of the Problem

Figure 1 demonstrates the usual process of care involving injectable antibiotics, starting with the order of prescription from the ward until the administration of medication in the ward. Critical steps where errors are more common were identified with asterisks. The Model of Good Care (MOGC), as shown in Table 1, highlights and further details the critical steps from the flowchart in Figure 1.

A total of 148 samples were recruited in the verification phase, which revealed that only 14.2% (n=21) of injectable antibiotics dilution and administration were appropriate. This was lower than the standard, set as 100%, leading to an Achievable Benefits Not Achieved (ABNA) of 85.8%.

Among the six aspects, the least percentages scored in terms of appropriateness was administration duration (18.9%), followed by reconstitution concentration (33.8%) and reconstitution diluents (74.4%) (Table 1). Two additional areas (results bolded) did not meet their standards, for which strategies were also implemented to address them.

As depicted in Table 2, dilution and administration procedures of amoxicillin/clavulanate, ceftriaxone, ampicillin/sulbactam, metronidazole, and cefuroxime were the most observed antibiotics, as they were commonly prescribed in HTK. Among them, only metronidazole achieved 100% appropriateness. This suggested that antibiotics without reconstitution and dilution, such as metronidazole, had fewer errors in addition to being convenient for the nurses.

On the other hand, some antibiotics such as cefepime, meropenem, piperacillin/tazobactam and vancomycin were inappropriately diluted and administered by the staff nurses. This was due to the initiation of these antibiotics by the visiting specialists and HTK staff nurses were less familiar with them. Hence, strategies targeting uncommon antibiotics were also devised.

Our study also showed that the most inappropriate administration duration occurred in slow intravenous (SIV) bolus antibiotics rather than intravenous infusion (IVI). Of the 148 samples in the verification phase, 102 received SIV bolus antibiotics, all of which were inappropriately administered within less than a minute.

In terms of reconstitution, 74.4% of the samples were reconstituted with appropriate diluents. Water for injection was more likely to be used appropriately as reconstitution diluent compared to sodium chloride 0.9% (NS), at 73.7% and 26.2%, respectively. Despite the common usage of amoxicillin/clavulanate in adult multidisciplinary wards, it was still reconstituted inappropriately. For instance, a 1.2g amoxicillin/clavulanate powder was reconstituted with 10 ml NS instead of 20 ml water for injection (WFI).

According to Pareto analysis (Figure 2), factors that majorly contributed to the inappropriate injectable antibiotics dilution and administration were being unaware of uncommon procedures, unavailability of local protocols, inadequate references, no reminders upon antibiotics' dispensing, insufficient knowledge or experience, and inadequate monitoring by pharmacists.

Strategy

Various remedial measures were implemented during the intervention phase from October to December 2018 to improve the appropriate practice. Firstly, a new approach, named "SWeFT", consisting of five different strategies, was implemented, where "S" represents Sticker, "W" represents an antibiotic wheel, "e" represents education material such as protocol, "F" represents form, and "T" represents a table.

A new administration sticker with a Quick Response code was designed and supplied together with uncommon injectable antibiotics by the inpatient pharmacy. The sticker acts as a means to alert nurses to be cautious of their dilution and administration. This sticker also contains medication details such as the generic and brand names, compatible diluents, reconstitution and dilution procedures, as well as storage

