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A Prospective Study of Poisoning Severity Score among Acute Antipsychotic Poisoned Cases Admitted to Menoufia Poison Control Center (MPCC) Throughout One Year

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Abstract **Introduction**: Antipsychotics rank in the top five substance classes involved in human exposures. Overdose of antipsychotic medications is common.
Aim of the work: to study antipsychotic drug poisoning cases that were admitted to MPCC during one year as regarding: socio demographic pattern, their clinical manifestation, investigation and outcome according to poisoning severity score (PSS). **Patients and Method:** Patients complaining of antipsychotic drug overdose admitted to MPCC from 1st October 2012 to 30th September 2013 were included. The socio-demographic and clinical data were collected from each patient in a designed clinical toxicological sheet. The studied cases were classified according to poisoning severity score. **Results:** The total patient's number was 60 patients. Females outnumbered males. Cases 33.3% below 10 years old were males, while females above 40 years old constituted 50.2%. Accidental poisoning was in males below age of 10 years from rural side, on the other hand 75% of females exposed to suicidal mode mainly from urban area. Regarding (PSS); most of cases were of moderate degree and the least were of severe and fatal degrees. Palpitation and abnormal movements were the commonest symptoms. Sinus tachycardia was the most prominent ECG changes seen in 20% of cases. ICU admission was indicated for 16.7% of cases. Improvement has occurred in 40% of cases, while only one case died. **Conclusion and Recommendation:** Significant relation was found between PSS and poison history as regard Co-ingestion and patients on antipsychotic therapy. Cases with moderate severity toxicity had palpation and abnormal movements. Acute antipsychotic overdose seldom results in death. Therefore it is recommended to improve awareness of physician about appropriate pharmacologic treatment of psychiatric problems.

Keywords Antipsychotics – toxicity- poisoning severity score.

Introduction

Major tranquilizer usually refers to antipsychotics (Ananth et al., 2004). Antipsychotics can abort specific psychotic symptoms without impairing intellectual ability and level of consciousness. In addition, they are referred to as neuroleptics because of the effective changes they induce, including decrease aggressive behavior and emotional liability (Kwiatkowsk, 2008).

Antipsychotic drugs were classified into first "typical" antipsychotics and second "Atypical" antipsychotics. The first-generation neuroleptic agents, also known as major tranquilizers, comprise a group of several classes of drugs (Butyrophenones, Dibenzoxazepines, Dihydroindolone, Diphenyl butylpiperidine, Phenothiazines, Thioxanthenes) (Haddad and Dursun, 2008).

Second "Atypical" antipsychotics the newer second-generation include Benzepines, Olanzapine, Quetiapienethe. (Shirzadi and Ghaemi, 2006). The newer atypical neuroleptics lack extrapyramidal effects as rigidity, tremor, bradykinesia, and akathesia which commonly occur with the first generation (Dubois, 2005).

Diagnose of antipsychotic overdoses can be through clinical manifestations symptoms and signs which include anticholinergic effects, extrapyramidal symptoms, neuroleptic malignant syndrome, seizures, and cardiac effects (Trenton et al., 2003).

Antipsychotic overdose toxidromes should be differentiated from other toxic and non toxic causes as rhabdomyolysis, status epilepticus, toxicity of anticholinergic, antidepressant, and antihistamine (Pacher and Kecskemeti, 2004).

Antipsychotics rank in the top five substance classes involved in human exposures (Correll et al., 2006). Overdose of antipsychotic medication is more common among psychiatric patients than other individuals, although unintentional ingestion by children is not uncommon (Gussow, 2012).

Aim of the Work

During the last few years, a large number of antipsychotic drug overdose cases were admitted to Menoufia Poison Control Center (MPCC) and the number of cases increases yearly so this work aims to study antipsychotic drug poisoning cases that were admitted to MPCC as regarding: socio demographic pattern, their clinical manifestation, investigation and outcome according to poisoning severity score.

