

DISCUSSION

Tramadol hydrochloride is a synthetic, centrally acting analgesic used both parenterally and orally for the treatment of moderate to severe pain. It has dual mechanism of action; weak agonistic effect at the μ -opioid receptor, as well as inhibition of monoamine (serotonin, norepinephrine) re-uptake.⁽⁸⁵⁻⁸⁷⁾

Numerous clinical trials have proven its efficacy and safety over a broad range of painful conditions, both acute and chronic; however, in severe pain morphine may be superior to tramadol. This combination of safety with good efficacy made tramadol unique analgesic.^(88, 89,90)

In over dose cases, Lethargy, nausea, tachycardia, agitation, seizure, coma, hypertension and respiratory distress are the more frequently reported symptoms and they are mostly attributable to the monoamine reuptake inhibition rather than its opioid effects^(86,87).

The present study was carried out on all patients with tramadol overdoses admitted to the Alexandria Poison Center and Intensive Care Unit (I.C.U.) at Alexandria Main University Hospital.

This included retrospective study patients with tramadol overdoses who were admitted from 1/1/2012 to 30/6/2012 (Sixty three patients) and prospective study patients with tramadol overdoses who were admitted from 1/10/2012 to 31/3/2013(fifty nine patients).

Personal data

Age and sex:

Tramadol overdose has been one of the most frequent causes of drug poisoning in the recent years, especially in young adult males.⁽⁹¹⁾

As regard age, in this study the mean age was 29.77 ± 6.94 years. Similar findings were obtained by Zhang, et al., (2013).⁽⁹¹⁾ and as the mean age was (23.4 ± 4.1) years 23.1 ± 6.3 years in their studies respectively. Also other studies reported near mean age (22.7 years).^(90,92)

This study, conducted on 122 patients, among which 87 (71.3%) were males and 35 (28.7%) were females. Hassanian-Moghaddam et al.,(2012)⁽⁹²⁾ reported similar finding where males predominately (70.1%) according to his study. Fawzi et al., (2011)⁽⁹³⁾, found that adult population have higher prevalence (67.9%) to children that presented only (32.1%) of the studied cases. The male sex prevalence was higher as well (77.2%) compared to (22.8%) females.

Similarly, Ahmadi et al.,(2012)⁽⁹⁴⁾, identified patients with tramadol poisoning as (78.5%) males and (21.5%) females. However, in a study conducted by Morteza, et al., (2012)⁽⁹⁵⁾, on 520 Tramadol intoxication patients during 2008-09 in kermanshah, the results showed that male was predominantly more than female (93.7% male and 6.3% female). Additionally, they demonstrated that, Tramadol intoxication was more common in young male patients (83.3%) where, 61.8% were between 20-40 years old.⁽⁹⁵⁾

Socioeconomic status and Residence:

Regarding current study, the higher percentage of cases 61.5% (n=75) were having middle socioeconomic status while poor status was reported in 35.2% (n=43) and high standards were only seen in 3.3% (n=4).

In this study, Most of the studied patients 81.1% were living in the city while 18.9% were living in the village.

Fawzi et al., (2011)⁽⁹³⁾, found that most tramadol addicts being unemployed, low socioeconomic status, suburbs residents uneducated or with minimal educational levels.

Reason for using tramadol:

In this study, 97.5% were self medicated and 2.5% were using tramadol as medically prescribed.

Hundred percent of tramadol abusers reported in a study by Zhang et al.,(2013)⁽⁹¹⁾, were self medicated.

The reason for presentation was intentional self-poisoning in (68.4%), abuse in (27.8%) and (1.5%) had accidental poisoning according to the study conducted by Hassanian-Moghaddam et al.,(2012)⁽⁹²⁾.

Petramfar et al.,(2008)⁽⁸⁵⁾, found that 81% of patients abused tramadol and the remaining cases consumed it for therapeutic purposes.⁽⁸⁵⁾

Life style habits:

In this study, most of the studied patients 95.9% were active smokers, 82.0% did not drink alcohol. Seventy six percent of the studied individuals (n=93) did not have any drug abuse as known by history taking.

