

Outcomes of Pharmacy Interventions on Pediatric Medication Prescribing Patterns in Taiwan

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KEY WORDS:

dosage switching guidelines; intervention; medication safety; pediatrics **Background/Purpose:** The aim of this study was to assess the long-term effect of pharmacy interventions on patients and health care providers, and switching from prescribing extemporaneous powder dosage forms to liquid dosage forms.

Methods: An education program for parents was conducted. An attitude, knowledge and behavior questionnaire was employed to measure the efficacy of the education program. Medication management policies were then executed by providing an in-service to pediatricians, establishing dosage-switching guidelines and adding liquid dosage forms of necessary medications into the hospital formulary. Dosage-switching guidelines of pediatric medications were established by surveying the most prescribed extemporaneous powder dosage forms at the Taipei Medical University–Wan Fang Hospital. These guidelines were introduced to every pediatrician, nurse and pharmacist. The prescribing rate of extemporaneous powder prescriptions was monitored to measure the outcomes of the interventions. **Results:** The mean scores of attitude, knowledge and practice significantly improved towards a positive use of commercially available liquid medications after the patient education program for the parents. Prescriptions for extemporaneous powder dosage forms significantly decreased from 1600 (2.54%) to 13 (0.022%) monthly in the 4th year and were reduced to zero in the 6th year.

Conclusion: This study demonstrated that the pharmacists' interventions were able to change the parents' knowledge, attitude and practice towards pediatric drug dosage forms and the prescribing pattern. Effective assurance in children's medication safety can be achieved through collaboration between medical professionals and parents.

1. Introduction

Pediatric patients comprise a large proportion of the patient population, but concern about their medication safety has been neglected for a long time. Approximately 75% of the prescription medications listed in

the Physician's Desk Reference lack pediatric labeling.¹ Most of the drugs prescribed for children have not been tested in the pediatric population.² Some of the reasons for this lack of testing are small financial benefits to pharmaceutical companies, difficulties in carrying out clinical studies in children, and ethical issues due to

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children not being able to make their own decisions to participate in a clinical trial.³ Therefore, many medications have not been approved by the Department of Health in Taiwan or the Food and Drug Administration in the United States for children.

Pediatric medication safety in Taiwan is compromised because of the traditional concepts of pediatricians and parents' lack of knowledge. While facing a lack of commercially available dosage forms appropriate for pediatric patients, in the United States and Canada, extemporaneous liquid dosage forms are prescribed.⁴ However, physicians in Taiwan tend to prescribe extemporaneous powder dosage forms. Extemporaneous powder has a short shelf-life due to break down of the original formulation and efflorescence. The risk of contamination with microorganisms or other medications is unavoidable. For those drugs that are commercially available in liquid dosage forms, physicians still prescribe extemporaneous powder dosages for pediatric patients.⁵ A survey carried out by the Taiwan Health Reform Foundation demonstrated the attitudes of physicians in prescribing extemporaneous powder dosage forms for pediatric patients. For example, the powder dosage form is requested by the parents and then supplied by a pharmacy service hoping to please its customers. Alternatively, there is a misconception that a powdered dosage form can provide a more accurate dose than the liquid form.⁶ Parents in Taiwan lack knowledge of the risks involved when their children take extemporaneous powder dosage forms and passively accept prescriptions from pediatricians without question.^{7,8}

Changing the prescribing habits of pediatricians from extemporaneous powder dosage forms to commercial liquid dosage forms requires effective strategies. The aim of our study was to assess the long-term effect on the prescribing pattern for the pediatric population after implementing strategic interventions to educate parents as well as pediatricians at Taipei Medical University–Wan Fang Hospital.

2. Methods

2.1. Patient education phase

An education program was conducted for randomly selected parents of pediatric patients admitted to the Taipei Medical University–Wan Fang Hospital in January 2003. Parents whose children were under 8 years old and admitted to the Wan Fang Hospital pediatric inpatient ward were included in the study. The included parents had to be able to understand their children's medication use. Parents who were illiterate or who had visual/listening disabilities, parents who were unwilling to attend the study, or situations where different parents filled out the pre- and post-questionnaire were excluded from the study.

