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Role of the Pharmacist in Identification of Medication Related Problems in the Icu: A Preliminary Screening Study in an Egyptian Teaching Hospital

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Abstract: Introduction Medication-related problems in the ICU are an important but poorly understood phenomenon. Many patients admitted to intensive care units consume long-term medication. New drugs may be commenced during intensive care intended for the short term or longer. Patients are often cared for by several teams during hospital admission and long-term medication may inadvertently be permanently discontinued. Aim: We sought to evaluate the frequency and incidence of medication-related problems in the ICU in one of the largest teaching hospitals in Egypt. Methodology: Prospective observational study was conducted to report and record the frequency of medication related problems in the ICUs. Patients: 220 patients were reviewed during a period of one year. Those patients were prescribed 2286 medications. Results: Medication review was done for 220 ICU patients. The average length of the period the patients stayed in the hospital was around 10.396 days. The 220 recruited patients, using a total of 2286 medicines, were classified into six major categories according to the BNF 2009. Cardiovascular conditions represented the principal reason for ICU admission. Cardiovascular agents counted for the majority of the medications consumed by the participants; anticoagulants and antiplatelets, nitrates and H_2-receptor antagonists were prescribed most frequently. About 97% of monitored patients were reported with one or more drug related problems. The problems were categorized into 13 different classes. Among the detected errors, incorrect dosing regimen represented the highest percentage (21.971%) followed by duplication and prescribing unnecessary medication representing around 12% each. Equal incidence of drugs being prescribed either in a lower dose, higher dose or had some degree of drug interaction (8.4 % each). Drugs that required therapeutic monitoring that was not done represented 7.27 % and antibiotic misuse represented 5.331 % of the total medication errors detected.

Key Words: Medication review, medication errors, prescription monitoring, medication related problems, drug related problems, adverse drug events, intensive care unit.

INTRODUCTION

Maximizing efficacy, minimizing risks, reducing costs and respecting patients' choices are the main features of good prescribing of medicines (Barber, 1995). In reality, this does not occur because medicines are sometimes prescribed inappropriately (Cantrill *et al.,* 1998) or because of inappropriate use of the prescribed medicines by the patients (McGavock, 1996). Medication-related problems (MRPs) can reduce the potential clinical benefits of treatment with medicines and waste the resources.

There are various definitions of medication-related problems (MRPs). MRPs can be defined from a narrow perspective of adverse drug reactions and undesirable drug interactions which relate to the pharmacology of the medicine. Definitions may also describe the medicine-taking behaviour of the patient or their non-adherence to the treatment. From a wider perspective, MRPs could encompass adverse drug reactions, patient medicine-taking behaviour and problems initiated from the prescribing of medicines.

Patient medication records (PMRs) and prescription monitoring is one of the methods that can be employed to identify any MRPs patients may suffer. The position of pharmacists at the interface between distributing the medications and using them makes their role in preventing inappropriate prescribing problems important (Rupp *et al.,* 1992).

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There is no universal classification of drug-related events but classification of MRPs is desirable for assessing the effectiveness of pharmaceutical care services.

There are a variety of ways in which MRPs have been classified. In some classifications, the causes of MRPs are separate from the problems. In other cases, classifications of the MRPs describe the causes behind these problems. Other classifications consider the interventions being employed to reduce these MRPs.

Critical care presents substantial patient safety challenges. It is fast-paced, complex, and commonly requires urgent high-risk decision-making, often with incomplete data and by physicians with varying levels of critical care training. These factors may lead to higher medical error rates than elsewhere (Beckmann *et al.,* 2003). Moreover, critically ill patients may be particularly vulnerable to iatrogenic injury because of the severity and instability of their illness and their frequent need for high-risk interventions and medications (Cullen *et al.,* 1997).

