Innovare
Academic Sciences

International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 6, Issue 8, 2014

Original Article

ASSESSMENT OF PHYSICIANS' RESPONSE TO TEXT ALERTS IN PATIENTS WITH REDUCED RENAL FUNCTION BY USING A TEXT MESSAGE ALERTING SYSTEM

AIDA SEFIDANI FOROUGH[1], MOHAMMAD FARAHBAKHSH[2], NIMA NADERI [3], FANAK FAHIMI [1, 4]

1 Clinical Pharmacy Department, School of Pharmacy, Shahid Beheshti University of Medical Sciences, 2 MD, Department of Infectious Diseases, Shahid Beheshti University of Medical Sciences, 3 Department of Pharmacology and Toxicology, School of Pharmacy, Shahid Beheshti University of Medical Sciences, 4 Chronic Respiratory Disease Research Center (CRDRC), NRITLD, Masih Daneshvari Hospital, Tehran, Iran.
Email: fanakfahimi@yahoo.com,

Received: 08 Jul 2014 Revised and Accepted: 07 Aug 2014

ABSTRACT

Introduction: Adverse drug events are mostly dose dependent and preventable. About 50% of these adverse effects are due to inappropriate dosing especially in patients with renal failure.

Objective: We aimed to determine the impact of short message alerting on physicians' drug dosing of patients with decreased renal function.

Methods: Eighteen physicians accepted to enroll in the study. Their patients who received at least one of the six selected drugs were selected for evaluation. The patients with an estimated glomerular filtration rate of 50 ml/minute or lower were randomly divided into two groups of case and control. An alert was sent to the physician in charge of the intervention (case) group. Physicians' reactions was recorded as "dose adjustment", "discontinuation of medication" or "none" and were compared in both groups. The reaction time of physicians before and after receiving alerts was recorded as well.

Results: One hundred and thirty seven patients entered the study. The study results showed a significant difference in overall changes between the two groups (*** $P < 0.001$). The rate of dose adjustment increased significantly after sending alerts to physicians (*** $P < 0.001$). However, there was not a significant difference regarding discontinuation of medication between groups ($P = 0.76$). On the other hand, prompt reaction of physicians (0-6 hours after sending short message) significantly increased after intervention (* $P < 0.05$). Nevertheless, physicians' reaction time in 6-24 hours and 24-48 hours was not changed significantly after intervention.

Conclusion: The results of this study show that informing physicians about the renal function of the patients leads to appropriate dosing.

Keywords: Acute Kidney Injury, Chronic Kidney Disease, Dosage adjustment, Creatinine clearance, SMS, Alerting system.

INTRODUCTION

Medication errors account for a large number (28%) of adverse drug events (ADEs) and can be prevented. Over 50% of these errors occur at the ordering stage [1], [2]. It has been documented that drug dosages should be adjusted for 20% to 46% of prescriptions due to changes in glomerular filtration rate [3]. Drug-prescribing practices may not routinely consider kidney insufficiency effects on the disposition of drugs. Decision aids may optimize prescribing behavior and control medical error incidence to some extent [4]. Many drug clearances are affected by kidney function, and this is more pronounced in the geriatric population. Hence, drugs need to be adjusted due to reduced renal function as a result of the aging process. Drug-induced kidney injuries are prevalent in 70% of elderly patients [5]. Prescription of the incorrect drug or dose often stems from the lack of information regarding the drug or the patient [6]. Even a small decrease in renal function of inpatients can be harmful both in short and long-term[7]. Van Dijk EA et al. found that at discharge 36.6% of patients had a calculated creatinine clearance less than 51 mL/min/1.73 m^2. Dosage adjustment based on renal function was necessary in approximately 24% of prescriptions. These adjustments were missed for almost 41% of the cases [8]. Treatment of serious clinical conditions in inpatients is usually delayed and the information technology can facilitate the clinical management of such conditions [9]. Since serious clinical conditions may require treatment immediately, an ideal alerting system would allow the physicians to take action spontaneously [9]. Rind et al. found that computer-based alerts have prevented serious renal impairment, preserved renal function, and are accepted by physicians [10]. It has been reported that physicians prefer to use pagers and mobile phones as their alerting tool [11]. The pharmacist is an important member of the health care team and is often the last barrier in receiving excessive or incorrect drug dosing by patients. Thus, when encountering a prescription, pharmacists should consider the patient's kidney function [12]. With the help of implementing a short message service (SMS) system for sending critical value alerts to phones, corrective actions were taken more promptly and treatment outcomes were improved in a recent study [11]. Pharmacists formulated therapeutic recommendations through a computer based alerting system in one study. Nearly 50% of these recommendations were agreed immediately by physician [13].

