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Drug-induced Adverse Events and Prescribing Cascades in Older Adults: Pharmacy Stakeholder Survey

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ABSTRACT

***Objectives**: The aim of this study was to assess pharmacists' and student pharmacists' understanding of drug-induced adverse events (DIAEs) and prescribing cascades (PC) and assess their willingness to use system-level approaches to identify DIAEs and PC for future patient interventions.*

***Methods**: Following a continuing education presentation on DIAEs and PC, pharmacists and student pharmacists completed a survey. A retrospective post-then-pre method was used to assess knowledge. McNemar tests and chi-square analyses were used to determine differences in understanding of DIAEs and PCs, as well as between pharmacists and student pharmacists.*

***Results**: A total of 53 participants completed the survey including pharmacists (n=39) and student pharmacists (n=14). Fewer participants had previously heard of the term (40%; p<0.001) and concept (60%; p<0.001) of PC compared to the term and concept (98% in both) of DIAE. Student pharmacists were less likely to have heard of the term PC (14%) compared to pharmacists (40%; p=0.029). There was no difference in knowledge of the concept of PC. Nearly all respondents were willing to assess for DIAE and PC in their patients, and over 75% of respondents were willing to receive systems-based alerts for DIAE and PC.*

***Conclusion**: There was a differential in understanding DIAE and PC among respondents. Programs aimed at building understanding, as well as systems-level alerts for PC, are needed.*

Keywords: drug-induced adverse events, education, prescribing cascade

BACKGROUND

Older adults are major consumers of prescription and non-prescription medications. Two-thirds of community-dwelling older adults (>65 years old) take five or more prescriptions, over-the-counter (OTC) products, and dietary supplements.[1] Additionally, 36% of older adults take five or more prescription medications. Institutionalized older adults consume greater numbers of medications, as approximately 50% of older adults in the long-term care setting take nine or more medications.[2] Taking multiple or inappropriate medications may predispose patients to drug-induced adverse events (DIAEs), along with changes in pharmacokinetics and pharmacodynamics associated with aging, being female, and having genetic factors, sustaining multiple co-existing medical problems, and having cognitive issues.[3]

DIAEs are unwanted, potentially harmful outcomes related to the utilization of a medication that may be idiopathic or related to its mechanism of action that typically require a dose reduction or treatment discontinuation.[4-6] The degree of the DIAE's severity may vary between patients and amongst different medications ranging from mild discomfort to hospitalization and death.[5] An unintended consequence of a DIAE is a prescribing cascade (PC). PC occurs when a DIAE is misinterpreted as a new medical condition, resulting in the prescription of a new, potentially unnecessary medication.[7]

Previous studies have identified DIAEs resulting in PC.[8-13] Yet there is no published information on any member of the healthcare team's knowledge of PC and how this knowledge can be used clinically. In particular, pharmacists' and student pharmacists' understanding of DIAEs and PC or their willingness to participate in interventions to mitigate DIAEs and PC is unclear. More information is needed on pharmacists' knowledge, as it may change a pharmacist's approach to medication review to include evaluating for PC. The aim of this study was to assess pharmacists' and student pharmacists' understanding of DIAEs and PC and assess their willingness to use patient- and system-levels approaches to identify DIAEs and PC for future patient interventions.

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METHODS

Measures

A 150-minute continuing education presentation over two sessions entitled "Drug-Induced Adverse Events and Prescribing Cascades in the Elderly" was delivered on July 18th, 2015 to pharmacists and student pharmacists attending the American Society of Consultant Pharmacists Midwest Regional Conference. The objectives of this presentation were to: 1) differentiate between DIAEs and PC in the elderly,

2) evaluate the primary literature regarding DIAEs and PC in the elderly, 3) identify and intervene on DIAEs and PC in the elderly given a patient case, and 4) create one's own PC case.

Following the presentation, participants were given ten minutes to complete a voluntary paper survey (available upon request) regarding the content. A retrospective post-then-pre method was used, which allows for participants to better assess their knowledge following the presentation.[14] As opposed to a pre-test post-test method, the post-then-pre method allows participants to assess a question with the same point of reference.[14] An issue with the pre-test post-test method is that the post-test may indicate there is a reduced knowledge of the educational outcome relative to baseline knowledge due to an overestimation of prior knowledge, thus resulting in an underestimation of true knowledge. The survey was reviewed by three colleagues with expertise in survey design for content validity. Alterations were made; however, no pilot testing was conducted. This study was approved by the St. Louis College of Pharmacy Institutional Review Board.

Variables

For comparison purposes, the answers to 'Yes' and 'No or Did Not Answer' questions were transformed to 'Yes' and 'No', respectively. The answers to 'Agree or Strongly Agree' and 'Neutral, Disagree, Strongly Disagree, or Did Not Answer' questions were transformed to 'Agree' and 'Disagree', respectively. The answers to 'Slightly Willing or Very Willing' and 'Neutral, Slightly Not Willing, Not Willing, or Did Not Answer' questions were transformed to 'Willing' and 'Not Willing', respectively.

