ORIGINAL ARTICLE

Development and Evaluation of the Impact of Validated Drug Dosing Pocket Guide in Pediatric Intensive Care Unit (PICU)

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ABSTRACT

Introduction: Pediatric intensive care unit (PICU) patients are constantly exposed to the risk of prescribing errors due to the complexity in drug dosing and administration. Hence, a measure to prevent these unwanted errors is necessary. **Objectives:** This study aimed to develop, validate and to assess the effectiveness of a drug dosing pocket guide in reducing the frequency of dosing-guide relevant pharmacist interventions in PICU and to explore the satisfaction as well as perception of the doctors. **Methods:** A drug pocket guide on commonly used drugs in the PICU was developed and validated. Copies of the guide were distributed to practicing doctors in the pediatric department of Hospital Pulau Pinang. The number of PICU ward pharmacist interventions, an indicator of prescribing errors, were collected and compared before and after using the guide. A run chart was plotted to evaluate the effectiveness of the pocket guide. A post-intervention questionnaire was used to gauge doctor satisfaction and perception towards the pocket guide. **Results:** Pharmacist interventions were reduced from eighteen (9.6%) to seven (3.5%) after introduction of the pocket guide, p=0.51. The run chart signaled a favorable shift below the median (median=5). The questionnaire revealed that 94.4% of the doctors were still using the pocket guide and all of them (n=18) agreed that the guide helped to improve patient safety. **Conclusion:** A validated drug dosing pocket guide reduced the frequency of pharmacist interventions which was sustained over time. This inexpensive and simple guide was generally well received by the doctors.

Keywords: Prescribing errors; Pediatric intensive care; Drug dosing guide; Pharmacist intervention

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INTRODUCTION

Safe and effective prescribing are fundamental to ensure patient safety. Nevertheless, concerns have been raised about the confidence and competency level among medical and house officers in prescribing [1]. In the United Kingdom, doctors especially junior doctors found prescribing to be very stressful and lacked the confidence to prescribe due to insufficient knowledge on drug dosing and administration [2,3].

In Malaysia, lack of knowledge and supervision were the most common contributing factors to prescribing errors in pediatric in-patient wards. A study by Khoo et al. reported 1637 prescribing errors among seventeen Malaysian hospitals [4]. Pediatric general wards had the most prescribing errors, followed closely by pediatric intensive care units (PICU), and neonatal intensive care units (NICU). This trend was most notable in key hospitals such as Hospital Kuala Lumpur and Hospital Pulau Pinang. Prescribing in pediatric patients is complex. Each dose is individualized based on a patient's various factors such as age, weight, body surface area and clinical condition. That each dose is calculated differently is a potential source of dosing errors [5,6].

Statistics from the Medication Safety team, Hospital Pulau Pinang revealed that the pediatric department topped the total number of reported medication errors in 2020, with a total of 10 cases (32.2%) out of 31 cases reported. This included medication errors reported from pediatric medical ward, neonatal ward, NICU, and PICU [7]. In 2021, there were three medication errors reported in PICU in the first quarter of the year, including one due to prescribing error. This has led to additional monitoring and treatment intervention to revert the harm caused. With an increase in the number of new junior doctors who were unfamiliar with the drug dosing, prescribing in PICU could be an overwhelming experience. These doctors rely highly on ward pharmacists to provide instant information and recommendations to accurately prescribe medications while avoiding errors.

Pharmacist intervention is defined as a recommendation provided by a pharmacist to the medical care team in response to the identification of a drug-related problem

in an individual patient. This intervention may be initiated at any point of the medication delivery process. A pharmacist would intervene in situations such as incidences of inappropriate or incomplete prescribing of a drug, its dose, its frequency, or duration of therapy, or when a therapy involves a drug that requires relevant laboratory monitoring. However, the ward pharmacist service may not be available for an entire 24-hour day or during public holidays. Moreover, the recent COVID-19 pandemic in 2020 – 2021 has shown that direct, face-to-face discussion on prescribing and pharmacist-to-physician interactions were negatively affected due to social distancing requirement and redistribution of manpower. Hence, this warrants for an easily accessible, self-educational intervention tool in the form of a pocket-size, dosing guide on commonly used medications that a PICU physician can use to assist drug prescribing.

