RESEARCH

Student Pharmacists' Ability to Organize Complex Medication Regimens According to the Universal Medication Schedule

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Objective. Pharmacists are medication experts with the capability and expertise to impact medication management and improve patient care, particularly when polypharmacy is present. This study aims to assess student pharmacists' ability to impact the administration of complex prescription regimens using the universal medication schedule in a standardized laboratory exercise.
Methods. P1 and P3 student pharmacists across three colleges of pharmacy completed a required activity during a laboratory sequence to simplify and organize a complex medication regimen. Students organized how and when they would advise a patient to take seven fictitious medications with distinct instructions over a 24-hour period using a medication box. Picture documentation of each students' activity was used for data analysis. Descriptive statistics were used to compare P1 versus P3 students' performance, and an independent t-test assessed the frequency of daily dosing. A chi-square analysis was used to compare differences between P1 and P3 students, and analysis of variance was used to compare differences among individual institutions.
Results. There were 459 P1 and 372 P3 students (98.7% RR; 831 total) that consented to participate. Student pharmacists recommended 5.1 (1.0) (Range 3 – 11) dosing intervals per 24 hours with 27% of students successfully organizing the regimen to 4 total intervals. P3 students were more effective than P1 students at the total frequency in dosing (4.89 vs. 5.35 per 24 hours).
Conclusion. Student pharmacists gain more effectiveness organizing complex medication regimens with curricular experience. Student pharmacists can translate this exercise to potentially improve patients' self-organized medication regimens.
Keywords: polypharmacy; complex medication regimen; pharmacy; teaching and learning; universal medication schedule

INTRODUCTION

Adverse drug events (ADEs) contribute to nearly 700,000 emergency department visits and 100,000 hospital admissions each year.[1,2] Numerous factors including patient-, clinician-, or drug-specific reasons contribute to ADEs. Polypharmacy has been identified as a significant risk factor for ADEs in the elderly.[3,4] ADEs due to medication non-adherence can occur when elderly patients are required to manage multiple medication regimens with complicated schedules and/or complex instructions. For example, when a patient is prescribed a medication dosed three or four times per day, they are less likely to take their medication correctly, compared to a medication prescribed only once daily.[5] Additionally, instructions to take a medication as "two tablets by mouth twice daily" often leads to the common misinterpretation by the patient to "take a pill twice a day." [6] Both the clinician who prescribes and the pharmacist who translates are culpable to prescription labeling issues potentially leading to unintended ADEs.

To address this problem, experts from policy, health literacy, and academia gathered at the National Academies (formerly the Institute of Medicine) to develop the universal medication schedule (UMS), which is intended to increase patient understanding and adherence to their medication instructions.[7,8] The UMS specifies four standard times (morning, noon, evening, and bedtime) to be used in the prescribing and labeling of medications. A study by Wolf et al, measured the ability of patients to adhere to and understand prescription labeling using the UMS.[9] Within the study, 464 hospitalized patients aged 55-74 were asked to organize a hypothetical, 7-drug medication regimen into a large pillbox with 24 slots representing each hour of the day. The investigators measured the accuracy and variability in the ways the subjects interpreted the medication regimen. On average, patients would take their medication six times per 24 hours, an increase of two dosing frequencies over the recommended four times per day. This increased frequency could result in an increased burden for patients who take multiple medications that could ultimately result in non-adherence, suboptimal dosing, and drug-food interactions.[6]

As medication experts, pharmacists have the capability and expertise to impact medication management to improve patient care, particularly in the elderly.[10,11] Currently, pharmacy schools are mandated to address both special populations and medication safety within their curricula.[12] Some pharmacy faculty have expanded upon this idea with the creation of multiple pedagogical approaches to increase empathy for geriatric patients and polypharmacy.[13-16] However, research assessing student pharmacists' ability to organize a complex medication regimen adherent to the UMS is unavailable. This study aims to assess student pharmacists' ability to organize and simplify a complex prescription regimen adherent to the UMS within a standardized laboratory exercise.

METHODS

Professional year 1 (P1) and professional year 3 (P3) student pharmacists completed a required activity during an ambulatory or community pharmacy-based laboratory sequence to organize and simplify a complex medication regimen. This activity simulated the research on the Universal Medication Schedule (UMS) using a similar approach published by Wolf and colleagues.[6] This activity occurred at three colleges of pharmacy located within research-intensive public universities (University of Kentucky, University of Illinois at Chicago, and Purdue University). This research protocol was approved at each respective university's institutional review board and all students who were included in analyses gave informed consent prior to participation.

