PREDICTORS OF OUTCOME AFTER TRAMADOL OVERDOSE

BY

Hany M. Tawfik and Aya S. Khater*

Poison Control Center, Ain Shams University Hospitals,

**Forensic Medicine and Clinical Toxicology department - Faculty of Medicine, Ain Shams University.*

ABSTRACT

Tramadol poisoning is a significant health problem and it is one of the most common reasons for visiting emergency departments (EDs). Factors that help to predict overall tramadol poisoning related fatality have rarely been elucidated. So, the aim of this work is to identify predictors for poisoning-related outcome in tramadol overdose by documenting the relationship between demographic, clinical characteristics, laboratory data, emergency interference and in-hospital mortality among patients presented with acute tramadol overdose in the Poison Control Centre (PCC), Ain Shams University Hospitals. Between the first of January 2011 and the end of December 2011 we prospectively recruited tramadol poisoned patients presented to the emergency department (ED) of Poison Control Center (PCC), Ain Shams University Hospitals in Egypt. Interviews were conducted with patients within 24 hours after admission. Comparisons between survived cases and deaths were done to identify predictors of fatality. A total of 1233 poisoning cases were recorded at the ED. Tramadol poisoning was common in the middle age (84.5%), 79.5% were males and history of addiction was reported in 76.6%. Tramadol abuse was detected in 80% of all mortalities. Deaths were common among males (80%). The significant predictors for fatality included delay time, abnormal heart rate, abnormal blood pressure, abnormal respiratory rate, skin changes, GCS ≤ 10, blood glucose, blood pH, endotracheal intubation, and need for mechanical ventilation. It could be concluded that abnormalities of heart rate, blood pressure, respiratory rate, conscious level, blood sugar, blood pH and the need for emergency respiratory interference are important predictors for the outcome of tramadol overdosed patients in the EDs.

Keywords: *Tramadol, Vital Signs, Glasgow, Intubation.*

INTRODUCTION

Tramadol overdose has been one of the most frequent causes of drug poisoning in recent years. Its use has been approved in some countries and became the most prescribed opioid worldwide (Shipton, 2000). It exerts its analgesic effect by inhibiting

the re-uptake of norepinephrine and serotonin and also by weak opioid receptor agonism (Shadnia et al., 2008). Some patients might exhibit a certain degree of tolerance to the drug after prolonged prior exposure, and it is emphasised that physicians must be more cautious when prescribing tramadol (Sohil and Ponampalam, 2011).

Lethal poisoning by tramadol seems to have been increased in recent years. Hence, finding a factor that can predict severity and mortality of tramadol overdose is important in improving the outcome. The mortality of acute poisoning depends on a number of factors such as nature of poison, dose consumed, level of available medical facilities and the time interval between intake of poison and arrival at hospital (De Decker et al., 2008).

AIM OF THE WORK

The aim of this study is to identify predictors for tramadol poisoning related outcome by documenting the relationship between demographic, clinical characteristics, laboratory data, emergency interference and in-hospital mortality among patients presented with acute tramadol overdose in the Poison Control Centre (PCC), Ain Shams University Hospitals.

METHODS

This research was conducted as a prospective study involving cases of acute tramadol overdose who presented between 1st of January 2011 and the end of December 2011 to the ED of the PCC, Ain Shams University Hospitals. All cases were enrolled within 24 hours of arrival. Information collected included general characteristics (age, sex, history of suicide or abuse and delay time), clinical data (pulse, blood pressure, temperature, respiratory rate, skin changes, GCS and seizures), in addition to laboratory data (random blood sugar and blood pH) and emergency interferences (e.g., endotracheal intubation, mechanical ventilation and use of naloxone). Diagnosis of tramadol poisoning was proved by history of ingestion of overdose of tramadol tablets and by positive urine screen for tramadol by enzyme immunoassay using Axizyem autoanalyser.

Statistical analysis:

The data was analyzed using SPSS statistical software (11.5.0; SPSS Inc., Chicago, IL). Differences between survivors and fatalities were tested using the chi-square test. P value < 0.05 is considered statistically significant. Logistic regression analyses were applied to adjust for confounders and to identify significant predictors of outcomes.

Ethical consideration:

Permission was obtained from the Director of the PCC, Ain Shams University

Hospitals and the regional ethics committee. All data were stored anonymously. Relatives of recruited patients provided written informed consent for participation.

