Assessment of APACHE II, Modified Early Warning (MEWS) and Worthing Physiological (WPS) Scores as Predictor for Mechanical Ventilation in Acute Organophosphorus Toxicity Patients

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ABSTRACT

Early assessment of patients presented with acute organophosphorus toxicity in the Emergency Department is an essential step to detect their pathway in the hospital. The present study aimed to assess the overall accuracy of Acute Physiology and Chronic Health Evaluation (APACHE II), Modifies Early Warning Score (MEWS), and Worthing Physiological Score (WPS) in predicting mechanical ventilation in acute organophosphorus toxicity patients. A cross-sectional cohort study was conducted on 132 patients presented with acute organophosphorus patients. From each patient, the following was collected: clinical data, routine laboratory investigations results, and blood samples for estimation of cholinesterase levels. The clinical and laboratory data were used to calculate APACHE II, MEWS, and WPS scores within six hours from admission. Statistical analysis revealed that the median values of APACHE II, MEWS, and WPS differed significantly between mechanically ventilated and non-mechanically ventilated patients. A strong significant negative correlation was detected between clinical severity and cholinesterase levels. WPS score showed the highest discriminatory power for predicting mechanical ventilation (area under the curve [AUC] 0.977). However, APACHE II and MEWS scores were nearly equal in their discriminatory power (AUC 0.924 and 0.927 respectively). Cholinesterase levels can be used as auseful diagnostic tool but are very poor in predicting patient outcomes (AUC 0.209 and 0.129 for acetylcholinesterase and butyrylcholinesterase respectively). In conclusion, using theWPS score for clinical evaluation of acute organophosphorus toxicity patients has valuable prognostic abilities for predicting patients' outcomes.

Introduction ·

Organophosphorus poisoning is considered one of the main causes of acute toxicities among adults and children with a reported mortality rate ofabout 10-20% (Hwan et al., 2013). In addition, up to 38% of

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acute organophosphorus toxicity patients may require mechanical ventilation (Eddleston et al., 2006).

Since morbidity and mortality represent a high percentage of these cases. On admission, patients in good condition may deteriorate rapidly and need intubation with mechanical ventilation. Thus, prediction of those who may require mechanical ventilation and categorizing patients to detect suitability forward, intermediate care‹ or intensive care admission will help in improving the outcome and decreasing waste of resources (Mohamed et al., 2019).

Several scoring systems were developed to predict patient outcomes in theemergency department. These scores are used to identify critically ill patients rapidly and accurately to provide necessary urgent intervention (Khater et al., 2019).

Acute Physiology and Chronic Health Evaluation series (APACHE) is one of the most well-known emergency assessment scores that measure the clinical severity and predict the outcome independent of the diagnosis. The APACHE score is based on acute physiological parameters and other clinical information (Chhangani et al., 2015). Previous studies evaluated the accuracy of the APACHE II scoring system in predicting the outcome of acute organophosphorus toxicity cases and it was above 90% accurate (Chhangani et al., 2015; Mohamed et al., 2019). However, still، the main drawback of this scoring system is therelative consumption of time and resources. Thus, using a simple score depending on clinical features is likely to be more efficient and applicable especially in low-income countries where most of the poisoning occurs (Abd Alkareem et al., 2019).

Modified Early Warning Score (MEWS) and Worthing Physiological Score (WPS) are scoring systems that are comprised of easily and rapidly obtainable parameters. They can be calculated by the bedside, allowing physicians to decide the pathway of their patients and predict outcomes Chang et al., 2018).

The present work aimed to assess the overall accuracy of APACHE II, MEWS، and WPS in predicting mechanical ventilation in acute organophosphate toxicity cases.

Subjects and Methods:
Subjects:

A sectional-cross cohort study was conducted on 132 patients presented with acute organophosphorus toxicity. The sample population was patients attending to toxicology unit at Mansoura University Emergency Hospital and Damietta general hospital.

