Pattern of Intensive Care Unit Admission Due to Drug Problems

KAMEL ABDELAZIZ MOHAMED, M.D.
The Department of Critical Care Medicine, Cairo University, Egypt

Abstract

Introduction: Drug related problems (DRPs) are of major concern, affecting patients of both sex. They impose considerable economic burden on the society and the health-care systems.

Aim of the Work: The aim of this work was to identify and categorise drug-related problems in adult intensive care unit.

Patients and Methods: The study was a prospective, observational study as eighty six patients were included. They were consecutively admitted to ICU through the emergency room or transferred from the general ward due to DRPs. Parameters included in the study as length of stay in ICU, need for cardiovascular support or mechanical ventilation, dialysis, as well as APACHE II score were recorded.

Results: Drug related problems represent 3.6% of the total ICU admission. The median (range) of APACHE II score for 86 patients included in the study was 17 (10-23), and length of ICU stay was 2.4 (1.5-4.2) days. In 45 patients (52%), DRP was drug over dose (group I), while other DRP was present in the other 41 patients (48%, group II). Patients in group 1 were older (39 years versus 32 years in group II), with significant impaired renal function. The need of inotropic drugs and mechanical ventilation as well as the length of stay (LOS) in ICU was significantly higher in group I. There were no significant difference in GCS between both groups, however APACHE II score was significantly higher in group I. Only four patients (4.6%) were admitted by suicidal attempt as well as three patients (3.4%) due to trauma drug-related admissions, all were in (group I). Nineteen percent of the patients had hypoglycaemic medication due to hypoglycaemic medication followed by (group 2). The total mortality rate was 4.6%, all of them were eventually non preventable.

Conclusion: The critically ill patients admitted due to drug related problems represented a small proportion (3.6%) of admissions to the ICU. Hypoglycaemic medication was one of the most common causes of admission by drug related problems.

Key Words: Drug related problems – ICU – Cost – Safety.

Introduction

OVER the past 40 years, advances in drug therapy have improved patient care but led to an apparent increase in the incidence of drug-related problems (DRPs) [1]. Drugs are usually prescribed with the goal of achieving an optimal therapeutic outcome. When the outcome is not optimal, DRP has occurred [2]. Although health care personnel are for patient’s safety, mistakes and errors inevitably occur, particularly in a complex environment such as the intensive care unit (ICU) [3].

The critically ill patients in ICU are more vulnerable to DRPs than others. Moreover, administration of multiple drugs is a common event in ICU that leads to an increased incidence of DRPs [4]. The incidence is variable and has been reported to be as high as 29.7 per 100 admissions in some medical centres [5]. Such errors have serious implications on patients, cost and safety [6]. DRPs can occur at any stage of the treatment. Only 25% of DRPs are either unpredictable or caused by an allergic reaction.

In most instances (>70%) of DRPs are related to dose of drug administered [7]. The adverse drug events may be attributable to the drugs, diagnostic agents, the biological, nutrients, fluids, electrolytes or even the common components of the drug delivery systems. Occasionally more than one agent is involved in causing the problem regardless of the route and mode of drug administration [8]. One factor that influences morbidity and mortality is a harmful, unpredicted reaction to a drug which is an almost daily occurrence in hospitals.

The ICU has been known to be the land of polypharmacy for many years. Polypharmacy is known to increase the risk of DRPs, drug-drug and drug-disease interaction [9]. It has been claimed that patients taking two drugs face 13% risk of
adverse drug interactions, rising to 38% when taking four drugs and to 82% if seven or more drugs are given simultaneously [9]. DRPs have been studied internationally, but local, relevant data are limited. A probability model estimated that morbidity and mortality associated with DRPs account for $76.6 billion in hospital cost, $17 million emergency room visits, and $8.7 million hospital admissions annually in the United States [6].

Aim of the work:

The aim of this work was to identify and categorize drug-related problems in adult intensive care unit.

Patients and Methods

The study was conducted as a prospective, observational study to evaluate admissions due to DRPs to general intensive care unit. All critically ill patients at the hospital were subjected to evaluation by consultants. The ICU is a closed unit staffed by in-house, full-time, certified intensivist. The data was collected over a period of two years (February 2010 to March 2012) in general intensive care unit that contains 22 beds in Riyadh care hospital, Saudi Arabia. The protocol was approved by the local hospital’s ethics committee.

The patients were collected consecutively after consent to determine the frequency of admissions to the emergency room or transfer from the ward to ICU as a result of DRPs. The study endpoints were assessed by the investigator. The patients were followed-up until discharge from the hospital or until death, whichever occurred first.

The inclusion criteria included:

- History of drug use within the preceding 12 hours.
- Positive blood or urine test for a drug that was not administered within the hospital.
- Written or other evidence of drug ingestion (e.g. suicide note or empty medication bottles).
- Trauma admissions with a clear history of prior drug use.