Because of the above mentioned reasons, because none of the published literatures reviewed medication errors in Egypt, and because the normal medication system in the study hospital does not involve any active role for the pharmacist, performing this study was essential. In this system, the physicians at the hospital currently write orders by hand, copies of which are sent to the pharmacy, where the satellite based pharmacists transcribe orders into the medication administration record (MAR) and dispense ready-to-administer doses to the floor, but do not actively participate in other activities, such as ward-based rounds or medication review. Because of these reasons arose the aim of the present study. The objective of the study is to gain a better understanding for the incidence and nature of serious medical errors in critical care settings, and describe the frequency and types of medication related problems in different intensive care units in one of the main teaching hospitals in Egypt. And to see the impact of the pharmacist in identifying medication related problems.

MATERIAL AND METHODS

Study site:

The participating institution was tertiary care teaching facility. Surgical, medical and mixed ICU, Kasr El-Aini Hospital, Cairo, Egypt, were included.

Study Design and Data Collection:

This is a prospective observational study. Patients admitted to the ICUs during the data collection shifts over the study period (November 2007 to November 2008) were systematically samples and followed until transfer, unit discharge, or death. All staff and patient-related data were confidential. A fourpronged approach was used to capture suspected adverse events and serious errors (collectively referred to as incidents). The primary method of data collection was direct continuous observation.

Healthcare professionals in the ICU were informed that the purpose of the research was to identify medication errors. There was no attempt to hide the intent of the study.

A special data collecting sheet was designed by the investigators for a structured patient information collection. This sheet was divided into several sections, the first was concerned with the patient demographic data. The second section was designed to gather any information regarding the reasons for hospital admission, history of the present illness, other co-morbidities together with all other relevant details like laboratory data. The main section was designed to record all the data regarding the patient medication, dates and times that a prescription was written, names of medication, dosage forms, doses, dosage regimens, starting dates and ending dates, if applicable, instructions, potential drug-drug interactions and any OTC medication being consumed by the patient.

Demographic information about patients was obtained from flow sheets and medication administration records. Laboratory results and results of diagnostic tests were used as necessary.

Data for recruited patients were collected by the investigators and by the based pharmacists in the different ICUs. The collected data were reviewed by the investigational pharmacists and rechecked with investigational clinician. The investigational pharmacists participated in the process of evaluation used a standard set of definitions related to medication errors and problems. Both terminologies “medication related problems (MRPs)” and “drug related problems (DRPs)” will be used interchangeably in this study to describe any problems connected with medications prescribed to the enrolled patients.

For accurate detection of drug-drug interactions, the prescriptions medications for all the enrolled patients were fed on Lexi-comp software and only major interactions (coded as X interactions) were reported as a medication related problems.

Data Analysis:

Descriptive statistics were generated, specifically means and standard deviations and ranges. The primary outcome of ICU visits that were drug-related is reported as a percentage. The other statistical comparisons were done by the Mann-Whitney for nominal continuous data, and the Chi-squared (X^2) test for categorical data with a P value of < 0.05 being considered significant. Statistical Package for Social Science (SPSS) was used for data analysis.

RESULTS AND DISCUSSION

Medication review was done for 220 ICU patients. Table 1 shows demographic description of patients recruited in this study. All the recruited patients were monitored during the total length of their hospital stay. The average length of the period the patients stayed in the hospital was around 10.396 days ranging from 2-20 days.

The 220 recruited patients were using a total of 2286 medicines classified into six major categories according to the British National Formulary (BNF 2009). The number and type of each category is shown in table 3. Cardiovascular conditions represented the principal reason for ICU admission of patients included in this descriptive study (55.742%) as shown in table 2. Cardiovascular agents counted for the majority of the medications consumed by the participants; anticoagulants and antiplatelets, nitrates and H_2-receptor antagonists were prescribed most frequently (table 3).

During the study period, patient's medication was reviewed by the investigators to identify and classify medication-related problems (MRPs). An initial assessment was made by the investigators regarding the MRPs identified. About 96.818% of the monitored patients were reported with one or more drug related problems. The problems were categorized into 13 different classes:

- •Therapeutic failure
- •Dosage problems
  - ○Lower doses
  - ○Higher doses
  - ○Incorrect regimen
- •Lack of therapeutics drug monitoring
- •Antibiotic misuse
- •Side Effects
- • Drug interaction
- • Contraindication
- • Stopping of necessary medication
- • Inappropriate medication
- • Duplication of medication
- • Using unnecessary medication
- • Unnecessary combinations
- • Others