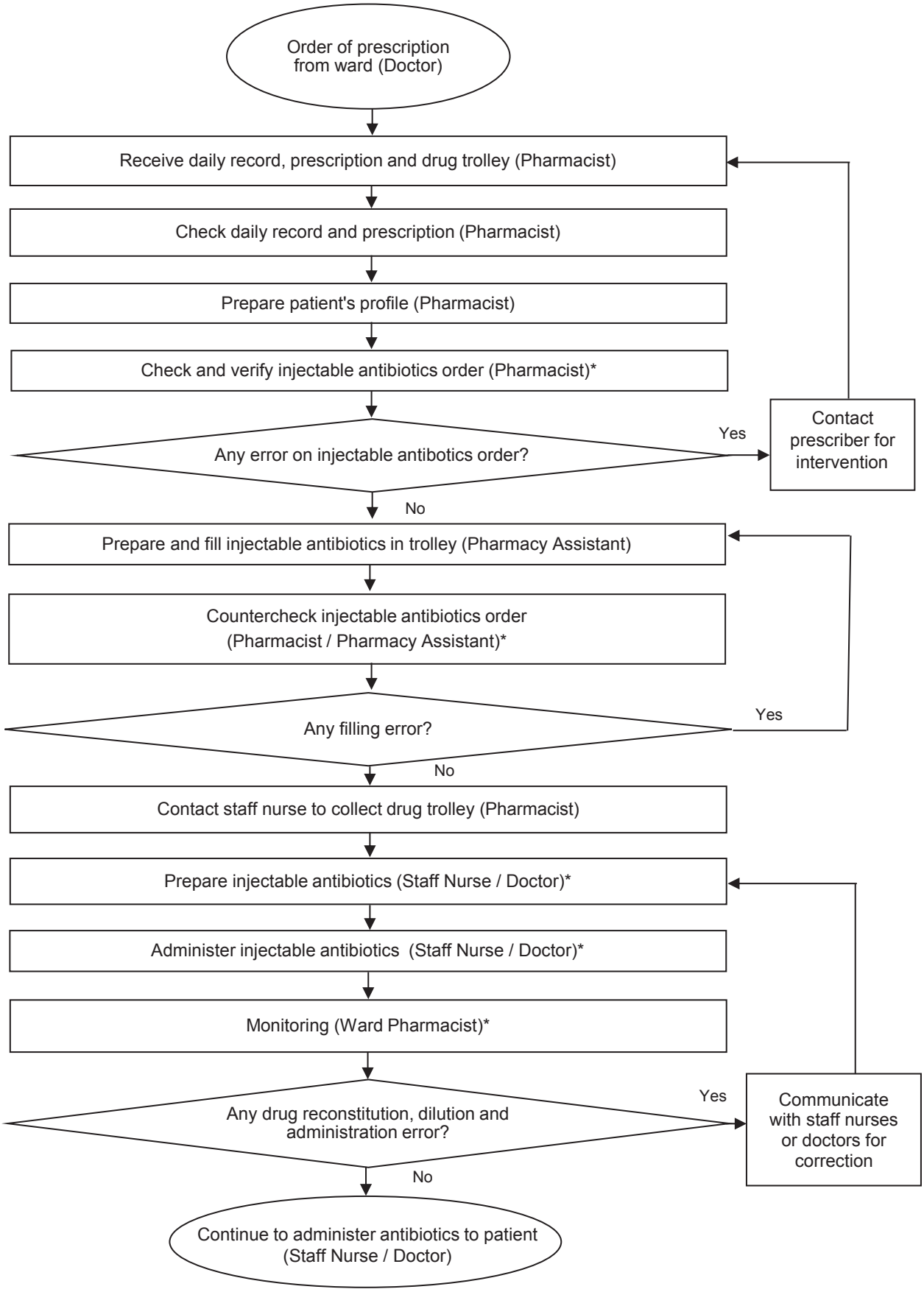


Figure 1: Process of care for injectable antibiotics (* indicates critical steps)

Table 2: Comparison of appropriate injectable antibiotics dilution and administration among different antibiotics between the verification and post-intervention phases

Injectable Antibiotics	Verification Phase		Post -Intervention Phase	
	Observed (n)	Overall Appropriateness, n (%)	Observed (n)	Overall Appropriateness, n (%)
Amoxicillin/Clavulanate	60	0 (0)	62	16 (25.8)
Ampicillin	NA	NA	1	0 (0)
Ampicillin/Sulbactam	15	0 (0)	17	7 (41.2)
Benzylpenicillin	1	1 (100)	1	1 (100)
Cefoperazone	3	3 (100)	NA	NA
Ceftazidime	1	0 (0)	NA	NA
Ceftriaxone	26	2 (7.7)	34	21 (61.8)
Cefuroxime	10	0 (0)	10	5 (50)
Cloxacillin	1	0 (0)	8	5 (62.5)
Metronidazole	15	15 (100)	3	3 (100)
Others				
Cefepime	1	0 (0)	5	5 (100)
Meropenem	10	0 (0)	2	2 (100)
Piperacillin/ Tazobactam	4	0 (0)	3	3 (100)
Vancomycin	1	0 (0)	2	2 (100)

NA: Drug not in use during the observation period
Others: Antibiotics that are infrequently used/rarely prescribed by visiting specialists (i.e., Cefepime, Meropenem, Piperacillin/Tazobactam and Vancomycin)