Eighty seven percent of the sample had no previous history of drug abuse before tramadol abuse in the study by Zhang.et al.,(2013)⁽⁹¹⁾.

However, there was a history of addiction to substances in (16.4%) according to study conducted by Hassanian -Moghaddam et al.,(2013).⁽⁹²⁾

The United States Drug Enforcement Administration warns that it is difficult to know the effect of any drug, particularly the first time patient use it. Even if it is a small dose, patient may experience serious negative side effects because everyone's body chemistry is different, and so his body's tolerance to drugs. Tramadol overdose symptoms may occur accidentally, because many people are unaware of how it interacts with other substances, even if they seem harmless.⁽⁹⁶⁾

If users are addicted to alcohol or drugs, and they are taking tramadol, The risks of experiencing tramadol overdose symptoms are significantly increased.⁽⁹⁶⁾

Psychiatric troubles:

In current study, the majority, of the studied patients have psychiatric troubles 84 (68.9%) in the form of depression as known by history taking. This is their reason for taking tramadol.

Actually this is explained by tramadol affects neurochemicals such as serotonin and norepinephrine. That means the drug behaves a little like antidepressants such as Zoloft (sertraline, which is an SSRI or selective serotonin reuptake inhibitor) or Effexor (venlafaxine an SNRI) in the brain, though the drug has not been approved to treat depression.^(87, 97)

Tramadol, unlike antidepressants, works quickly so its antidepressant effects begin quickly after taking it. Antidepressants typically take at least two weeks for any effect and up to 4 weeks before full effects.

Antidepressant should not be taken in combination with tramadol, there is a risk of serotonin syndrome. Actually there have been times when tramadol has been prescribed to people with severe refractory depression however it is extremely rare and only done under severe circumstances⁽⁹⁸⁾.

Poisoning conditions:

In this study, non-toxic doses were detected in 63.9% of cases, where as toxic doses were found in 33.6% and fatal doses were reported in 2.5% only. Accidental poisoning was reported in most of the studied individuals 94.3%, while suicidal poisoning was found in 7 cases (5.7%) and ingestion was reported as the only route of administration in all studied individuals.

Similarly, in Zhang et al.,(2013)⁽⁹¹⁾, oral intake was found in (100%) of reported tramadol abusers.⁽⁹¹⁾

Further more, the route of exposure was oral in all patients according to study conducted by Hassanian-Moghaddam et al.,(2013).⁽⁹²⁾

Also, Fawzi et al., (2011)⁽⁹³⁾, reported that the oral route of intake was the highest among route of intake forms as being more prevalent (96.8%). Shadnia et al., (2008)⁽⁹⁹⁾, found oral route of administration in (98.25%), whereas only (1.75%) had used tramadol parenterally

General signs:

In this study, disturbed consciousness level was found in most of the studied individuals (80.3%) while, 19.7% of patients were fully conscious. Glasgow coma score ranged between 9.0-15.0 with the mean of 12.94±1.16. Pulse rate ranged between 56.0-149.0 beat/min with the mean of 102.77±20.33.

Systolic blood pressure ranged between 110.0-140.0 mmHg with the mean of 120.074±9.308. Diastolic blood pressure ranged between 60.0-90.0 mmHg with the mean of 76.91±8.20. Temperature ranged between 36.60-37.80 degree with the mean of 37.17±0.40. Normal pupil size was seen in the majority of patients included in the study (91.8%, n=112), whereas constricted pupil was reported in 9 cases (7.4%) and pinpoint pupil was met in only one patient (0.8%). Respiratory rate ranged between 16.0-28.0 rate/min with the mean of 21.50±3.54.

