Pharmacy Education (2021) 21(2) 93 - 97
https://doi.org/10.46542/pe.2021.212.9397

IAI CONFERENCE

RESEARCH ARTICLE

The evaluation of compounding prescription and its availability of a licensed product for children at a private hospital in Yogyakarta, Indonesia

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Keywords
Compounding
Extemporaneous preparation
Licensed drug formula
Prescribing profile

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Abstract

Introduction: The availability of licensed drug formulas for paediatric patients is still limited, so compounded drugs still exist, especially in the form of divided medicinal powder. **Aim**: This study aimed to determine the profile of divided medicinal powder prescription and its availability in licensed drug formula for paediatric patients. **Methods**: This research was a cross-sectional study. Prescriptions containing order to compound divided medicinal powder at a ublic Hospital in Yogyakarta Special Region from January to March 2019, were collected and analysed descriptively. **Results**: The total collected prescriptions were 152. The total of active substances given to paediatric patients was 38. The most prescribed drug in the hospital was Triamcinolone. There are 34 active substances already available in licensed drug formulas for paediatric patients, so it is better not to be compounded. However, four active substances are not available as licensed product in the drug information handbook in Indonesia, so, it is reasonable to compound to provide a suitable medication (dose and dosage form) for paediatric patients.

Introduction

Providing medicine for paediatric patients is a huge challenge, including the lack of information on drug dosages and the availability of dosage to form the formulas. Medication errors and serious risks are also more common in children than adults (C. Wiedyaningsih *et al.*, 2012). Besides, the need for treatment in paediatric patients is certainly not the same as in adults because the physiology of the paediatric patients' bodies must be considered different in terms of pharmacokinetics, dosage, route of administration and adherence. That is the reason why a study for paediatric medication is required.

An extemporaneous preparation or compounded drug is commonly used as a medication for paediatrics (Widyaswari & Wiedyaningsih, 2012). Compounding is an activity of changing dosage form or mixing drugs into a new dosage form which is needed for the patient (Jackson & Lowey, 2010). It has a high risk and should be of concern because there are many undesirable events such as pharmaceutical problems, drug interactions, medication errors, quality of concoctions, and bacterial contamination problems. However, drug compounding is generally a solution to the limitation of drug formulas for paediatrics (C. Wiedyaningsih *et al*., 2012).

There are some alternatives to drug compounding for paediatric patients. Divided medicinal powder, syrup, dispersible powder/tablet, etc., are some dosage formulations that are commonly used. The study from Virginia (2014) showed that 73% of paediatric patients were more likely to get divided medicinal powder as a medication. Divided medicinal powder, also known as "puyer" in Indonesia, has several advantages, such as flexibility in dose adjusting, easy administration, and

simplicity to use (Virginia, 2014). However, it also has some disadvantages, including the possibility of adverse events, drug interactions, incompatibilities, and other risks (Rochjana *et al*., 2019).

A study of the profile and determinants of compounding services in the Yogyakarta Special Region showed that most community pharmacists (94%) dispensed prescriptions with compounding. Prescription-required compounding accounted for 11.55% of prescriptions dispensed within one month (Kristina *et al*., 2018). There is a high risk of medication error with compounding. This high compounding frequency rate and its risk make it important to do research on the profile of the compounding prescription in every health facility. The risk and negative effects of drug compounding should be minimised by using a licensed product for paediatric medication. Thus, it is necessary to carry out an analysis of the availability of licensed products for medicines formulated in a pharmaceutical installation. Studies have been conducted regarding the profile of the compounding prescription and also the evaluation of its availability as licensed products in a primary health facility in Yogyakarta (Widyaswari & Wiedyaningsih, 2012). In that study, it was found that there are still some drugs intended for children, not available in the form of a licensed formula.

This study aimed to determine and evaluate the compounding prescription profile, especially in divided medicinal powder form, and its availability as a licensed product in a public hospital in Yogyakarta Special Region. The results of this study are expected to provide long-term benefits in decreasing the frequency of compounding drugs for active substances available in licensed dosage forms for children.

Methods

This study was an analytical observation with a retrospective cross-sectional design. This study had an ethical clearance certificate from the Ethical Commission of the University of Respati Yogyakarta, no 130.3/FIKES/PL/V/2019. The population were all prescribed medicines in the hospital. The samples of prescriptions were collected by purposive sampling method in a pharmacy department at a public hospital in Yogyakarta Special Region. The inclusion criteria for the sample was that prescriptions contain an order to compound the divided medicinal powder for paediatric patients (0-18 years old) from January to March 2019. The exclusion criteria were unreadable prescriptions (illegible handwriting).

