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Role of Clinical Pharmacists in Early Detection, Reporting and Prevention of Medication Errors in a Medical Ward

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ABSTRACT

Background: Drug utilization evaluation (DUE) is an effective process in order to identify variability in drug use and subsequent application of effective interventions for improving patient outcomes. In this study, appropriate uses of drugs were evaluated by clinical pharmacy service.
***Methods*:** A prospective, interventional study from January to September 2015 was designed for determining frequency and type of clinical pharmacists' interventions and medication errors occurred in the infectious disease ward of Loghman hospital, affiliated to Shahid Beheshti University of Medical Sciences, Tehran, Iran.
Results: During the 8 months of the study period, 498 errors were detected among 419 patients that admitted to infectious disease ward of Loghman hospital. Most common errors were related to deep vein thrombosis (DVT) prophylaxis, stress ulcer prophylaxis (SUP) and vancomycin monitoring.
Conclusion: Our result showed that clinical pharmacy interventions can have an important role in reducing adverse drug events and their activities can be effective for reduction of medication error.

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Introduction

Rational use of medication has an important role for producing desirable outcomes in medicine. As a member of a patient's health care team, pharmacists and especially clinical pharmacists, providing comprehensive drug management to patients and providers; not only play a vital role in saving lives, enhancing patients' quality of life and reducing length of hospital stay, but also can make therapeutic interventions which are significantly decreasing treatment complications and also lessen costs (1-3). Pharmaceutical care provided by well-skilled clinical pharmacist has been started since 2005 in the hospital wards at Shahid Beheshti University of Medical Science, Tehran, Iran. In these teaching hospitals setting, clinical pharmacist focus on activities including safe and cost-effective drug administration (4), monitoring of drug utilization pattern (5-7), providing drug information for health care professionals (8) and reducing potential risks of medication related errors (9, 10). Medication errors are common in hospitalized patients (11). These errors are responsible for considerable costs, mortality and morbidity, whereas two-third of them can be preventable (12). Recently, many interventions have been taken to reduce the number of medication errors which are a major concern to health care institutions (13-15). In addition to this issue, appropriate use of stress ulcer prophylaxis (SUP) and deep vein thrombosis (DVT) prophylaxis are

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Table 1. Thrombotic risk factors for Deep Vein Thrombosis (DVT).

Each box = 1 risk point	
• Patient's age 40-60 y/o • Smoker (present) • Family history of DVT/PE • History of Heart Failure • Ischemic stroke (Past& present) • Leg swelling , ulcers , stasis , peripheral vascular diseases , varicose veins, vasculitis • Acute infections including pneumonia	• Obesity (> 120% IBW) • Current use of oral contraceptives, estrogen therapy, Hormone replacement therapy or drugs such as Tamoxifen, Thalidomide, Lenalidomide • Nephrotic syndrome • Pregnancy or postpartum (< 1 month) • Indwelling central venous catheter(present) • Sickle cell disease • Immobility
Each box= 2 risk points	**Each box= 3 risk points**
• Patients > 60 years old • Documented history of DVT / PE • Acute Heart Failure	• Multiple trauma (present) • Chemotherapy (current course) • Cancer (past & present) • Inherited thrombophilia* • Antiphospholipid antibody syndrome • Myeloproliferative disorders (Polycythemia vera, Essential thrombocythemia) • Paroxysmal nocturnal hemoglobinuria • Orthopedic surgery (below waist) • Pelvic / thoracic / abdominal surgery (≤1 month) • Spinal cord injury (≤1 month) or paraplegia • Surgery lasting > 30 minutes • Sepsis