In study of Shadnia, et al., (2008)⁽⁹⁹⁾, (23.42%) of cases were unconscious. The pulse rate, ranged between 60 and 130 bpm with an average of 77.06 ± 16.90 bpm. Systolic and diastolic blood pressure ranged between 60–140 mmHg with an average of

107.4 mmHg, 50–110 mmHg with an average of 69.73 mmHg. Whereas respiratory rate, and body temperature of the patients were 4–38/min with an average of 14.80/min, and 36–38 °C with an average of 36.95, respectively.

Sohil, et al., (2011)⁽¹⁰⁰⁾, during examination of their cases of tramadol overdose, they found that, patients were and tachycardic with a heart rate of 142 beats per minute and respiratory rate was 18 per minute. Their initial temperature was 36.5°C and the blood pressure was 130/82 mmHg and remained stable throughout. The patients's oxygen saturation on room air was 100%. The pupils were bilaterally reactive to light.

Neurological signs and symptoms:

Regarding neurological signs and symptoms in current study, dizziness was reported in 44.3% of patients while 55.7% of them did not suffer from dizziness. Anxiety was detected in 21.3% of patients only. Delirium was reported as complain in 7 cases only. While euphoria was reported in 58.2% of the studied individuals.

Confusion was detected in 66.4% of the studied cases (n=81) whereas 57.4% suffered from headache.

Convulsion was reported in 27 of the studied individuals (22.1%). Slurred speech was detected in only 2 patients of the cases (1.6%). Coma was reported in 23 patients only (18.9%).

The most common symptoms of tramadol overdose are central nervous system (CNS) depression, and seizures.⁽⁸⁵⁾

It has been reported that 15% to 35% of hospital referred patients with tramadol poisoning experience seizures.^(86,87)

These neurological findings are comparable to symptoms reported by Farzaneh et al.,(2012)⁽¹⁰¹⁾, with overdose were: lethargy (30%), agitation (10%), seizures (8%), (5%) of coma in their study conducted

While Shadnia et al.,(2008)⁽⁹⁹⁾ noticed the commonly observed symptom was vertigo (62.3%), Headache (38.6%) and Anxiety(27.2%).

Contrarily, Sohil et al.,(2011),⁽¹⁰⁰⁾ who examine the cases with overdose of tramadol, found that, their neurologic examination was normal with normal deep tendon reflexes and no rigidity or clonus was noted.

Tonic-clonic seizures occurred in 46.1% according to study conducted by Hassanian-Moghaddam et al.,(2012).⁽⁹²⁾ Where as Ahmadi et al.,(2012)⁽⁹⁴⁾ founded that 41.8% of cases have symptoms of seizure and other cases haven't.

Morteza et al.,(2012)⁽⁹⁵⁾, reported central nervous system (CNS) depression (57%), agitation (25.2%).and , seizure (20.3%) were the most apparent symptoms among cases with tramadol over dose.⁽⁹⁵⁾

Kunig et al.,2006⁽¹⁰²⁾, Seizures have been reported in patients receiving the normal recommended dose. The risk for seizures is increased with doses above the recommended range. He added that nervous system side effects occur frequently. Dizziness, headache, and somnolence have been reported in more than 25% of treated patients during the first three months of therapy. CNS stimulation, including nervousness, anxiety, tremor, agitation, euphoria, emotional liability and hallucinations, has also been reported.

Confusion, sleep disorders, and coordination disturbances have been reported in less than 5% of patients. Seizures have been reported in over 200 cases. Cases of long-lasting delirium have been reported in two elderly patients. A case of serotonin syndrome triggered by tramadol has also been reported.

Tramadol overdose might also present with features of the serotonin syndrome due to the Serotonin-Norepinephrine Reuptake Inhibitor (SNRI) properties of the drug, which may include neuromuscular hyperactivity (myoclonus and hyper reflexia), autonomic hyperactivity (tachycardia and pyrexia) and altered mental state (usually agitation, excitement and later confusion)⁽¹⁰⁰⁾. A prospective multicentre evaluation of tramadol exposure suggested that much of the toxicity in tramadol overdose can be attributed to the monoamine uptake inhibition rather than its opioid effects and agitation, tachycardia, confusion and hypertension suggest a possible mild serotonin syndrome.⁽¹⁰¹⁾

Cardiovascular signs and symptoms:

In this study, regarding cardiovascular signs and symptoms, (62.3%) of patients complained of palpitation precordial pain was only reported in 13.1% of cases. Neither Syncope nor cardiac arrest was detected in all patients.