Individual students were given seven fictitious medication names and instructions (Table 1). The medication regimens were complex requiring patients to take medications multiple times per day: at bedtime, and/or with food. Students were asked to fill a 24-hour medication box (Midnight to 11PM) in the same way they would instruct a hypothetical patient to take these medications. The box also included the hypothetical patient's daily schedule with wake, meal, and sleep times (wakes (5am); ate breakfast (8am), lunch (12pm), and dinner (6pm); and goes to bed (9pm)). Students were given the following instructions to begin the exercise: "Imagine a physician has prescribed these medications for your patient. Please show me how you would suggest the patient take these medicines over the course of one day." Administration frequency was defined as the total number of dosing intervals represented by the number of bins used within the medication box. This subsequently represented the amount of times the patient would need to take medication during the day to complete the complex medication regimen. Time between doses was measured for each medication and grouped based on alignment with the hypothetical patient's daily schedule.

Assessment

After completion of the exercise, a de-identified picture of each 24-hour medication box was taken. Pictures were entered into an Excel spreadsheet by two individuals at each institution, and discrepancies were resolved by the lead investigator at each institution. Demographic information outside of year in pharmacy school was not obtained to ensure the anonymity of results for each student.

Given the importance of accurate recommendations for dosing regimens by student pharmacists, errors were measured to capture discrepancies identified between the instructions on the label and the organization of the complex medication regimen. For reporting purposes, errors were categorized into two categories: frequency and quantity. A frequency error was defined as a subtherapeutic (eg, once daily when written for twice daily) or supratherapeutic (eg, twice daily when written for once daily) discrepancy based on total number of daily doses. A quantity error was defined as the inappropriate number of tablets or capsules at a given dosing interval (eg, two tablets were dosed when written for one tablet).

Statistical Analyses

The primary outcome of interest is the percent of students that followed the UMS four times per day regimen. Secondary analyses included the mean (or median if not normally distributed) number of times per day students instructed a hypothetical patient to take medications, percent of students who filled in less than or equal to 4 different slots in a 24-hour period, and percent of students who filled in greater than or equal to 7 or more slots in a 24-hour period. It also included percent of students who had frequency errors defined as either no dose given or an extra dose given (eg, once daily when it should have been twice daily) and percent of students who had quantity errors defined as the incorrect number of tablets. Additionally, it included the number of hours between doses of twice daily and three times daily medications.

Descriptive statistics were reported as percentages for each outcome and stratified by year in school and by each institution. Differences in each outcome between P1 versus P3 students and of each individual institution were assessed. An independent t-test was used to assess the number of times per day students instructed a hypothetical patient to take medications. A chi-square analysis was used to compare differences between P1 and P3 students. Analysis of variance (ANOVA) was used to compare differences between individual institutions. Odds ratios (OR) were calculated to compare among student pharmacists (P3 vs. P1 students). All analyses were conducted using IBM SPSS Statistics Version 23 (Armonk, NY).

RESULTS

A total of 831 student pharmacists consented across the 3 colleges of pharmacy (98.7% Response Rate; 831/842). This included 459 P3 students and 372 P1 students with 296 students represented from the Purdue University College of Pharmacy (Purdue), 268 from the University of Illinois at Chicago College of Pharmacy (UIC), and 267 from the University of Kentucky College of Pharmacy (UK).

The mean frequency of dosing for the fictitious medication regimen across all student pharmacists was 5.1 (1.0) dosing intervals over the 24-hour period (Range 3-11). There was no statistical difference across the 3 colleges of pharmacy in total number of bins (p=.74). Only 27% of student pharmacists organized the medication regimen according to the UMS of 4 or less standard intervals of dosing while 10% of students recommended 7 or more frequencies per day. Differences between each college of pharmacy student pharmacist cohort are summarized in Table 2.

Time between doses was measured for each medication to determine potential causes of increased dosing frequency. Of the medications dosed twice daily (Table 1), 79% of student pharmacists separated the two Colesevlam doses by 9 – 11 hours; 67% separated Disopyramide by 12 hours; and 40% of student pharmacists separated Pimvampicillin doses by 9 – 11 hours while 31% separated Pimvampicillin by 12 hours. Specific hours between doses 1 and 2 are summarized in Table 3.