A total of 619 MRPs were detected and indexed in a total of 213 patients, i.e. only 3.182% of the monitored patients were free of any medication related problems. Table 4 represents the most commonly reported medication related problems in the ICU. Among the detected errors, incorrect dosing regimen represented the highest percentage (21.971%) followed by duplication and prescribing unnecessary medication representing around 12% each. Equal incidence of drugs being prescribed either in a lower dose, higher dose or had some degree of drug interaction (8.4 % each). Drugs that required therapeutic monitoring that was not done represented 7.27 % and antibiotic misuse represented 5.331 % of the total medication errors detected.

Table 1: Demographic description of recruited patients

Parameter	Patients with MRPs	Patients without MRPs	P
	N = 213	N = 7	
Average age in years (S.D)	55.530 (16.025)	53.019 (4.891)	0.0521*
Age range	19-90	45-59	
Weight (S.D)	69.909 (11.193)	72.912 (3.120)	0.0601*
Gender distribution (male %)	142 (66.667)	5 (71.429)	0.0657**
Average number of medication taken (S.D)	10.515 (3.1)	10 (1.310)	0.0416*
Average length of hospital stay in days (S.D)	13.920 (361)	6.871 (4.500)	0.0021*

*Statistical level of significance, Mann-Whitney U-test, $p<0.05$ between the two groups

** Statistical level of Significance at $p<0.05$, Chi-squared test

MRPs: Medication related problems

SD: Standard deviation

P: Level of significance

Table 2: Frequencies and percents of the main reasons for ICU admission and the other most commonly diagnosed medical problems

Principle Conditions for admission	Frequency (%)*	Co-morbid conditions	Frequency (%)*
	Cardiovascular conditions		
Myocardial Infarction	75 (17.943)	Hypertension	97(16.870)
Heart Failure	42 (10.048)	Ischemic Heart Disease	65 (11.111)
Acute coronary syndrome	36 (8.612)	Myocardial Infarction	45 (7.692)
Atherosclerosis	22 (5.263)	Ischaemic dilated cardiomyopathy	26 (4.444)
Unstable angina	15 (3.589)	Atrial Fibrillation	26 (4.444)
Atrial Fibrillation	13 (3.110)	Dyslipidemia	13 (2.222)
Infective endocarditis	8 (1.914)	Congestive Heart Failure	10 (1.709)
Cardiac arrest	8 (1.914)	Angina	7 (1.197)
Coronary artery bypass graft	7 (1.675)		
Ischemic dilated cardiomyopathy	7 (1.675)		
Total	233	Total	282
	Endocrinological conditions		
Diabetic ketoacidosis	15 (3.589)	Diabetes (type II)	78 (13.333)
Hypoglycaemia	7 (1.675)		
Hyperthyroidism	6 (1.435)	Hypothyroidism	19 (3.248)
Hypothyroidism	6 (1.435)		
Total	34	Total	97
	Respiratory conditions		
Chest infection	15 (3.589)	Pneumonia	7 (1.197)
Acute pulmonary oedema	8 (1.914)		
Respiratory distress	8 (1.914)		
Severe cough	8 (1.914)		
Pneumothorax			
Total	39	Total	7
	Electrolyte imbalance		
Acute periodic hypokalemic paralysis	8 (1.914)		
Hyperkalemia	6 (1.435)		
Total	14		
	Renal disorders		
Renal Impairment	34 (8.134)	Renal impairment	26 (4.444)
		Renal stones	7 (1.197)
		Bladder carcinoma	8 (1.368)
		Urinary Tract Infection	6 (1.026)
Total	34	Total	47
	Others		
Shock	20 (4.785)	CVS	19 (3.248)
Decreased Conscious Level	8 (1.914)	Depression	15 (2.564)
Limb ischemia	8 (1.914)	Cirrhosis	14 (2.393)
PCI	8 (1.914)	Rheumatic Arthritis	14 (2.393)
Post portum eclampsia	7 (1.675)	Raynaud's syndrome	14 (2.393)
Cellulitis	7 (1.675)	Ascites	13 (2.222)
Post operative	6 (1.435)	Bed sore	13 (2.222)
		Deep Vein Thrombosis	13 (2.222)
		Epilepsy	13 (2.222)
		Hepatomegaly	8 (1.368)
		Peptic ulcer	8 (1.368)
		PACs	7 (1.197)
		Dermatitis	7 (1.197)
		Transiet Ischemic Attack	7 (1.197)
		Tumour	6 (1.026)
Total	98	Total	152
Grand Total	418		585

*Column percent calculated by dividing the total number of conditions in each disease category by the total number of conditions.