* Factor V Leiden, Antithrombin deficiency , Protein C/ S deficiency, Prothrombin 20210A,Antiphospholipid syndrome, Dysfibrinogenemia, Lupus anticoagulant

important concerns of health care providers. Despite of believing in the harmlessness of acid suppressive therapy in hospitalized patients, it can have adverse effects like increasing risk of *Clostridium difficile* associated disease and hospital and community acquired pneumonia (3, 16-19). Moreover, the cost of unnecessary stress ulcer prophylaxis in general medicine can be considerable (20). Venous thromboembolisem, including DVT and pulmonary embolism (PE) is an important cause of mortality and morbidity. Considering that 70% to 80% of DVTs are silent or asymptomatic, prophylaxis is the most effective way for reducing mortality and morbidity in susceptible patients, but the inappropriate and extra dosage of anticoagulants may lead to an increase in cost and 2-fold risk of bleeding (21). On the other hand, lower dose of anticoagulant can be problematic and increase the risk of DVT in hospitalized patients. This study was conducted to evaluate the type and frequency of clinical pharmacists' interventions and their role in early detection, reporting and prevention of medication errors such as proper administration of DVT and SUP.

Methods

A prospective, interventional study was designed for determining frequency and type of clinical pharmacists' interventions and medication errors occurred in the infectious disease ward of Loghman hospital, affiliated to Shahid Beheshti University of Medical Sciences, Tehran, Iran. Patients that were admitted in this ward were considered for inclusion during the study period. A clinical pharmacist spent 6 hours per day to collect data during the study and reviewed all patients' medical records, medication history and monitor patients' drug treatment regimens to complete pharmacotherapy monitoring forms and extracting medical errors during 8 months period of study from January to September 2015.

The well documented drug information in optimal dose, drug utilization of anticoagulants was carried out by using the DVT risk factors and orders mentioned in caprini risk assessment model (22). PPIs or ranitidine for acid suppressive therapy for stress ulcer prophylaxis (SUP), and heparin or enoxaparin for deep vein thrombosis (DVT) prophylaxis are approved by the pharmacy and therapeutic committee.

Appropriate utilization of SUP based on American Society of Health-System Pharmacists (ASHP) guideline and articles was recommended in patients:

- Requiring mechanical ventilation > 48 hr.
- Coagulopathy (defined as PLT < 50000 or INR > 1.5 or PTT > 2 normal value)
- History of gastrointestinal bleeding or peptic ulcer disease within 1 year
- Traumatic brain injury, traumatic spinal cord injury

Table 2. Orders for Deep Vein Thrombosis (DVT) prophylaxis.

Low Risk (≤ 1 risk point TOTAL)	Moderate Risk (2 risk points TOTAL)	High Risk (≥3 risk points TOTAL)
• Early ambulation: • Out of bed to chair • Out of bed with assistance • SCD (Sequential compression device) • Plexi - pulse	• Heparin 5000 U SQ q12 h • Heparin 5000 U SQ q 8 h • Enoxaparin 40mg SQ q 24h • Enoxaparin 30mg SQ q 24h (if CLcr < 30 ml/min) • SCD • Plexi- pulse	• Heparin 5000 U SQ q 8 h • Enoxaparin 40mg SQ q 24h • Enoxaparin 30mg SQ q 12h (Orthopedic surgery , major trauma , spinal cord injury) • Enoxaparin 30mg SQ q 24h (if CLcr < 30 ml/min) • In addition to the above (optional): • SCD • Elastic stocking • plexi-pulse

Severe burns (>35 percent of the body surface area With at list two of following risk factors: sepsis ,occult Gastrointestinal bleeding lasting ≥6 days, glasgow coma score of ≤10 (or the inability to obey simple commands), intensive critical unit (ICU) patients with partial hepatectomy may also benefit from prophylaxis, ICU patients with multiple trauma (Injury Severity Score of ≥16), transplantation patients in the ICU preoperatively, renal insufficiency, hepatic failure, enteral feeding, glucocorticoids using(> 250 mg Hydrocortison), heparin or LMWH uses, warfarin using, history of use of Nonsteroidal Anti-inflammatory Drugs (NSAIDs) > 3 month (especially for age>65 years old, high dose NSAIDs, concurrent use of steroids or anticoagulant or aspirin), an ICU stay of more than 1 week (23-28).