Inclusion criteria were patients above 18 years old presented with acute organophosphorus toxicity. Exclusion criteria included patients with prehospital treatment, emergency intubation as first aid measures, any condition which reduces cholinesterase activity (e.g Parenchymal liver disease, acute infection, metastatic carcinoma, dermato-myositis, early pregnancy and patients exposed to toxicants like carbon disulfide, cocaine، and solanines or drugs like birth control pills) (Mohamed et al., 2019). The written informed consent was obtained from all studied patients participating in the study to use their clinical and laboratory data.

Methods:
Clinical data:

1. History including age, elapsed time since ingestion, any prehospital treatment.

2. Clinical examination: including respiratory rate/min, heart rate /min, conscious level, temperature ◦C, arterial blood pressure (mmHg), Glasgow Coma Score (GCS).

3. General laboratory investigations, including PaO2 (mmHg), arterial pH, Serum HCO3 (mEq/L), sodium (mEq/L), potassium (mEq/L), creatinine (mg/dl), hematocrit (%), white blood cells count (×1000/mm3).

4. Toxicological investigations: Five ml of blood were collected for estimating acetylcholinesterase (ACHE) and butyrylcholinesterase (BuCHE) levels using previously described methods (Silk et al., 1979; Brogdon, 1987). Stomach content was collected and detection of

organophosphates compounds using the previously described method was done.

Clinical scoring of patients:

The data were collected within six hours from admission. If multiple values of the same parameter were collected, the worst value was used for calculating the score. From collected clinical and laboratory data, three scores were calculated for each patient.

1. Acute Physiology and Chronic Health Evaluation II score (Akavipat *et al.*, 2019): the score includes 13 clinical and laboratory parameters that are temperature, mean arterial blood pressure, pulse rate, respiratory rate, oxygenation, arterial pH, serum HCO3, serum sodium level, serum potassium level, creatinine, hematocrit value, total leukocytic count, GCS. Each of the previous points was scored from zero to four according to theseverity from normal to abnormal values. The sum of these values plus points adjusting to patients' age and chronic health condition to get the overall score. The score is ranging from (0 to 71).

2. Modified early warning scores (Chang *et al.*, 2018): the score includes documenting systolic blood pressure, heart rate, respiratory rate, temperature, and AVPU score. These parameters are scored from 0 to 3 from normal to abnormal value according to severity. The minimum score is 0 and the maximum is 15.

3. Worthing Physiological Score (Duckitt *et al.*, 2007): the score includes documenting ventilatory frequency, pulse rate, systolic blood pressure, temperature, oxygen saturation, and AVPU score. These parameters are scored according to severity. The minimum score is 0 and the maximum is 14.

Statistical analysis:

Data were analyzed using the Statistical Package of Social Science (SPSS) program for Windows (Standard version 21). The normality of the data was first tested with a one-sample Kolmogorov–Smirnov test. Proper statistical tests were selected. Sensitivity and specificity at different cut-off points were tested by the ROC curve. For all above mentioned statistical tests done, the threshold of significance is fixed at a 5% level (p-value).

Results:

The study included 132 patients from which 46 (34.8%) cases were mechanically ventilated, and 86 (65.2%) cases passed without mechanical ventilation. Descriptive statistics of different recorded clinical and laboratory parameters with the difference between mechanically ventilated and non-mechanically ventilated patients are illustrated in the table (1). As regard cholinesterase levels, it was significantly correlated with the severity of poisoning as illustrated in table (2). On assessing their importance as a predictive factor for the probability of mechanical ventilation, AUC was 0.219 and 0.129 for ACHE and BuCHE respectively.

The three selected scoring systems were calculated for all patients. The descriptive statistics of the three studies' scores and the differences between both mechanically ventilated and non-mechanically ventilated patients are illustrated in table (3).

