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Research Article

Pharmacists' Interventions in A Paediatric Haematology-Oncology Pharmacy: Do They Matter to Minimise Medication Misadventure?

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Abstract

Paediatric patients with cancer are a high-risk patient population for medication misadventures. This study aimed to document and evaluate the role of pharmacists' interventions during dispensing-related activities in minimising the occurrence of medication misadventure in haematology-oncology patients. The primary investigator observed and documented all clinical interventions during dispensing-related activities performed by clinical pharmacists in a haematology-oncology pharmacy during 33-day. A total of 359 interventions were performed for 1028 patients. The rates of intervention were 20.04 per 100 medication orders and 34.92 per 100 patients. Provision of drug information was the most common interventions constituting more than three quarters of all interventions. According to therapeutic groups, cytotoxic antineoplastics made up more than half of all interventions. Of all interventions, 22 involved recommendations leading to changes in patients' treatment (active interventions), and all recommendations were accepted. The top three medication errors were due to inappropriate dosing, labelling error, and unfulfilled indication. Clinical pharmacists' intervention during dispensing in a paediatric haematology-oncology pharmacy improved medication safety and patient care by minimising the incidence of medication misadventures.

Key words: Haematology-oncology, medication misadventure, paediatrics, pharmacists' intervention

Intervensi Farmasis pada Pasien Pediatrik di Apotek Hematologi-Onkologi: Apakah Farmasis dapat Mengurangi Kecelakaan dalam Pengobatan?

Abstrak

Pasien kanker pediatrik merupakan kelompok pasien berisiko tinggi mengalami kecelakaan pengobatan. Penelitian ini bertujuan untuk mendokumentasikan dan mengevaluasi peran intervensi farmasis selama dispensing (peracikan dan penyerahan obat) obat untuk meminimalisir kecelakaan pengobatan pada pasien hematologi-onkologi. Peneliti utama mengobservasi dan mendokumentasikan intervensi klinis selama dispensing oleh farmasis klinis di sebuah apotek satelit hematologi-onkologi selama 33 hari. Sebanyak 359 intervensi diberikan pada 1028 pasien. Prevalensi intervensi sebesar 20,04 tiap 100 obat yang diresepkan dan 34,92 tiap 100 pasien. Pemberian informasi obat adalah intervensi yang paling umum diberikan (lebih dari tiga per empat dari semua intervensi). Berdasarkan terapetik obat, antineoplastik sitotoksik terkait dengan lebih dari setengah intervensi. Sebanyak 22 intervensi melibatkan rekomendasi yang mengarah pada perubahan pengobatan pasien (intervensi aktif) dan semua rekomendasi diterima oleh dokter. Adapun tiga besar kesalahan pengobatan disebabkan dosis tidak sesuai, kesalahan pelabelan, dan indikasi yang tidak terobati. Intervensi farmasis klinis selama dispensing di apotek satelit hematologi-onkologi pediatrik dapat meningkatkan keselamatan pengobatan dan asuhan pasien dengan meminimalisir kecelakaan pengobatan.

Kata kunci: Hematologi-onkologi, intervensi farmasis, kecelakaan pengobatan, pediatrik

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Introduction

Children are not "mini adults". Unique characteristics of children are the wide variation in size from infancy through adolescence and the associated physiological maturational changes which occur throughout childhood that can affect drug variations pharmacokinetics and these present practical difficulties.^{1,2} Children with cancer receiving chemotherapeutic agents present further challenges to health care providers in this vulnerable area. Chemotherapy medications are among the most potent medications given to children and have narrow therapeutic window with high potential for toxicity unlike those experienced by other chronically ill populations.

Administration of chemotherapy is error prone for many reasons and even small errors can cause major harm.3-5 Additionally, some chemotherapy agents are given in various ways (e.g via intravenous, intrathecal) in various doses (e.g standard versus high) over various periods of time (e.g bolus, continous infusion). Some chemotherapy agents can be given safely by one route but not by another.6 Dosage formulations are often extemporaneously compounded to meet the need for small doses in these Moreover, the process from patients. prescribing to monitoring chemotherapy involves individuals from multiple health care disciplines whose efforts must be coordinated to minimise the risk. ⁷Hence, the greater number of medications administered will be related to the increased potential for causing errors. Hence, cancer patients should be identified as high-risk to suffer the consequences of an untoward event associated with medication misadventure.