We aimed to develop, validate, and evaluate the effectiveness of the drug dosing pocket guide in reducing frequency of pharmacist interventions related to dosing guide. Additionally, we aimed to evaluate the users' particularly doctors' satisfaction level and perception for this simple, self-help interventional tool.

MATERIALS AND METHODS

This is a prospective interventional study conducted in the Pediatric Department, Hospital Pulau Pinang, Malaysia from September 2021 to February 2022. This study consisted of two phases, namely development and validation of the drug dosing pocket guide and evaluation of its effectiveness in reducing pharmacist intervention, as well as physician satisfaction and perception of the pocket guide. The study was registered in the National Medical Research Registry (NMRR-22-00105-TX2) and has obtained Medical Research Ethics Committee approval.

Development and validation of drug dosing pocket guide

A comprehensive drug dosing guide on commonly used medications in the PICU was developed by a PICU ward pharmacist. The selection of medications in the pocket guide was based on PICU drugs listed in the Ministry of Health Malaysia Pediatric Pharmacy Services Guideline [8]. Some medications were included based on pediatricians' requests and frequency of the drugs involved in the medication errors that occurred in the PICU for the year 2021. Antibiotics and anti-epileptics were excluded because antibiotic guidelines and a pediatric neurology dosing guide were available.

The prototype dosing pocket guide was validated by five experts that consisted of a consultant pediatrician, pediatric specialists and PICU pharmacists. The content validation involved the grading of accuracy, usability, suitability, and ability to reduce medication error using an investigator-developed questionnaire with 4-point Likert scale (1 for not relevant to 4 for highly relevant) (Figure 1). The content validation was done using a non-face-to-face approach via an online Google form sent to the experts.

Evaluation of the efficacy, satisfaction and perception of the drug dosing pocket guide

The validated drug dosing guides were then distributed to all medical doctors practising in the Pediatric Department, Hospital Pulau Pinang. Universal sampling method was used to recruit doctors. Informed consent was obtained from the recruited doctors. Doctors who received the drug dosing pocket guide were included whereas doctors who were on maternity leave and transferred out of the department during the study period were excluded. Instructions on the use of the drug dosing pocket guide were provided. The doctors were informed to use the pocket guide. After two months of usage and familiarization of the pocket guide, the doctors filled up the questionnaire that were sent to them via Google form through WhatsApp message. A 12-item questionnaire was adopted from Reynolds et al. [9]. This questionnaire permits for unrestricted use, distribution and reproduction in any medium. The questionnaire was divided into three sections, namely (1) the use of the drug dosing pocket guide; (2) format of the drug dosing pocket guide; and (3) content of the drug dosing pocket guide. Data collected were descriptively summarised and responses were expressed in percentage (%) with the number of respondents to each question as a denominator.

One certified PICU based ward pharmacist performed interventions and answered inquiries as a routine activity daily in the PICU. All relevant interventions and inquiries related to the drugs listed in the dosing guide during the study period were included. Any interventions and inquiries not related to the drug listed and irrelevant information such as availability, brand name and others on the drug listed were excluded. Baseline data on all relevant interventions that were done and inquiries that were answered by the PICU ward pharmacist was collected over a two-month period before introducing the drug pocket guide. Two months after the distribution of the pocket guide, a post-intervention set of data was collected over another two-month period. Similarly, all relevant interventions done, and inquiries answered by the same PICU ward pharmacist were collected. The two sets of data were retrieved from the ward pharmacist daily activity form.

A run chart was plotted to evaluate the success of the drug dosing pocket guide to be as close to real time as possible. A run is a series of points in a row on one side of median. Data was collected from the monthly report of the frequency of relevant pharmacist intervention since January 2021 to identify a shift or trend before the

introduction of drug dosing guide. At least ten points were needed for the run chart to be applicable [10].