Farzaneh et al., (2012)⁽¹⁰¹⁾, reported that: tachycardia and hypertension were (13%) and (2%) of the studied group respectively. While hypotension was reported in (10.5%) according to Morteza et al., (2012).⁽⁹⁵⁾

Shadnia et al.,(2008)⁽⁹⁹⁾ reported palpitation in (14%) of the studied group.⁽⁹⁴⁾

Respiratory signs and symptoms:

Regarding respiratory signs, in this study, Dyspnea was detected in 40 patients (32.8%) whereas Cough was not reported in all patients. There were no rhonchi detected in any patient of the studied group. Crepitations were found in only 8 (6.6%) of the studied patients while stridor was not found in all studied cases (100%).

(2%) of tramadol overdosed patients suffered from respiratory depression⁽¹⁰¹⁾ furthermore apnea was observed in (3.6%) of patients according to study conducted by Hassanian-Moghaddam et al.,(2012)⁽⁹²⁾. Shadnia et al.,(2008)⁽⁹⁹⁾, observed dyspnea in (10.5%) of the studied cases.

Stephan, et al.,(2000),⁽¹⁰³⁾ showed that, respiratory depression with tramadol is less pronounced, and occurs less often, in comparison to equianalgesic doses of morphine. In large clinical and post-marketing studies including over 21,000 patients, no clinically relevant respiratory depression was reported. However, respiratory depression can occur, in particular with overdose as in children or with impaired renal function, possibly due to retention of the active metabolite M1.

Gastrointestinal signs and symptoms:

Regarding this study, gastrointestinal signs, anorexia was not detected in all individuals. Nausea was reported in 79 patients of the studied cases (64.8%). Only 21 patients out of the total 122 suffered from vomiting representing only (17.2%). Abdominal colic was reported as a complain in only three patients representing (2.5%). In all studied patients (n=122) there was neither diarrhea. nor constipation detected in any patient.

Shadnia et al.,(2008)⁽⁹⁹⁾, observed that the most commonly presented symptoms were nausea (76.32%) whereas Farzaneh et al.,(2012)⁽⁹⁹⁾, observed nausea in (14%) only of his studied cases. While vomiting was a sign in Shadnia et al.,(2008) (43.86%).

Also, Ripamonti et al., (2004)⁽¹⁰⁴⁾, reported that gastrointestinal side effects are common. Nausea and constipation occur within the first 90 days of therapy in 40% and 46% of treated patients, respectively. Vomiting, diarrhea, dyspepsia, anorexia, flatulence, abdominal pain, and dry mouth have also been reported Stephan, et al., (2000)⁽¹⁰³⁾ found that, the most common adverse events reported in clinical trials and post-marketing studies were, in decreasing order of frequency: nausea, dizziness, drowsiness, tiredness, fatigue, sweating, vomiting, dry mouth and postural hypotension. Nausea, a well-documented opioid side effect, seems to occur with an incidence comparable to that in other opioids, while vomiting is less common.

The incidence of nausea varied with route and setting of administration from 3% in controlled trials of oral medication, to 21% with IV use via patient controlled analgesia (PCA) pumps in the postoperative period. Another opioid side effect, which is reduced with tramadol use, is constipation. Clinically this has proven to be a significant advantage with long-term therapy, but could also be beneficial in the prevention of ileus postoperatively.⁽¹⁰³⁾

Skin signs and symptoms:

In the current study, no skin signs were observed, in all patients except coldness that was detected in 4.1% of the studied patients (n=5).