Medication misadventure itself has been defined by Mannasse as "any iatrogenic hazard or incident associated with drug therapy". This definition embraces three

subtypes of medication safety terms including adverse drug events (ADE), medication errors, and adverse drug reactions (ADRs).⁸ Medication misadventures impose a threat on the safety of our patients and impart a high financial burden on the healthcare system. It is the evident that little studies have been done to investigate the incidence and the nature of medication misadventures in children, being a very vulnerable patient population.^{9,10}

Aside from limited established literature on the incidence and nature of medication misadventure in the paediatric patients, there is another concern regarding the justified attempts to minimise the misadventure. 11 It has been well-reported in previous studies emphasising the contribution of clinical pharmacists to patient safety in a range of clinical settings. ^{12–16} Unfortunately, there have been limited studies specifically documenting the interventions of clinical pharmacists in paediatric area, in particular haematologyoncology pharmacy setting. Therefore, this study aimed to document and evaluate the role of pharmacists' interventions during dispensing-related activities in minimising the incidence of medication misadventure in this crucial area.

Methods

This study was conducted in an haematologyoncology unit at a major paediatric teaching hospital in Perth, Western Australia. There were two pharmacies available in this hospital: one central/main pharmacy and one satellite pharmacy for haematologyoncology patients either outpatients attending clinic or inpatients on the ward. In addition to do clinical activities on the ward. haematology-oncology pharmacists were also responsible to dispense medications including cytotoxic chemotherapy orders and fluid therapy orders. A combination of computerised system for parenteral

chemotherapy orders and handwritten ordering process for oral chemotherapy and non-chemotherapy orders was used for inpatients and outpatients. The oncology pharmacists entered the chemotherapy orders into computer after reviewing the specific cancer management protocol for each patient, patient's demographic information, laboratory parameters, any associated dose modifications (i.e. based on body surface area). Then, the pharmacists produced the pre-printed parenteral cytotoxic sheet and fluid therapy order sheet. Meanwhile, oral chemotherapy orders and non-chemotherapy medication orders were written by physicians on medication chart (for inpatients) and prescription (for outpatients).

During observation, the primary investigator collected the data including the patient's demographic data, date of admission to clinic/ward, diagnoses on admission (using the International classification of Childhood Cancer 3rd edition with slight modification to accommodate hematologic and immune diseases)¹⁷, inpatient/outpatient category, the number of cytotoxic and non-cytotoxic medication orders dispensed from oncology pharmacy for each patient, the description and the type of the intervention, the medications involved, the intervened health care personnel (doctors, nurses, pharmacists), the acceptance degree of the intervention (yes/no/pending).

medications involved the interventions categorised were using Australian Medicines Handbook 2014 (AMH) drug classes.¹⁸ The type of intervention was categorised by major type with further characterisation as described by Condren et al 19 with slight modification. The rate of interventions was defined as the number of interventions per 100 medication orders and the number of interventions per 100 patients. In addition, the interventions were divided into active and passive interventions. An active intervention was defined as any action

by a pharmacist that directly resulted in a change to patient management or therapy.²⁰ All other care-centred activities were considered as passive interventions.

The pharmacists' active intervention data was analyzed to identify the occurrence of medication misadventure (if any) and the type of medication misadventure (adverse drug event, adverse drug reaction and medication error). If medication misadventure involved any medication error, the error was further classified according to the type of error and the severity of the outcomes using the National Coordinating Council for Medication Error Reporting and Prevention Taxonomy.²¹ The rate of medication error was defined as the number of errors intercepted through pharmacists' interventions per number of pharmacists' intervention and the number of errors intercepted through pharmacists' interventions per number of patient.

Demographic variables, pharmacists' intervention and medication misadventure data were summarised using descriptive statistics (mean±standard deviation for variables measured on a continuous scale, and frequencies and percentages for categorical variables) carried out using the SPSS® version 22.0 statistical package.

Results

During the 33-day data capture period, there were 1028 patients admitted to haematology-oncology unit with slightly more patients present to the clinic as outpatients than being hospitalised to the ward as inpatients. As expected, the majority of the patients came to this unit to receive medications with the remainders were admitted for regular medical examinations without involving any medication such as undertaking blood tests and imaging procedures. The characteristics of the patients during the study period are detailed in Table 1 and the top five of patients'

Table 1 Characteristics of Patients in Haematology-Oncology Unit

Patients' Characteristics	Values
Total number of patients	1028
Number of patients each week day, Mean \pm SD	31.69 ± 5.53
(Range)	(21–43)
Number of patients receiving medications (%)	845 (82.2%)
Source of patients	
Inpatients	430 (41.8%)
Outpatients	598 (58.2%)
Age in years, Mean±SD	7.25±4.96
(Range)	(0.35-18.00)
Gender (%)	, , , , , , , , , , , , , , , , , , ,
Male	635 (61.8%)
Female	393 (38.2%)

cancer diagnoses are outlined in Figure 1.