The pre-intervention knowledge-attitude-practice questionnaire was filled out by the parents and the education program was conducted on the following day. The education program lasted approximately 20 minutes. The pharmacists used PowerPoint slides to illustrate the correct concept, knowledge, advantages and disadvantages of the extemporaneous powder forms and liquid forms, and also the process of making the extemporaneous powder dosage form. Each parent participated in the education program individually with the pharmacist. After completion of the program, the parents were asked to fill out the post-intervention knowledge and attitude questionnaire. Three months later, follow-up phone calls were made to survey the impact of the education program on the parents' practice (Figure 1).

2.2. Questionnaire development

Phase I. Parent survey

The questionnaire was initially designed by pharmacists and five pediatric physicians. Three specialists in medicine, pharmacy and public health were then invited to





Figure 1 Study flow chart. K=knowledge; A=attitude; P=practice or participants' behavior.

assess the content validity of the questionnaire. After the completion of content validity assessment, 30 parents were invited to assess the face validity. In a pilot study, the 30 parents assessed the knowledge and practice questionnaire for test–retest reliability, and the attitude questionnaire for internal consistency.

The questionnaire consisted of three main parts. (1) Knowledge related to two aspects of powder or liquid dosage forms (dichotomous questions, scored with the summation of correct answers). Each aspect contained five questions. (2) Attitudes toward the administration of powder and liquid dosage forms (scored on a 5-point Likert scale; lower scores for preference to powder dosage forms and higher scores for liquid forms). Each aspect also contained five questions. (3) The practice of administering medications to their children in powder (5 questions) or liquid dosage forms (3 questions). These eight questions were on a 5-point Likert scale. Another three multiple-choice questions were employed to survey the decision that the parents made between powder and liquid dosage forms. The English version of the questionnaire is included in the Appendix, and its Chinese version is available from the corresponding author.

2.3. Medication management phase

In this phase, three major medication management policies were executed: (1) pharmacy-offered in-service to pediatricians; (2) addition of necessary liquid dosage form medications for the pediatric population into the hospital formulary; and (3) establishment of dosageswitching guidelines. The prescription rate of extemporaneous powder dosage forms, defined as the number of extemporaneous powder dosage forms prescribed divided by the total summation of pediatric prescriptions, was used as an indicator to measure the outcome. Follow-up was carried out from January 2003 to January 2008 (Figure 1).

The pharmacy in-service to pediatricians was opened to demonstrate the standard operating procedure of milling and making extemporaneous powder drugs, the risk and cost of extemporaneous powder drugs and the KAP (K=knowledge; A=attitude; P=practice or participants' behavior) results of the patient education program. The in-service then led to common interests of the pediatricians and a pharmacist-conducted survey on the prescribing pattern at the hospital. The pharmacy tried to identify the most commonly prescribed extemporaneous powder dosage form drugs in the hospital by reviewing all prescriptions prescribed in 3 consecutive days. This analysis included 1806 prescriptions for 744 patients. After thorough discussions, the Departments of Pediatrics and Pharmacy finally reached a consensus to establish dosage-switching guidelines and also added liquid dosage forms of necessary medications into the hospital formulary system.

2.4. Introduction of the dosage-switching guidelines

Guidelines for pediatric medication were established based on the analysis of the 3-day pediatric prescriptions. The most prescribed extemporaneous powder dosage form drugs were selected and included in the guidelines. Nine pharmacological classes of medications included in the guidelines were simple analgesics, antihistamines, bronchodilators, mucolytic agents, antiflatulents, aminopenicillins, first-generation cephalosporins, macrolides, and sulfonamides/trimethoprim. The equivalent doses for switching were established by referencing the dosage listed in the Physician's Desk Reference and the Harriet Lane Handbook. The drugs in the guidelines were grouped according to their pharmacological class, along with the generic name, solid dosage form, recommended liquid dosage form and dosage (Table 1). The physicians were able to switch the dosage form simply by referring to the guidelines.