The receiver operating characteristic (ROC) curve was obtained for predicting the risk of mechanical ventilation using a continuous variable. ROC curve was used to find out the value of different scoring systems obtaining maximum sensitivity and specificity as shown in table (4). The continuous measurement scale in the present study

resulted in the different cut-off values and different corresponding sensitivity and specificity. A summary of the relationship of

APACHE II, MEWS, and WPS scores are shown in the ROC curve graph (Figure 1).

Table (1): Descriptive statistics of different clinical and laboratory parameters in all studied patients (n: 132 patients).

	Non mechanically ventilated patients (86 patients)					Mechanically ventilated patients (46 patients)				
	Mean	**SD**	**Median**	**Minimum**	**Maximum**	**Mean**	**SD**	**Median**	**Minimum**	**Maximum**
Age (years)	29.59	11.41	26	18	59	31.57	11.50	25.5	18	57
MAP (mmHg)	87.00	8.47	87	63	117	85.78	29.44	83	45	147
SBP (mmHg)	114.24	12.07	115	90	160	113.78	39.88	105	55	180
Pulse /min	80.08	12.78	79	50	145	97.50	34.67	105	35	150
Respiratory rate/min	21.88	6.14	20	17	50	25.98	15.91	21	5	60
PaO2	73.84	6.77	74	44	88	61.04	11.96	60	43	88
Arterial pH	7.34	0.08	7.35	7.17	7.67	7.20	0.14	7.19	6.9	7.55
Serum HCO3	17.90	2.93	18	12	22	14.45	4.40	13	9	30
Creatinine (mg/dl)	0.85	0.31	0.8	0.5	1.8	1.47	0.30	1.6	0.8	1.9
Serum Na (mEq/L)	140.62	3.69	142	135	145	144.30	5.44	143	136	160
Serum K (mEq/L)	3.53	0.49	3.5	2.1	4.6	3.36	1.08	3.5	1.8	6.5
Hematocrit (%),	32.55	4.14	34	23	39	33.29	3.51	34	25	39
WBCs (×1000/mm3),	12529.53	6068.68	12000	3000	30000	19856.52	8213.58	18000	10000	45000
ACHE (μ moles/ ml red cells/ min)	5.39	5.1	1.75	1.3	8.2	3.57	1.27	3.4	1.3	7
BuCHE (IU)	1630.84	580.34	1700	454	2720	760.59	463.24	805	124	1990

MAP: mean arterial blood pressure, SBP: systolic blood pressure; min: minute; Pa O2: oxygen tension; WBCs: white blood cells; Na: sodium, K: potassium; ACHE: Acetylcholinesterase; BuCHE: Butyrylcholinesterase, SD: Standard deviation.

Table (2): Correlation between cholinesterase levels and the three studies scores

	Acetylcholinesterase		Butyrylcholinesterase	
	r	**p**	**r**	**p**
APACHE II score	-.631[*]	<0.001*	-.750[*]	<0.001*
MEWS score	-.584[*]	<0.001*	-.620[*]	<0.001*
WPS score	-.552[*]	<0.001*	-.600[*]	<0.001*

APACHE II: Acute Physiology and Chronic Health Evaluation II; MEWS: Modified Early Warning Score; WPS: Worthing Physiological Score. P-value <0.05 is significant. *: significant.

Table (3): Difference in APACHE II, MEWS, and WPS scores in both mechanically ventilated and non-mechanically ventilated patients (n: 132 patients).

	Non mechanically ventilated patients (86 patients) Median (min-max)	Mechanically ventilated patients (46 patients) Median (min-max)	p-value
APACHE II score	3 (0-33)	24 (7-34)	<0.001
MEWS score	2 (1-9)	6 (1-10)	<0.001
WPS score	2 (0-8)	8 (3-10)	<0.001

APACHE II: Acute Physiology and Chronic Health Evaluation II; MEWS: Modified Early Warning Score; WPS: Worthing Physiological Score. Min: minimum; max: maximum. P-value <0.05 is significant. *: significant.