RESULTS

Table (1) showed that tramadol poisoned patients represent 7.4 % (1595 out of 21550 poisoned patients) during the year 2011.

Characteristics of the poisoned cases were demonstrated in table (2). As regards the age group, most of tramadol cases were in the middle age 14-40 years (84.5%) as well as most of deaths (9 cases out of ten). Most of cases were males (79.5%) as well as the majority of deaths (8 males out of 10 cases). It was also noted that 76.6% of cases were due to tramadol abuse, 13.2% were suicidal and 10.2% was accidental mainly in the children. The majority of cases presented with delay time <6 hours (92.8%). A significant difference was found between survivors and group of deaths concerning delay time.

Table (3) illustrated the clinical status of the poisoned cases. 7.5% of patients had abnormal body temperature (91 patients with hyperthermia and two patients with hypothermia), 7.8% had abnormal heart rate (82 patients with tachycardia and 14 cases with bradycardia), while 3.3% presented with abnormal blood pressure (21 cases had hypotension and 20 patients had hypertension). In addition, GCS < 10 was found in 11.1%.

Statistical analysis revealed that the group of deaths showed significant predominance of abnormal heart rate, abnormal blood pressure, abnormal respiratory rate, abnormal skin changes and GCS ≤ 10 ($p < 0.05$) when compared with the survivors group.

As shown in table (4), 5.3% of cases had abnormal blood sugar while acidosis was detected in 7.4%. Both were predominant among the group of deaths when compared with the survivors group ($p < 0.05$).

Table (5) demonstrated the emergency interference done in the poisoned cases. Endotracheal intubation (ETI) was performed in 5.6% of cases, 2% of patients were mechanically ventilated and 6.4% received naloxone.

Statistical analysis revealed that the group of deaths showed significant predominance of using ETI and mechanical ventilation ($p < 0.05$) when compared with the group of survivors.

Logistic regression analysis is shown in tables (6, 7, 8, 9). It revealed that the delay time > 6 hours, abnormal heart rate,

abnormal blood pressure, abnormal respiratory rate, skin changes, GCS ≤10, abnormal blood glucose, acidosis, ETI and need for mechanical ventilation all are predictors of in-hospital mortality.

Table (1) : Percentage of tramadol patients in the year 2011.

Year 2011	No of patients	%
Total no of patients	21550	100%
No of tramadol patients	1595	7.4 %

Table (2) : Statistical analysis of the demographic general characteristics for survived and dead groups.

Parameters	Deaths (n = 10)	Survivors (n=1223)	Total (%) (n =1233)	*Chi-square test* (χ^2)	P
Age (years)					
≤ 5 years	-	102	(8.3 %)	***1.5***	***0.7***
6-13 years	-	23	(1.9 %)		
14-40	9	1034	(84.5%)		
> 40 years	1	64	(5.3 %)		
Gender					
Male	8	972	(79.5 %)	0.002	0.96
Female	2	251	(20.5 %)		
Mode of poisoning					
Suicidal	2	161	(13.2 %)	1.4	0.5
Accidental	-	126	(10.2%)		
Abuse	8	936	(76.6 %)		
Delay time					
> 6hours	3	86	(7.2 %)	7.8	0.005*
≤ 6 hours	7	1137	(92.8)		

* P ≤ 0.05 is significant.

Table (3) : Statistical analysis of clinical parameters for survived and dead groups.

Parameters	Deaths (n = 10)	Survivors (n = 1223)	Total (%) (n = 1233)	*Chi-square test* (χ^2)	P
Body temperature					
Abnormal	2	91	(7.5 %)	2.2	0.13
Hyperthermia	(1)	(90)			
Hypothermia	(1)	(1)			
Normal	8	1132	(92.5 %)		
Heart rate (HR)					
Abnormal	4	92	(7.8 %)	14.6	0.0001*
Tachycardia	(4)	(78)			
Bradycardia	(0)	(14)			
Normal	6	1131	(92.2 %)		
Blood pressure (BP)					
Abnormal	5	36	(3.3 %)	68.3	0*
Hypotension	(5)	(16)			
Hypertension	(0)	(20)			
Normal	5	1187	(96.7 %)		
Respiratory rate (RR)			**%**		
Abnormal	5	30	(2.8 %)	81.3	0*
Bradypnea	(3)	(9)			
Tachypnea	(2)	(21)			
Normal	5	1193	(97.2 %)		
Skin changes					
Abnormal	6	40	(3.7 %)	88.9	0*
Cyanosis	(5)	(18)			
Pallor	(1)	(22)			
Normal	4	1183	(96.3 %)		
Seizures					
Seizures	1	108	(8.8 %)	0.017	0.9
No seizures	9	1115	(91.2 %)		
Coma					
GCS ≤ 10	7	130	(11.1%)	35.4	0*
GCS > 10	3	1093	(88.9 %)		