After establishing the guidelines, they were introduced to the pediatricians and in-ward nurses in the morning meetings for 4 weeks. The content of the presentation placed emphasis on: (1) the risks of drug instability and dosage uniformity for extemporaneous powder dosage forms because of a lack of standard procedure for preparation; and (2) utilization of the dosage-switching guidelines. After each presentation, physicians, nurses and pharmacists had further communication and discussion on the topic.

2.5. Statistical analysis

During guestionnaire development, Cronbach's α value was used to measure the internal consistency of the attitude questionnaire. Spearman's correlation test was then used to examine the test-retest reliability and a level above 0.7 indicated good reliability. To determine the knowledge, attitude and behavior change between pre- and post-education, binomial variables were tested using the χ^2 test (with or without Yate's correction) or the Fisher's exact test if necessary. For numerical variables, normality was examined by the one-sample Kolmogorov-Smirnov test. Normally distributed continuous variables were tested with a paired sample t test, while other continuous data were tested using the Wilcoxon signed-rank test. NcNemar's χ^2 test was used to compare binomial data in paired samples. Computations were performed using SPSS version 10.0 (SPSS Inc., Chicago, IL, USA) for Windows. A two-tailed p < 0.05 was considered statistically significant.

3. Results

The questionnaire had good validity as assessed by the specialists and parents by multiple adjustments.

Pharmacologic class	Generic name	Brand name of solid dosage form	Brand name of liquid dosage form	Recommended dose of liquid dosage form
Simple analgesics	Acetaminophen	Panadol 80 mg/tab	Anti-Phen 24 mg/mL	10–15 mg/kg/dose Q4–6H MAX 5 dose/d
Antihistamines	Cetirizine	Zyrtec 10 mg/tab	Zyrtec 1 mg/mL	2–5 yr: 2.5 mg QD, MAX 5 mg/d 6–11 yr: 5–10 mg/d
	Cyproheptadine	Pilian 4 mg/tab	Cyproh 0.4 mg/mL	0.25 mg/kg/d 2–6 yr: MAX 12 mg/d 7–14 yr: MAX 16 mg/d
Bronchodilators	Fenoterol	Frandyl 2.5 mg/tab	Berotec liquid 0.5 mg/mL	0.1 mg/kg/dose Q6H syrup
	Procaterol HCl hemihydrate	Meptin-mini 25 μg/tab	Meptin liquid 5 μg/mL	≥6 yr: 25 µg QD-BID <6 yr: 1.25 µg/kg QD-BID
Mucolytic agents	Ambroxol Bromhexine	Axol 30 mg/tab Bisolvon 8 mg/tab	Mucosolvan 3 mg/mL Bisolvon 2 mg/mL	1.5–2 mg/kg/d <5 yr: 4 mg (2 mL) BID 5–10 yr: 4 mg (2 mL) QID
	Pseudoephedrine 60 mg Triprolidine 2.5 mg	Peace Tab	Peace syrup	6–12 yr: 1/2 tab TID-QID 5 mL TID
Antiflatulents	Simethicone	Kascoal 50 mg/tab	Gascon drop 20 mg/mL	<2 yr: 20 mg (1 mL) QID 2–12 yr: 40 mg (2 mL) QID
Aminopenicillins	Amoxicillin Amoxicillin/ clavulanate potassium	Amoxicillin 250 mg/cap Augmentin tab	Amolin 25 mg/mL Augmentin syrup	20–50 mg/kg/d (1–2 mL/kg/d) <40 kg: 20–90 mg/kg/d (amox comp) (divided Q8–12H)
1 st Generation cephalosporins	Cephalexin	Ulex 250 mg, 500 mg/cap	Ulex 25 mg/mL	Mild/moderate: 25–50 mg/kg/d, MAX 4 g/d Severe infections: 50–100 mg/kg/d
Macrolides	Erythromycin	Erythromycin 250 mg/tab	Ulosina 25 mg/mL	30–50 mg/kg/d
Sulfonamides and trimethoprim	Sulfamethoxazole trimethoprim	"Chemix" SMZ 400 mg/tab TMP 80 mg/tab	"Trimerin syrup" SMZ 40 mg/mL TMP 8 mg/mL	Pneumocystis pneumonia: 15–20 mg TMP/75–100 mg SMZ/ kg/d (divided Q6H); UTI: 8 mg TMP/kg/d (divided BID