Statistical Analyses

Descriptive statistics were used to describe characteristics and responses in three categories: all respondents, pharmacists only, and student pharmacists only. Next, questions on DIAEs were compared to questions on PC to determine if there were differences in understanding and identification, using the McNemar Test among all respondents, pharmacists, and student pharmacists. Chi-square analysis (or Fisher's Exact Test, when appropriate) were used to compare pharmacists' to student pharmacists' responses. All data were considered two-sided with an *a priori* level of significance of 0.05. All statistical analyses were performed using IBM-SPSS, version 22.0 (IBM Corp., Armonk, NY).

RESULTS

A total of 53 participants completed the survey, including 39 pharmacists and 14 student pharmacists. A majority of respondents were female, 80% of pharmacists had at least 15 years of practice experience, and approximately 50% of pharmacists practiced in the long-term care setting (Table 1).

Table 2 compares knowledge of DIAE versus PC among all respondents, pharmacists, and student pharmacists. Overall, greater than 95% of respondents had previously heard of the term and concept of DIAE, while significantly fewer respondents had previously heard the term (40%, $p<0.001$) and concept (60%, $p<0.001$) of PC (Table 2). A higher proportion of all respondents had previously identified DIAEs in patients compared to PC ($p<0.001$).

Table 3 assesses differences in knowledge between pharmacists and student pharmacists regarding DIAE and PC. Student pharmacists were also significantly less likely to have previously heard of the term PC compared to pharmacists ($p=0.029$), but there was no difference in previously being aware of the concept of PC ($p=0.773$). Pharmacists identified more DIAEs ($p<0.001$) and PC ($p=0.004$) in practice compared to student pharmacists.

Ninety-eight percent (n=52) of respondents were likely to look for DIAEs and PC in their future patient interventions. Additionally, 88.7% and 77.4% of respondents were willing to receive systems-based notifications to confirm both DIAEs and PC, respectively, in their future patient interventions. When asked about their preference for identifying DIAEs and PC on their own versus a systems-based approach, 53% (n=28) and 49% (n=26) of all respondents had no preference for either method of identifying DIAE and PC, respectively.

Over 90% of respondents recommended that this topic be presented to their colleagues in pharmacy and healthcare. Moreover, approximately 90% of respondents would read future publications and incorporate publications into practice regarding DIAE and PC. Three-quarters of respondents recommended that this topic be discussed with older adult patients.

DISCUSSION

To the authors' knowledge, this is the first study to identify pharmacists' and student pharmacists' knowledge of DIAEs and PC and their willingness to identify DIAEs and PC in future patient interventions. Nearly all respondents had previously heard of the term and concept of DIAE with no difference between pharmacists and student pharmacists. However, pharmacists were less likely to be aware of PC compared to DIAE, as less than 50% had previously heard of the term and approximately 60% had previously heard of the concept of PC. In general, this may be an overestimation as these pharmacists were attending a geriatric pharmacy conference; therefore, many respondents work with the geriatric population and are more likely to encounter patients with a PC. Only 15% of student pharmacists had previously heard of the term PC, while 57% were aware of the concept. The Geriatric Curriculum Guide, 3rd Edition suggests incorporating adverse events into the geriatric curricula; however, it does not specifically include PC.[15] At least one school of pharmacy, the University of Charleston School of Pharmacy, incorporates PC into its curricula.[16] 'The Prescribing Cascade Game' introduces the concept, term, and examples of PC to student pharmacists

in the second year of their professional program. This learning activity can be emulated by other schools of pharmacy as a method of introducing student pharmacists to PC. However, it is currently unclear the proportion of pharmacy school curricula covering PC within geriatric modules.

Based on this survey, both pharmacist and student pharmacist respondents will actively and passively investigate DIAEs and PC in future patient interventions. There are few studies that have confirmed PC using pharmacoepidemiological techniques that can be used by pharmacists to justify interventions.[8-13] Approximately 90% of respondents in our study were willing to read and incorporate future studies on DIAEs and PC in future patient interventions. Therefore, this may be an area of educational need and potential for expanded observational and interventional research.

Currently, there are no interventional studies that aim to reduce PC; however, several studies have used systems-based approaches to identify adverse events.[17] Pharmacists play a vital role as the "safety-net" for healthcare providers in medication utilization and are essential to the identification of PC in a variety of practice settings.[18] Based on our study, approximately 75% of participating pharmacists were willing to receive systems-based alerts so that DIAEs and PC can be confirmed and intervened. Pharmacists' willingness to engage in these interventions can further justify performing future quasi-experimental or experimental research on interventional techniques. For example, a systems-based approach can identify a PC (e.g., lisinopril and a new order for cough medication) and alert the pharmacist to differentiate between an angiotensin-converting enzyme inhibitor (ACE inhibitor)-induced cough and cough secondary to an infection.[19] The pharmacist is in an ideal situation to communicate with the patient and/or physician or review a medical record to confirm the PC and suggest changes in therapy. This action can reduce medication burden and costs for patients, improve quality of life, and mitigate downstream consequences of PC.