P3 student pharmacists were more effective at organizing complex medication regimens than P1 students. The average administration frequency of P3 students was 4.9 (0.9) versus 5.3 (1.1) (p<.001) in P1 students. When stratified by year in pharmacy school, P3 students were significantly more likely to organize the medication regimen according to the UMS than P1 students (OR 2.81, 95% CI 2.03 – 3.91)). P3 students were also significantly less likely to dose the regimen 7 or more times per day compared to P1 students (OR 0.46, 95% CI 0.29 – 0.73). This difference was primarily driven by significant differences between P3 and P1 student performance at Purdue (4.9 (0.8) vs 5.3 (1.1) p<.001) and UK (4.6 (0.7) vs 5.6 (1.0) p<.001) with no significant difference at UIC (5.1 (1.1) vs. 5.0 (1.0) p=.75).

A total of 17% of student pharmacists' regimens contained greater than or equal to 1 quantity error(s) and 11% contained greater than or equal to 1 frequency error(s). Progression in the pharmacy program was a significant effect as P3 students made fewer frequency errors compared to P1 students (7% vs 16%; p<.01). However, there was no significant difference for quantity errors when comparing P3 to P1 students (16% vs 19%; p=.84). Differences in quantity and frequency errors between each college of pharmacy student pharmacist cohort are also summarized in Table 2.

DISCUSSION

This study aimed to assess student pharmacists' ability to impact patients' administration of complex prescription regimens by replicating a dosing activity examined by Wolf et al. using the UMS construct. P3 students were more likely to organize a medication regimen using the UMS than P1 students without any specific instruction or guidance. In all three schools, this was the first-time students had been exposed to the activity whether they were a P1 or P3 in any curriculum. These results demonstrate students tend to gain effectiveness in managing complex prescription regimens just with curricular experience and increased time as a student pharmacist. These skills would not only increase the depth of pharmacy curricula but provide additional skills to help graduates in practice.

The primary driver for the increase in dosing frequency over the UMS was individual prescription instructions. A secondary analysis of the timing between medications describes the most likely cause of the increase in frequency. For example, of the 3 medications dosed twice daily, the instructions had a significant impact on the number of hours between dose 1 and dose 2 as described in Table 3. When the label instructions indicated that the medication Colesevlam was to be dosed with meals and liquid, a significant majority of student pharmacists separated the doses consistent with the patient's schedule. When the label indicated that the medication Disopyramide was to be dosed every 12 hours, most separated it by 12 hours. Given that Pimvampicillin did not have a specific time or dietary requirement, and simply indicated 'twice daily', student pharmacists split the second dose between 9 – 11 hours or 12 hours, effectively splitting the 3rd twice daily medication between the other 2 medications. Many students used these times to administer the medications; however, the instructions on one medication were "take 2 tablets by mouth every 12 hours." Because the times given did not provide an exact 12 hour spread, many students administered a medication at a time that was exactly 12 hours after the first dose but was not at a time the patient ate a meal or was going to bed. It is realistic that a patient's daily activities may not perfectly align with ideal medication administration times.

This study used a similar methodology to the research described by Wolf et al.[6] Compared to the general population of older adults as represented by this previous research, student pharmacists reduced the medication regimen frequency by approximately one time per day compared to the previous patient population (5.1 vs. 6.0 per 24 hours). It should be noted that while P1s and P3s students improved from previous patient populations, they still did not meet the standard proposed with UMS. However, student pharmacists were 2.15 times more likely to organize the medication according to the UMS and were 73% less likely to dose the regimen seven or more times per day (10.1% vs 29.3%) compared to older adults. As such, student pharmacists can potentially improve patients' self-organized medication regimens, which could in turn, result in fewer administration errors and improved medication adherence.

While student pharmacists reduced the medication regimen frequency by approximately one time per day compared to the general population, the P3 student cohort decreased the frequency by approximately 1.5 times per day compared to the general population. A study examining how pharmacists with varying years of experience and/or training complete the same activity would further inform the profession if and how complex medication regimens are simplified in practice. Future research could focus on the addition of realistic medication names to student pharmacists and the role of extended-release formulations and the impact on medication regimens.