VTE prophylaxis were considered in medical patients older than age 40 who have limited mobility for 3 days (at least 50% of times on the bed), and have at least one of the thrombotic risk factors shown in Table 1 (22).

Orders for DVT prophylaxis are shown in Table 2 (22).Medication error was defined as " any preventable incident that may cause or lead to an improper medication use or patient injury while in the control of the health care professional, patient or consumer''(29). Clinical pharmacist interventions which were used in this study are classified as following activities:

Drug discontinuation, the addition of a drug to treat regimen, dose adjustment (29), changing from one to another drug, dosage form change, drug interaction management, medication error prevention, therapeutic drug monitoring, lab data request, checking drug compatibility and stability, adverse drug reactions (ADRs) prevention and management or report and patient education (25). Information was collected by reviewing physicians' orders and drug Cardex of patients The frequency of observed errors was reported.

Results

During the 8 months of the study period, 498 errors were detected among 419 patients that admitted to infectious disease ward of Loghman hospital. Type and frequency of errors in the medical process are shown in Table 3. All of the recorded errors were detected by clinical pharmacists and their recommendations were accepted by the health care provider team who were responsible for patient drug therapy.

Discussion

Monitoring of medication errors is one of the most important issues for clinical pharmacists. They provide pharmaceutical care including therapeutic drug monitoring, review patients' medical records, attending in medical wards and education of health care workers and patients about drug therapy in teaching hospitals of the Shahid Beheshti University of Medical Sciences. In the present study, the most common intervention that has done by the clinical pharmacist was requested for checking vancomycin level in the patients. One of the prescribed antibiotics in infectious disease ward of Loghman hospital was vancomycin, which its initial dosing is based on glomerular filtration rate (GFR) and disease type. The monitoring vancomycin trough level is important for therapeutic outcomes and preventing drug induced nephrotoxicity. In one study, Barrier et al., suggested high trough levels of vancomycin does not result in improving clinical responses ,but likely increase the incidence of nephrotoxicity (30). In another study done by Bosso et al., higher vancomycin trough levels were associated with increased risk of nephrotoxicity (31). In another study that was done in Tabriz, 69.3% of patients received vancomycin inappropriately (32). Also, in a study that was done in Iran, 97.7% of the study population, received an inappropriate dosing regimen of vancomycin and inappropriate indication as well (33). Another study showed that pharmacist involvement can improve achievement of timely adequate vancomycin trough levels by using dosing protocol of vancomycin at the Intensive Care Unit (34). Due to the importance of appropriate dosing of vancomycin, Glomerular filtration

Table 3. Type and frequency of clinical pharmacist's interventions in an infectious ward (n=498).

Type of intervention	Medicine (s)	example	N (%)
Lab data request	• SrCr (14), electrolytes level (21), BUN (2), SUA (2), lipid profile (9), albumin (2),BS (5), HbA1c (16), 2hPP (1), LFT (7), FBS (2), CBC (4), platelet (5), Iron profile (8), Vitamin B12 (1), • Digoxin level (2), vancomycin level (16) • INR (6), PTT (4), • stool exam (2), BP (2), • PSA (2), TFT(3), BMD (1), thyroid sonography (1)	In some cases, pharmacist wasn't able to adjust the dose of AKI patient due to lack of SrCr level.	28
Adding a drug to treatment regimen	• Heparin(11), atorvastatin(5), ACEI+HCTZ(5),Aspirin(5), enoxaparin(3), amlodipin(2), metoprolol(1), enelapril(1), losartan(1), tamsulosin(1) • Pantoprazole(10), lactulose(4) • Salmeterol(1) • Glibenclamide(2), insulin(2), metformin(1)Isoniazid(2), Ethambutol (2), Pyrazinamide (1) • KCl(6), ferrous sulfate(3), Calcium-D (2), Mg(1), folic acid(1), calcitiol(1), high pr ensure(1) • Pack cell(1), normal salin(N/S) IV fluid (2) • Lorazepam(3), methadone(2), gabapentin(1), levodopa-benserasid(1), donepezil(1), phenytoin(1)	Pantoprazole was not started for a patient that SUP was necessary	17
Changing from one to another drug	• Captopril to losartan (1), valsartan to captopril (1), propranolol to metoprolol (1), atenolol to amlodipine (2), enoxaparin to heparin (1), metoprolol to cavedilol (1), heparin to enoxaparin(2), carvedilol to losartan(1), • chlordiazepoxide to lorazepam (1), phenytoin to valproate (1), clomipramine to fluvoxamine (2), alprazolam to lorazepam (1), • MOM to lactulose (1), omeprazole to pantoprazole (7), ranitidine to pantoprazole (1), pantoprazole to omeprazole(5), cimetidine to pantoprazole(10), pantoprazole to ranitidine(1), • ceftriaxone to tazocin(1), ciprofloxacin to levofloxacin(1), meropenem to tazocin(3) • Normal saline IV fluid to 1/3 Normal saline and 2/3 Dextrose IV fluid (1), folic acid to folinic acid(1), atrovent to salbutamol(1), Calcium Carbonate to Calcium-D (1),	Omeprazole was changed to pantoprazole in a patient with coadministration of Clopidogrel.	10