trimethoprim; UTI=urinary tract infection.

Spearman's rho for test–retest reliability was 0.81 for the knowledge questionnaire and 0.71 for the practice questionnaire. Cronbach's α of internal consistency was 0.86 for the aspect related to powder dosage forms and 0.79 for liquid dosage forms in the attitude questionnaire.

A total of 121 parents met the inclusion criteria. There were 13 parents excluded from the study because of illiteracy or inability to communicate (3 subjects), unwillingness to attend the study (4 subjects), and one parent filled the pre-questionnaire and the other filled the post-questionnaire (6 subjects). Six parents dropped out of the study since their children were discharged earlier than expected and they did not have the opportunity to fill out the post-questionnaire. Therefore, 102 parents completed the pre-education and post-education questionnaires and 92 (92.2%) of them answered the follow-up phone calls (Figure 1). The demographic information for the parents is shown in Table 2.

The education program resulted in marked improvement in the parents' knowledge related to both dosage forms, with the mean total score increasing from 4.93 to 9.11 (maximum score=10, p<0.001; Table 3). The mean knowledge scores for both liquid and powder dosage forms were significantly increased after the education. There was an 84.7% increase in the knowledge score.

Table 2	Demographic parents*	characteristics	of	participating
Sex, fema	ale			90 (88.2)
Age, yr				33.8±6.8
Educatio	n			
Elemei	ntary school			1 (1.0)
Junior	high			1 (1.0)
Senior	high			52 (51.0)
Colleg	e			32 (31.4)
Above	college			16 (15.7)

*Data presented as n (%) or mean ± standard deviation; [†]ages of all children of the participating parents were obtained and calculated.

 1.7 ± 0.7

 4.6 ± 3.4

Number of children

Age of children, yr[†]

The mean post-intervention attitude score was significantly higher than the pre-intervention score (p < 0.001; Table 3). The mean attitude score for extemporaneous powder forms was significantly increased (p < 0.001), indicating that the parents were becoming worried about administering the extemporaneous powder dosage forms to their children after the education program. The attitude score for liquid dosage forms failed to show a significant improvement following the education program (p=0.932). However, this is because the baseline attitude score for liquid dosage forms was already high, indicating a high acceptance of liquid dosage forms.

Similar to the attitude scores, the mean practice score was significantly increased from a baseline of 22.4 \pm 3.5 to 23.7 \pm 4.2 in the 3rd month of the phone survey (p=0.003). The baseline practice score of the liquid dosage form was 9.8 \pm 2.6, which was not significantly different from 9.7 \pm 3.0 in the 3rd month (maximum score = 15, p < 0.799). The practice score of the powder dosage form was significantly improved after the education program (p < 0.001), indicating that the practice of parents for using this dosage form could be effectively changed.

The results of the multiple-choice questions for practice revealed some interesting findings. The most common reasons for choosing extemporaneous powder dosage form drugs were that they were "easy to feed" and "recommended by the physician", and there was no difference before and after the education program. With regard to the reason for choosing liquid dosage forms for children, the item "recommended by the physician" had also increased after the education program from 38 (41.3%) parents to 50 (54.3%) parents. A total of 16 (17.4%) parents switched their choice from extemporaneous powder forms to commercially available forms (liquid or pills); however, this behavior change did not achieve statistical significance (p=0.505, NcNemar's test).