Table 3: BNF Categories and frequencies of medication prescribed in the ICU

Medications Prescribed	Frequency (%)*
Gastrointestinal medications	
H2 antagonists	155 (6.780)
Proton Pump Inhibitors	65 (2.843)
Osmotic laxative	7 (0.306)

Table 3: Continue

Cardiovascular medications	
Antiplatelets	252 (11.024)
Parenteral anticoagulants	220 (9.624)
Nitrates	213 (9.318)
Lipid regulating drugs	136 (5.949)
Loop diuretics	104 (4.549)
Anti-ischemic	103 (4.506)
Beta-blocker	99 (4.331)
ACEIs	98 (4.287)
Potassium Sparing Diuretics	52 (2.275)
Calcium Channel Blockers	46 (2.012)
Cardiac glycosides	45 (1.969)
Inotropic sympathomimetics	33 (1.444)
Vasoconstrictor sympathomimetics	32 (1.400)
Antiarrythmias	32 (1.400)
Oral anticoagulant	21 (0.9189)
Centrally acting antihypertensives	13 (0.569)
Others	26 (1.137)
Antibiotics	
Cephalosporins	104 (4.549)
Penicillin	71 (3.106)
Metronidazole	55 (2.406)
Clindamycin	48 (2.100)
Quinolone	26 (1.137)
Beta-lactamase inhibitors	13 (0.569)
Aminoglycosides	7 (0.306)
Vancomycin	7 (0.306)
Antidiabetic medication	
Insulin	14 (0.612)
Sulphonylureas	7 (0.306)
Thyroid dysfunction medication	
Thyroid hormone	33 (1.444)
Anithyroid drug	8 (0.350)
Other	
Anxiolytics	55 (2.406)
Antiepileptics	33 (1.444)
Glucocorticoids	26 (1.137)
Nephroprotective agent	20 (0.875)
Allergic emergencies	13 (0.569)
Immunosuppressants	13 (0.569)
Drugs suppress rheumatic disease	13 (0.569)
Drugs used in nausea & vertigo	7 (0.306)
Erectile dysfunction	6 (0.262)
Total	2286

*Column percent calculated by dividing the total number of medications in each category by the total number of prescribed medications.

Table 4: Most commonly reported Medication related problems in the ICU

Reported medication related problems	Frequency (%)
Inappropriate regimen	136 (21.971)
Dosage error	104 (16.800)
Lower dose	52 (8.400)
Higher dose	52 (8.400)
Unnecessary medication	72 (11.632)
Duplication	72 (11.632)
Drug interaction	52 (8.400)
Lack of monitoring	45 (7.270)
Antibiotic misuse	33 (5.331)
Stopping necessary medication	13 (2.100)
Unnecessary combination	13 (2.100)
Inappropriate medication	7 (1.131)
Contraindication	7 (1.131)
Total	619

*Column percent calculated by dividing the total number of medications in each category by the total number of prescribed medications.

Discussion:

Medication errors are an important cause of patient morbidity and mortality (Hussain and Kao, 2005). In 1999 Institute of Medicine (IOM) report, *To Err is Human: Building a Safer Health System*, drew public attention and considerable interest by the medical community to the importance of patient safety (Kohn *et al*, 1999). However, to date, there is little evidence that patient safety has improved (Leape and Berwick, 2005).

The ICU combines the presence of high-risk patients and interventions in a complex environment. The single strongest predictor of an ADE is patient illness severity (Giraud *et al*, 1993). Critically ill patients are prescribed twice as many medications as patients outside the ICU (Cullen *et al*, 1997).

