



Beliefs about the Use of Extemporaneous Compounding for Paediatric Outpatients among Physicians in Yogyakarta, Indonesia

Chairun Wiedyaningsih^{1*}, Sri Suryawati², Yati Soenarto², Muhammad Hakimi²

1Faculty of Pharmacy, Universitas Gadjah Mada, Yogyakarta, Indonesia, 55281.

2 Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta, Indonesia, 55281.

*Corresponding author's E-mail: chairun_wied@ugm.ac.id

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ABSTRACT

Many drugs used in paediatrics are not commercially available in suitable dosage forms. Therefore, the drugs often prescribed in extemporaneous compounding dosage form. Compounding can pose health risks include poor quality and unsafe products. Studies of compounding have primarily focused on prescription profiles, reasons of prescribing never be explored. The study was conducted to identify factors influencing physicians' decision to prescribe extemporaneous compounding dosage form for paediatric outpatients. Qualitative semi-structured interviews were conducted with 15 general physicians and 7 pediatricians to identify the reason of prescribing extemporaneous compounding. The interviews were transcribed and analysed using thematic analysis. Factors underlying prescribing of compounding could be categorized to therapy, healthcare system, patient and past experience. The primary reasons of therapy factors were limited availability of drug compositions, dosages or formulas specific for children. Beliefs in efficacy of the compounding forms were higher when the drugs used primarily to overcome complex cases. Physicians did not concern about compounding form containing several active substances because manufactured syrups may also contain several active substances. Although medicines were available in manufactured syrups, limited institutional budget was healthcare system factor of compounding prescribing. The prescribing factors related to patients include easy to use, efficient and lower price. The prescribing factors related to past experience were physicians' beliefs to the progress of patient's health status.

Keywords: Compounding; interview; physician; prescription.

INTRODUCTION

Concerns about the use of drugs for children continue to rise. Children are particularly vulnerable to unwanted drug effects. In daily practice, finding appropriate medicines for the children have variety of challenges. In Indonesia, many of medicines are then administered in the extemporaneously compounding dosage forms. The medicines were usually prescribed with a product prepared extemporaneously using traditional compounding technique by crushing manufactured tablets or opening capsules. Little is known about the possible drug interaction inherent in this type of prescription. Risks such as errors may occur in adjusting doses and preparing formulations. Compounding medications is individualized, therefore, there are not many reports related to this study. The practice of compounding has not been well standardized. Therefore it may lead to contamination or products did not have high quality.

Prescribing may be influenced by many factors; not only medical but also non-medical. Differences in prescribing may also occur for other reasons, such as professional isolation in rural locations. Prescribing for children is complex, since it requires an understanding of the kinetics of the drug in several stages of physiological development.¹ The use of extemporaneous compounding medicines for children needs a lot of consideration. This

relates to the emphasis for treatment to be based on scientific evidence.

The aims of the current study were conducted to identify factors influencing the physicians' decision to prescribe extemporaneous compounding dosage form for paediatric outpatients.

MATERIALS AND METHODS

Study design

The study was designed in cross sectional survey.

Subjects

Interviews were conducted with 15 general physicians and 7 paediatricians for their paediatric outpatients. Participants were purposively selected in such a way as to ensure diversity of age, gender, professional experiences, clinical type and area to maximise the range of views expressed. The interviews and the analyses were conducted simultaneously, so that the researchers could control for topic saturation.

Interviews

Following the approvals of local government and research ethics committee for the study protocol, appointment of interviews were made to participants. Participants were interviewed in their work environments. The interviews with audio-tape recorded, which lasted between 30 and 60 minutes were conducted to elicit factors that influence



participants' decision in prescribing extemporaneous dosage forms.

Analysis

Detailed transcripts were reviewed by participants. The interview transcripts were then examined. Descriptive categories were given either based on the words used by the participants, or from the researchers' theoretical knowledge. Transcript interviews were then analysed thematically. Each theme presented in the results was supported by quotations. The quotations cited here were translated from Indonesian into English. In translating the quotations from Indonesian to English, effort was put into preserving the meaning of the quotation, rather than literally translating word for word. Parts of the quotations that were unnecessary or repetitious were excluded and indicated with an / . . /. Additions of words to facilitate the understanding of the quotation were put in square brackets.