After the data were collected, they were analysed descriptively into two sections, including:

a. The profile of divided medicinal powder prescription:

   The profile analysis of prescription includes the characteristics of the subject, the age, the number of compounding, and the number of active substances contained in the preparations. The data were analysed descriptively and presented in the form of tabulation of frequency and percentage.

b. The analysis of the availability of a licensed product for paediatric patients:

The availability of the licensed product for paediatric patients (syrups, dry syrups, powder drops, suspensions, lozenges, and chewable tablets) was seen from the literature. The literature was MIMS Consultation Guidelines 2019/2020 and ISO Indonesia volume 52 (2019).

Results

In this study, the profile of divided medicinal powder prescriptions was analysed from all prescriptions that met the inclusion criteria. There are 152 prescriptions from the observation. In Figure 1, the profile of the subject was clearly shown that compounded drug was highly prescribed for paediatrics under five years old. Meanwhile, there are about 3% of the patients with the age range 12-18 years old also get a divided medicinal powder.

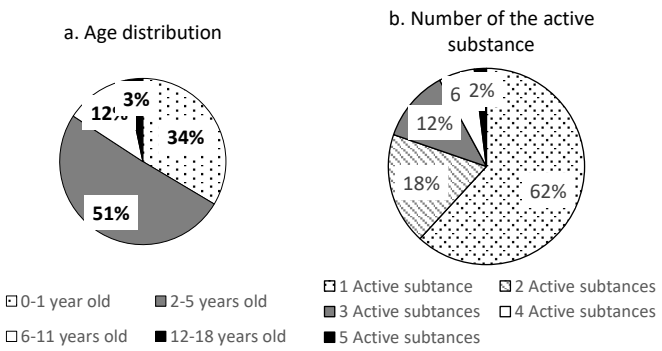

Figure 1: The profile of compounding prescription

The number of active substances that were compounded in one dosage form was also analysed. It was shown that more than half of all compounded drugs were containing one active substance. The highest number of active ingredients containing in a prescription were five substances; this kind of prescription-only appear in a low frequency (2%).

The availability of the licensed product for paediatric patients was analysed from all the active substances that compounded. The results showed that from 152

prescriptions obtained; there are 38 active substances prescribed for compounding (Table I). The top five frequently prescribed were Triamcinolone, Phenobarbital, Salbutamol Sulfate, Levotiroksin sodium, and Bromheksin. Most of them were drugs that indicated respiratory disease.

Table I: Active substances that undergo compounding along with the frequency of prescription

Active substances	Frequency	Percentage	Active substances	Frequency	Percentage
Triamcinolone	45	17.65 %	Ambroxol HCl	2	0.78 %
Phenobarbital	30	11.76 %	Methylprednisolone	2	0.78 %
Salbutamol Sulfate	25	9.80 %	Loratadine	2	0.78 %
Levotiroksin Sodium	17	6.66 %	Lisinopril	2	0.78 %
Bromheksin	15	5.88 %	Spironolactone	2	0.78 %
Terfenadine	12	4.70 %	Triheksiphenidil	2	0.78 %
Pseudoephedrine HCl	12	4.70 %	Ursodeoksikolat	2	0.78 %
Captopril	10	3.92 %	Risperidone	2	0.78 %
Piracetam	9	3.52 %	Vitamin B6 (Pyridoxine)	1	0.39 %
Furosemide	9	3.52 %	Ranitidine	1	0.39 %
Cefixime	9	3.52 %	Alprazolam	1	0.39 %
Phenytoine	7	2.74 %	Buspirone	1	0.39 %
Cetirizine	5	1.96 %	Haloperidol	1	0.39 %
Asam Folat	5	1.96 %	Amoxicillin	1	0.39 %
Diazepam	4	1.56 %	Mebendazole	1	0.39 %
Mebhydrolin	4	1.56 %	Clindamicin	1	0.39 %
Vitamin B1 (Thiamin)	4	1.56 %	Clobazam	1	0.39 %
Paracetamol	3	1.17 %	Levotiroksin	1	0.39 %
Niacin	3	1.17 %	Isoniazid	1	0.39 %

Discussion

The profile of divided medical powder prescriptions was analysed from the subject (patients) and the object (drug). In this study, 152 prescriptions suited the inclusion criteria to analyse its profile. The profile of the prescription was presented in Figure 1. It was shown that children from 0-5 years old were likely to get a divided medicinal powder as the medication. It is reasonable because, at those ages, they may have difficulty in taking a tablet or comply when given more than one drug (dosage form). Besides, the licensed product is also considered expensive (Setyani & Putri, 2019; C. Wiedyaningsih *et al*., 2012). This phenomenon was also shown in a study by Piliarta (2012), which stated that children under five years old tended to get compounded drugs than the older children (Piliarta *et al*., 2012). Meanwhile, there are about 3% of the patients with the age range 12-18 years old also get a divided medicinal powder. At this age, children should be able to get a pill or tablet as a medicine to reduce the number of compounded drugs.