It is important to remember that critically ill patients have fewer defences against adverse events than other patients do. They have limited ability to participate in their medical care and they lack the physiological reserve to tolerate additional injury. Moreover, they are reliant on sophisticated technologies and equipment to deliver essential care and yet relatively little is known about medical equipment failures and the associated safety risks. Finally, lack of continuity of care at discharge from the ICU is a well known feature putting the patient at risk for errors and highlights the importance of communication with the future caregivers (Campbell *et al.,* 2006).

None of the published studies focusing exclusively on medication administration errors in the ICU have been performed in developing countries. There are a variety of similarities and differences between our evaluation and the studies done in western industrial (developed) countries. In common were the ICU environment, the types and definitions of errors and the use of pharmacy personnel as independent observers. A limitation to some of these studies, as well as ours is the observation of a relatively small number of patients (Tissot *et al*, 1999). Many of these studies involved paediatric patients (Tisdale, 1986; Schneider *et al*, 1998).In some studies, unlike ours, the pharmacists were active members of the healthcare team who provided clinical advice, which may account for the difference in the incidence of errors (Calabrese *et al*, 2001). This was quite difficult in the present study for two reasons, firstly; the description of clinical pharmacist and his/her role in MRPs interventions has not been defined yet, secondly; the investigators were not permanently working in the above mentioned ICUs. Another limitation and inherent problem of most of published studies that tend to focus on chart review, like our study, is the possibility of unrecorded information and missing documentation of actual or potential incidents (Manias, 2007).

The incidence of MRPs varies widely between the different clinical settings and patient populations and between the different studies. Among critically ill adults, the rate of medication errors ranges from 1.2 to 947 errors per 1,000 patient ICU days with a median of 106 errors per 1,000 patient ICU days (Kane-Gill and Weber, 2006). It was difficult to calculate the actual incidence of MRPs in this study because the investigators have not screen all the patients admitted to the ICUs during the study period. Instead we calculated the average number of MRPs with respect to the total number of patients screened and there were 2.814 problems/patient identified. It was difficult to compare our reported value to the published ones for several reasons reported by Moyen *et al*, first, the definition of medication error is critical. Furthermore, should medication errors be reported per patient, patient day, medication day, or dose administered? Second, the process node (prescription, transcription, and so on) under investigation will influence incidence estimates. Third, the method of reporting medication errors influences rate estimates. (Moyen *et al.,* 2008)

The 13 MRPs categories developed in this screening were not designed to be a definitive set of categories, but aimed to integrate all the types of MRPs identified in this setting. It is worth mentioning that parentral nutrition and intravenous admixtures were not included in the screening process.

The most commonly identified problem was incorrect regimens were dosage errors where medications were prescribed either in doses lower that officially stated or the opposite. The drug most commonly prescribed in a dose higher that anticipated was spironlactone where the normal dose of spironlactone in heart failure in the presence of ACE inhibitors should not exceed 25mg (BNF 2009), but a large number of screened patients were prescribed spironlactone doses ranging between 50-100 mg. On the opposite, atoravastatin was prescribed in lower doses than those required for some cases.

Duplication was the second most commonly encountered problem where nitrates in different dosage forms were used concurrently i.e., the same patient was administered glycerly trinitrate as tablets and transdermal batches simultaneously.

The most commonly prescribed medication with no clear indication was metronidazole, which was prescribed for a sole reason which is prophylaxis, regardless the patient case, kidney and liver function.

There was no special pattern for the identified drug-drug interactions in the screened patients. Only major interactions as classified using the Lexi-comp software were reported. This included prescribing sildenafil together with the nitrates. Another major interaction case was reported when verapamil was prescribed together with bisoprolol for a patient with congestive heart failure. Regarding the lack of therapeutic drug monitoring, among the 220 patients reviewed, 110 (50%) received one or more of those drugs described as having narrow therapeutic index and required careful monitoring. Out of those 110 patients only 7 patients (6.364%) were monitored for those medications. This lack of monitoring can be attributed to several factors, the major will be cost related. Not all the physicians were familiar with which drugs should be closely monitored and even

those who were familiar did not know the availability of the monitoring tests in their hospital. When the physicians were verbally asked about the importance of therapeutic drug monitoring some of them believed that clinical manifestation would be the best indicator to count on rather than the drug plasma sample.