Setting

Daerah Istimewa Yogyakarta (DIY) Province, Indonesia ie: City, Sleman, Bantul, Kulonprogo, and Gunungkidul Districts

RESULTS AND DISCUSSION

Twenty-two participants were participated. Besides practicing as private clinicians, participants spent most of their time in institutional clinical care (primary health care, hospital). There were only two general practitioners who did not practice in government and one general practitioner who did not practice in private. Characteristics of participants are given in Table 1.

Four categories were identified from the results of interviews regarding of compounding prescription, i.e., therapy-related factors, healthcare system factors, patient factors and past experiences.

The therapy-related factors

Prescribing in extemporaneous compounding, physicians can modify composition and dose of drugs as expected, i.e., as indication of the therapy. Although medicines were available in manufactured syrup, but the composition, dose, or formula were not available as physician desired. Even extreme participant's opinion stated that the drug compositions in manufactured syrup sometimes were vague. The examples of their opinion can be seen from the following quotes,

"Because we can do as what we need, not as what the drug manufacturer made"

"Many of drugs composition in syrup [manufactured products] were not appropriate"

"For the formula [manufactured product], there is one combination, which makes me do not agree, for example in a syrup contain two substances gg [glyceril guaicolate] and dmp [dextromethorphan], here is the opposite"

"/.../for example there is ephedrine in formula [manufactured product] for children but we do not want it, [therefore] we finally prescribe compounding as what we want"

Extemporaneous compounding was prescribed especially if the patient in a complex case or really did not cure with the manufactured formula. Although some physicians prefer to prescribe manufactured syrup with one active substance, but other physicians prescribed compounding since the manufactured syrup formula did not contain some active substances that can treat to some symptoms, for examples, the statements as follow,

"Because we can choose the drugs so the chances for recovery can be expected"

"I think almost all physicians for certain cases were also not free from formulas [manufactured product] because I want to achieve targets which are not met by the formula"

Paediatric population is a challenge for pharmaceutical care, involved such as lack of availability pediatric formula.² If there is a medicine available, paediatric patients may require adjustment composition or dose. The current interviews with physicians in DIY province also showed these problems. Physicians prescribed the drugs in extemporaneous compounding dosage form because of the limited manufactured formula suitable for children. Problems of drug formula for children was not only occurred in Indonesia or developing countries, but also occurred in developed countries.³⁻⁵

The healthcare system factors

Generally, physicians stated that compounding prescriptions were still needed in Indonesia. The reason was limited availability of drug dosage forms suitable for pediatric outpatients (syrups) in some health institutions. Primary health cares or public hospitals generally only provided medicines in the forms of tablets or capsules. For examples,

"Because patients cannot swallow the tablets and only tablets are available"

"In primary health cares, paracetamol, ctm, gg available separately, so it must be formulated [compounded]"

"For example in primary health cares, erythromycin never available in syrup"

In general, procurement of medicines in health institutions was based on the formulary. Medicines in private are more variable than in public institutions. Physicians in private institutions rarely prescribed extemporaneous compounding dosage form. In public and primary health care, however, multivitamin were generally not available. For this need, physicians had to ask hospital pharmacy to prepare compounding medicine that contains of several vitamins.



"For example, if we would like to give multivitamin syrup; it's not available, usually only available separately on vitamin C tablet, and vitamin B complex tablet"

"I feel the difference in private and local government practice, in private institutions asthma syrup already exists [some drugs in one formula]"

Shortage of budgets led to the limited availability of formulas and dosage forms suitable for paediatric outpatients. Majority of paediatric outpatients in primary health cares and public hospitals were covered by government health insurance. Budgets for drug supply and government insurance were limited to oral medications which generally more likely to be provided in the form of tablets or capsules. Hence physicians prescribed the extemporaneous dosage form, such statements follow,

"The oral only those, no other choices".