* P ≤ 0.05 is significant. N.B. abnormal temperature (≤ 36.0°C or ≥ 37.5°C) – abnormal HR (< 60 or > 120 beats/min) – abnormal BP (SBP < 90 or > 160/100 mmHg) - Respiratory distress (RR <10 or >24 breaths / min).

Table (4) : Statistical analysis of laboratory parameters for survived and dead groups.

Parameters	Deaths (n= 10)	Survivors (n =1223)	Total (%) (n = 1233)	*Chi-square test* (χ^2)	P
Random blood glucose (mg/dl)					
Abnormal Hyperglycaemia Hypoglycaemia	5 (4) (1)	61 (57) (4)	(5.3%)	39.7	0.0001*
Normal	5	1162	(94.7%)		
Blood pH					
Acidosis	10	81	(7.4%)	126.5	0.0001*
Normal	-	1142	(92.6%)		

* P ≤ 0.05 is significant.

Table (5) : Statistical analysis of emergency interference for survived and dead groups.

Parameters	Deaths (n = 10)	Survivors (n= 1223)	Total (%) (n =1233)	*Chi-square test* (χ^2)	P
Endotracheal intubation					
Yes	10	59	(5.6 %)	170	0*
No	0	1164	(94.4%)		
Mechanical Ventilation					
Yes	10	15	(2 %)	487	0*
No	0	1208	(98%)		
Naloxone					
Yes	2	77	(6.4 %)	3.1	0.08
No	8	1146	(93.6%)		

* P ≤ 0.05 is significant.

Table (6) : Logistic regression analysis of general characteristics as predictors associated with tramadol-related mortality.

Parameters	Deaths (n = 10)	Survivors (n =1223)	OR (95% CI)	P
Age (years)				
≤ 5	-	102	0.5 0.03-8.9	0.5
6-13	-	23	2.4 0.1-42.7	0.5
14-40	9	1034	1.6 0.2-13.1	0.6
>40	1	64	2 0.3-16.1	0.5
Gender				
Male	8	972	1 0.2 - 4.9	0.97
Female	2	251		
Mode of poisoning				
Suicidal	2	161	1.6 0.3-7.8	0.5
Accidental	-	126	2.4 0.1-41.5	0.5
Abuse	8	936	1.2 0.3-5.8	0.8
Delay time				
> 6 hours	3	86	5.7 1.4 to 22.3	0.01*
≤ 6 hours	7	1137		

* P ≤ 0.05 is significant.

OR = odds ratio, CI = confidence interval.

Table (7) : Logistic regression analysis of clinical parameters as predictors associated with tramadol-related mortality.

Parameters	Deaths (n = 10)	Survivors (n = 1223)	OR (95%CI)	P
Body temperature(BT)				
Abnormal	2	91	3.1	0.2
Normal	8	1132	0.7 -14.9	
Heart rate (HR)				
Abnormal	4	92	8.2	0.001*
Normal	6	1131	2.3 -29.6	
Blood pressure (BP)				
Abnormal	5	36	33	0.0001*
Normal	5	1187	9.1 -119	
Respiratory rate (RR)				
Respiratory distress	5	30	39.8	0.0001*
RR 10 - 24/min	5	1193	11 - 144.7	
Skin changes				
Pallor or Cyanosis	6	40	44.3	0.0001*
None	4	1183	12 - 163.4	
Seizures				
Seizures	1	108	1.2	0.9
No seizures	9	1115	0.1 - 9.1	
Coma				
GCS ≤ 10	7	130	19.6	0.0001*
GCS > 10	3	1093	5.0 - 76.8	

* P ≤0.05 is significant.