Sohil, et al., (2011)⁽¹⁰⁰⁾, found that, skin color was normal with a good capillary refill and there was no sweating or dryness of oral mucosa in patients with overdose of tramadol. Sweating is a side effect specific to tramadol, due to its monoaminergic effects, and it can be quite distressing to a small number of patients. In rare situations, sweating may be severe enough to necessitate discontinuation.

Genitourinary signs and symptoms:

In this study, no genitourinary signs were found in patients with tramadol over dose although in FDA report, in 2013 genitourinary side effects including urinary retention and urinary frequency that have been reported in less than 5% of tramadol over dosed patients⁽¹⁰⁵⁾.

Laboratory investigations:

In this study, regarding laboratory investigations, results showed that, most of the studied samples were normal in urea, creatinine, random blood glucose levels, also complete blood picture and liver functions tests. This was in agreement with Sohil, et al., (2011) who reported the same normal results for the investigations.⁽¹⁰⁰⁾

Electrocardiogram:

In current study, the reported heart rate was between 60 and 100 beats/min in 58% of cases (n=71), whereas 40.2% (n=100) had the heart rate beat/min over 100 and only 2 patients (1.6%) had it below 60 beat/min.

Regular rhythm was found in most of the studied patients 119 (97.5%). Normal P-wave were found in the majority of the studied individuals 119 (97.5%), Normal QRS-wave was reported in 65.6% of patients (n=80), whereas 22.1% (n=27) had

shortened QRS-wave and 15 patients (12.3%) had prolonged QRS-wave. T-wave was found normal in the majority of the studied individuals 120 (98.4%), while flattened T wave was detected in 2 (1.6%). Normal ST segment was found in 120 (98.4%) and normal PR interval were found in 80 (65.6%). PR interval were found normal in 80 patients (65.6%), whereas 22.1% (n=27) had shortened PR interval and 15 patients (12.3%) had it prolonged.

Many studies recorded sinus tachycardia with a normal QRS/QTc duration as Electrocardiogram abnormalities.^(101,103,106)

Cole, et al., (2012)⁽¹⁰⁷⁾, They revealed no previous human cases of tramadol overdose causing ECG changes consistent with sodium-channel blockade.

Treatment:

In this study, emesis was used for decontamination in 15 (12.3%), gastric lavage was practiced in 104 patients (85.2%), activated charcoal was used in 3 patients (2.5%).

Intravenous fluids were administered in most of the studied individuals 118 (96.7%). Oxygenation was needed in 109 of the studied cases (89.3%). Mechanical ventilator was only required in 9 cases (7.4%).

Anticonvulsive therapy was required in 27 (22.1%) of the studied patients. Intravenous hydrocortisone was only used in 13 (10.7%) of the studied patients. Sodium bicarbonate was included in the treatment of 14 (11.5%) of the patients.

Antidote usage was needed in only 27 patients (22.1%) of the studied group. Most of them 88 (72.1%) required hospitalization for just one day, 27 patients (22.1%) stayed for three days and 7 patients (5.7%) stayed in hospital for two days.

In study conducted by Hassanian-Moghaddam et al.,(2013)⁽⁹²⁾, treatment for apnea included intubation and ventilation in (84.2%), and naloxone administration in (15.8%).

The treatment of tramadol overdose is mainly supportive, with careful monitoring. Symptom onset is rapid, requiring administration of activated charcoal within 1–2 hours of ingestion.