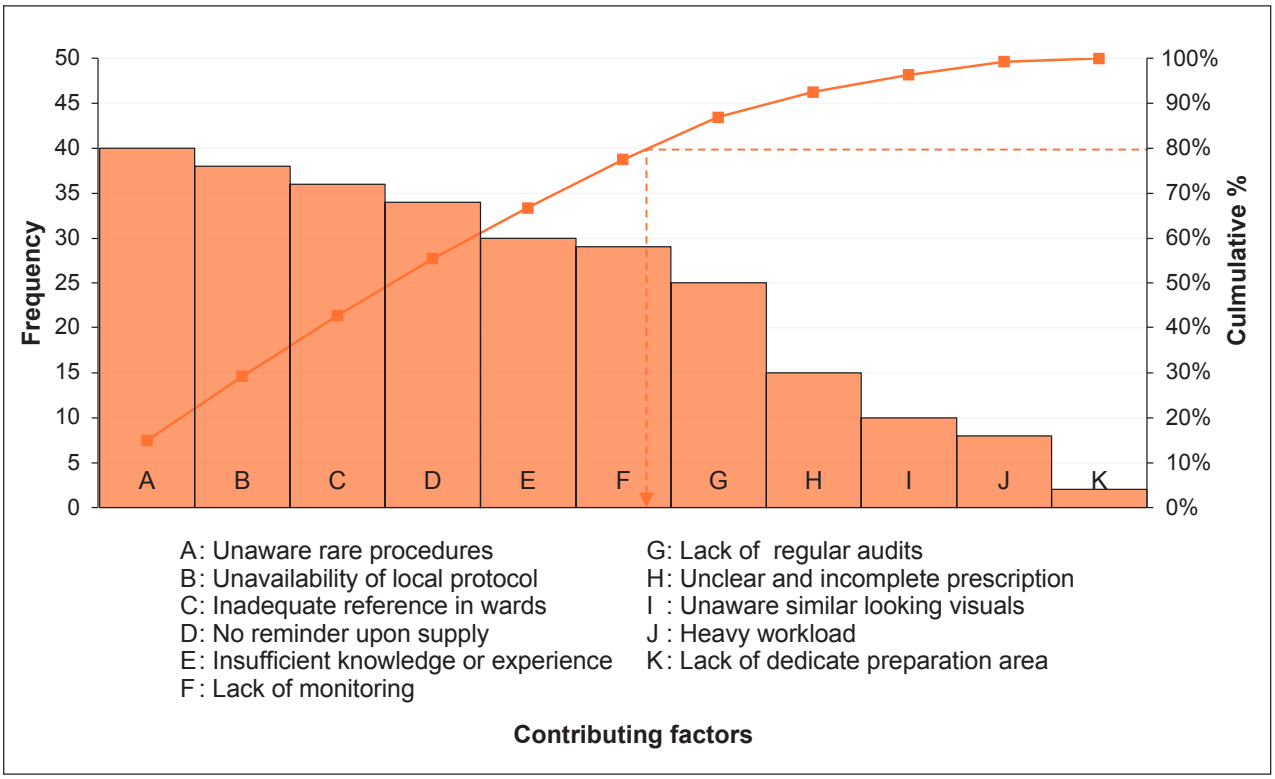


Figure 2: Factors contributing to the low incidence of appropriate injectable antibiotics dilution and administration

requirements. It was attached to the new medication administration form (HTK/531 form) and kept in the medication chart for easy access for the nurses and served as a guide for the administration of unfamiliar antibiotics. Prior to this, there were no reminder stickers with QR codes provided upon dispensing antibiotics to the wards.

A Summary Wheel and the Summary Table, which contained summarised information on all available injectable antibiotics in HTK, were also designed and kept beside the drug trolley. Previously, there were inadequate references regarding all injectable antibiotics in the wards. Hence, with this more readily and easily available information, the usage of inappropriate diluents and administration duration was hoped to be reduced.

Additionally, knowledge empowerment and adherence to the latest dilution protocol were enforced through the distribution of Dilution Protocol HTK 2018/2019 to each ward. This local protocol consists of information on reconstitution, dilution, diluents, routes, administration rates and stability for all antibiotics available in the HTK formulary. The protocol was developed based on the latest product information and guidelines, as well as the state dilution protocol. Before this, no proper references or local protocols were kept in the wards. This strategy can improve the knowledge and understanding of the various medication preparations and administrations among nurses.

The role of ward pharmacists, too, was enhanced by increasing pharmacist rounds, frequent monitoring of injectable antibiotics and better cooperation through a multidisciplinary team, especially the Antimicrobial Stewardship (AMS). Pharmacist-led education sessions or small group training in the ward provided nurses with regular updates on the knowledge of injectable antibiotics. Nurses were also educated on the correct clinical practices regarding dilution and administration of injectable antibiotics, risk factors, signs and symptoms, as well as complications if antibiotics were not diluted and administered appropriately. They were also encouraged to consult inpatient or ward pharmacists whenever there were doubts related to the dilution and administration of injectable antibiotics.

Although a better outcome was anticipated, some unexpected factors may have affected the strategy outcomes. For instance, it was acknowledged that more time and effort were required to change personal behaviours, especially for those with longer working experiences. More efforts were also needed to advocate using correct references and guidelines instead of merely following routine practices. In addition, the high workload in the wards may also influence adherence to the strategies implemented.