Table 3	Knowledge, attitude and participating parents'
	behavior for conventional available liquid forms
	versus extemporaneous powder forms*

Pre-education score	Post-education score	р
2.93 ± 1.12	4.75 ± 0.55	< 0.001
2.00 ± 1.00	4.35 ± 0.67	< 0.001
4.93 ± 1.74	9.11 ± 0.97	< 0.001
12.3 ± 5.0	18.5±5.2	< 0.001
17.9±4.9	17.9±4.3	0.932
30.2 ± 3.9	36.4±5.7	< 0.001
12.7±2.3	14.0±2.5	< 0.001
9.8±2.6	9.7±3.0	0.799
22.4 ± 3.5	23.7±4.2	0.003
	Pre-education score 2.93±1.12 2.00±1.00 4.93±1.74 12.3±5.0 17.9±4.9 30.2±3.9 12.7±2.3 9.8±2.6 22.4±3.5	Pre-education score Post-education score 2.93±1.12 4.75±0.55 2.00±1.00 4.35±0.67 4.93±1.74 9.11±0.97 12.3±5.0 18.5±5.2 17.9±4.9 17.9±4.3 30.2±3.9 36.4±5.7 12.7±2.3 14.0±2.5 9.8±2.6 9.7±3.0 22.4±3.5 23.7±4.2

*Data presented as mean±standard deviation; [†]tested using Wilcoxon signed-rank test, $\alpha = 0.05$; [‡]normal distribution of variables was confirmed using the one-sample Kolmogorov-Smirnov test, tested using the paired sample *t* test, $\alpha = 0.05$.



Figure 2 Proportion of prescriptions that contained extemporaneous powder forms in the period 2003–2008. The numbers in the graph indicate the number of prescriptions containing extemporaneous powder forms and the percentage of the total number of prescriptions in the outpatient setting.

The monthly prescriptions of extemporaneous powder dosage forms significantly decreased from 1600 (2.54%) to 13 (0.022%) in January 2006 and to zero in January 2008 (Figure 2).

4. Discussion

The pharmacy interventions in this study were associated with an increase in parents' knowledge, attitudes and practice towards using liquid dosage forms and with a decreased rate of prescriptions in extemporaneous powder dosage forms. The study initially integrated medical and pharmaceutical expertise into a pediatric team by using the patient education data to support the proposal. The positive attitude and practice of parents on extemporaneous powder dosage forms changed to negative, indicating that pharmacists can change parents' attitude and practice through effective education. The attitude change also suggested strong counterevidence to the concept of physicians that "extemporaneous powder dosage forms are requested by the parents". Children are not simply little adults; their anatomy and physiology are quite different from adults, ^{9–11} and thus the administration of drugs is a particular concern.

Communication using evidence-based data is the key to successful intervention demonstrated in this study. Education programs addressing correct attitudes toward the use of pediatric medications, instead of updated knowledge, might be more effective in influencing the quality of care for pediatric patients.^{12,13} Communication and discussions involved in this study, including analysis of current pediatric prescriptions and introduction of the dosage-switching guidelines, provided pediatricians with information on the safety problems associated with extemporaneous powder dosage forms and played a major role in the positive and sustained outcome in this study. Our results are consistent with a previous study by Fortescue et al for preventing pediatric medication errors, which showed that improved communication between physicians, nurses and clinical pharmacists in the ward was one of the most useful strategies.¹⁴

The implications of our study are in agreement with results from previous studies related to pediatric dosage forms in Taiwan.^{8,15,16} The extemporaneous powder dosage form lacked uniformity because of the high and unacceptable variation in the weights and the content of major ingredients.^{8,15} There are no standards to test the sterility and particles for the environment and related equipment used to compound the extemporaneous formulations in hospitals.¹⁶ The Taiwan government was aware of the concern for pediatric medication safety, and started to provide incentives to pharmaceutical companies with the aim of encouraging the manufacture of more pediatric products. Effective assurance in children's medication safety can only be achieved through collaboration among the government, medical professionals and parents.