Patients, Material and Methods

In this study, patients complaining of antipsychotic drug overdose admitted to MPCC from 1st October 2012 to 30th September 2013 were included. The study was carried out in an ethical manner following guidelines set by the Ethical Committee of Faculty of Medicine, Menoufia University. Informed valid consent was taken from the patients or from the patient's guardian and approval of head of MPCC before the study. Patients suffering from any systemic diseases and who didn't give informed consent were excluded from the study. The socio-demographic and clinical data were collected from each patient in a designed clinical toxicological sheet. Serum electrolytes, arterial blood gas, liver and kidney function tests, creatine phosphokinase (CPK) level were assessed. ECG was performed for each patient and was thoroughly analyzed. The studied cases were classified according to poisoning severity score. The clinical severity of poisoning was graded according to the method described by Persson et al., (1998) and developed by the International Program on Chemical Safety, the European Community, and the European Association of Poisons Centers and Clinical Toxicologists (IPCS/EC/EAPCCT) (Fruchtengarten, 2006). The poisoning severity score (PSS) is a four-scale grading as (0) none, (1) minor, (2) moderate, (3) severe, and (4) fatal. It was determined at the time of initial inquiry and following recovery, using examination findings including the Glasgow coma score, pupil size, convulsion, respiratory rate, pulse rate, blood pressure, body temperature, ECG findings, pain assessment, and laboratory presentations (serum glucose, potassium (K), sodium (Na), calcium (Ca), pH, and bicarbonate in arterial blood gases). The data collected were tabulated and analyzed by SPSS (statistical package for social science) version 17.0 on IBM compatible computer. Chi-square test (χ^2) was used to study association between two qualitative variables. P-value of < 0.05 was considered statistically significant (Elliott and Woodward, 2007).

Results

Sex differentiation in age groups demonstrated in table (1) where the relation between sex and different age groups was significant (P= 0.002). Females and males comprised (33.5%) and (25%) respectively in the age group 20-<40 years.

Table (2): Shows that there was highly significant relation between age and mode of poisoning as P= 0.000 and significant relation between gender and residence as regard to mode of poisoning where P = 0.03 and 0.04 respectively. All cases under 10 years had taken the drug accidentally (84.1%). The highest percent of cases committed suicide was in age group 20- < 40 (42.5%). Only one male case exposed to homicidal intake in age group 20-< 40 from urban area. Females and males constituted (77.5%) and (73.7%) for suicidal and accidental exposure respectively. The accidental mode was higher in rural side (89.5%) of cases. On the contrary, suicide was (75%) of cases from urban areas.

Table (3): shows that there was significant relation between PSS and co-ingestion, patients who were on psychic therapy and seasonal variation where P = 0.048, 0.004 and 0.003 respectively. Regarding co-ingestion, (60 %) of cases were of moderate severity grade while one case (100%) of fatal grade. Patients who were on psychic therapy and summer season predominance were (100%) of cases of severe and fatal grades for each one. Also there was no significant relation between PSS and drug type (typical and atypical), delay time of presentation and mode of exposure where P= 0.333, 0.082 and 0.786 respectively.

Table (4): Reveals significant relation between poisoning severity grades of the studied cases according to PSS and vomiting (P < 0.01), where vomiting was presented in (100%) of cases of fatal grade followed by (73%) and (60%) of cases were of minor and moderate grades respectively. Similar significant result was found with loss of consciousness, which it was of severe and fatal grades (100%) for each followed by (28%) of moderate severity grade. Regarding dizziness, it was represented minor and moderate grades (53.3%) and (8%) respectively. This relation was significant (P <0.01). Similar significant result (P <0.01) was found as regard convulsions where, severe and fatal severity grades were in (100%) of cases for each, while (48%) of cases were of moderate severity grade. Cases complained from palpitation (60 %) were of moderate grade. Abnormal movements represented moderate severity grade in (60%) of cases. All cases (100%) of the" none" grade of severity score had no complain. The relation between PSS and palpitation, abnormal movements and no complain was highly significant as P =0.00.

Table (5): Shows a highly significant relation between PSS and ICU admission (P= 0.000), where (100%) of cases were of both severe and fatal grades while (32%) of cases were of moderate grade. On the other hand, all of severe and fatal grades cases (100%) and (40%), and (6.6%) of cases of moderate and minor grades respectively needed emergency stabilization in

the form of supplemental oxygen, Coma Cocktail (Naloxon, Dextros, fluids and Thiamine) and intubation. The relation between PSS and emergency stabilization was significant as P =0.019.