Our objective was to study the correct dose adjustments of the six selected medications based on kidney function, with and without sending a short text message alert to mobile phones of the physicians in charge of the patient with reduced renal function.

MATERIALS AND METHODS

Setting

This study was performed from August 2012 to June 2013 at Masih Daneshvari Hospital, a 446-bed teaching affiliate of Shahid Beheshti University of Medical Sciences in Tehran, Iran. The hospital consists of surgical, oncology, intensive care unit (ICU) and internal wards and is the educational collaboration center of the WHO Eastern Mediterranean region, the Middle East office of the International Union against Tuberculosis and Lung Diseases (IUATLD) and the reference center for TB educational and research programs in the country.

Design

The study was a single center, randomized, single-blind, crossover study to evaluate the reactions of physicians to short message alerts in clinical setting. Twenty nine physicians including attendings and fellow physicians were asked to participate in the study. Eighteen physicians including 16 attendings and 2 fellow physicians agreed to receive short text message alerts if their patients' renal function was decreased. However to prevent observer induced bias, the physicians were not aware of the exact purpose of the study. Initially, in the permission letter sent to the physicians it was stated that the project was a part of pharmacy healthcare improvement program. Physicians in each ward were then randomly selected and put in one of the intervention and no intervention groups. The data was then analyzed using demographics and the physicians remained anonymous. Six medications including ciprofloxacin (IV), vancomycin (IV), amikacin (IV), ranitidine (IV), ranitidine (PO) and digoxin (PO) were selected for this study. This selection was based on our previous study [14] which indicated commonly prescribed drugs with high rates of inappropriate dosing based on renal function. The inclusion criteria consisted of patients of the participated physicians with an estimated glomerular filtration rate (eGFR) less than 50 ml/min/1.73 m^2. Also, the patients should have received at least one of our studied medications inappropriately based on their renal function to be included in our study. Furthermore, patients undergoing dialysis or discharged from the hospital before our evaluation were excluded from the study. Demographic and laboratory data were then retrieved from the charts. Serum creatinine was checked daily for these patients and creatinine clearance (or GFR) was estimated using the appropriate equation on daily basis. Cockcroft & Gault formula was used in our study to calculate estimated GFR because of the fact that most of the dose adjustment guidelines in renal impairment are based on this formula. Since our hospital beds are not equipped with scales, for critically ill patients whose actual body weights were not available, we calculated ideal body weight (IBW) based on existing formulas by measuring the height of the patient. Dosages, dosing intervals and dose adjustments of the studied drugs were investigated based on the calculated creatinine clearance. These were then evaluated using the dose adjustment guidelines. The appropriate dosage data for each drug in different GFR ranges were collected from five different references[ ], [16], [17], [18], [19].Required dosage adjustments were based on the level of kidney function impairment which was divided into three categories (eGFR<10 ml/min/1.73 m^2, eGFR 10 to 50 ml/min/1.73 m^2, eGFR> 50 ml/min/1.73 m^2).

The final guideline was obtained by choosing the widest acceptable dosage range in different GFRs. We used correction factor as a tool to remove between session variations (the number of observations for each medication was different). All available data are equally weighted using correction factor. Correction factor expresses the number of opportunities for errors for each prescribed medication. It is calculated by multiplying the number of observations by the number of opportunities for errors. In other words, corrected percentage of error for each selected drug was calculated by using the number of errors divided by factor correction multiplied by 100. Patients with an estimated GFR lower than 50 ml/min/1.73 m^2 who were prescribed at least one of the 6 target medications that required dose adjustment, were monitored for 24 hours and if no adjustment was applied by physician during the 24-hour period, a short message alert was sent to the responsible physician as a reminder of the patient's impaired renal function. Patients were observed for 48 hours after sending alerts. Any change in prescribed drugs including dose adjustment or discontinuation of medication was recorded.

At the same time the physicians in no intervention group did not receive any alert. Due to ethical issues the physicians in control group received a short message alert 48 hours after GFR drop if they did not make any adjustment. In the second phase of the study, we did a crossover between intervention and no intervention physician groups. Expected reactions from physicians both in intervention and no intervention groups was divided into three categories: 1) drug dose adjustment 2) drug discontinuation 3) no action.