There were two major limitations in this study. The sample size of the patient education program was small and further large studies might be needed to confirm the results. The study on the patient education program also lacked a control group, but subjects were compared before and after the program. The second limitation was the lack of clinical and economical outcomes after switching the dosage forms. More complete studies in the future may be warranted to survey the full impact of pharmacy interventions on switching dosage forms for pediatric patients.

Pediatric patients represent a group that needs intensified care. With a lack of suitable drugs for pediatric patients, physicians tended to prescribe extemporaneous powder dosage forms in Taiwan. This study demonstrated that pharmacists' interventions were able to change the parents' knowledge, attitude and practice towards pediatric dosage forms. Pediatric physicians also accepted the correct concept and changed their prescribing habits. Through effective communication and discussion among pediatricians, nurses, pharmacists and parents, we achieved the ultimate goal of changing the administration of pediatric drugs in an appropriate and safe way.

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Appendix Pediatric Medication Use Questionnaire

Your gender: 🛛 Male	🗆 Fema	le							
Your age: yr									
Your education level:	🗆 Elem	nentary s	chool	🗆 Juni	or high	🗆 Sen	ior high	□ College	□ Above college
How many children do you	have?	□1	□ 2	□ 3	□4	□ 5	□ More t	:han 5: (_)
Average age of your childr	en:	yr							

Part 1: Please choose the most appropriate answer

	Yes	No	Unknown
1. Powder medicine should be discarded if it has been clumping			
2. Liquid medicine should be discarded if it has precipitated			
3. All kinds of powder medicine can be mixed with food (e.g., milk, juice)			
4. All kinds of liquid medicine can be mixed with food (e.g., milk, juice)			
5. Powder formula can become contaminated during the compounding process			
6. Drinking lots of water should be avoided if taking liquid medicine as it will dilute the medication			
7. Expiration dates will be shortened if pills are compounded to powder dosage formulation			
8. Powdered antibiotic formula can be stored for up to 7–14 days after mixing with water			
9. All kinds of liquid medicine should be stored in the refrigerator			
10. All kinds of pills can be compounded to powder dosage formulation			

Part 2: Please mark the response that best expresses your opinion

In general, I believe that	Always concerned	Usually concerned	Sometimes concerned	Seldom concerned	Never concerned
When my children take medicine in powder form dosage					
1. with different amounts of dosages in every pack					
2. with different amounts of contents in every pack					
3. with errors in formula preparation					
4. which is contaminated during the compounding and delivery process					
5. which is clumping (e.g., hygroscopic)					
When my children take medicine in liquid form dosage					
1. which contains large amounts of sugar					
2. which has broken down (i.e., precipitation)					
3. which contains preservatives					
4. which contains alcohol					
5. which is not easy to feed my children					

Part 3-1: Please mark the response that best expresses your practice					
When your children get sick,	Always	Usually	Sometimes	Seldom	Never
1. are they unwilling to take powder dosage form because of its bitterness?					
2. are they unwilling to take liquid dosage form because of its bitterness?					
3. is it difficult to coax them into taking powder dosage form?					
4. is it difficult to coax them into taking liquid dosage form?					
5. did you have experience in asking for a powder formulation?					
6. did you have experience in asking for a solution formulation?					
7. have you ever encouraged them to take pills instead of powder form?					
8. have you ever encouraged them to take solution instead of powder form?					

Part 3-2: Please mark the response that best expresses your opinion

In general,

1. My reasons for choosing my children's medicine in powder dosage form is because (maximum: 3 items)

□ easy to feed □ good taste □ convenient to carry □ easy to store □ recommended by physician

other reasons _____

2. My reasons for choosing my children's medicine in liquid dosage form is because (maximum: 3 items)

🗆 easy to feed 🛛 good taste 🖾 convenient to carry 🖾 easy to store 🖓 recommended by physician

other reasons _____

3. When my children get sick, I would choose

□ powder medications □ liquid or solid pill medications