Table (4): Area under the curve (AUC), optimal cut-off point, sensitivity, specificity, identified scores with overall accuracy using receiver operating characteristic (ROC) method for predicting mechanical ventilation in acute organophosphorus toxicity cases

	AUC	95% CI		Cutoff	Sensitivity	Specificity	PPV	NPV	Accuracy
		Lower	Upper						
APACHE II score	0.924	0.878	0.970	11.5	0.913	0.198	89.53%	80.43%	86.36%
MEWS score	0.927	0.877	0.977	2.5	0.978	0.221	93.02%	80.43%	88.64%
WPS score	0.977	0.956	0.998	3.5	0.978	0.128	95.35%	91.30%	93.94%

APACHE II: Acute Physiology and Chronic Health Evaluation II; MEWS: Modified Early Warning Score; WPS: Worthing Physiological Score. AUC: area under the curve, CI: confidence interval, PPV: positive predictive value, NPV: negative predictive value.
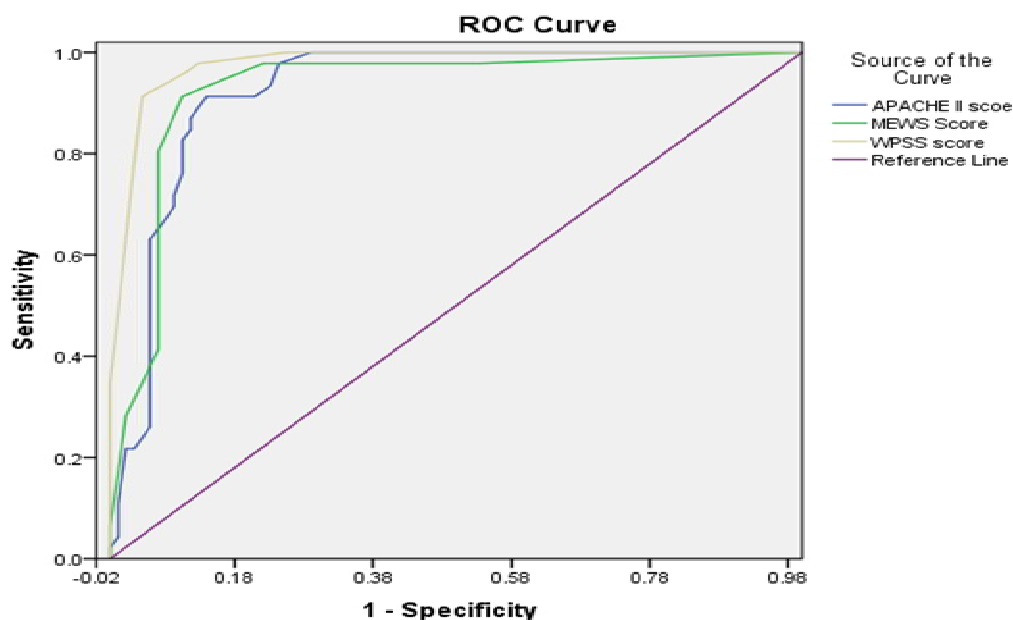

Fig. (1): Receiver operating characteristic (ROC) graph showing sensitivity, specificity, and area under the curve for APACHE II, MEWS, WPS scores. APACHE II: Acute Physiology and Chronic Health Evaluation II; MEWS: Modified Early Warning Score; WPS: Worthing Physiological Score.

Discussion:

Predicting the outcome and need for mechanical ventilation is an essential step during the initial assessment of any toxicological patient to detect his pathway. This will help in improving the outcome by decreasing bed occupancy time (Oprita et al., 2014). Thus, the present work aimed to assess the overall accuracy of APACHE II, MEWS, and WPS scores in predicting mechanical ventilation in acute organophosphate toxicity cases.

The percentage of organophosphate poisoning that needed mechanical ventilation was 34.8%. This ratio is similar to a previous study done by Amin et al. (2018) who reported mechanical ventilation in 34.21% of cases but different from that of Elagamy and

Gabr (2019) and Sam et al. (2009) who reported mechanical ventilation in 20% and 56.3% of cases respectively. The variability in the ratio can be attributed to the difference in the severity of enrolled cases in the study.