Table (6): Shows there was significant relation between serum potassium level and poisoning severity grades of the patients (P= 0.002). Hypokalemia was in (100%) of cases of both severe and fatal grades, meanwhile it was (32%) and (6.7%) of moderate and minor grades respectively. There was no significant relation between PSS and serum Na, and Ca levels where (P= 0.449 and 0.575 respectively). As regards liver function tests, (100%) of severe grades cases, presented with elevated liver function tests followed by (38.9%), (26.7%), and (20%) in "none", minor and moderate grades respectively. On the other hand elevated renal function occurred in all severe and fatal severity grades cases. The relation was highly significant between PSS and liver and kidney function tests (P =0.001). Increased CPK level was in all cases of severe and fatal grades followed by (12%) of cases in moderate severity grade. The relation between PSS and CPK level was significant as (P= 0.05).

Frequency distribution of ECG changes among antipsychotic poisoned cases, ECG was normal in (66.6%) of cases, on the other hand sinus tachycardia, wide QRS and depressed ST segment were (20%), (6.6%) and (6.6%) respectively as shown in table (7) and graphs (1, 2).

Table (8): Shows there was a highly significant relation between PSS and ECG changes (P= 0.000), where (100%) of cases of both severe and fatal grades had sinus tachycardia and wide QRS respectively. Cases of moderate poisoning severity score had sinus tachycardia, prolonged QT and wide QRS (40%, 16% and 4%) respectively.

Table (9): Shows highly significant relation between poisoning severity grades and mode of treatment as regards activated charcoal and sedatives where P=0.000, all the studied cases of different poisoning grades received activated charcoal while 100% and 56% of severe and moderate poisoning grades respectively received sedatives. $NaHCO_3$ given to cases of severe, moderate and minor poisoning severity grades 100%, 48% and 26.7%, respectively. 100% of cases of severe and fatal PSS treated with vasopressor drugs. Cases of moderate poisoning severity grade 48% given Diphenhydramine. The relation between PSS and mode of treatment as regards to $NaHCO_3$, Vasopressor and Diphenhydramine was significant as P=0.005, 0.008 and 0.032 respectively.

Table (10): Shows that there was highly significant relation between poisoning severity grades and outcome of the patients (P= 0.000). Improvement occurred in (100%), (48%), (38.9%) and (26.7%) of severe, moderate, "none" and minor grades respectively. Only one case (100%) died who had fatal severity grade.

Table 1: Statistical Analysis Chi-square (χ^2) of gender of studied cases versus age (No=60).

	Gender of studied group No= 60					
Age in years	**Male No = 24**		**Female No = 36**		**Test of significance χ^2**	**P value**
	No	**%**	**No**	**%**		
< 5 yrs	5	20.8	6	16.7	19.11	0.002*
5 – < 10 yrs	3	12.5	2	5.4		
10 – < 20 yrs	5	20.8	10	27.7		
20 – < 40 yrs	6	25.0	12	33.5		
≥ 40yrs	5	20.8	6	16.7		

** P value <0.05 = significant, No= number of cases*

Table 2: Statistical Analysis Chi-square (χ^2) and Fisher's Exact Test of the mode of exposure in correlation to the age, gender and residence of the studied cases (No=60).

	Mode of exposure No=60						**Test of significance**	**P- value**
	Accidental No=19		**Suicidal No=40**		**Homicidal No=1**			
	No	**%**	**No.**	**%**	**No.**	**%**		
Age								
< 5 years	11	57.8	0	0	0	0	χ^2 25.283	0.000 **
5 – < 10 years	5	26.3	0	0	0	0		
10 – < 20 years	2	10.6	13	32.5	0	0		
20 – < 40 years	0	0	17	42.5	1	100		
≥ 40 years	1	5.3	10	25.0	0	0		
Gender								
Male	14	73.7	9	22.5	1	100	Fisher's Exact test 2.297	0.03*
Female	5	26.3	31	77.5	0	0		
Residence								
Rural	17	89.5	10	25.0	0	0	χ^2 10.76	0.04*
Urban	2	10.5	30	75.0	1	100		

** P value <0.05 = significant, ** P value <0.001 = highly significant,No= number of cases*

Table 3: Statistical Analysis Chi-square (χ^2) of the relation between poison history and poisoning severity grades of the studied cases according to PSS (No=60).