Although antibiotic misuse was not among any of the published lists of medication related problems neither in the primary care nor in the secondary care, we could not ignore it in this observational study as a major category in the screened patients. About 13% of the prescribed medications during the ICU stay were antibiotics. Around 50% of those prescribed antibiotics were misused. In this piece of work antibiotic misuse meant

- •Prescribing unnecessary antibiotic
- • Prescribing inappropriate antibiotic
- • Prescribing different antibiotics covering the same spectrum for the same patient
- • Starting and discontinuation of antibiotics within an awkward timescale. Interestingly regarding this point, some of the screened patients were prescribed four different antibiotics consequently within a period of three days.
- • Inappropriate regimens for the prescribed antibiotics

Stopping necessary medications and unnecessary duplications have the same weight (2.1%) in this screening study. Atorvastatin and ACE inhibitors were the most important medications stopped despite the urgent need for them in the screened patients. Ranitidine and omeprazole combination represented the most unnecessary combination specially when used as prophylaxis against stress ulcer in the ICU. Two different loop diuretics were prescribed simultaneously in several patients without any literature or reference support. Also two dihydropyridine calcium channel blockers were prescribed simultaneously.

Contraindications represented the least committed problems. Despite the fact that they were minor in frequency; they were major in severity. One of the major contraindications reported was prescribing diltiazem in patients suffering from congestive heart failure.

When the average length of hospital stay for the screen patients were compared with the average length of hospital stay for selected sample of ICU patients without any identified MRPs, it was reported that there was significant difference in the mean length of stay between patients with or without drug-related problems. It was quite difficult for the investigators at this stage to compare this difference on the basis of pharmacoeconomy.

Moyen *et al*, 2008, proposes three simple strategies to change medicine's approach to medication errors: a) recognize the inadequacy of the current approaches for preventing medication errors; b) improve the error reporting system, avoid punishment and focus on identifying performance improvement opportunities; and c) understand and enhance human performance within the medication use process (Crane, 2000).

Limitations:

Our study has several limitations. First, the role of investigators was limited only to the reporting of the medication related problems and no intervention was generally done, which may look unethical. To avoid ethical dilemmas, the investigators reported potential serious problems identified in the screened patients to senior medical staff in the ICUs on several occasions intended for that purpose during the study period. Another potential concern is the effect that an observer may have on participants being observed (e.g. the Hawthorne effect) (Manias, 2007). Also, the data collected did not consider the impact of the identified medication related problems on the total cost during patient hospital stay.

Another problem is that the process of identification of the MRPs depended mainly on an observational experience which is more subjective and may be a source of bias. A more structured interview should be designed to guarantee the consistency of the process of identifying the MRPs, although this may be a bit difficult in an ICU setting as many of the enrolled patients were on mechanical ventilation or not conscious enough to be interviewed.

Another limitation is that the study was restricted to one hospital and one health authority; therefore it cannot be assumed that the results are representative of other hospitals and other health authorities.

Finally, calculating the percent of the MRPs for the total number of medication prescribed/patient was not the most accurate way of assessment due to the great variation between the numbers of medication each patient was prescribed.

Future research should focus on studying the optimal strategy to improve prescribing practices and monitoring, particularly among high-risk patients or patients taking high-risk medications and studying interventions performed to prevent potential problems or correct any actual problems reported.

Conclusion:

Patient safety is an important health care issue because of the consequences of iatrogenic injuries. Medication errors in critical care are frequent, serious and predictable. A promising way to reduce human error is to identify failures and redesign faulty systems.

Recommendation:

Emphasizing the role of clinical pharmacist as an inpatient services, with a great stress on his/her role as a medication reviewer.

Establishing a method for reporting any identified medication related problems and the optimal strategy for solving the identified problems.

Efforts must be directed towards improving communication between the different healthcare providers in the ICUs to ensure proper delivery of the seamless care.

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