Data analysis

Content validity index (CVI) and scale-level content validity index (S-CVI) were calculated to establish the validity of the dosing pocket guide [11]. A minimum CVI of 1 (for five experts) was considered acceptable [12,13]. A CVI form is shown in Figure 1. The data was analyzed using IBM Statistical Package for Social Sciences (SPSS) software Version 26. Data in categorical values were presented in frequency and analyzed using Fischer exact test. Results were significant if p-value were less than 0.05. There were three probability-based rules namely the shift, trend and run rules which were used to objectively analyze a run chart or evidence of non-random partterns in the data based on an alpha error of $p<0.05$ [10]. The median was calculated and used as the chart's centre line to interpret a run chart. Critical values were used to determine if too many or too few runs exist in the run chart. The lower limit for the number of runs was set at 6 and the upper limit at 16 [9, 14, 15].

Questions	Relevance
1. The drug doses in this drug dosing pocket guide are accurate	1 2 3 4
2. The drug dilutions in this drug dosing pocket guide are accurate	1 2 3 4
3. The drug doses mentioned in this drug dosing guide are suitable for infants and children	1 2 3 4
4. The list of drugs in this guide comprises of the commonly used medications in paediatric intensive care unit	1 2 3 4
5. The guide serves as a quick access to information on drug dosing and administration in paediatric intensive care unit	1 2 3 4
6. The guide is useful to support prescribing among the doctors in paediatric intensive care units	1 2 3 4
7. The drug dosing pocket guide will help to reduce medication error	1 2 3 4
8. The drug dosing guide is simple and easy to use	1 2 3 4
Scale Content Validity Index (S-CVI)	

Figure 1 : Content validation index (CVI) form.

RESULTS

The final drug dosing pocket guide consisted of 26 drugs. Information regarding the dose, dilution, method of administration and strength of the drugs were included in the pocket guide. The content validation included five experts who consisted of one consultant pediatrician, two PICU specialists, and two PICU pharmacists. All the experts agreed and graded the content to be relevant. Scale level content validity i ndex (S-CVI) was calculated to be 1, which was an acceptable CVI value.

Questionnaire survey

A total of 29 medical officer doctors in the Pediatric Department received the physical copy of drug dosing pocket guide, accounting for 88% (29/33) of doctors in the department. However, two doctors were excluded as they transferred out during the study period and did not respond to the questionnaires. The response rate was 62% with eighteen doctors who responded and completed the questionnaires. Most of the doctors 17/18 (94.4%) were still using the drug dosing pocket guide. Majority of the doctors (88.9%) were at least satisfied with the material, colour and size of the drug dosing guide. None of them are dissatisfied with the pocket guide material. Thirteen of the respondents (72.2%) preferred the dosing guide to be printed as both plastic card and in PDF format. One respondent suggested for an online link which is continuously updated is the way to go rather than replacing and reprinting new cards for the updated version. Majority of the respondents, 13 participants (72.2%) were satisfied with the content in the dosing chart and have no further comments or suggestions; while 5 other participants (27.8%) gave suggestions such as to include information regarding common antibiotics dosing, potassium chloride corrections and renal dose adjustment for end stage renal failure patients. All respondents agreed that the drug dosing pocket guide would improve patient safety and were in complete agreement for ongoing production of the guide for future doctors (Table I).

Frequency of ward pharmacist interventions

A total of 188 ward pharmacist interventions and inquiries were retrieved at baseline and 199 pharmacist interventions and inquiries during the post-intervention periods. The pharmacist interventions and inquiries reduced from 9.6% to 3.5% after introducing the drug dosing pocket guide (Table II).