Poison history	Poisoning Severity Score No=60										Test of significance χ^2	P value
	None No = 18		Minor No = 15		Moderate No = 25		Severe No = 1		Fatal No = 1			
	No	%	No	%	No	%	No	%	No	%		
Drug type												
Typical	4	22.2	3	20.0	9	36.0	1	100.0	1	100.0	6.328	0.333
Atypical	14	77.8	12	80.0	16	64.0	0	0	0	0		
Co- ingestion												
Yes	8	44.4	8	53.3	15	60.0	0	0	1	100.0	3.036	0.048*
No	10	55.6	7	46.7	10	40.0	1	100.0	0	0		
Delay of presentation												0.082
< 1 hr	3	16.7	2	13.3	0	0	0	0	0	0	4.582	
≥ 1 hr	15	83.3	13	86.7	25	100.0	1	100.0	1	100.0		
Mode of exposure												0.786
Accidental	5	27.8	2	13.3	5	20.0	0	0	0	0	4.498	
Suicidal	13	72.2	12	80.0	20	80.0	1	100.0	1	100.0		
Homicidal	0	0	1	6.7	0	0	0	0	0	0		
On antipsychotic therapy											7.947	0.004*
Yes	6	33.3	3	20.0	4	16.0	1	100.0	1	100.0		
No	12	66.7	12	80.0	21	84.0	0	0	0	0		
Season												
Summer	10	55.6	6	40.0	11	44.0	1	100.0	1	100.0		
Spring	2	11.1	4	26.7	6	24.0	0	0	0	0	10.98	0.003*
Autumn	2	11.1	3	20.0	6	24.0	0	0	0	0		
Winter	4	22.2	2	13.3	2	8.0	0	0	0	0		

** P value <0.05 = significant P value >0.05 = non significant No= number of cases*

Table 4: Statistical Analysis Chi-square (χ^2) of the relation between clinical manifestations and poisoning severity grades of the studied cases according to PSS (No=60).

Clinical manifestations	Poisoning Severity Score, No=60										Test of significance χ^2	P value
	None		minor		Moderate		Severe		Fatal			
	No=18	%	No=15	%	No=25	%	No=1	%	No=1	%		
Vomiting												
Yes	1	5.6	11	73.3	15	60.0	0	0	1	100	20.3	<0.01*
No	17	94.4	4	26.7	10	40.0	1	100	0	0		
Loss of consciousness												
Yes	0	0	1	6.7	7	28.0	1	100	1	100	16.992	<0.01*
No	18	100	14	93.3	18	72.0	0	0	0	0		
Dizziness												
Yes	0	0	8	53.3	2	8.0	0	0	0	0	19.872	<0.01*
No	18	100	7	46.7	23	92.0	1	100	1	100		
Convulsions												
Yes	0	0	0	0	12	48.0	1	100	1	100	25.118	<0.01*
No	18	100	15	100	13	52.0	0	0	0	0		
Palpitations												
Yes	0	0	0	0	15	60.0	0	0	0	0	28.0	0.00**
No	18	100	15	100	10	40.0	1	100	1	100		
Abnormal movements											28.0	
Yes	0	0	0	0	15	60.0	0	0	0	0		0.00**
No	18	100	15	100	10	40.0	1	100	1	100		
No complaint												
Yes	18	100	1	6.7	0	0	0	0	0	0	55.68	0.00**
No	0	0	14	93.3	25	100	1	100	1	100		

**P value <0.05 = significant, ** P value <0.001 = highly significant P value >0.05 = non significant, No= cases number*

Table 5: Statistical Analysis Chi-square (χ^2) of the relation between poisoning severity grades in the studied cases according to PSS and their need for ICU admission and emergency stabilization.