Reaction time of physicians was defined as time elapsed from the moment that alert was sent until we detected a reaction from the physician. Review of the orders was performed 6, 24, and 48 hours after sending the text message. Statistical analysis was performed using Graph pad Prism 5.0.

Table 1: Inappropriate dosage adjustment for the studied drugs with and without correction factor

Drug	Number of observations	Number of errors	Number of errors after applying correction factor	Percentage of errors without correction factor	Percentage of errors after applying correction factor
Ciprofloxacin (IV)	159	64	40.25	26.78	18.29
Vancomycin(IV)	114	61	53.50	25.52	24.31
Ranitidine (PO)	73	20	27.39	8.36	12.44
Ranitidine (IV)	89	46	51.68	19.24	23.48
Amikacin(IV)	90	26	28.88	10.87	13.12
Digoxin(PO)	120	22	18.33	9.20	8.33
Total	645	239	220.03	100	100

RESULTS

A total of 152 patients were evaluated. After excluding 15 patients who were discharged or underwent dialysis, further evaluation was done for 137 patients. Mean age ± SD was 66.41 ± 13.51 years and male: female ratio was 90:47. Mean serum creatinine ± SD was 2.08 ± 1.25. Mean estimated GFR ± SD of patients was 32.99 ± 11.42. One hundred and twenty five patients had the eGFR range of 10-50 ml/min while for 12 patients eGFR was less than 10 ml/min. Among 645 observations of the studied medications, renal dose adjustment was required for 239 (37.05%) cases. Ciprofloxacin (IV) had the highest rate of inappropriate dosing among six medications with 64 (26.78%) cases while ranitidine (PO) had the lowest rate of inappropriate dosing with 20 (8.36%) cases. Vancomycin, ranitidine (IV), amikacin (IV), and digoxin (PO) had the inappropriate dosing rates of 25.52%, 19.24%, 10.80% and 9.20% respectively. After applying correction factor, vancomycin rated as the most inappropriately prescribed medication.

Fifty four (39.41%) patients required dose adjustment for only one drug in their prescription, 64 (46.71%) patients required dose adjustment for 2 drugs and 19 (13.86%) patients required dose adjustment for 3 drugs according to their renal function. One hundred and nineteen inappropriate dosing out of 239 prescriptions was found in internal ward, while 58, 26, 25 and 11 cases were recorded in medical ICU, infectious diseases ward, surgical ICU and cardiology ward respectively. Regarding the specialty of physicians, 5 intensive care unit physicians, 9 internists, 2 infectious disease specialists and 2 cardiologists participated in our study. During the study period, 102 short message alerts were sent to the physicians. Sixty eight alerts were sent to the physicians in the intervention group. Thirty four alerts were sent to the physicians in intervention group during the first phase of the study while remaining 34 alerts were sent to the physicians during the second phase of study after doing crossover between physicians. Fifty three alerts (77.94%) of 68 sent alerts led to a change in patients' medications as dose adjustment or discontinuation. Reaction time of physicians was categorized into 0-6 (quick reaction time), 6-24 (moderate reaction time) and 24-48 hour (delayed reaction time) intervals. Eleven changes out of 53 (20.75%) were applied during the first six hours after sending short message alert, 30 (56.60%) changes were applied in 6-24 hour time period and 12 (22.64%) changes occurred within 24-48 hour time period. Physicians were divided in two groups. Group A included the physicians who received alerts during the first phase of the investigation while group B physicians started to receive alerts after cross-over. The overall reaction of physicians (including dose adjustment and discontinuation of medication) significantly increased after the short message intervention, regardless of the group of the study (*** P <0.001). More detailed analysis indicated that only drug dose adjustment based on reduced renal function significantly increased after sending alerts (*** P <0.001). However, there was not a significant change when discontinuation of medication in intervention and no-intervention groups was considered (P=0.76). A comparison showed that the overall changes did not differ significantly between group A and group B during no-intervention stage (P= 0.46).