In the data set before introduction of the pocket guide, 18/188 interventions and inquiries were relevant to the drug dosing pocket guide. The highest number of interventions involved inotropes (9/18, 50%); followed by miscellaneous drugs (5/18, 27.7%), sedatives (3/18, 16.7%) and neuromuscular blocking agents (1/18, 5.6%) (Table III). Among the pre-intervention data collected, there were two near-missed errors involving 10× higher doses of atropine and ketamine prescription. These were intercepted by the PICU ward pharmacist, and the doses were adjusted accordingly. Overdosing of these medications may have caused detrimental toxic effect to the patients such as compromising airway patency, causing cardiac decompensation and delirium [16, 17]. Hence, timely pharmacist interventions had helped to avoid unwanted medication errors and harm to the patients. As for pharmacist inquiries, which involve responding to specific concerns from mainly medical officers in PICU helped to clarify and provide accurate information from dilution to dosing and administration of drugs. This can therefore indirectly prevent erroneous prescriptions, and ensuring safe and effective medication use. All in all, the outcome of a pharmacist intervention is the improvement of treatment effectiveness by providing recommendations on the

Table I : Responses to post-implementation of the pocket drug dosing guide questionnaire

Section 1: Use of drug dosing card

	Yes	No
Have you received a drug dosing card?	18 (100%)	
If so, are you still using the drug dosing card?	17 (94.4%)	1 (5.6%)

Section 2: Format of drug dosing card

	Very Satisfied	Satisfied	Neutral	Unsatisfied	Very unsatisfied
How satisfied are you with the material (color, size, etc) of the drug dosing card?	6 (33.3%)	10 (55.6%)	2 (11.1%)	0 (0%)	0 (0%)

Section 3: Content of drug dosing card

Do you think the drug dosing card will improve patient safety? Why?	18 (100%) Yes	
In your opinion, should we produce cards for future MOs?	18 (100%)	
	No	Suggestions
Do you have any further comments or suggestions?	13 (72.2%)	□ An online link that is continuously updated would be great. This ensures that the most up to date version is always readily available to all. Replacing and printing new cards for new versions wouldn't be the most cost effective I assume. □ Include antibiotic dosage □ KCL correction. □ Please provide to all MOs, its super useful □ Include renal adjusted dose for ESRF patients □ Hope that this initiative is continued

Table II : Number of relevant interventions recorded pre- & post-introduction of the pocket drug dosing guide

	Pre-intervention	Post-intervention	p-value*
Total interventions, n (2 months)	188	199	
Total relevant interventions	18	7	
• No. of interventions	2	0	0.51
• No. of inquiries	16	7	
Percentage of relevant interventions (%)	9.6	3.5	

* Fischer exact test

drug related problems to ensure the rational drug use [18].

In the data set post-introduction of the pocket guide, 7/199 interventions were relevant to the drug dosing guide. There were no prescribing errors related to drugs included in the pocket guide throughout the two-month period. Only 7 relevant inquiries were identified from the ward pharmacist daily activity form. Most of the inquiries were also related to inotropes (3/7, 42.9%); followed by other medications (2/7, 28.5%), sedatives (1/7, 14.3%) and reversal agents (1/7, 14.3%) (Table III). There were no relevant prescribing or dilution error after the introduction of the drug pocket guide.

Run chart analysis

The run chart (Figure 2) shows higher numbers of relevant interventions with median=5 prior to implementation

Table III : Potential Error rate in prescribing medications

Types/Categories	Pre- intervention, n (%)	Post- intervention, n (%)
Inotropes	50 %	42.9 %
Sedation & Pain	16.7 %	14.3 %
Neuromuscular Blocking Agent (NMBA)	5.6 %	0 %
Reversal	0 %	14.3 %
Others*	27.7 %	28.5 %

**Others: Inj Atropine, Inj Calcium Gluconate, Inj Magnesium Sulphate, Inj Sodium Bicarbonate, Inj Dextrose 10% & 50%, Inj 3% saline, Inj Human Albumin 5% & 20%, IVI Actrapid, Inj Salbutamol, Inj Heparin and Inj Labetalol*

of the dosing guide. Also, there was a shift (>6 points above the median line, from April to October 2021) which signaled a non-random pattern. This translated to the high incidence of relevant pharmacist interventions occurring not by chance. Following the pocket guide introduction, the median has reduced to 2. There was a steady trend of reduction in the frequency of interventions (up to four consecutive points) after the introduction of the pocket guide. However, this downward trend was not sustained as a rise in the number of interventions was observed toward the end of April to May 2022. An established trend requires at least five consecutive points moving upward or downward and this trend was not found in the run chart. Nevertheless, there was a valid shift reduction in interventions with nine points below the median=5. A total of 20 data points on the run chart did not fall on the median. The number of runs identified was 4, which was less than the expected runs.