Supportive measures (including oxygen and vasopressors) should be employed in the management of circulatory shock and pulmonary edema accompanying overdose as indicated. Cardiac arrest or arrhythmias may require cardiac massage or defibrillation.⁽¹⁰⁷⁾

While naloxone will reverse some, but not all, symptoms caused by overdosage with tramadol, the risk of seizures is also increased with naloxone administration. In animals convulsions following the administration of toxic doses of ULTRAM (tramadol HCL) could be suppressed with barbiturates or benzodiazepines but were increased with naloxone. Naloxone administration did not change the lethality of an overdose in mice. Hemodialysis is not expected to be helpful in an overdose because it removes less than 7% of the administered dose in a 4-hour dialysis period.⁽¹⁰⁸⁾

Prognosis:

In this study, complete recovery and discharge was the fate in a large number of the studied samples 88 (72.1%), while 27 patients (22.1%) required ICU admission and 7 patients (5.7%) needed to be put under observation. Recovery is probable after an oral dose. If patient has taken a high dose of tramadol and experience adverse side effects, prognosis and recovery without long term damage is possible if breathing has not been compromised. During these more serious cases of tramadol overdose, doctors may administer oxygen to help his breath better. But to be clear: tramadol overdose can be deadly. Furthermore, the lack of oxygen reaching the brain due to depressed breathing can cause permanent brain damage. Luckily, it's hard to accidentally take this much tramadol. ^(109, 110)

There are some warning symptoms and signs for tramadol prognosis seizure (convulsions); weak or shallow breathing; high levels of serotonin in the body--agitation, hallucinations, fever, fast heart rate, overactive reflexes, nausea, vomiting, diarrhea, loss of coordination, fainting; or severe skin reaction--fever, sore throat, swelling in your face or tongue, burning in your eyes, skin pain, followed by a red or purple skin rash that spreads (especially in the face or upper body) and causes blistering and peeling. ⁽¹¹¹⁾

The most dangerous complication of tramadol overdose is slow or shallow breathing. Tramadol overdose can even cause breathing to stop completely. Other medications combined with the tramadol may also cause overdose, or make these effects more pronounced. ⁽¹¹⁰⁾

Ahmadi et al.,(2012) ⁽⁹⁴⁾, found the duration of hospitalization for 94.2 % of cases shorter than 48 hours whereas(10%) of the admitted cases died. In Morteza et al., (2012)⁽⁹⁵⁾, (3.1%) of patients had to be transmitted to ICU. Similarly, (15%) of patients were admitted to an intensive care unit in study conducted by Spiller et al., (1997). ⁽¹¹²⁾

Shadnia et al., (2008) ⁽⁹⁹⁾, the admission period ranged between one and twenty one days with average of 2.75 days.(7.02%) of cases admitted in intensive care unit (ICU).

In this study, multivariate logistic regression analysis of predictor variables contributing to adverse outcome of tramadol overdosage patients, these were age ,smoking, illicit drugs use ,self use of tramadol,poisonous amount dose and disturbed conscious state. Fakhreddin et al 2011⁽¹¹³⁾ studied demographic information, clinical findings, and blood tramadol concentrations. There were 401 patients with a history of tramadol overdose; 121 (30.2%) with a history of seizure and 14 (3.5%) with a history of unconsciousness were included. Most of overdoses involved men (83%). The mean age was 22.9 years (range, 14–50 years). Intentional overdose was the most common mode of poisoning (51.9%). The mean dose ingested was 1,511 mg (SD, 1,353; range, 200–7,000).

Another study of total 114 cases of intentional tramadol intoxications revealed that the median age of 23.66 ± 6.87 years, male dominate females (82 men and 32 women). Other illicit drugs were found to be used in combination with tramadol in some of the cases, which among them benzodiazepines were the most common. Tramadol overdose has been one of the most frequent causes of drug poisoning in the country in the recent

years, especially in male young adults with history of substance abuse and mental disorders. Nausea, vomiting, Central Nervous System (CNS) depression, tachycardia, and seizure are the most common findings in this kind of poisoning.⁽¹¹⁴⁾

On contrary, gender of people who have cigarette smoking when taking tramadol was females (77,78%) and males (22.22%) and age of people who have Cigarette smoking when taking Tramadol 66.67% in 40-49 years followed by 13.33% 50-59 years.⁽¹¹⁵⁾

SUMMARY

Tramadol is one of the analgesic drugs, related to opioids and it is preferred in a wide range of painful conditions commonly used in the treatment of moderate to severe pain because of acceptable side effects.