An additional consideration for future implementation and research is the medication regimen complexity index (MRCI).[17] The MRCI is an observational tool that can categorically determine medication complexity. While the MRCI calculation requires an evaluation by an observer, there is no clinical judgement involved and higher MRCI scores have been associated with increased mortality, medication nonadherence, and hospitalizations.[17] The regimen in this study had an MRCI score of 30.5, representing a complex regimen, especially for older adults. In previous population-based studies reviewing MRCI, this patient's medication regimen would fall into the top quadrant (MRCI >20) of a sample of older adults.[18] Further variation in level of student and level of complexity using MRCI could further validate student pharmacists' ability to simply complex medication regimens on behalf of patients.

Limitations of this study include lack of student accountability and variance in activity timing across universities. Students were not formally assessed on their individual performance on the activity, which they knew prior to and while completing the activity. Additionally, the use of fictitious and historical drug names, while negating clinical knowledge between P1 and P3 students, may have led to students not taking the activity seriously or putting forth their maximal effort. Any comparisons to the previous study by Wolf et al. compared older adults and interpretation may be limited based on the homogeneity of the student pharmacist population. Moreover, there were limited and varying opportunities to place the activity within the three skills laboratory curricula, which led to activity implementation at different points (weeks) of the academic year and may have also influenced results. Lastly, although students across institutions were in the same class (P1 or P3), they may have different levels of training and personal experiences at the time they completed the activity.

CONCLUSION

Pharmacists are uniquely positioned to impact care of patients by simplifying medication regimens. The UMS is intended to assist patients in adhering to their medications by simplifying the schedule but is underutilized in both practice and education. Student pharmacists were more likely to organize a medication regimen according to the UMS than patients, and the effectiveness improved with student pharmacist experience. Student pharmacists may be well-equipped to educate and simplify complicated regimens for patients and could impact patient care through effective interventions regarding UMS. Implementation of UMS instruction and/or practice exercises in skills-based courses could address polypharmacy issues, including what should be done in similar situations to optimize patient care. However, given potential improvements UMS may have on medication adherence with little to no foreseen consequences, the authors recommend the profession adopt a formal position on the UMS, guiding its implementation in curricula and practice.

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Table 1. Medications Used in the Complex Medication Activity[a]

Drug Name	Instructions
Pimvampicillin 700 mg	Take 1 tablet by mouth twice daily for 10 days
Disopyramide 400 mg	Take 2 tablets by mouth every 12 hours
Zoplicone 7.5 mg	Take 1 tablet by mouth at bedtime
Colesevlam 1875 mg	Take 1 tablet by mouth twice daily with meals and liquids
Trimipramine 100 mg	Take 1 tablet by mouth 3 times daily
Cephalothin 500 mg	Take 1 tablet by mouth 3 times daily
Pinaverium 50 mg	Take 2 tablets by mouth 3 times daily with food and water

[a] Adapted from Wolf et. Al[9]

Table 2. Student Pharmacist Performance Characteristics by University

	Differences Among Universities				
Medications	**Purdue N (%)**	**UIC N (%)**	**UK N (%)**	***p* value****	**Total N (%)**
Administration Frequency ≥7*	32 (10.8)	29 (10.8)	23 (8.6)	.62	84 (10.1)
Administration Frequency <5*	79 (26.7)	79 (29.5)	70 (26.2)	.66	228 (27.4)
Range of Frequency	3-10	3-11	3-9	--	3-11
Quantity Errors	66 (22.3)	35 (13.1)	44 (16.5)	.01	145 (17.4)
Frequency Errors	25 (8.4)	19 (7.1)	48 (18.0)	<.001	92 (11.1)
	M (SD)	**M (SD)**	**M (SD)**		**M (SD)**
Total Administration Frequency	5.12 (1.02)	5.06 (1.07)	5.10 (1.01)	.74	5.10 (1.03)

Abbreviations: SD=standard deviation, M=mean, N=number of students, UIC=University of Illinois Chicago, UK=University of Kentucky

*Administration frequency was measured over a 24-hour period

**Analysis of Variance (ANOVA)

Table 3. Dosing Intervals for Twice daily Medications

	Hours between Dose 1 and Dose 2 (% of total students)			
Medications	**<8**	**9 - 11**	**12**	**13+**
Colesevlam	18	78	2	1
Disopyramide	1	7	67	26
Pimvampicillin	7	40	31	21

Colesevlam 1875 mg Instructions (SIG): Take 1 tablet by mouth twice daily with meals and liquids

Disopyramide 400 mg Instructions (SIG): Take 2 tablets by mouth every 12 hours

Pimvampicillin 700 mg Instructions (SIG): Take 1 tablet by mouth twice daily for 10 days