Clinical Investigation

Applicability of different scoring systems in outcome prediction of patients with mixed drug poisoning-induced coma

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ABSTRACT

Background: Mixed drugs poisoning (MDP) is common in the emergency departments. Because of the limited number of intensive care unit beds, recognition of risk factors to divide the patients into different survival groups is necessary. Poisoning due to ingestion of different medications may have additive or antagonistic effects on different parameters included in the scoring systems; therefore, the aim of the study was to compare applicability of the different scoring systems in outcomes prediction of patients admitted with MDP-induced coma. **Methods:** This prospective, observational study included 93 patients with MDP-induced coma. Clinical and laboratory data conforming to the Acute Physiology and Chronic Health Evaluation (APACHE II), Modified APACHE II Score (MAS), Mainz Emergency Evaluation Scores (MEES) and Glasgow Coma Scale (GCS) were recorded for all patients on admission ($time_0$) and 24 h later ($time_{24}$). The outcome was recorded in two categories: Survived with or without complication and non-survived. Discrimination was evaluated using receiver operating characteristic (ROC) curves and area under the ROC curve (AUC). **Results:** The mortality rate was 9.7%. Mean of each scoring system was statistically significant between $time_0$ and $time_{24}$ in the survivors. However, it was not significant in non-survivors. Discrimination was excellent for GCS_{24} (0.90±0.05), APACHE II_{24} (0.89±0.01), MAS_{24} (0.86±0.10), and APACHE II_0 (0.83±0.11) AUC. **Conclusion:** The GCS_{24}, APACHE II_{24}, MAS_{24}, and APACHE II_0 scoring systems seem to predict the outcome in comatose patients due to MDP more accurately. GCS and MAS may have superiority over the others in being easy to perform and not requiring laboratory data.

Key words: Acute physiology and chronic health evaluation II, coma, glasgow coma scale, mainz emergency evaluation system, outcome, poisoning

INTRODUCTION

The most severe cases of patients who have overdosed on drugs usually require intensive care unit (ICU) admission. Knowing risk factors that can divide poisoned patients into different survival groups is necessary because of limited ICU beds. Various scoring systems have been performed as a tool for triage and ICU quality management.

The Glasgow Coma Scale (GCS) scoring has been used for outcome and recovery evaluation of patients admitted to an ICU following drug overdose[1] as a tool for the evaluation of mental status of poisoning patients,[2] the need for intubation in patients with antidepressant poisoning[3] and for predicting acute and delayed poisoning outcome.[4-9]

The Initial Acute Physiology and Chronic Health Evaluation (APACHE II) score has been used as a useful prognostic indicator in cases of organophosphate (OP) poisoning,[10,11] evaluating the severity of acute paraquat poisoning,[12,13] identifying acetaminophen-poisoned patients needing a liver transplant[14,15] and as a prognostic factor in aluminium phosphide poisoning.[16]

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Comparison for effectiveness of different scoring systems has also been illustrated in studies for OP,[17-20] OP and carbamate,[21] aluminum phosphide[22] and carbamazepine poisoning.[23]

Although several severity scores have been proposed for evaluating poisoned patients on admission to the emergency department or ICUs, these have not been compared for patients with mixed drug poisoning (MDP) at different times. Because of the potential drug–drug interactions between MDPs, there could be a dominant additive or antagonistic toxidrome of various drug combinations. Therefore, there arises a need to compare the scores of individual drug combinations or various classes of drug combinations.

METHODS

The poisoning emergency department at our university hospital, Noor and Ali Asghar (PBUH) Medical Center in which this study was conducted, is the main referral centre for the central provinces of Iran, exclusively for poisoned patients. Approximately 400 patients are admitted per month and patients are managed under the supervision of an anaesthesiologist and intensive care specialist, a forensic medicine specialist, a clinical pharmacy specialist and a medical toxicologist.