It is a centrally acting synthetic analgesic compound that is not derived from natural sources. Tramadol produces its anti-nociceptive and analgesic effects via opioid and non-opioid mechanisms. The opioid component involves low affinity to μ -opioid receptors and the non-opioid component inhibits the reuptake of serotonin and norepinephrine neurotransmitters.

Initially this new opioid painkiller medication was introduced as having safe and low abuse liability and widely used throughout the world. However, after a while, it was revealed that this agent has significant risks when overdose occurs. Nowadays, tramadol abuse has become a common medical emergency.

An increasingly alarming phenomenon of tramadol drug abuse has been demonstrated in the Egyptian community in the last four years. Although the issue of drug abuse is not a newcomer to the Egyptian society, tramadol has been associated with a wide range of drug abuse and its illegal drug transactions had made it easily accessible and readily provided at cheap costs despite of its being a scheduled drug. The alleged usages of tramadol had also contributed greatly to its popularity and massive use especially among Egyptian youth.

This study was carried out on all patients with tramadol overdoses admitted to the Alexandria Poison Center and Intensive Care Unit (I.C.U.) at Alexandria Main University Hospital from 1/1/2012 to 30/6/2012 and from 1/10/2012 to 31/3/2013. It aimed to study the epidemiologic, clinical and laboratory patterns of tramadol over dosage among users. Also, determined the association between these patterns and patients' outcome.

In the present study, included a total of 122 patients, ranged between 18.0-40.0 years old among which (71.3%) were males and (28.7%) were females. The higher percentage of cases (61.5%) were having middle socioeconomic status while poor status was reported in (35.2%) and high standards were only seen in (3.3%). Most of them (81.1%) were living in city while patients representing (18.9%) were living in the village.

The major of the studied patients have psychiatric troubles (68.9%) as known by history taking and (94.3%) did not have any previous suicidal attempts.

Most of the studied cases (95.9%) were active smokers were (82.0%) do not drink alcohol. Seventy six percent of the studied individuals did not have any drug abuse.

Self medicated were found in most of the studied patients (97.5%) while only three individuals (2.5%) were using treatment as medically prescribed.

Non-toxic doses were detected in (63.9%) individuals, toxic doses were found in (33.6%) and fatal doses were reported in (2.5%). Accidental poisoning

was reported in most of the studied individuals (94.3%), while suicidal poisoning was found in cases (5.7%). Ingestion was reported as the only route of administration in all studied individuals. The majority of patients included in the study (82%) did not receive any prehospital management.

Disturbed consciousness level was found in most of the studied individuals (80.3%) while, (19.7%) of patients were fully conscious, Glasgow coma score ranged between 9.0-15.0, Pulse rate ranged between 56.0-149.0, Systolic blood pressure ranged between 110.0-140.0, Diastolic blood pressure ranged between 60.0-90.0, Temperature ranged between 36.60-37.80, Respiratory rate ranged between 16.0-28.0. Normal pupil size was seen in the majority of patients included in the study (91.8%), whereas constricted pupil was reported in (7.4%) and pinpoint pupil was met in only (0.8%).

Dizziness was reported in (44.3%) patients while (55.7%) of patients did not suffer from dizziness, Anxiety was detected in only (21.3%), Delirium was reported as complain in only (5.7%), Euphoria was represented in (58.2%) of the studied individuals, Confusion was detected in (66.4%), (57.4%) suffered from headache, Convulsion was reported in (22.1%), Slurred speech was detected in only (1.6%) and Coma was reported in (18.9%) of the studied group.

Precordial pain was only reported in (13.1%) of cases, (62.3%) complained of palpitation while no Syncope or cardiac arrest were not detected.

Dyspnea was detected in (32.8%) and Crepitations were found in only (6.6%). No Cough, Rhonchi or Stridor were detected.