A recent commentary from Steinman stated that providers currently do not have methods to evaluate ongoing medications for adverse events or to determine the necessity of medications and called for systems to periodically assess benefits, harms, and ongoing needs of medications to inform prescribers.[20] The approach of identifying DIAEs through PC may be one such method to provide individualized assessments to identify potentially unnecessary medications that may be contributing to adverse events.

Limitations

There are some limitations to this study. Using a post-then-pre method, there may be an unconscious desire of the respondent to answer survey questions in a way that the researchers would want him or her to respond; however, this approach allows respondents to more accurately answer questions regarding baseline knowledge. Additionally, information from this survey was drawn from a non-random sample of pharmacists and student pharmacists from the Midwest, who attended a regional pharmacy conference. These results may not be generalizable to other regions of the country or to pharmacists who do not attend these types of conferences. Multiple types of educational interventions may also be needed as one educational session may not be enough to change behavior.

CONCLUSION

A stakeholder survey of pharmacists and student pharmacists at a geriatric regional conference suggested differences in understanding of the terms and concepts of DIAEs and PC. These results identify a potential knowledge gap, specifically in PC, and call attention to the need for increased continuing education on PC and the integration of PC in pharmacy curricula. This survey suggests expanding research efforts in identifying DIAEs and PC, as pharmacist engagement is vitally important to the success of this type of intervention. Furthermore, this survey suggests a potential willingness for pharmacists to engage in interventions aimed to reduce DIAEs and PC in older adults and justifies continued expansion in this area of research.

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Table 1: Participant Characteristics

	All Respondents n (%) (n=53)	Pharmacists n (%) (n=39)	Student Pharmacists n (%) (n=14)
Gender			
Male	19 (35.8)	18 (46.2)	1 (7.1)
Female	34 (64.2)	21 (53.8)	13 (92.9)
Years of Practice			
Student	14 (26.4)	--	14 (100)
< 5 years	5 (9.4)	5 (12.8)	--
5 to 15 years	3 (5.7)	3 (7.7)	--
> 15 years	31 (58.5)	31 (79.5)	--
Practice Setting			
Academia	1 (1.9)	1 (2.6)	--
Clinical	4 (7.5)	4 (10.3)	--
Community	4 (7.5)	4 (10.3)	--
Hospital	3 (5.7)	3 (7.7)	--
Independent Living Facility	1 (1.9)	1 (2.6)	--
Long-Term Care Setting	25 (47.2)	25 (64.1)	--
Student	14 (26.4)	0 (0)	14(100)
Did Not Answer	1 (1.9)	1 (2.6)	--
Geographic Region of Practice			
Midwest	49 (92.5)	36 (92.3)	13(92.9)
South	2 (3.8)	2 (5.1)	0 (0)
Did Not Answer	2 (3.8)	1 (2.6)	1(7.1)

Table 2: Current Understanding of Drug-Induced Adverse Events and Prescribing Cascades

	DIAE – n (%)	PC – n (%)	P-Value*
All Responders (n=53)			
Prior to the Presentation, I have heard of the term:	52(98.1)	21(39.6)	<0.001
Prior to the Presentation, I have heard of the concept of:	52(98.1)	32(60.4)	<0.001
I have identified a ___ in a Patient?	42(79.2)	21(39.6)	<0.001
Pharmacists (n=39)			
Prior to the Presentation, I have heard of the term:	38(97.4)	19(48.7)	<0.001
Prior to the Presentation, I have heard of the concept of:	39(100)	24(61.5)	<0.001
I have identified a ___ in a Patient?	36(92.3)	20(51.3)	<0.001
Student Pharmacists (n=14)			
Prior to the Presentation, I have heard of the term:	14(100)	2(14.3)	<0.001
Prior to the Presentation, I have heard of the concept of:	13(92.9)	8(57.1)	0.063
I have identified a ___ in a Patient?	6(42.9)	1(7.1)	0.063

*=Comparison using McNemar Test
DIAE = Drug-Induced Adverse Events; PC = Prescribing Cascades

Table 3: Current Understanding of Drug-Induced Adverse Events and Prescribing Cascades by Experience

	Pharmacists (n=39) – n(%)	Student Pharmacists (n=14) – n(%)	P-Value*
Prior to the Presentation, I have heard of the term:			
DIAE	38(97.4)	14(100)	1.00
PC	21(39.6)	2(14.3)	0.029
Prior to the Presentation, I have heard of the concept:			
DIAE	39(100)	13(92.9)	0.264
PC	24(61.5)	8(57.1)	0.773
I have identified a ___ in a Patient?			
DIAE	36(92.3)	6(42.9)	<0.001
PC	20(51.3)	1(7.1)	<0.001

*=Comparison using Chi-Square Test or Fisher's Exact Test
DIAE = Drug-Induced Adverse Events; PC = Prescribing Cascades