DISCUSSION

Considerable attention has been drawn to electronic alerting systems in clinical setup as a means of reducing prescription and medication errors. We implemented short message alerting system for informing physicians about the renal function of the patients. The intervention by sending short message alerts was associated with a significant increase in rate of drug dose adjustment based on impaired renal function. However, there was not a significant difference between intervention and control group in discontinuation of drugs which shows that physicians mostly tended to adjust the doses rather than ceasing the medication. In one study Sellier et al [3] implemented an alerting system for adjusting drug doses for inpatients with renal insufficiency. The intervention led to a significant decrease in inappropriate dosages from 67% to 54%. Similarly, Oppenheim et al implemented an alert system displaying the correct dosage of a drug when a wrong dosage was selected by a physician and half of the orders were adjusted in response to alerts [20]. In these two previous studies, the exact dosage was suggested to the physician, whereas we only provided the eGFR values to the physicians, asking them to check their patient's status. Previous studies showed that there is a significant difference between responses of residents and senior physicians to alerts. Residents tended to improve their performance in prescribing drugs whereas senior physicians tended to make more errors [3]. What makes our study different from this aspect is that all included physicians in our study were attending and fellow physicians. Results from our study showed that all of the dose adjustments after sending alerts were within the acceptable range of dose. There can be two reasons for this: 1) knowledge of the participated physicians about dose adjustment in renal failure 2) choosing the widest acceptable renal dose range for studied drugs. Although all physicians were aware of the study, the exact purpose of the study was unknown to them. In this way we prevented observer induced bias in the study. Time of corrective actions in renal impairment is of a great clinical importance. Several studies have shown that early detection of renal failure has positive prognostic outcomes and reduces the rate of mortality [21]. In our study, quick reaction of physicians (response during the first six hours after sending message) considerably increased which was statistically significant, indicating that physicians in intervention group took a quicker action compared to non-intervention group. Physicians' early reaction (during 0-6 hours after sending alerts) significantly increased after receiving short message alerts (* P < 0.05). However there was not a significant difference in moderate (6-24 hours) and delayed (24-48 hours) reaction times between intervention and no-intervention groups (P = 0.63 and 0.09 respectively). The results also indicated that ICU physicians tended to respond to the alerts quicker than physicians in other studied wards.

Table 2: Reaction time of physicians in studied wards

Ward	0-6 hrs (%)	6-24 hrs (%)	24-48 hrs (%)
ICU	17 (73.91)	24 (51.06)	5 (41.66)
Internal	4 (17.39)	13 (27.65)	6 (50)
Infectious diseases	2 (8.69)	7 (14.89)	1 (8.33)
Cardiology	-	3 (6.38)	-
Total	23 (100)	47 (100)	12 (100)

Because of various interfering factors in discontinuation of a drug, its clinical value may not be as important as drug dose adjustment in renal failure since other factors such as inadequate clinical response, development of side effects or unavailability of a drug may result in discontinuation. This may be the reason of non-significant difference in discontinuation of medication in both group A and group B. Non-significant difference between no-intervention periods of group A and group B may be resulted from a potential dependence of the physicians to receive short messages to make changes.

This study was subject to several limitations. First, the intervention was conducted in only one hospital with limited number of patients and physicians. Second, lack of a consistent renal dosing guideline was a problem. having the potential to change therapeutic outcomes. According to a study by Fahimi et. al using different dosing guidelines results in an inconsistency in decision about dose adjustment [21].

It should be taken into consideration that for some medications like vancomycin, taking blood concentration levels would be the most proper way to decide whether to adjust the dose or not. However, taking blood concentration levels of drugs is not routinely performed in our hospital, so we had to rely on the dosing guidelines gathered from available resources. Concomitant illnesses such as hypothyroidism, hepatic impairment and chronic heart failure have the potential to interfere with the existing renal impairment and should be scrutinized in detail to understand their impact on renal dosing. Moreover, one limitation of the study was that we were not certain if the alert was received or seen by the physician or not. On the other hand, there are different GFR estimation equations which could be used to calculate creatinine clearance. Among commonly-used equations for estimating GFR, certain equations are preferred in different patient populations as suggested by previous studies (14). We mainly used Cockcroft & Gault equation in our study since most of renal dosing guidelines are based on this equation. Patients with no weight record were evaluated with IBW calculation. Moreover, the relation between the demographic qualities of physicians (specialty, gender, work experience) and the rate of responses to alerts can be a subject for future studies.

CONFLICT OF INTERESTS

Declared None

ACKNOWLEDGMENTS

We would like to thank all the physicians involved in our study. We also acknowledge Dr. Shahdi Ziaee for her contributions.

This study was done as a Pharm D thesis.