	Poisoning severity score No=60										Test of significance χ^2	P value
	None No = 18		Minor No = 15		Moderate No = 25		Severe No=1		Fatal No=1			
	No	%	No	%	No	%	No	%	No	%		
ICU admission												
Yes	0	0	0	0	8	32.0	1	100.0	1	100.0	20.832	0.000**
No	18	100.0	15	100.0	17	68.0	0	0	0	0		
Emergency stabilization												
Yes	0	0	1	6.6	10	40.0	1	100.0	1	100.0	11.761	0.019*
No	18	100.0	14	94.4	15	60.0	0	0	0	0		

** P value <0.05 = significant ** P value <0.001 = highly significant No= number of* cases

Table 6: Statistical Analysis Chi-square (χ^2) of the relation between poisoning severity grades in the studied cases according to PSS and laboratory investigations (No=60).

Laboratory investigations	Poisoning severity score No=60										Test of significance χ^2	P value
	None No = 18		Minor No = 15		Moderate No = 25		Severe No = 1		Fatal No = 1			
	No	%	No	%	No	%	No	%	No	%		
Na												
Hyponatremia	0	0	0	0	3	12.0	1	100.0	1	100.0	26.987	0. 449
Hypernatremia	0	0	0	0	1	4.0	0	0	0	0		
Normal	18	100.0	15	100.0	21	84.0	0	0	0	0		
K												
Hypokalemia	0	0	1	6.7	8	32.0	1	100.0	1	100.0	17.432	0.002*
Normal	18	100.0	14	93.3	17	68.0	0	0	0	0		
Ca												
Hypocalcemia	0	0	0	0	2	8.0	0	0	0	0		
Normal	18	100.0	15	100.0	23	92.0	1	100.0	1	100.0	2.897	0.575
Liver function tests												
Increased	7	38.9	4	26.7	5	20.0	1	100.0	0	0		
Decreased	0	0	0	0	0	0	0	0	0	0	7.844	0.001**
Normal	11	61.1	10	73.3	20	80.0	0	0	1	100.0		
Kidney function test												
Elevated	2	11.1	0	0	2	8.0	1	100.0	1	100.0	19.802	0.001**
Normal	16	88.9	15	100.0	23	92.0	0	0	0	0		
CPK												
Normal	18	100.0	15	100.0	22	88.0	0	0	0	0	30.207	0.05*
Increased	0	0	0	0	3	12.0	1	100.0	1	100.0		

** P value <0.05 = significant, ** P value <0.001 = highly significant P value >0.05 = non-significant No= cases number*

Table 7: Frequency distribution of ECG changes of the studied cases (No=60).

ECG changes	No.	%
Normal	40	66.6
Wide QRS	4	6.7
Depressed ST segment	4	6.7
Sinus tachycardia	12	20.0
Total	60	100.0

Table 8: Statistical Analysis Chi-square (χ^2) of the relation between poisoning severity grades in the studied cases according to PSS and ECG changes (No=60).

ECG changes	Poisoning Severity Score No=60										Test of significance χ^2	P value
	None No = 18		Minor No = 15		Moderate No = 25		Severe No = 1		Fatal No = 1			
	No	%	No	%	No	%	No	%	No	%		
Normal	18	100.0	12	80.0	10	40.0	0	0	0	0	51.431	0.000**
Wide QRS	0	0	2	13.3	1	4.0	0	0	1	100.0		
Prolonged QT	0	0	0	0	4	16.0	0	0	0	0		
Sinus tachycardia	0	0	1	6.7	10	40.0	1	100.0	0	0		

*** P value <0.001 = highly significant No= number of cases*

Table 9: Statistical Analysis Chi-square (χ^2) of the relation between poisoning severity grades in the studied cases according to PSS and mode of treatment (No=60).