This study involved prospective data collection followed by retrospective analysis, and was conducted by the Anesthesiology Research Department. The protocol of this prospective and observational study was reviewed and approved by the Institutional Ethics Committee of our university (research project number 385535). This study included consecutive hospitalizations of 93 patients with MDP-induced coma on admission. Patients whom were transferred or referred from elsewhere were not included in the study. Patients admitted after the first 24 h of ingestion were also excluded. Patients with OP, carbamate, paraquat, acetaminophen, carbamazepine and aluminium phosphide poisoning were also excluded. Gastric evacuation and activated charcoal administration occurred across patient groups in accordance with our local guidelines, which were interpreted inclusively rather than exclusively.[24]

The following data were collected by a well-trained staff physician: Demographics, APACHE II, Mainz Emergency Evaluation Scores (MEES), GCS and Modified APACHE II System (MAS) scores. APACHE II_0, MAS_0, $MEES_0$ and GCS_0 data were obtained on admission, whereas APACHE II_{24}, MAS_{24}, $MEES_{24}$ and GCS_{24} data were obtained 24 h later in patients who stayed for 24 h or more.

To calculate the APACHE II score,[25] 12 common physiological and laboratory values (temperature, mean arterial pressure, heart rate, respiratory rate, oxygenation, arterial pH, serum sodium, serum potassium, serum creatinine, haematocrit, white blood cell count and GCS) were marked from 0 to 4, with 0 being normal and 4 being the most abnormal. The sum of these values was added to a mark adjusting for patient age and a mark adjusting for chronic health problems (severe organ insufficiency or immunocompromised patients) to arrive at the APACHE II score.

We also calculated the score of the MAS without parameters of biochemical tests [arterial oxygen tension (PaO_2), arterial pH, serum sodium, serum potassium, serum creatinine, haematocrit, white blood cell count] for each patient.[18]

The GCS was determined based on three components: Eyes (4 = opens, 3 = to verbal command, 2 = to pain, 1 = none), verbal (5 = oriented, 4 = disoriented, 3 = inappropriate words, 2 = incomprehensible sounds, 1 = none) and motor (6 = obeys, 5 = localizes pain, 4 = withdrawal, 3 = abnormal flexion, 2 = abnormal extension, 1 = none).

To calculate MEES,[26,27] seven parameters (GCS, heart rate, respiratory rate, cardiac rhythm, pain, blood pressure, oxygen saturation) were marked. The scores of the APACHE II, MAS, MEE and GCS were determined by the emergency physician, formally trained in the procedures by the attending toxicologist. All other available data including toxic agent, gender and age were also recorded in a checklist. Continuous variables were compared by the standard t-test.

The binary logistic regression analysis (backward conditional stepwise method) was employed to calculate the odds ratio (OR) of different parameters of APACHE II, MAS and MEES for the occurrence of the outcomes. For simplicity, outcomes were recorded in two categories: (1) non-survived and (0) survived with or without complication. Discrimination was tested using the receiver operating characteristic (ROC) curves and by comparing areas under the curve (AUCs).[28] AUCs between 0.7 and 0.8 were classified as "acceptable" and between 0.8 and 0.9 as "excellent" discrimination.[29] For the different scoring systems tested, the sensitivity,

specificity and the best cutoff point given were determined.[30] This cutoff point was also used to calculate the predicted and observed mortality. In this study, h_0 hypothesis for statistical analysis was there is not any significant difference between the outcome of survivors and non-survivors in $time_0$ (on admission) and $time_{24}$ (24 h later) using APACHE II, MAS, MEES and GCS mean scores. The Chi square or Fisher's exact test was applied to compare the rate of mortality below and above the best cutoff points for the scoring systems. The data was analyzed using the Statistical Package for Social Sciences version 17.0 (SPSS Inc., Chicago, IL, USA) and Med-Calc (Med-Calc Software Inc., Mariakerke, Belgium) statistical software. A *P*-value less than 0.05 was considered to be statistically significant.

RESULTS

Of the 93 eligible patients, 50 (53.76%) were female and 43 (46.24%) were male. The mean age for survivors was 28.64±12.05 years and for non-survivors was 38.66±14.98 years (*P* value = 0.055). The most prominent drugs involved in poisoning were tricyclic antidepressant (33.3%), benzodiazepines (19.4%), anti-convulsants (11.8%), anti-psychotics (6.5%), opioids (5.4%) and others (23.6%). All the poisoning cases were intentional.