Table (8) : Logistic regression analysis of laboratory parameters as predictors associated with tramadol-related mortality.

Parameters	Deaths (n = 10)	Survivors (n=1223)	OR (95%CI)	P
Random blood glucose (mg/dl)				
Abnormal	5	61	19	0.0001*
Normal	5	1162	5.3 - 67.6	
Blood PH				
Acidosis	10	81	294.4	0.0001*
Normal	-	1142	17 - 5068.8	

* P ≤ 0.05 is significant.

Table (9) : Logistic regression analysis of emergency interference as predictors associated with tramadol-related mortality.

Parameters	Deaths (n = 10)	Survivors (n= 1223)	OR (95%CI)	P
Endotracheal intubation				
Yes	10	59	411	< 0.0001*
No	0	1164	23.8 - 7098	
Mechanical Ventilation				
Yes	10	15	1637.3	< 0.0001*
No	0	1208	91.8 -29196.5	
Naloxone				
Yes	2	77	3.7	0.1
No	8	1146	0.8 - 17.8	

* P ≤0.05 is significant.

DISCUSSION

Among 21,550 patients visited the PCC, Ain Shams University Hospitals during the year 2011, 1595 cases (7.4%) were tramadol overdose. The study included only 1233 patients. The other 362 cases were excluded due to mixed overdose or refusal to complete treatment. Mortality rate among the tramadol poisoned cases was 0.8%. The most common age of poisoning was 14 - 40 years (84.5%), followed by age < 5 years (8.3%). Most of patients were males 79.5% and 20.5% were females. History of addiction was reported in 76.6%, while suicide accounted for 13.2% and accidental ingestion was (10.2%) mainly in children. Death due to abuse represented (80%), 90% were in the middle age and 80% were males. A significant difference between survivors and death groups as regards delay time was found.

A similar study was done in Iran by Ahmadi et al. (2012) who reported that the total number of tramadol overdose cases was 0.1 % and mortality rate was 0.97%. Adults between 16 - 35 years represented 93.3%, children < 15 years of age were 2.2% and males accounted for 78.5%. The mean age of death was 30 years and 90% of them were males. In contrast, they found that tramadol addiction was reported only in 29.6%, while suicide attempts accounted for 55.1% and the common cause of death was suicide (60%).

In accordance with the present findings,

Morteza et al. (2012) found that 61.8% of tramadol overdose was between 20-40 years old and it was more common in males (83.3%).

The current study revealed that there was a predominance of abnormal heart rate, abnormal blood pressure, abnormal respiratory rate, abnormal skin changes and GCS ≤ 10 ($p < 0.05$) in the dead group. While non significant difference was detected between both groups as regards body temperature and seizures. Our results revealed that 7.5% of the cases had abnormal temperature.

Mulpur et al. (2004) attributed hyperthermia which occur in tramadol poisoning to be a feature of serotonin syndrome while hypothermia due to decreased muscle activity, cutaneous vasodilatation and effect on the hypothalamic heat regulation. Moreover, 7.8% of our patients had abnormal heart rate. Similar results were noticed by Marquardt et al. (2005) who reported that tachycardia was found in 17.4% of tramadol overdose cases.

Lewis (2006) explain the bradycardia by increased parasympathetic activity and tachycardia is due to serotonin syndrome as discussed by Jones and Story (2005).

In the current study, 3.3% of cases had abnormal blood pressure. Flacke et al. (2006) found that tramadol overdose produced hypotension which may be due to arteriolar and venous dilatation and also due to histamine release. Moreover, Daubin et al. (2007) noted that tramadol may cause refractory shock and asystole. Whereas Jones and Story (2005) reported that tramadol overdose might present with features of serotonin syndrome with hypertension.

Regarding respiratory distress, it was reported in 2.8% of our patients. Dvir, (2008) reported that respiratory depression was due to depressive opioid effect, while tachypnea occurs due to pulmonary edema and autonomic hyperactivity. Moreover, opioids decrease the minute volume, respiratory rate and tidal volume by altering the sensitivity of the brainstem respiratory center to carbon dioxide concentrations (Lewis, 2006).

In the current study, seizures were found in 8.8% of our patients. In contrast, Ahmadi et al. (2012) found that 41.8% of their cases had seizures which were also detected in 70% of deaths. Moreover, Marquardt et al. (2005) reported that seizures were seen in 13.7% of their cases and they were probably a feature of serotonin syndrome.