As regard cholinesterase levels, the mean levels in mechanically ventilated patients were 760.59 IU and 3.57 μ moles/ ml red cells/ min for BuCHE and ACHE respectively. These results were very close to previously reported results by Amin et al. (2018) but lower than that reported by Agrawal et al. (2018) and Brahmi et al. (2006). This discrepancy in estimated cholinesterase levels can be attributed to the affection of their levels by environmental exposure to different types of pesticides (Othman et al., 2018). On correlating with the severity of cases, a significant negative correlation was detected. This is like previous studies which reported a significant negative correlation between cholinesterase levels and severity of poisoning (Elagamy and Gabr, 2019; Honnakatti et al., 2018). However, despite the correlation of cholinesterase levels with clinical severity, they are very poor predictors for the probability of mechanical ventilation. This finding is by previous studies that cholinesterase is a good diagnostic investigation but cannot be used as a predictor for the outcome (Aygun et al., 2002; Eddleston et al., 2008; Yuan et al., 2018; Bhat et al., 2021; Mahmoud et al., 2021). Thus, a grading system to predict the patient outcome based on cholinesterase levels is most likely unreliable.

As regarded the studied scores, on comparing the median scores on admission between patients who were later mechanically ventilated and those that were not, a significant difference was detected between the two groups. This indicates a potential role for these scoring systems in predicting the need for mechanical ventilation. This is

similar to the previously reported significant value for APACHE II score and other emergency scoring systems for predicting outcomes in acute organophosphate poisoning cases (Sam et al., 2009; Shahin and Hafez, 2020).

Regarding the APACHE II score, it serves as a useful index for evaluating the severity of poisoning due to multiple organ system involvements (Hwan et al., 2013). In the present study, the median value for patients who did not require mechanical ventilation was 4 and this value was similar to previous studies on patients who survived without intubation (Eizadi-Mood et al., 2007; Shahin and Hafez, 2020). Meanwhile, the median value for patients who required mechanical ventilation was 24, and this much higher than that reported by Shahin and Hafez (2020) and Eizadi-Mood et al. (2007) which were 17 and 13.5 respectively. The difference in the estimated values could be explained by severe cases enrolled in the present study.

The AUC for APACHE II score in the present study was 0.924 with an overall accuracy of 86.36% indicating its strong predictive value for mechanical ventilation. This accuracy is very close to previous studies that reported excellent predictive power of more than 0.9 (Eizadi-Mood et al., 2007; Shahin and Hafez, 2020). In addition, the cut-off point in the present study was 11.5 which is very close to that reported by (Shahin and Hafez, 2020) that was 9 but higher than reported by (Eizadi-Mood et al., 2007) which was 7.

Modified Early Warning Score and WPS are simple rapid scoring systems in the emergency department. The present study, according to our knowledge, is the first to use these two emergency scoring systems to predict the outcome in acute organophosphorus toxicity. However, they proved their relative efficacy in the

emergency department in general. In the present study, AUC was 0.927 and 0.977 with overall accuracy 88.64 and 93.97% for MEWS and WPSS respectively indicating a very high predictive value for these scores. The cut-off values were 2.5 and 3.5 for MEWS and WPS respectively. The estimated predictive values in the present study are much higher with lower cut-off points than previously reported results (Bulut et al., 2014; Gök et al., 2019; Wei et al., 2019). This discrepancy is mostly due to the nature of cases selection, as previous studies were evaluating all medical and surgical cases presented to the emergency department not specified to toxicological cases. In addition, they were evaluating ICU admission and hospital mortality not the probability of mechanical ventilation. As regards the most predictor score, WPS was the best one as a predictor and this was in agreement with previous studies that favored WPS as a predictor emergency scoring system (Gök et al., 2019; Rahmatinejad et al., 2021).