Thirty-one patients were discharged as being well during the first 24 h of hospitalization. The remaining (62 patients) were included in the other analysis. The mortality was 9.7%. Comparison of major complications between survivors and non-survivors were as follows: Intubation (83.90% and 100%), mechanical ventilation (39.30% and 66.70%) and aspiration pneumonitis (17.90% and 16.70%).

Table 1 shows that there were significant differences in APACHE II, MAS, MEES and GCS mean scores between survivors and non-survivors in $time_0$ (on admission) and $time_{24}$ (24 h later). The mean of each scoring systems was statistically significantly different between $time_0$ and $time_{24}$ in the survivors; however, it was not significant in non-survivors [Table 1].

Between survivors and non-survivors, there was only a significant difference of GCS in $time_0$ and $time_{24}$ [Table 2].

Binary logistic regression analysis was employed to calculate the OR as the estimate of the relative risk of the APACHE II, MAS and MEES determinants on $time_0$ and $time_{24}$ for the occurrence of outcomes. For simplicity, the outcomes were recorded in two categories: (1) non-survived and (0) survived with or without complication. Table 3 reports the parameters of the different scoring systems influencing outcomes in the patients. GCS, respiratory rate, age and mean arterial pressure in MAS_0 and GCS in MAS_{24} were identified as independent risk factors for predicting outcome. There were no specific determinant parameters in $APACHE\ II_0$, $APACHE\ II_{24}$, $MEES_0$ and $MEES_{24}$ for the outcome prediction. Although the type of MDP combinations ingested and their possible proportions or dosage ingested could be a significant factor affecting the severity scores, the analysis did not support it.

Predictive values of the various scoring systems calculated at the best cutoff point have been shown in Table 4. Discrimination was excellent for GCS_{24} (0.90±0.05), $APACHE\ II_{24}$ (0.89±0.01), MAS_{24} (0.86±0.10) and $APACHE\ II_0$ (0.83±0.11) and acceptable for MAS_0 (0.81±0.11), $MEES_{24}$ (0.80 ± 0.08), GCS_0 (0.77±0.09) and $MEES_0$ (0.75±0.09) AUC.

DISCUSSION

The applicability of APACHE II, MAS, MEES and GCS were evaluated in predicting outcomes in

Table 1: Comparison of APACHE II, MAS, MEES and GCS scores between survivors and non-survivors in $time_0$ (on admission) and $time_{24}$ (24 h later)

Scoring system	Survivors (mean±SD)	Non-survivors (mean±SD)	*P* value	Mean differences (mean±SE)	95% CI of difference	
					Lower	Upper
$APACHE\ II_0$	15.87±3.76	20.66±3.26	0.004	−4.79±1.59	−7.99	−1.59
$APACHE\ II_{24}$	10.03±6.28	21.83±6.94	0.000	−11.79±2.72	−17.24	−6.34
MAS_0	12.30±2.60	15.50±2.58	0.006	−3.19±1.11	−5.43	−0.95
MAS_{24}	8.07±5.05	15.16±4.35	0.002	−7.09±2.14	−11.39	−2.79
$MEES_0$	18.64±2.41	16.83±1.83	0.08	1.80±1.01	−0.22	3.84
$MEES_{24}$	20.69±3.35	16.66±2.94	0.007	4.02±1.43	1.14	6.90
GCS_0	5.35±1.43	4.16±0.98	0.052	1.19±0.60	−0.01	2.39
GCS_{24}	9.55±3.61	4.83±1.72	0.000	4.72±1.50	1.71	7.72

APACHE II: Acute Physiology and Chronic Health Evaluation; MAS: Modified APACHE II system; MEES: Mainz Emergency Evaluation Scores; GCS: Glasgow Coma Scale; CI: Confidence interval; SD: Standard deviation; SE: Standard error

Table 2: Comparison of different parameters of scoring systems between survivors and non-survivors in $time_0$ (on admission) and $time_{24}$ (24 h later)