The divided medicine powder can contain one or more active substances, which are mixed into one dosage form. The amount of active substances given to the patient depends on the severity and the doctor's diagnosis based on the symptoms and condition of the patient (C. Wiedyaningsih *et al.*, 2012). An analysis of the number of active substances in each prescription is useful to evaluate the prescription profile. There were 62% of prescriptions that were prepared with only one active substance. As seen in Figure 1b, the compounding order containing five active substances had the lowest frequency. This result shows that compounding practice in the hospital has compromised the potency of the compounded drug, thus increasing incompatibility and instability. The incompatibility and instability in the compounded drug will increase as more active substances are added (Setyani & Putri, 2019; C. Wiedyaningsih *et al*., 2012).

Compounding drugs using one type of active substance is usually carried out for several reasons, such as because of the limited licensed preparations for

children (syrup, drop) or because the available licensed preparations are not affordable (Setyani & Putri, 2019). In this study, the active substances that were compounded were recorded, and their frequency was calculated. From the 152 collected prescriptions, 38 active substances were compounded (Table I). These active substances were then examined for their availability in licensed products for paediatric patients.

Based on Table I, the five types of active substances mostly compounded into divided medicine powder were Triamcinolone acetonide as an anti-inflammatory drug, Phenobarbital as antiepileptic, Salbutamol as an anti-asthmatic drug, Levotiroxin Na as an antithyroid drug to treat hyperthyroidism, and Bromhexine as a mucolytic agent. In March 2020, it appeared that there are certain drug prescriptions that are higher than other months. It is because the weather and climatic condition in Yogyakarta Special Region from January to March 2020 was cold and rainy. It caused the children with low immunity to have a common cold, asthma, rhinitis allergic, etc. It was reasonable that these drugs have a high prescribing frequency. The results of this study are in line with the research of Wiedyaningsih and Oetari (2005), who also found that compounded drugs are prescribed primarily for the purpose of treating respiratory diseases and allergies.(Chairun & Wiedyaningsih. 2005).

The availability of licensed products for paediatric patients was analysed from all the active substances that were compounded. The results showed that from 152 prescriptions obtained, 38 active substances were prescribed for compounding (Table 1). The evaluation of their availability in licensed products for paediatrics based on the literature (MIMS Consultation Guidelines 2019/2020 and ISO Indonesia volume 52 (2019) showed that four drugs were not available for paediatrics. Specifically, these drugs were not available in a single composition with a suitable dosage form for children, and there was no available information on the paediatric dose. These four drugs were Thiamin, Niacin, Pyridoxine, and Buspirone. However, the other active substances that were available in licensed products were still compounded.

There are some limitations in this study that might be improved. Observation for the reason to compound the drug from the doctor should also be considered in this study. It will give more information why a lot of drug which already available in the licensed product was still compounded. Drug compounding has some issues about the stability of the compounded products, the accuracy in dose strength, and the lack of standard protocol (Gudeman *et al*., 2013; Kristina *et al.*, 2017). The pharmacy department should conduct a risk assessment of active substances that are routinely used or have a high frequency of compounding. It may prevent medication errors in the dispensing stage. If the results of the risk assessment and risk analysis show that there is a potential risk (either related to quality, efficacy, or safety) to the compounded drugs, it will be better if the drugs are delivered with the available licensed products to minimise or eliminate the risks (Jackson & Lowey, 2010).

Conclusion

The profile of divided medical powder prescriptions in this hospital from January to March 2020 were mostly written for paediatrics patients under five years old. The most compounded drug contained one active substance. There are 34 active substances available as licensed products for children. However, there are four active substances that are not available as licensed products for children, namely Thiamin, Niacin, Pyridoxine, and Buspirone. The results of this study are very useful for hospitals to identify what drugs are actually available in licensed products, to minimise the frequency of compounding and reduce the risk of medication errors in drug compounding. To minimise the risk of errors at the dispensing stage, it is recommended that these 34 active substances are delivered in available licensed products. Comprehensive research is needed to better describe the profile of compounding prescription, so it can assist pharmacists in hospitals in formulating strategic steps to reduce the risk of medication errors due to drug compounding.

Acknowledgements

This study was funded by DRPM-RisTekDikTi with contract number: DIPA-042.06.1.401516/2019. The authors would like to thank the hospitals in the Wates area, Yogyakarta Special Region, and Danis, Kandela, Prima, Olin, Advent, Simon, There, and Gita, who had helped the authors with technical matters.

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