The exclusion criteria included:

- If the admission was solely related to alcohol abuse (although it was rare).
- The drug use was not positively identified (even though there may have been a high index of suspicion).
- When the patient denied drug use within the previous 12 hours.

Data collected were patient demographics, category of drug involved and identification of drug problem. Data were classified into the next categories, overdose, adverse reactions, subtherapeutic dose or failure to be received and even if the drug was given without indication.

Other parameters as the reason for ICU admission, duration of ICU stay, clinical assessment of the patient, need for cardiovascular support or mechanical ventilation and dialysis were recorded. The other information collected were Glasgow coma scale (GCS) score on presentation to hospital, Acute Physiology and Chronic Health Evaluation (APACHE) II score and predicted mortality (10). The results of laboratory study and computed tomography (CT) brain scanning if needed were recorded as well as the discharge status of the patient. Additional morbidity as a result of the admission was only attributed to patients who did not regain their previous functioning level by the time of hospital discharge.

Distributed variables were expressed as median with interquartile range: Q1, Q3 (IQR: Q1-Q3). The differences of all variables between groups and categorical data were assessed using the chi-square test, p-value <0.05 was considered statistically significant. In order to determine if there is a significantly higher or lower number of deaths than expected, it is necessary to compute a standard error or confidence intervals (at 95%) for the standardized mortality ratio (SMR). The statistical analysis was performed using minitab for windows (version 13.1, State College, PA, USA).

Results

1- Demographic data and patient characteristics:

Out of 2389 patients admitted to ICU during the period of study, only 86 patients admitted by drug-related problems representing 3.6% of total admission. The characteristics data for those patients included in the study are presented in (Table 1). The median (range) age was 36 (22-48) years. Fig. (1) showed age distribution of patients admitted by drug-related problems. The male to female ratio was 59:27. Fifty five Patients had been associated with chronic diseases e.g. diabetic, hypertensive, asthmatic and epileptic, those patients represented 63% of total patients in the current study. The most common leading cause of admission in this study was disturbed conscious level (23 patients) followed by convulsion (12 patients). Three patients (3.4%) were admitted to ICU due to trauma related to drug (tranquillizer). Another three patients (3.4%) were readmitted to ICU more than one separate occasion.
In our study two patients were transferred to a psychiatric hospital after resolution of their acute medical problem without mechanical ventilation or inotropic drugs. Only one had their discharge delayed owing to lack of available ward beds. Four cases presented by suicidal attempts were recorded (4.6%), two of them received paracetamol and another two patients used tranquilizer. Three patients admitted after cardiac arrest which was related to injection of drugs (one patient was received antibiotic & two patients were injected by narcotic overdose).

Table (1): Characteristics of 86 patients admitted to intensive care.

<table>
<thead>
<tr>
<th>Patients characters</th>
<th>Median (range)</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td>36 (22-48)</td>
<td></td>
</tr>
<tr>
<td>Gender:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>59 (69)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>27 (31)</td>
<td></td>
</tr>
<tr>
<td>GCS at presentation</td>
<td>10 (5-14)</td>
<td></td>
</tr>
<tr>
<td>APACHE II score</td>
<td>17 (10-23)</td>
<td></td>
</tr>
<tr>
<td>APACHE II predicted mortality</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>29 (33)</td>
<td></td>
</tr>
<tr>
<td>Inotropic support</td>
<td>2.4 (1.5-4.2)</td>
<td></td>
</tr>
<tr>
<td>Renal replacement therapy</td>
<td>19 (22)</td>
<td></td>
</tr>
<tr>
<td>Intensive care length of stay in days</td>
<td>7 (8.1)</td>
<td></td>
</tr>
<tr>
<td>Intensive care mortality</td>
<td>4 (4.6)</td>
<td></td>
</tr>
<tr>
<td>Discharged directly to home</td>
<td>8 (9)</td>
<td></td>
</tr>
<tr>
<td>Transferred to other hospital</td>
<td>2 (2.3)</td>
<td></td>
</tr>
</tbody>
</table>

II- Type of drug related problems:

Drug overdose was the leading most common definite DRP admission in the current study as 45 (52%) patients included in this category. Adverse drug effect like anaphylaxis and hypotension was the second most common cause (22%) followed by failure to receive medications (15%) as antiepileptic (Table 2). One of the most common drugs associated with definite DRPs were hypoglycaemic medication mostly insulin, tranquilizer and antiepileptic drugs came next (Fig. 2).

Because 52% of patients were admitted as a result of drug over dose, hence the patients were divided into two groups.

Group 1: Included 45 patients admitted by drug over dose.