Variables	Survivors (mean±SD)	Non-survivors (mean±SD)	*P* value
T_0	37.17±0.47	37.05±0.58	0.56
T_{24}	37.72±0.76	37.55±0.47	0.59
MAP_0	84.09±15.17	71.94±14.46	0.07
MAP_{24}	86.02±11.32	69.44±28.78	0.21
HR_0	88.14±19.53	92.50±27.81	0.62
HR_{24}	94.76±16.01	97.00±15.44	0.74
RR_0	16.78±9.34	18.50±16.84	0.69
RR_{24}	16.37±10.73	10.00±16.29	0.19
$PaO_{2(0)}$	74.71±35.09	75.16±23.77	0.97
$PaO_{2(24)}$	87.64±49.65	62.20±16.45	0.26
Arterial pH_0	7.34±0.08	7.33±0.06	0.62
Arterial pH_{24}	7.41±0.04	7.42±0.11	0.80
Na_0	136.67±4.41	136.16±4.26	0.78
Na_{24}	137.70±2.70	138.00±6.72	0.91
K_0	3.95±0.73	4.30±0.64	0.26
K_{24}	3.78±0.44	4.65±1.09	0.11
WBC_0	8308±2965	7600±3854	0.59
WBC_{24}	8749±3393	7880±3378	0.58
HCT_0	41.16±5.36	43.00±2.52	0.41
HCT_{24}	40.73±4.26	37.38±4.72	0.10
Cr_0	1.06±0.22	1.42±0.42	0.10
Cr_{24}	0.93±0.11	1.80±0.89	0.06
GCS_0	5.35±1.43	4.16±0.98	0.052
GCS_{24}	9.55±3.61	4.83±1.72	0.000

*P<0.05, comparison of values among different patients groups, n: Number of patients; T: Temperature (ºC); MAP: Mean arterial pressure (mmHg); HR: Heart rate (per minute); RR: Respiratory rate (per minute); PaO_2: Arterial oxygen tension; Na: Serum sodium (mMol/L); K: Serum potassium (mMol/L); WBC: White blood cell count; HCT: Haematocite; Cr: Serum creatinine (mMol/L); GCS: Glasgow Coma Scale

Table 3: Relative risk of the determinants for the occurrence of the outcomes

Scoring systems	Variable	B	OR (95% CI)	*P* value
MAS_0	RR	0.76	2.15 (1.04–4.59)	0.04
	GCS	0.78	2.19 (1.03–4.68)	0.04
	Age	1.08	2.95 (0.94–2.26)	0.06
	MAP	0.84	2.31 (0.84–6.35)	0.10
MAS_{24}	GCS	1.47	4.36 (1.33–14.26)	0.01

B: Estimated coefficient; OR: Odds ratio; CI: Confidence interval; RR: Respiratory rate; MAP: Mean arterial pressure; GCS: Glasgow Coma Scale; MAS_0: Modified APACHEII system in $time_0$ (on admission), MAS_{24}: Modified APACHEII system in $time_{24}$ (24 h later). *OR relates to a unit change on the score of that variable in the scoring systems

MDP-induced coma at different times; on admission and 24 h later.

There was a significant difference in the reported mean values of each scoring system between $time_0$ and $time_{24}$ in the survivors; however, it was not significant between $time_0$ and $time_{24}$ in non-survivors. The APACHE II_{24} mean values were found to be higher for non-survivors than survivors on $time_{24}$ (21.83±6.94 and 10.03±6.28, respectively) and $time_0$ (20.66±3.26 and 15.87±3.76). Because one parameter of APACHE II (GCS) was significantly different between survivors and non-survivors, this might be the reason of the observed higher scores in non-survivors.

Applicability of APACHE II and GCS in different poisoning has been evaluated previously. Initial assessment of GCS may help the clinician to identify advanced grade of OP poisoning patients, which has been illustrated by Akdur *et al*.[20] GCS has been used for predicting delayed neuropsychological sequels of carbon monoxide (CO) poisoning.[5] GCS score equal to or less than 14 had been associated with myocardial injury in CO poisoning.[9] GCS less than eight was more associated with mortality in a study by Budhathoki *et al*. about the outcome of children presenting with poisoning or intoxication.[4]