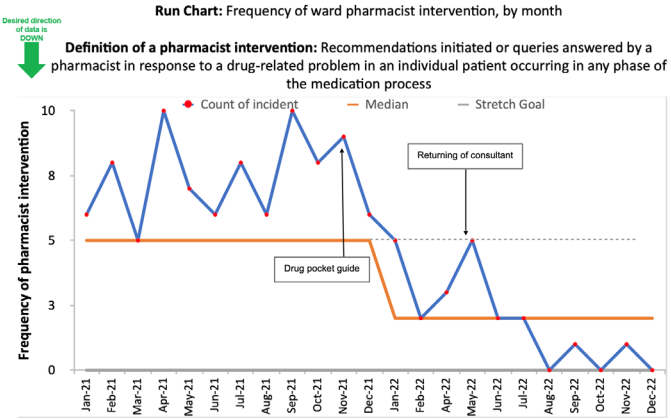

Figure 2 : Run Chart.

DISCUSSION

A validated drug dosing pocket guide was developed as an educational tool for pediatric medical doctors particularly working in the PICU. To our knowledge, this was the first study to evaluate the effectiveness of a validated drug dosing guide in reducing pharmacist interventions in the ward in Malaysia. This comprehensive, easy to use reference included concise information needed to prescribe commonly used medications safely and effectively in the PICU. Moreover, the medical doctors were generally satisfied with the pocket guide. Additionally, there were no medication errors in the period after introducing this drug dosing pocket guide.

Medication errors were generally three-fold higher among pediatric patients as compared to adults and usually occurred during prescribing [19]. A similar trend was observed in our local setting prior to introduction of this drug dosing pocket guide. A major cause towards the occurrences of such errors is performance and knowledge deficits among the healthcare providers [20]. In this respect, this drug dosing pocket guide served as a guiding tool as well as an educational device to prevent unwanted medication errors for common drugs in the PICU setting.

Sutherland et al. [21] showed that paucity of quality and accessible information on pediatric medicines contributed to the cognitive burden among doctors in the PICU setting. Prescribers often committed errors that were due to a lack of knowledge about dosing and administration, and they were unsure of reference sources to be used on the unit. One of the insights gained through qualitative interviews was that the vast range of dosing, dilution and administration references were available led different teams to administer the same drug doses using different concentrations. Thus, the authors advocated standardized infusion concentrations or formularies to tackle this issue at the organizational level. For instance, there are various dilution methods for inotropes in the widely used pediatric pocket book by Frank Shann [22], which may lead to differences in dilution patterns and confusion to the junior medical doctors. In this pocket guide, a specific dilution was adopted as standard dilution to cater for general prescribing for most of the PICU patients. Another example is there are wide range of dosing in the use of hypertonic 3% saline from 0.1-1mL/kg/hr as the maintenance treatment for raised intracranial pressure (ICP) in pediatric patients with traumatic brain injury [23]. Some guideline recommended using continuous infusion of 3% saline at rates of 0.5 - 1.5 mL/kg/hr adjusted to maintain ICP <20 mmHg [24]. This information on hypertonic saline is not available in the Frank Shann guide. This has led to different prescribing patterns in dosing based on specialists' preferences in

the PICU, whereby some may go overboard; while some maybe insufficient to achieve desired sodium serum level (145-155mmol/L) for effective ICP reduction [25]. Hence, a standard starting dose was set at 0.5ml/kg/hr and to titrate accordingly in our PICU setting. This was observed to achieve the desired sodium level quicker and maintaining cerebral protection. The PICU is one of the units with high usage of intravenous drugs that are considered as High Alert Medication such as the inotropes, sedatives, and neuromuscular blockers. Any potential medication errors in delivering these drugs such as dilution, dosing, and rate of infusion errors can be detrimental to patient care [26]. Hence, a standardized dosing, dilution and administration guide developed tailored to our local setting to be used as a standard of reference in the PICU developed in this study appears most pertinent.