"Availability medicines used in the institutions are limited, if syrup [manufactured product], it is too expensive, if tablets, [save budgets], its can be used for some patients"

"Medicines for Jamkessos [government insurance] only those [mostly in generic products and in tablet/capsules dosage form], could not find other drugs"

"if Jamkesmas [government insurance] patients, the generic drugs will be used, therefore a lot of more puyer [crushed tablets]."

In general, medicines are controlled by the Health Department of each region based on the policy of the Department of Health, Republic of Indonesia. Medicines for paediatric patients in private institutions depend on their budget and formularies. Procurements of the medicines in institutions often did not correspond to the real needs. This problem was prevalent in primary health cares and public hospitals in the DIY province. Therefore, the current study showed that physicians prescribed compounding medicine due to the limitations of drug dosage form and drug formulation. Drug expenditure budget was the cause of the problem. The difficulty raised more pronounced when physicians were practicing in remote areas. Medicines were generally provided only by quota. Complaints did not only the availability syrup dosage form, but also the availability of medicines. Some medicines exhausted at the end of fiscal year. Irrational medication when viewed from the current research may also be caused by the limitations of the budget. Paediatric outpatients in primary health cares and public hospitals were mostly in government health insurance. Budgets for drug supply were limited to the government insurance. Paediatric medicines mostly are provided in the form of generic tablets or capsules. Therefore the current study showed that treatment of paediatric outpatients, especially in the peripheral areas cannot be separated from generic tablets dosage form.

The patient factors

Paediatric patients, especially those less than 5 years old are generally unable to administer tablets. However, the drugs only were available in this form. Physicians and parents expected the medicines can be administered easily. Therefore, extemporaneous dosage form was prescribed,

"Useless if given a tablet but cannot be administered, our goal is not achieved"

"if tablet...cannot be swallowed, may need bananas. In villages, patients sometimes use banana to administer the medicine"

Parents expected that their children were not given too many drugs. Several active substances are expected to be given in one formula of extemporaneous dosage form, such statements follow.

"Simplify the number, for example, had to administer five drugs, if it could be mixed [in compounding prescription] so can only be administered once..."

"Sometimes the patient (the patient's parents) when given syrup, ... given just two [syrups] sometimes protest, why given too many drugs?"

"In fact if it it not compounding too many drugs, might be up to six bottles"

Ease in measuring volume of the drug was another reason. Parents sometimes gave medicines to their children using tablespoon or teaspoon. Parents have difficulty to measure the drug appropriately, especially, if the drug was given in manufactured syrup. Dividing the tablet into half, third, eighth, etc. were also considered by participants Examples of physician's statements are as follow,

"Manufactured products have standard spoon, for example one cth is 5 ml, but [parents] spooned not appropriately, they only know that teaspoon is spoon that usually used to stir [a cup of tea]"

"usually parents did not spoon appropriately /.../ e.g. baby weight 3 kg, would be given antibiotic syrup 1/3 tablespoons, it is difficult to measure, but if we use puyer [divided powder in small sachets], milligram [the weight] will be accurate"

"if the tablet should be divided equally, it's difficult, especially for 1/8"

"on average, we give paediatrics with puyer [crushed tablet] because I believe that parents cannot divide tablet equally, a quarter of can be?"

"Because I really believe that a small dose, such as one-tenth [1/10 tablet],.....can we give it without compounding?"

Treatments for pediatric outpatients, especially in peripheral regions cannot avoid from the compounding prescriptions since its can be more save costs. The



manufactured product actually was suitable, but the price was not suitable. Manufactured syrup with varied drug composition was believed to be quite expensive. Single formula in manufactured syrup was also expensive because patients will require some sort of syrups. Pediatric patients required the drug in small quantities. The manufactured products only provided the drugs in a large volume. Physicians expected that the pharmaceutical industry produce the drugs (syrup) is small quantity dosage forms. Some statements on the issues are following,

“I emphasize the issue of cost of the syrup. Unless there is a small package”

“If in the form of puyer [crushed tablets and given in small sachets], price is cheaper, the price of bottle [manufactured product] how much?”