A total 359 interventions were observed and documented during data collection period. Further, there were 1791 medication orders processed and dispensed by haematology-oncology pharmacists. The categories of interventions performed by the pharmacists during dispensing-related activities are shown in Figure 2. The rates of interventions were 21.29/100 medication orders and 35.18/100 patients. It can be estimated that there were

approximately 11 interventions performed each week day.

Regarding the sources of information used by haematology-oncology pharmacists as the triggers for making interventions, the most common trigger used to initiate an interventions was inquiry by other pharmacist where this trigger was responsible for almost half of the interventions. The second common triggers were inquiry from fellow medical staff and reviews of medication orders with

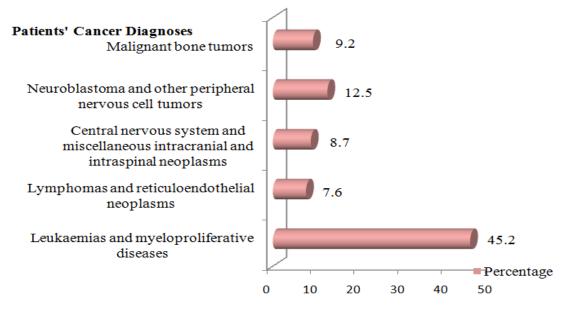


Figure 1 The Top Five Patients' Diagnoses on the Haematology-Oncology Unit during the Study

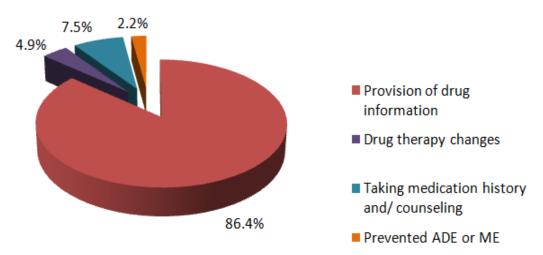


Figure 2 Categories of Pharmacists' Interventions during Dispensing-related Activities in Haematology-Oncology Pharmacy

23.1% and 17.3%, respectively.

Provision of drug information was the most common interventions performed by haematology-oncology pharmacists when processing and dispensing the medication orders, with this activity constituting more than three quarters of all interventions. Meanwhile, taking medication histories and/ patient counselling and drug therapy changes accounted for 12%, leaving the intervention category of prevented adverse drug events and medication errors with just 2% of the interventions. The majority of recommendations in drug therapy change category were due to the necessity to reduce the doses and add medications. Other drug therapy changes recommended included dosage form adjustment and dose increase. When categorised according to antineoplastics and therapeutic groups, immunomodulators were found to be the most common group implicated in the intervention with approximately 80%, followed by antiinfectives (10.9%) and gastrointestinal drugs (4.2%). Further, the breakdown of therapeutic groups uncovered cytotoxic antineoplastics made up more than half of all interventions, while another one-third involved

non-cytotoxic antineoplastics (i.e. PEG-asparaginase, tretinoin), immunosuppresants, drugs used with antineoplastics (i.e. mesna, calcium folinate, colony stimulating factor), antibiotics, and antiemetics.

Of interventions, there were interventions regarded active as interventions. The degree of acceptance of active interventions was very high where all of recommendations being accepted by either medical staff or fellow pharmacists. Further, all active interventions detected the occurrence of medication errors where almost all errors being intercepted before reaching and harming patients. There was one medication error that reached a patient due to inappropriate regimen of oral mercaptopurine where the patient receive extra dose of 25 mg/ week for 3 months. The types of medication errors detected through pharmacists' active interventions are depicted in Figure 3.

The most common category of medication errors was associated with Inappropriate dosing of correct medications comprising more than one-third of the erroneous medication orders mostly related to orders with high dose. The other common medication errors were associated with labelling errors

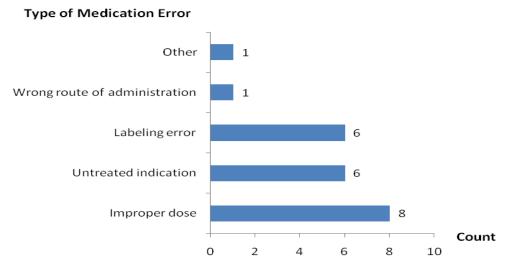


Figure 3 Types of Medication Errors Detected through Active Pharmacists' Interventions during Dispensing-Related Activities

(27.3%) and untreated indications (27.3%). These top three of medication error types were responsible for more than 90% of all errant orders. Overall, the rates of medication errors detected by dispensing haematology-oncology pharmacists through their recommendations were 1 medication error per 16 interventions, 1 medication error in 81 medication orders, and 1 medication errors in 47 patients.