Although GCS is an important factor in predicting outcome in poisoning, other variables such as the kind of toxic agent,[19,31,32] the use of an antidote[33] and the kind of intervention by different physicians[34] are also effective variables at predicting outcome. In the study by Davies *et al*. on acute OP poisoning, apart from admission GCS, the kind of pesticide affected the outcome.[19]

In our study, discrimination was excellent for GCS_{24}, APACHE II_{24}, MAS_{24} and APACHE II_0. There is no study to compare the scoring systems at different times in

Table 4: Classification table for the scoring systems in $time_0$ (on admission) and $time_{24}$ (24 h later)

Scoring systems	ROC area (95% CI)	*P* value	Best cutoff point	Sensitivity (%)	Specificity (%)	Survived		Died	
						PS	PD	PS	PD
$APACHEII_0$	0.83 (0.71–0.91)	0.61	20	83.33	78.57	69	18	1	5
$APACCEII_{24}$	0.89 (0.78–0.96)		14	100	64.29	67	20	0	6
MAS_0	0.81 (0.69–0.89)	0.69	14	83.33	67.86	63	24	1	5
MAS_{24}	0.86 (0.75–0.94)		10	100	60.71	64	23	0	6
$MEES_0$	0.74 (0.62–0.85)	0.69	≤16	66.67	80.36	74	13	2	4
$MEES_{24}$	0.80 (0.67–0.89)		≤18	83.33	73.47	74	13	1	5
GCS_0	0.77 (0.64–0.86)	0.10	≤5	100	60.71	59	28	0	6
GCS_{24}	0.90 (0.79–0.96)		≤5	83.33	94.64	84	3	1	5

ROC: Receiver operating characteristic; CI: Confidence interval; PD: Predicted to die; PS: Predicted to survive; APACHEII: Acute Physiology and Chronic Health Evaluation; MAS: Modified APACHEII system; MEES: Mainz Emergency Evaluation Scores; GCS: Glasgow Coma Scale

MDP poisoning patients; however, our results for initial evaluation of APACHE II and GCS discrimination compare with those published in OP poisoning.[17,18] In their study, the prognostic value of APACHE II was as good as that of GCS in predicting outcome patients hospitalized for OP poisoning, although no information regarding evaluation of scoring systems at different times had not been assessed. We found that an APACHE II_0 score greater than 20 and an APACHE II_{24} score greater than 14 predicted a poor outcome with 83.33% and 100% sensitivity and 64.29% and 78.57% specificity, respectively. In acute paraquat poisoning cases, an APACHE II score greater than 13 predicted in-hospital mortality, with 67% sensitivity and 94% specificity,[13] and in the patients with OP poisoning, the initial APACHE II score of 26 or higher had been a good predictor of mortality.[10] Difference in APACHE II score in different studies may be due to different toxic agents studied, poisoned patient population and evaluating outcomes at different times.

CONCLUSION

In conclusion, because of the potential drug–drug interactions between MDPs, there could be a dominant additive or antagonistic toxidrome of various drug combinations. Therefore, there arises a need to compare the scores of individual drug combinations or various classes of drug combinations. The results showed that the four scoring systems had an acceptable to excellent outcome prediction in patients with MDP-induced coma. The GCS_{24}, APACHE II_{24}, MAS_{24} and APACHE II_0 scoring systems seem to predict the outcome in patients with MDP more accurately. GCS and MAS may have superiority over the other systems in being easy to perform and not requiring laboratory data.

Our study has some limitations:

1. It was performed in a referral university teaching hospital and, therefore, it may not be applicable to institutions with different patient populations.
2. Patients admitted after 24 h of their presentation were excluded from our study thus resulting in a mortality rate of 9.7%. It could be stated that excluding these patients may weaken our study because patients who are sicker on admission are more likely to die.
3. We did not make an adjustment in our results for the intensity of treatment, which may affect the rate of mortality.
4. We did not include the "poison severity scale" recommended by the toxic exposure surveillance system (TESS) as one of the scaling systems for outcome prediction in our study to show how the employed "physiological scales" differ or comply with the poisoning risk assessment scales.
5. The scores were evaluated twice within a span of 24 h and not later. Certain biochemical parameters like liver or kidney function tests may take days for recovery. We may suggest comparing the trend of scoring system each day during patients' hospitalization for outcome prediction.

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