Skin changes occur in 3.7% of the patients either cyanosis due to respiratory depression with apnea or pallor due to hypotension and shock. Coma and

disturbed level of consciousness were present in 11.1% of our cases with GCS < 10. However, Eizadi et al. (2011) found that 57% of their patients were comatose (out of 184 tramadol cases). In addition, Marquardt et al. (2005) detected coma in 27.4% of their patients and it was attributed to central nervous system depressive effect of opioid receptors.

Our study revealed that there was a significant predominance of abnormal blood sugar and acidosis ($p < 0.05$) in the dead group. Mugunthan and Davoren (2012) reported a case of prolonged hypoglycaemia that necessitated treatment for 24 hours after tramadol overdose. Also, Loughrey et al. (2003) found liver injury and hypoglycaemia in a case with accidental tramadol overdose. Chandrasekaran et al. (2007) reported mixed respiratory and metabolic acidosis in patients with tramadol overdose and it was explained by presence of respiratory depression or lactic acidosis due to shock or hypoxia.

The present work revealed predominant use of ETI and mechanical ventilation ($p < 0.05$) in the dead group. 5.6% of cases were subjected to endotracheal intubation as a protection of airway in comatose patients or due to respiratory distress, 2% of cases were subjected to mechanical ventilation either due to respiratory failure or pulmonary edema and 6.4% received naloxone as an antidote in case of predominant opioid effect with impending respiratory failure.

Similar results were obtained by Hassanian et al. (2012) in a study conducted on 525 patients with acute tramadol poisoning and found that nineteen patients (3.6%) experienced apnea and received respiratory support (84.2%) or naloxone administration (15.8%) within 24 hours of ingestion.

Logistic regression analysis revealed that delay time > 6 hours, abnormal heart rate, abnormal blood pressure, abnormal respiratory rate, skin changes, GCS ≤10, abnormal blood glucose, acidosis, endotracheal intubation and the need for mechanical ventilation were good predictors for hospital mortality.

CONCLUSION

It is important for physicians to be aware of tramadol lethal effects, particularly if prescribed in large doses. Triage vital signs, conscious level, blood sugar and blood pH together with the need for emergency respiratory interference are all important for evaluation of outcome in tramadol overdose patients presented to the emergency department. Identification of those predictors may help risk stratification and the development of preventive interventions.

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REFERENCES

Ahmadi, H.; Rezaie, M. and Hoseini, J. (2012):"Epidemiological analysis of poisoning with tramadol". J. Forens. Res., 3:151-153.

Chandrasekaran, D.; DeSilva, P.; Dhatariya, K. (2007): "The dangers of underestimating tramadol". J. Med. Sci. Res., 1 (1):59–61.

Daubin, C.; Quentin, C.; Goulle, D. et al. (2007): "Refractory shock related to tramadol overdose".Clin. Toxicol., 45 (8):961–964.

De Decker, K.; Cordonnier, J.; Jacobs, W. et al. (2008): "Fatal intoxication due to tramadol". Forens. Sci. Int., 175: 79–82.

Dvir, Y. (2008): "Serotonin syndrome: A complex, easily avoidable condition". Gen. Hosp. Psych., 30: 284–287.

Eizadi, N.; Sabzghabaee, A.; Safdari, A. et al. (2011): "Outcome of tramadol intoxication". J. Isfahan Med. School, 28:117-120.

Flacke, J.; Flacke, W.; Bloor, B. et al. (2006): "Histamine release by four narcotics". Anesth. Analg., 66:723-730.

Hassanian, H.; Farajidana, H.; Sarjami, S. et al. (2012) : "Tramadol- induced apnea". Am. J. Emerg. Med., 16:150- 154.

Jones, D. and Story, D. (2005): "Serotonin syndrome and the anaesthetist". Anaesth. Intens. Care, 33(2):181–187.

Lewis, S. (2006): Opioid. In:Goldfrank's Toxicologic Emergencies. Flomenbaum, E.; Goldfrank, R.; Hoffman, S.; Howland, A; Lewin, A.; Nelson, S. (Eds.), McGraw-Hill; Ch. 38, P.P. 590- 612.