“If large volume, 60cc used and patient only uses 2-3 times, it's a pity if the rest of drug be discarded”

However, price did not really influence to the patients in government insurance because all medical expenses not be charged to them. The insurance has platform. Every patient with any particular treatment has a definitive tariff. Limited funding and formulas more likely affected to prescribe the extemporaneous dosage form. Price was more influential when the physician was in private institution or private practice. Puyer price tended to be cheaper. Prices will be far different if the compounding were formulated from branded names. Some statements are followed,

“But if branded medicine, it is more expensive, because if only using ¼ tablets, the price calculated for one tablet”

“Anyway, if I prescribed, [manufactured syrup], [patients] are not purchased”

Although sometimes prices did not affect in prescribing, lower price continued to be an option. Therefore, for patients with a weak economy, extemporaneous dosage form remained an option of prescription. Physicians and parents still emphasized the cost, especially if for temporary use. For example,

“Domperidon ,it would not be possible to spent in one bottle of syrup, especially for children, unless there is a small package”

Age of children to administer tablets should be considered. Management of the use of drug dosage form for children requires knowledge of pharmacology with respect to the period of child development.⁶ The current study indicated that physicians prescribed compounding because of the parents requested. Patients may be more practical and easier in administering the compounding form. However, the problem of bitter taste was expressed by physicians as patients complaint. Development of drug dosage formulations for oral use in children remains a challenge for scientists.^{6,7} The bitter taste problem should be noted. There is a lack of suitable and safe drug

formulations for children.⁸ Therefore it is expected to develop a child's preferred drug formulation.

The accuracy of treatment for children can be affected by dose measuring device. In current study, the easiness of measuring the drug dose was the reason of physicians to prescribe compounding medicines. Manufactured syrup generally accompanied with measuring spoon. However, in reality, pharmacies often did not enclose the manufactured spoon. If the pharmacies enclosed the spoon, problems may still occurred when parents used the measuring spoon. Puyer, crushed tablets which given in small sachets was the physicians choices since the medicines have been divided into measured dose regimens.

Drug prices tend to rise each year. Patients' ability to pay for medicines is becoming limited by increasing prices. This was even more burdensome for the child's medication, as drug formulations for children were more expensive than drugs for adults. Some medicines needed by developing countries usually obtained from import; therefore this will make difficulty in providing medicines for children. Regulations on intellectual property make more difficulty access of paediatric medicines in poor countries.⁸ The system made the limitations of patented medicine drug availability in poor countries.⁸ Prescribing compounding therefore is the solution of these problems. However, compounding medicines are not based on scientific evidence, and usually prepared in poor quality standard. Problems include under or over concentration of active ingredients, contamination, poor stability and inadequate packaging may occur. Therefore, initiatives have to be undertaken by health policy makers to address these issues.

Past experiences

Parents or physicians' past experiences affected to compounding prescriptions. Physicians generally believed in the efficacy of their formulas by looking at the progress of the patient's health status and repetition of patients demand. Parents and grand parents in rural areas asked for puyer rather than syrup (manufactured product) because it assumed that the puyer can cure faster. They usually asked for compounding prescription at the next visit.

“As far as I handle paediatric patients, compounding prescriptions can still be used, the important is in right dose, in fact, many patients return for treatment”

“There is no evidence which is more effective between the puyer and syrup”

Past experiences of parents and physicians toward the use of extemporaneous dosage form affect the choice of compounding prescriptions. An Indonesian paediatrician⁹ argued that prescribing is part of the culture. She even suggested that physicians tended to prescribe compounding by using the same sort of template, regardless of the individual. This may be caused by



childhood diseases were generally about the same in the area of physician's practices, as what have been stated from the current study.

CONCLUSION

In conclusions, extemporaneous dosage form was still prescribed to pediatric outpatients. To reduce the risk of extemporaneous dosage form, pediatric studies of drugs used for children have to be the priority. Providing drugs in variety of formulas based on local area needed and in small volume packages were necessary.

Prior Postings and Presentations

The manuscript has not been published and is not being considered for publication elsewhere, in whole or in part, in any language. An abstract of this manuscript has been submitted in International Conference on Pharmacy and Pharmaceutical Science, Zurich Switzerland July 2014. The abstract has been published at World Academy of Science, Engineering and Technology International Journal of Pharmacological and Pharmaceutical Sciences Vol:1, No:7, 2014.

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