Type of intervention	Medicine (s)	example	N (%)
Changing the frequency, duration or dose of drugs	• Heparin(10),enoxaparin(5), N.C(2), atorvastatin(4), digoxin(3), losartan(2)amlodipine(2),ASA(1), pentoxyphylline(1), gemfibrozil(1), metoprolol(1), fursemide(1), warfarin(1) • Oral anti-diabetic agent(1), insulin(2) • Vancomycin(12), acyclovir(7), meropenem(6), tazocin(4), ciprofloxacine(4), oseltamivir(2), ampicillin(2), cefazolin(1), ceftriaxon(2), amantadin(1), imipenem(1),zidovudin(1), ceftazidim(1), amikacin (1), clindamycin(1), azitromycin(2), • N-acetylcystein(1), hydroxyzine(1), dexamethasone(1), prednisolon(2) • Sodium valproate (2), acetaminophen (2), phenytoin(1), methadone(1), spironolactone(1), clidinume C(1), citaloperam (1), ferrous sulfate(1), folic acid(1), levethiracetam(1)	The interval of vancomycin administration was decreased due to low GFR.	20
Reminding missing drugs	• Mycophenolate mofetil (2), cyclosporine(1) • Amlodipin(2), Aspirin(2), atorvastatin(2), Nitroglycerin(1), captopril(1), diltiazem(1), carvedilol(1), losartan(1), enalapril(1) • Calendula cream(1), zinc cream(1), phenytoin cream(1) • Methimazole(1), levothyroxin(1) • Budesonide-formoterol(1), salbutamol(1), prednisolon(1)	The interval of vancomycin administration was decreased due to low GFR.	5
Drug discontinuation	• Pantoprazole (6), amp ranitidine (1), omeprazole(2), cimetidine(1) • Ampule dexamethasone (1), betamethasone Long Acting (1) • ciprofloxacin (2), vancomycin (1), • heparin (8), ASA(1), clexan(3), osvix(1), colestiramin (1), vitamin K (1), KCl (1), Nitroglycerin (1),atenolol(1), pioglitazone (1), metoprolol (1) • alprazolam (1), zolpidem(2), lopramide(1), hydrocortisone(1), atrovent(1), Ritalin(1), theophylline(1), acetaminophen(2), acetaminophen codein(1), expectorant codein(1), pioglitazon(1), gemfibrozil(1)	Heparin as deep vein thrombosis prophylaxis was discontinued in a patient without definite indication	10
Management of drug interactions	• Omeprazole (4), clopidogrel vs omeprazole(3), depakin vs meropenem(3), quetiapin vs. azithromycin (1), Ca vs. ferrous sulfate (1), ciprofloxacin vs. warfarin (1), ceftriaxone vs. heparin (1), methylphenidate vs phenytoin(1), Aspirin vs bruphen(1), enoxaparin vs heparin(1)	Omeprazole was coadministered with clopidogrel, instead of pantoprazole.	3