REFERENCES

1. Bates DW, Cullen DJ, Laird N, Petersen LA, Small SD, Servi D, *et al*. Incidence of adverse drug events and potential adverse drug events: implications for prevention. J Jama 1995;274(1):29-34.
2. Bobb A, Gleason K, Husch M, Feinglass J, Yarnold PR, Noskin GA. The epidemiology of prescribing errors:the potential impact of computerized prescriber order entry. J Arch Intern Med 2004;164(7):785-92.
3. Sellier E, Colombet I, Sabatier B, Breton G, Nies J, Zapletal E, *et al*. Effect of alerts for drug dosage adjustment in inpatients with renal insufficiency. J Am Med Inform Assn 2009;16(2):203-10.
4. Chertow GM, Lee J, Kuperman GJ, Burdick E, Horsky J, Seger DL, *et al*. Guided medication dosing for inpatients with renal insufficiency. J Jama 2001;286(22):2839-44.
5. Kohli HS, Bhaskaran MC, Muthukumar T, Thennarasu K, Sud K, Jha V, *et al*. Treatment-related acute renal failure in the

elderly:a hospital-based prospective study. J Nephrol Dial Transpl 2000;15(2):212-7.

6. Raschke RA, Gollihare B, Wunderlich TA, Guidry JR, Leibowitz AI, Peirce JC, *et al*. A computer alert system to prevent injury from adverse drug events:development and evaluation in a community teaching hospital. J Jama 1998;280(15):1317-20.
7. Kellum JA, Bellomo R, Ronco C. Definition and classification of acute kidney injury. J Nephron Clin Pract 2008;109(4):c182-c7.
8. van Dijk EA, Drabbe NR, Kruijtbosch M, De Smet PA. Drug dosage adjustments according to renal function at hospital discharge. J Ann Pharmacother 2006;40(7-8):1254-60.
9. Kuperman GJ, Teich J, Bates D, Hiltz F, Hurley J, Lee R, *et al*. editors. Detecting alerts, notifying the physician, and offering action items:a comprehensive alerting system. Proceedings of the AMIA Annual Fall Symposium. J American Medical Informatics Association 1996.
10. Rind DM, Safran C, Phillips RS, Wang Q, Calkins DR, Delbanco TL, *et al*. Effect of computer-based alerts on the treatment and outcomes of hospitalized patients. J Arch Intern Med 1994;154(13):1511.
11. Park H-i, Min W-K, Lee W, Park H, Park C-J, Chi H-S, *et al*. Evaluating the short message service alerting system for critical value notification via PDA telephones. J Ann Clin Lab Sci 2008;38(2):149-56.
12. Nguyen TV. Practical Assessment Tools for Identifying Kidney Disease 2010. Available from:http:// www.uspharmacist.com/ content/d/feature/i/1045/c/19882/.
13. Geerts AF, Scherpbier-de Haan ND, de Koning FH, van der Sterren TM, van Weel C, Vervoort GM, *et al*. A pharmacy medication alert system based on renal function in older patients. Brit J Gen Pract 2012;62(601):e525-e9.
14. Emami S, Riazi Esfahani H, Farokhi FR, Fahimi F. Assessment of drug dose adjustment in patients with kidney disease: opportunities for pharmacist involvement. Int J Pharm Pharm Sci 2012;4.
15. Marry Anne K, Lloyd Yee Y, Brian K, Robbin L, Joseph G, Wayne A, *et al*. Applied Therapeutics, The Clinical use of Drugs. The Point Lippincott Williams & Wilkins;2009.
16. Schrier RW. Manual of nephrology:Lippincott Williams & Wilkins;2008.
17. CF L. Drug Information Handbook (APhA) International:Lexi-Comp Inc;2009.
18. CF L. Drug Information Handbook (APhA) International:Lexi-Comp Inc;2010-2011.
19. Bennett WM, Aronoff G, Morrison G, Golper T, Pulliam J, Wolfson M, *et al*. Drug prescribing in renal failure:dosing guidelines for adults. Am J Kidney Dis 1983;3(3):155-93.
20. Oppenheim MI, Vidal C, Velasco FT, Boyer AG, Cooper MR, Hayes JG, *et al*. editors. Impact of a computerized alert during physician order entry on medication dosing in patients with renal impairment. J Proceedings of the AMIA Symposium American Medical Informatics Association 2002.
21. Fahimi, Fanak, Sepideh Emami, and Farin Rashid Farokhi. The rate of antibiotic dosage adjustment in renal dysfunction. Iran. J. Pharm. Res.11.1 (2012): 157.
22. Gettings L, Reynolds H, Scalea T. Outcome in post-traumatic acute renal failure when continuous renal replacement therapy is applied early vs. late. J Intens Care Med 1999;25(8):805-13.