Conclusion:

In conclusion, cholinesterase levels can be a useful tool for diagnosis and assessing the severity of organophosphorus poisoning at initial presentation but not predicting the outcome. APACHE II, MEWS, WPS scores were significant in predicting mechanical ventilation for acute organophosphate poisoning cases with the WPS score providing the best predictive value.

Recommendation:

Initial evaluation of acute organophosphorus toxicity cases using WPS score is recommended to decide their pathway and predict the outcome.

Conflicts of interest statement:

The authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest or non-financial in the subject matter or materials discussed in this manuscript. **Abdel Aziz A. Ghanem** is one of the coauthors and an editor of the Mansoura Journal of Forensic Medicine & Clinical Toxicology journal. He declares that he did not review the paper nor was included in the team handling the paper till acceptance by independent reviewers who were blind about the authors of the paper.

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تقييم مقاييس علم وظائف الأعضاء الحاد وتقييم الصحة المزمنة والإنذار المبكر المعدل ونتائج الجدارة الفسيولوجية كوسيلة للتنبؤ باستخدام جهاز التنفس الصناعي بمرضى التسمم الحاد بالمبيدات الحشرية الفسفورية العضوية

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٢ قسم الطب الشرعي والسموم الإكلينيكية كلية الطب جامعة الأزهر (أسيوط)

٣ قسم الطب الشرعي والسموم الإكلينيكية كلية الطب بنين جامعة الأزهر

يعد التقييم المبكر للمرضى الذين يعانون من سمية المبيدات الحشرية الفسفورية العضوية في قسم الطوارئ خطوة أساسية للكشف عن مسارهم في المستشفى. كان الهدف من هذه الدراسة هو تقييم الدقة الكلية لمقاييس علم وظائف الأعضاء الحاد وتقييم الصحة المزمنة (APACHE II) ودرجة الإنذار المبكر المعدل (MEWS) والنتيجة الفسيولوجية الجديرة (WPS) في التنبؤ باحتمالية استخدام جهاز التنفس الصناعي بهم. أجريت هذه الدراسة على ١٣٢ مريضًا يعانون من التسمم الحاد بالمبيدات الحشرية الفسفورية العضوية. تم جمع ما يلي من كل مريض: البيانات السريرية ونتائج الفحوصات المخبرية الروتينية وعينات الدم لتقدير مستويات الكولينستريز بالدم. تم استخدام البيانات السريرية والمخبرية لحساب (APACHE II) و(MEWS)و(WPS) لجميع المرضي في غضون ست ساعات من دخولهم المستشفى. أظهر التحليل الإحصائي أن القيم المتوسطة لـ (APACHE II) و(MEWS) و(WPS) مختلفة إحصائيًا بين المرضى الذين تم وضعهم علي أجهزة التنفس الصناعي ومن لم يحتاجوا له. كما أظهر التحليل الإحصائي ارتباطًا سلبيًا قويًا بين درجة صعوبة الحالة ومستويات الكولينستريز بالدم. أظهرت مقياس (WPS) أعلى قوة تمييزية للتنبؤ باحتمالية استخدام جهاز التنفس الصناعي (المنطقة تحت المنحنى 0.977) ومع ذلك، كانت مقاييس (APACHE II) و(MEWS) متساوية تقريبًا في قوتها التمييزية (المنطقة تحت المنحنى 0.924 و0.927) على التوالي. بالإضافة لذلك يمكن استخدام مستويات الكولينستيراز كأداة تشخيصية مفيدة ولكنها ضعيفة جدًا في التنبؤ باحتمالية استخدام جهاز التنفس الصناعي (المنطقة تحت المنحنى 0.129 و0.209) لأسيتيل كولينستراز وبيوتيل كولينستراز على التوالي. وكاستخلاص للبحث فإن استخدام مقياس (WPS) للتقييم السريري لمرضى التسمم الحاد بالفوسفور العضوي في قسم الطوارئ له قدرات تنبؤية قيمة للتنبؤ بنتائج المرضى.