Results

The post-intervention evaluation was conducted from January to February 2019. It showed improvement in the appropriate antibiotic dilution and administration percentage from 14.2% (n=21) to 49.3% (n=73). However, it did not achieve the standard target of 100%.

Upon re-evaluation, all uncommon antibiotics initiated by the visiting specialist demonstrated substantial improvements, thus meeting the 100% standard (Table 2). The “SWeFT” approach, particularly the HTK/531 form with the sticky reminders and QR codes, showed its effectiveness in improving the dilution and administration of uncommon antibiotics.

Post-intervention, the reconstitution concentration and administration duration, which were initially the least appropriate scoring aspects, demonstrated the most improvements, from 33.8% to 93.8% and 18.9% to 52.7%, respectively (Table 1). There was, however, only a marginal improvement in the appropriate reconstitution diluents aspect (Table 1).

It was noted that more SIV bolus antibiotics were generally administered appropriately for up to 3 minutes. Before the strategies, the SIV bolus antibiotics were administered in less than 1 minute. Despite improvement in the administration duration, about 66% of all SIV bolus antibiotics were

still inappropriately administered. This was likely due to inadequate infusion pumps, which can regulate drug delivery at the recommended duration. It was also noted that some staff nurses found it difficult to adhere to the administration duration, as they found it increased their workload burden over time. Despite being the most widely used antibiotic, amoxicillin/clavulanate was found to be the most inappropriately reconstituted antibiotic compared to ampicillin/sulbactam and cefuroxime.

Overall, the ABNA was successfully reduced from 85.8% to 50.7%. All six critical aspects, which were subpar prior to the interventions, showed improvements following the implementation of the strategies. Nonetheless, there is room for improvement as it has yet to achieve its standard of 100%.

Lessons and Limitations

This study looked into more specific aspects of dilution and administration of antibiotics in the non-specialised hospital setting in Malaysia. The "SWeFT" approach also appears feasible and generalisable to other hospitals, as it can be easily conducted with minimal cost. Through this study, this approach has proven beneficial in improving appropriate antibiotic dilution and administration outcomes. However, it has yet to achieve its target of 100%.

Despite the success, this study has several limitations and challenges. One of the limitations recognised was the presence of an observer, which may have affected the nurses' behaviour. In addition, when the data was analysed later on, a trend was noted wherein most of the data collected by the observer occurred during the peak hours of antibiotic administration (1100H – 1300H). This could lead to the predictability of when an observation would be done and the possibility of night observations being missed out. Another possible limitation was the biases among the different observing pharmacists. A simple interrater reliability measure was conducted to minimise the bias. However, there might still be biases among the two pharmacists observing these processes during the verification and post-intervention phase.

Insufficient equipment in this resource-limited setting amplified the nurses' difficulty in administering SIV bolus antibiotics. This was one of the setbacks to which limited strategies could be implemented currently. This study has only completed one Plan-Do-Study-Act (PDSA) cycle so far, which may also be a limitation. In the future, there is a need to focus on SIV bolus antibiotics as they contribute largely to the inappropriate administration duration.

Furthermore, this study did not assess the clinical effects of inappropriate administration, such as thrombophlebitis risk. It was difficult to identify the clinical consequences of the errors due to the delay between the occurrence of complications and the identification of medication errors. It will be of value if future studies explore the incidences of complications due to inappropriate antibiotic dilution and administration.

Conclusion and the Next Steps

This study added value by identifying critical errors in injectable antibiotics dilution and administration as well as the factors causing them. By formulating relevant strategies that targeted these factors, the percentage of appropriate injectable antibiotics dilution and administration improved to 49.3%. These strategies incurred minimal cost and were self-sustainable for the next cycles. Further innovative strategies will be implemented in the subsequent cycles to achieve the standard of 100%. One of the proposed strategies was the innovation of a syringe that allows only safe and slow IV administration of antibiotics. This can allow nurses to continue with other work during antibiotics administration.

Moreover, regular updates of reference guides, continuous education and training, and more involvement with the antimicrobial stewardship team, especially for new staff, are essential in achieving the standards. Periodic audits on antibiotics' dilution and administration

are also useful in identifying the aspects requiring further remedial actions. These audits can be applied to counter-check and provide feedback on aspects of practice that are not compliant with the standard of procedure. In the future, studies can be expanded to include other injectable medications and all disciplines in HTK to ensure patients' overall clinical outcomes and safety.

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Conflict of Interest

The authors declare that there was no conflict of interest.

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