From the study, we found that interventions on inotropes were the highest in both pre- and post-introduction of the pocket guide. Milrinone was being enquired repeatedly regarding its dilution and doses possibly because it was not as frequently used as other inotropes and hence, the prescribers' unfamiliarity with the drug and the need to inquire. The most frequently used inotropes were epinephrine, norepinephrine, dopamine and dobutamine in children of all ages [27]. Milrinone would only be started for patients with poor cardiac output after failing other alternatives. A randomized controlled trial compared the use of dobutamine or milrinone in low cardiac output showed that both were safe, well tolerated, and equally efficacious in preventing low cardiac output syndrome often encountered after heart surgical procedures [28]. In uncomplicated cases, dobutamine might be preferred because milrinone was more expensive than dobutamine. Thus, the usage of milrinone was not common and necessitates intervention by ward pharmacist even with the pocket guide in hand.

The number of relevant interventions has increased at the end of April to May 2022 as seen in the run chart (Fig. 2) notably because of new pediatrician from Australia being brought into the PICU. This might be due to differences in dosing and dilution practice between Malaysia and Australia. Nevertheless, after introducing the dosing drug pocket guide, the number of runs identified was lower than the median value. This suggested that the dosing drug pocket guide had made a significant change in the prescribing practice among the doctors. The introduction of the pocket guide was associated with a sustained reduction in the frequency of pharmacist intervention over time.

With the emergence and advancement of smartphones, a growing number of quick guide or flashcards had been converted into 'apps'. In the era of digitalization, most doctors have come to accept the smartphone in their daily clinical practice. During the COVID-19 pandemic, the role of smartphones was of paramount importance when regular face-to-face consultation became less feasible. A recent study revealed that almost 50% of junior doctors claimed high reliance on smartphones in searching for dosing related information [29]. Currently, more than 350,000 healthcare apps are available on the global market [30]. There was widespread access to healthcare apps, however the absence of clinical evaluation for these apps raised potential patient safety issues [31]. Thus, we produced a validated physical dosing guide which was easy to use, quick and portable in pocket size for the PICU setting and evaluated its effectiveness. The dosing guide is presently in a PDF file that could be accessible using the phone in response to the request from the doctors in the questionnaire survey.

The strengths of this study were the validated drug dosing guide developed at low cost, portable and provide great convenience to medical doctors. Nevertheless, this drug dosing guide was developed by one PICU ward pharmacist, tailored to the practice and request by the pediatricians. Thus, this pocket guide might not be generalizable nationwide as it was developed only for the PICU setting in one hospital. This was a single centre study whereby with only two months of data collection pre- and post-usage of the pocket guide. Nevertheless, a run chart approach was employed in this study to address this limitation and to evaluate the success of this dosing drug pocket guide over the time in an objective way. The drugs included in the dosing guide were commonly used drugs. PICU is an intensive care unit for pediatrics with general diseases, hence the intervention by the pharmacist was still high especially when prescribing uncommon drugs. The questionnaire surveys were sent via google form instead of a face-to-face approach due to the COVID-19 pandemic. Information regarding the selection of drugs into this pocket guide were not conveyed to the respondents which had led to suggestion on antibiotic doses to be included in the future updated version. Nevertheless, the dosing requested already existed in the National Antibiotic Guideline and pediatric protocol (under AKI section) which were available as references [32, 33].

CONCLUSION

The validated drug dosing pocket guide has been successfully developed and can improve prescribing accuracy overtime. The dosing guide was well received, applied to use by a majority of pediatric medical doctors who agreed that it helped in improving patient safety. Future plans involve continuous updates through a dynamic QR code and incorporating some suggestions from the doctors.

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