Group 2: Included 41 patients with other drug related problems.

Table (2): Causes of admission due to DRPs.

<table>
<thead>
<tr>
<th>Type of DRP</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug overdose</td>
<td>45 (52)</td>
</tr>
<tr>
<td>Adverse drug effect</td>
<td>19 (22)</td>
</tr>
<tr>
<td>Failure to receive drug</td>
<td>13 (15)</td>
</tr>
<tr>
<td>Sub therapeutic dosage</td>
<td>6 (7)</td>
</tr>
<tr>
<td>Drug use without indication</td>
<td>3 (3)</td>
</tr>
</tbody>
</table>

Fig. (1): Age distribution of patients admitted by drug-related problems.

Fig. (2): Frequency of drugs involved in the study.

III- Comparison between group I & group II:

Patients in group 1 were older (39 years versus 32 years in group II). The median (range) length of ICU stay was significantly longer in group 1 (3.1 (1.7-9.3) days versus 1.7 (1.1-4.5) days in group 2) (p-value 0.01). There were no significant difference in GCS between both groups; however APACHE II score was significantly higher in group 1.

The need of mechanical ventilation was significantly higher in group 1 compared to group 2 (46% versus 19%). Also usage of inotropic medication was significantly higher in group 1 (33%) compared to group 2 (9%). Laboratory study showed significant impaired renal function in group 1 and out of total seven patients who needed renal replacement therapy six patients were related to this group.
IV- Intensive care mortality:

The predicted mortality in the study based on the APACHE II score was 18% and the standardized mortality ratio (SMR) was 0.25 (95% confidence interval 0.12-0.54). The total number of non survivors was four cases (4.6%) and deaths were inevitable. Two non survivors had anoxic encephalopathy as they were admitted due to cardiac arrest after drug injection (one patient had anaphylaxis and the other one was narcotic overdose) and died later after ICU admission. The third mortality case presented by massive intracranial haemorrhage due to oral anticoagulation (the patient did not follow his INR for more than five months). The cause of death in the fourth case was paracetamol induced fulminant hepatic failure that was considered unsuitable for liver transplantation.

Table (3): Comparison between both groups included in the study.

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>39 (22-46)</td>
<td>32 (27-48)</td>
<td>0.03</td>
</tr>
<tr>
<td>ICU LOS</td>
<td>3.1 (1.7-9.3)</td>
<td>1.7 (1.1-4.5)</td>
<td>0.01</td>
</tr>
<tr>
<td>BMI</td>
<td>32.03 (30.2-34)</td>
<td>30.35 (29.3-31.6)</td>
<td>0.31</td>
</tr>
<tr>
<td>GCS</td>
<td>9 (4-14)</td>
<td>11 (5-14)</td>
<td>0.5</td>
</tr>
<tr>
<td>APACHE II</td>
<td>19.2 (12-23)</td>
<td>16.3 (10-20)</td>
<td>0.04</td>
</tr>
<tr>
<td>Bilirubin mmol/l</td>
<td>8 (7-22.5)</td>
<td>9 (7-22)</td>
<td>0.85</td>
</tr>
<tr>
<td>Creatinine mmol/l</td>
<td>110 (42-141)</td>
<td>45 (29.5-72)</td>
<td>0.02</td>
</tr>
<tr>
<td>Lactic acid mmol/l</td>
<td>1.9 (0.97-4.45)</td>
<td>1.5 (0.9-2.9)</td>
<td>0.04</td>
</tr>
<tr>
<td>INR</td>
<td>1.1 (1-1.3)</td>
<td>1.02 (0.9-1.22)</td>
<td>0.33</td>
</tr>
<tr>
<td>Use of MV</td>
<td>21 (46%)</td>
<td>8 (19%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Use of inotropes</td>
<td>15 (33%)</td>
<td>4 (9%)</td>
<td>0.01</td>
</tr>
<tr>
<td>MV days</td>
<td>3 (1.7-9.3)</td>
<td>1.4 (1-4.2)</td>
<td>0.04</td>
</tr>
<tr>
<td>Mortality</td>
<td>3 (6.5%)</td>
<td>1 (2.4%)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

ICU LOS : ICU length of stay.
MV : Mechanical ventilation.
LOS : Length of stay.
BMI : Body mass index.
GCS : Glasgow coma score.
INR : International normalized ratio.
MV : Mechanical ventilation.

Data are shown as median (interquartile range, Q1-Q3) or number (%).