Discussion

It has been recognised that pharmacists have been actively providing clinical pharmacy services and involving in patient care as the part of health care professionals. One of the major outputs of clinical pharmacy services is the generation of interventions directed at preventing or reducing drug-related harm and enhancing the efficacy of drug treatment.²² Consequently, the interventions require appropriate and adequate documentation to substantiate the contribution of pharmacists. Nonetheless, the lack of the documentation remains the widespread concern among pharmacists working in varied health care

settings.23,24

Morethanthree-quarters of the interventions in our study were related to chemotherapy medications. As with our study, Waddell et al analysing the interventions performed by oncology pharmacy staff found pharmacy staff performed around 2 interventions each day, much lower rate than that of our study. Corresponding well with our study, the majority of the interventions demonstrated in that study was provision of drug information/consultation to other health care providers.²⁵

Further, an intervention study by Wong and Gray in haematology-oncology clinics in Virginia providing ambulatory cancer services for adults and children demonstrated less number of interventions per day, half as much, as opposed to our study.² Wong and Gray found patient counselling and therapeutic recommendations (i.e. cessation of drugs without clear indications, dose recommendation and drug selection) as the leading categories of interventions. Contrast to our study, that study revealed that more than 80% of interventions were non-chemotherapy related. The distinct rate and pattern of the interventions between

our study and Wong study can be explained by the complexity of the disease states of the patients in that study given the fact that the studies did not specifically focus on paediatric oncology patients. It can be expected the adult patients in those studies present with more comorbidities in addition to their malignancies.

In addition, the incorporation of nonclinical pharmacists' interventions in Waddell et al study (i.e. interventions performed by oncology technicians and pharmacy students) might result in differences in the rate of the intervention. By contrast, a retrospective analysis of 2-year interventions by oncology pharmacists in an ambulatory oncology clinic for adults reported much higher rate of intervention In comparison to our study. That study demonstrated 583 clinical intervention for 199 patients with the rate of approximately 3 interventions performed for each patient and the most frequent intervention was pertinent to patient education.²⁶ A similar tendency of intervention type has been found in a prospective US study in adults with cancer and a paediatric oncology study in Jordan where both studies found patient counselling as the most common intervention accounting for more than a quarter of all interventions.^{2,27}

With regard to active interventions, our study observed and documented low rate with 0.67 interventions per 100 medication orders. Nonetheless, our finding is consistent previous studies undertaken general patient settings where those studies demonstrated the rates of active interventions per 100 medication orders in the range between 0.7% and 8.5%. 13,14,28-30 Specifically haematology-oncology intervention studies, Shah et al retrospectively analysed the documented clinical pharmacy activities a haematology-oncology outpatient practice. During that 12-month study, Shah et al found the rate of 0.73 interventions for each outpatient, much higher than

that of our study. Further, the top three interventions performed and documented in that study included drug addition, drug discontinuation and dose adjustment which were quite similar with that of our study.³¹ Further, it is worthwhile noting that all of recommendations in our study were accepted either by doctors, nurses or other pharmacists. A considerably high rate of acceptance to pharmacists' interventions in this highrisk area has also been reported in some studies.^{2,25,26,32} The high acceptance rate is the positive indicator that pharmacists are well accepted and considered as reliable source of information by other health care providers.

Medication errors are common during paediatric hospitalisations, occurring in nearly 6% of all medication orders for paediatric general inpatients.^{33,34} With respect to the use of chemotherapeutic medications, these highrisk medications were responsible for more than 20% of fatal adverse effects including disabilities.35,36 Our findings demonstrated inappropriate doses of medications were the leading category of medication errors in oncology pharmacy constituting more than one-third of all errors. As with our study, some studies documenting interventions for children and adult patients undertaken by haematology-oncology pharmacy staff also demonstrated improper dosing as the most common drug related problem.^{25, 37}

In addition, a study using multidisciplinary health care professionals for detecting medication errors in an adult haematology-oncology unit in Spain demonstrated a similar pattern where errors in dosing being accountable for the majority of the errors.³² Interestingly, this Spanish study showed that more than two-thirds of the errors were detected by pharmacists while the remaining cases were intercepted by medical and nursing staff. The problem associated with inappropriate dosing seemed not specific to oncology area as some non-oncology

paediatric studies also revealed the same tendency. 14, 33, 38, 39 It is important to note that almost all medication errors in our study can be detected earlier and corrected before harming patients. Our finding was more favourable compared to a paediatric oncology study by Frances et al where they found 13% of medication errors reached patients and a small proportion of the incidents resulted in temporary patient harm requiring medical intervention. Nonetheless, in keeping with our finding, this study also found the majority of errors originated from the discrepancies during prescribing. 40

Conclusions

Our findings justify the evidence substantiating the role of pharmacists through their interventions during dispensing-related activities in improving medication safety and patient care in paediatric haematologyoncology area.

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Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article

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