Loughrey, M.; Loughrey, C.; Johnston, S. et al. (2003): "Fatal hepatic failure following accidental tramadol overdose". Forensic. Sci. Int., 134: 232-233.

Marquardt, A.; Alsop, A. and Albertson, E. (2005): "Tramadol exposures reported to state wide poison control system". Ann. Pharmaco. Ther., 39(6):1039-1044.

Morteza, R.; Ali, R.; Farzaneh, B. et al. (2012): "Clinical and laboratory findings in patients with tramadol intoxication referred to Razi Hospital during 2005-2006". J. Toxicol., 6 (16): 605-609.

Mugunthan, N. and Davoren, P. (2012): "Danger of hypoglycemia due to acute tramadol poisoning". Endocr. Pract., 18(6): 151-152.

Mulpur, A.; Mirsadraee, S.; Hassan, T. et al. (2004): "Refractory ventricular fibrillation in accidental hypothermia". Perfusion, 19:311-314.

Shadnia, S.; Soltaninejad, K.; Heydari, K. et al. (2008): "Tramadol intoxication". Hum. Exp. Toxicol., 27: 201–205.

Shipton, E. (2000): "Tramadol-present and future". Anaesth. Intens. Care, 28: 363–374.

Sohil, P. and Ponampalam, R. (2011): "Tramadol overdose". Healthcare, 20 (3): 200-203.

التنبؤات بالنتيجة بعد جرعة زائدة من عقار الترامادول

المشتركون فى البحث

د. هانى محمد توفيق و د. آيـــة خاطر*

من مركز علاج التسمم بمستشفيات جامعة عين شمس وقسم الطب الشرعى والسموم الاكلينيكية*

كلية الطب – جامعة عين شمس

يعد التسمم بعقار الترامادول مشكلة صحية كبيرة حيث أنه من أكثر الأسباب شيوعا لزيارة أقسام الطوارئ، ولكن العوامل التى تساعد على التنبؤ بالوفاة نتيجة التسمم بعقار الترمادول نادرا ما تم دراستها. وتهدف هذه الدراسة إلى تحديد التنبؤ بالنتيجة جراء التسمم بالترامادول عن طريق تقييم الخصائص الديموغرافية والسريرية، والبيانات المختبرية، والتدخلات العلاجية الطارئة فى المرضى الذين يعانون من تناول جرعة زائدة من عقار الترامادول. فى الفترة من أول يناير الى آخر ديسمبر ٢٠١١ قمنا بدراسة حالات التسمم بجرعة زائدة من عقار الترامادول الواردة الى مركز علاج التسمم بمستشفيات جامعة عين شمس .وقد تم مناظرة جميع الحالات في غضون ٢٤ ساعة من وصولها. تم مقارنة حالات الأحياء والوفيات لتحديد تنبؤات الوفاة. تم تسجيل عدد ١٢٣٣ حالة تسمم بالترمادول فى هذه الفترة . وأظهرت النتائج أن التسمم بجرعات زائدة من عقار الترامادول كان شائعا فى منتصف العمر (٥ , ٨٤٪) وبلغت نسبة الذكور ٥ , ٧٩٪ وبلغت نسبة الإدمان (٦ , ٧٦٪) ومحاولات الانتحار (٢ , ١٣٪). وتبين أن إدمان الترامادول شمل ٨٠٪ من جميع الوفيات وكانت معظمها من الذكور فى الفئة العمرية المتوسطة. و أثبتت النتائج الإحصائية أن التنبؤات المعنية للوفاة هى تأخير وقت الوصول للمستشفى، واضطرابات كل من ضربات القلب، و ضغط الدم ومعدل التنفس ، وكذلك التغيرات الجلدية، ومقياس جلاسكو للغيبوبة اقل من ١٠ وتغير نسبة السكر في الدم، وزيادة حموضة الدم، بالاضافة الى الحاجة لتركيب أنبوبة حنجرية و استخدام جهاز التنفس الصناعى . وقد خلصت هذه الدراسة إلى أنه يتعين فحص حالات التسمم بالترامادول في أقسام الطوارئ بواسطة العلامات الحيوية ، ومستوى الوعى ومستوى السكر في الدم، ودرجة حموضة الدم وكذلك الحاجة للتدخل العاجل في حالات الاضطرابات التنفسية للتنبؤ بنتائج مرضى تسمم الجرعات الزائدة من الترمادول.