Nausea was reported in (64.8%) of the studied group, Only (17.2%) patients out of the total suffered from vomiting and Abdominal colic was represented as a complain in (2.5%). Anorexia, Diarrhea and Constipation were not detected in any patient.

No Diaphoretic, skin, Cyanosis, Redness, Hotness, Coldness or Rash were detected in skin manifestations.

Dysuria, Oliguria, Anuria, Haematuria or Renal colic were not detected in genitourinary signs.

Urea level in blood ranged between 4.30-8.50, Creatinine level in blood ranged between 0.80-1.30 of Renal function. Random blood glucose level ranged between 80.0-120.0, Haemoglobin level ranged between 13.50-15.50, Haematocrit level ranged between 40.0-45.0, Red Blood Cells ranged between 4.50-5.70 million, Platelets count ranged between 151.000-446.000, Wight Blood Cells ranged between 4.0-10.40 million, Neutrophils ranged between 40.0-60.0, Lymphocytes ranged between 20.0-40.0, Eosinophils ranged between 1.0-4.0, Basophils ranged between 0.50-1.00. Liver function ALT ranged between 17.0-35.0, AST ranged between 19.0-35.0.

The heart rate was between 60 and 100 in (58%), whereas (40.2%) had the heart rate over 100 and only (1.6%) had it below 60 beats per minut. Regular rhythm were found in most of the studied patients (97.5%). Normal P-wave were found in the majority of the studied individuals (97.5%), while flattened p-wave was detected in (0.8%) and inverted p-wave was detected in (1.6%). Normal QRS-wave was reported in (65.6%) of patients, whereas (22.1%) had shortened

QRS-wave and (12.3%) had prolonged QRS-wave. normal ST segment were found in (98.4%) and normal PR interval were found in (65.6%). T-wave were found normal in the majority of the studied individuals (98.4%), while flattend T wave was detected in (1.6%). Normal ST segment was detected in (98.4%), while depressed ST segment was detected in (1.6%). PR interval were found normal (65.6%), wherears (22.1%) had shortened PR interval and (12.3%) had it prolonged.

Emesis was used for decontamination in (12.3%), gastric lavage was practiced in (85.2%), activated charcoal was used in (2.5%). IV fluids were administered in most of the studied individuals (96.7%). Oxygenation was needed in (89.3%) of the studied group. Mechanical ventilator was only required in (7.4%) of the studied group. Anticonvulsive therapy was required in (22.1%) of the studied patients. IV hydrocortisone was only used in (10.7%) of the studied samples. Sodium bicarbonate was included in the treatment of (11.5%) of the studied patients. Antidote usage was needed in only (22.1%) of the studied group.

Most of the studied samples (72.1%) required hospitalization for just one day, (22.1%) stayed for three days and (5.7%) stayed in hospital for two days.

On doing multivariate logistic regression analysis of predictor variables contributing to adverse outcome of tramadol overdose patients, it was found, age, smoking, illicit drugs use, self use of tramadol, poisonous amount dose and disturbed conscious state were the Predictors of adverse outcome of tramadol overdose.

CONCLUSIONS

1. The incidence of tramadol poisoning was found to be high rate in males than femals aged between 18-40 years old with middle socioeconomic status living in the city.
2. The present study showed that the majority of the patients have psychiatric troubles, smokers, do not drink alcohol, did not have any drug abuse and did not have any previous suicidal attempts. Self prescribed were found the most way to get tramadol.
3. The study has also thrown a light on vital signs and systemic presnetations which varies according th severity and doses taken by patients.
4. The major side effects found with this study were the neurological, gastrointestinal , cardiovascular and respiratory manifestations.
5. These manifestations include: anxiety, dizziness, confusion, convulsion, headache, euphoria, coma and nausea.
6. The present work shows that most of investigations done were within normal ranges.
7. In this study the line of treatment include gastric lavage, supportive treatment and use of antidote (narcen). Duration of hospitalization decided according to severity of manifestations.