Discussion

This study highlights the unique characteristics of critically ill patients admitted due to drug related problems. Those patients represent a small proportion of the hospital ICU admissions (3.6%) which was comparable to reports from developed countries [11]. Drug related problems are of major concern, affecting patients of both sex and patients belonging to all age groups [12]. They impose considerable economic burden on the society and the already stretched health-care systems [13]. In the current study thirty percent of the patients were between the age of thirty and thirty nine years which was unexpected and alarming for a real problem. The relatively young age of patients indicates the high potential for chronic morbidity and mortality, with many years of life likely to be affected or lost. On the other hand only 10% of the patients above the age of fifty nine which could be explained by either strict medical care and follow-up, or major insults that interfere or prevent their admission. The study population had an age distribution similar to other studies reporting drug-related hospital admissions [14,15]. Although unlike other self-poisoning study reported by Henderson A et al., we found that a high proportion of our patients in this study were males [16].

Drug overdose was one of the most common causes of admission to ICU with drug related problems (45 patients 52%), which was comparable to that reported by O’Brien et al., in 2009 [17]. The administered drugs can produce predictable or unpredictable toxicity which is related to the pharmacological actions of these compounds. Regrettably, the adverse reactions to the medications are generally not well studied and the mechanism of some in causing the ADRs remains poorly described [18].

In this study, adverse drug reactions encountered 22% of DRPs, while it was reported to be 29% by Bowman et al., in 1990 [8]. The median LOS for all patients was slightly higher than mentioned by Liisanantti et al., [19], which could be explained by the association of chronic diseases in 63% of the total number of our patients. The cost of one day admission (estimated as 3000 SR) had given us an idea of how much DRPs would propose a financial burden. The international program for resource use in critical care has evaluated international cost comparisons; however, the difficulties in finding a universal and meaningful unit of cost persist [20,21].

The median (range) length of ICU stay in group 1 was 3.1 (1.7-9.3) days versus 1.7 (1.1-4.5) in group 2 (p-value=0.01). The need of mechanical ventilation was significantly higher in group I (46%) compared to group 2 (19%). Also the usage of inotropic was significantly higher in group I. This significant difference between both groups could be explained by higher APACHE score in group I. In addition the impaired renal function that was significantly observed in group I could be a direct effect from the drug problem or result from deterioration of the condition, as out of total seven patients needed renal replacement therapy six patients were in group I. Another important finding was that the most common DRP was related to hypoglycaemic medications (19%) followed by...
tr tranquillizers and antiepileptic. In contrast to other study; antidepressant medications represent the most common cause of DRPS [4]. That difference could be attributed to the drug commonly used in community and prevalence of chronic diseases like diabetes mellitus. This also reflect the prevalence of diabetic patients in saudi arabia as reported by Al-Nozha et al., which could soon reach 50% in those over 50 years of age [22]. Approximately 4.6% of the patients with drug related admissions to the intensive care unit were due to suicidal attempt, which was lower if compared to other societies [23]. This could be explained by the nature of the community in saudi arabia. From previous follow-up studies it has been reported that approximately 3% of patients admitted for self-poisoning will die from suicide in the following ten years [24]. Self-discharge or patient refusal to be reviewed by these services did not occur in the study. This could be explained by the emergency situation facing both patients and relatives accompanying. Concerning the drug-related trauma in the study, three patients (3.4%) were admitted to ICU due to trauma related to tranquilizer intake. On the other hand, Soderstrom et al., found that up to 36% of intentional injury victims have a drug dependency problem and 17.7% of seriously injured trauma victims are dependent on drugs other than alcohol [25,26]. The lower percentage in our study could be explained by denying any history of drug intake due to legal aspect and also difficulty of doing routine drug screening that request consent from either patients or relatives. The results in this respect go nearer to that found in South Western Sydney (i.e. 4%) [27]. The mortality rate in this study was comparable to that recorded by Cretikos et al., [11]. The predicted mortality rate based on the APACHE II score was higher to that found in our study [10,28]. This observation could be explained by the treatable nature of the conditions that originally lead to ICU admission.

A factor limiting the scope of this study was the fact that, only patients who were admitted were assessed, so a significant number of patients with minor DRP who were not admitted may have been missed. Also some DRPs may have been underestimated as it may be difficult to detect contraindications, medications with no indication without access to each patient’s medical chart. Another limitation was that all data were collected in a single institution although this was partially compensated by prolongation of the study. Also there were confounding variables as the treating physicians, hospital discharge, and in-puts from the patient’s families. We controlled such factors by strict following the policy of ICU discharge beside that the treating physicians were not aware about the study.

**Conclusion:**

Critically ill patients admitted due to drug related problems represent a small proportion of the hospital ICU admissions. Hypoglycaemic medication was one of the most common causes of admission by drug related problems. The results confirmed that identification of a drug-related illness is important if the patient requires admission to an intensive care unit. This is necessary not only to improve the quality of acute care but also to allow early and appropriate treatment. Particular effort should be made to prevent DRPs in diabetic patients.

**References**