Type of intervention	Medicine (s)	example	N (%)
Changing the dosage forms (intravenous to oral)	• Pantoprazole(5), ranitidine (3)	Intravenous pantoprazole was changed to oral pantoprazole.	2
Therapeutic drug level monitoring	• Vancomycin (3), digoxin (1), meropenem(2)	Vancomycin level was required to adjust the doses in an AKI patient.	1

Acute kidney injury; AKI, Angiotensin-converting-enzyme inhibitor; ACEI, Bone marrow density; BMD, Blood pressure; BP, Blood urea nitrogen; BUN, Blood sugar; BS, Cell blood count, CBC, Fasting blood sugar; FBS, Hydrochlorothiazide; HCTZ, International ratio; INR, Potassium chloride; KCL, Liver profile test;(LFT), Partial thromboplastin time; PTT, PDH; past drug history, Prostate specific antigen; PSA, Serum creatinine; SrCr, Serum uric acid; SUA, Two hours post prandial;2hpp, Thyroid function test; TFT.

rate (GFR) was calculated for all patients by the clinical pharmacist in initial dosing and 16 requests for checking vancomycin trough level by the clinical pharmacist of the ward resulted in changing the drug dose in 12 patients in this study. Another common intervention that was done by the clinical pharmacist in our research, was adding a drug to the treatment regimen and changing the frequency, duration or dose of drugs. Among these interventions, SUD and DVT prophylaxis were observed more than other drugs. By considering the importance of appropriate drug use with an optimal dose for VTE prophylaxis in mortality and morbidity (21, 22), Heparin adding, dose changing and discontinuation in drug regimen was done in 11, 10 and 8 of the patients respectively.

In a study conducted by Khalili et al., about anticoagulant utilization evaluation, approximately half of patients were candidate for DVT prophylaxis during drug monitoring and 25% of them needed drug dose adjustment (35). Also, another study showed that a program that was developed by a pharmacy service was associated with a reduction of the occurrence of DVT (36). In Dobesh et al study, they concluded pharmacists can play a key role in helping health care professionals to improve prevention of venous thrombosis (37). In Fahimi et al., study, which was done in Masih Hospital in Tehran, Iran, enoxaparin utilization on 147 inpatients was reviewed. Their results showed that inappropriate dosing, administration and prescribing of enoxaparin is common in Masih hospital and they need educational programs and implementation of protocols to control prescribing patterns (7). Therefore, regarding our result, educational programs and implementation of protocols are necessary for control of prescribing patterns. In addition, gastric ulcer prophylaxis (GUP) indication with appropriate drug dosing regimen was monitored in this study. Pantoprazole was added to the drug regimen of 10 patients and discontinued in 6 cases. In Khalili et al., study the appropriate use of GUP was evaluated in 30 patients that were candidates for receiving GUP and the authors concluded that clinical pharmacists interventions were associated with reduction in use of acid suppressive therapy (38). Because of the potential inhibitory effect of Cimetidine on CYP450 which can result in interaction with other drugs in patients' drug regimen (in comparison to pantoprazol) (39), changing a drug regimen from Cimetidine to Pantoprazole was done in 10 cases. Based on clinical cultures, meropenem was changed to piperacillin/tazobactam in 3 patients during the study. In a study done by Haroutiunian et al., the interaction between meropenem and valproic acid (VPA) causes a significant decrease in VPA plasma concentration (40) which was detected in 3 cases in our study. By considering the effect of medication errors on cost of care , mortality and morbidity (12), clinical pharmacy interventions can have an important role in reducing adverse drug events and their activities can be cost effective (41).

In conclusion, our result showed that clinical pharmacy interventions can have an important role in reducing adverse drug events and their activities can be effective for reduction of medication error.

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