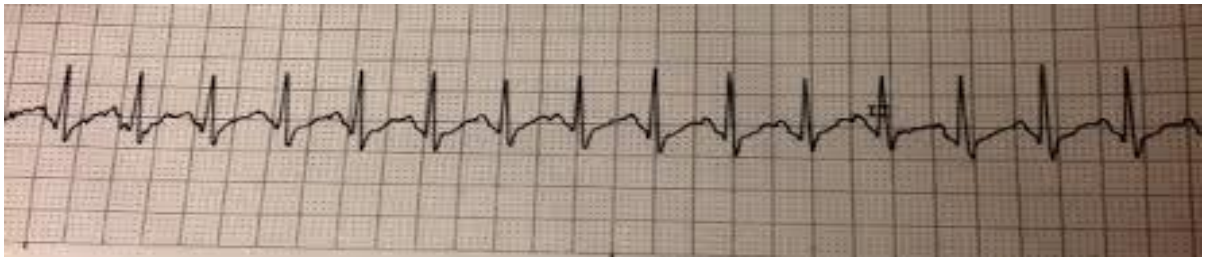
Mode of treatment	Poisoning severity score No=60										Test of significance χ^2	P value
	None No = 18		Minor No = 15		Moderate No = 25		Severe No = 1		Fatal No = 1			
	No	%	No	%	No	%	No	%	No	%		
Activated charcoal												
Yes	18	100.0	15	100.0	25	100.0	1	100.0	0	0	60.000	0.000**
No	0	0	0	0	0	0	0	0	1	100.0		
Sodium bicarbonate ($NaHCO_3$)											14.824	0.005*
Yes	0	0	4	26.7	12	48.0	1	100.0	0	0		
No	18	100.0	11	73.3	13	52.0	0	0	1	100.0		
Vasopressors												
Yes	2	11.1	1	6.7	3	12.0	1	100.0	1	100.0	13.692	0.008*
No	16	88.9	14	93.3	22	88.0	0	0	0	0		
Sedatives												
Yes	1	5.6	1	6.7	14	56.0	1	100.0	0	0	4.0	0.000**
No	17	94.4	14	93.3	11	44.0	0	0	1	100.0		
Diphenhydramine												
Yes	3	16.7	1	6.7	12	48.0	0	0	0	0	10.534	0.032*
No	15	83.3	14	93.3	13	52.0	1	100.0	1	100.0		

** P value <0.05 = significant,** P value <0.001 = highly significant, No= number of cases*

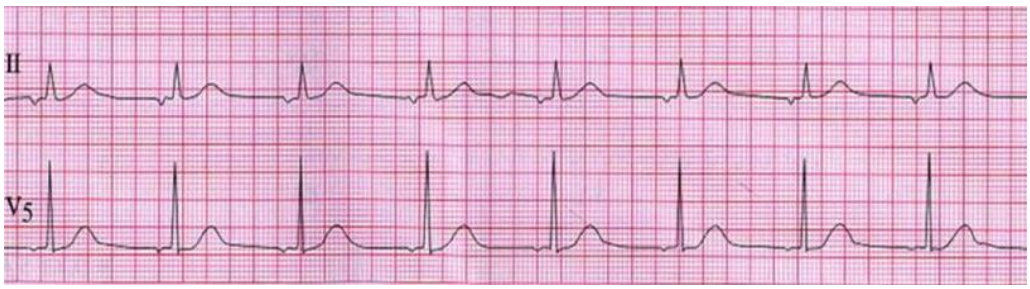
Table 10: Statistical Analysis Chi-square (χ^2) of the relation between poisoning severity grades in the studied cases according to PSS and outcome (No=60).

Outcome	Poisoning severity score, No=60										Test of significance χ^2	P value
	None No = 18		Minor No = 15		Moderate No = 25		Severe No=1		Fatal No=1			
	No	%	No	%	No	%	No	%	No	%		
Improved	7	38.9	4	26.7	12	48.0	1	100.0	0	0	65.848	0.000**
Discharged on request	7	38.9	5	33.3	4	16.0	0	0	0	0		
escaped	4	22.2	6	40.0	9	36.0	0	0	0	0		
dead	0	0	0	0	0	0	0	0	1	100.0		

***P value <0.001 = highly significant No= number of cases.*



Graph 1: ECG strip showing sinus tachycardia: heart rate is 128/min and regular in Clozapine overdose.



Graph 2: ECG strip showing wide QRS complex (0.14 s) in a case of Haloperidol overdose (normal QRS complex is <3 small squares i.e. <0.12 s).

Discussion

Poisoning occurs in all regions and countries and represents a leading cause of death in some countries (Bohnert et al., 2010).

Drug overdose is one of the easiest methods of attempting suicide, which is one of the major health problems world-wide (Aslan et al., 2011).

Poisoning due to medical drugs is a major problem in children as well as adults (Arokiasamy, 1994). The study showed that females outnumbered males. This result agreed with Doshi et al., (2005) who found that female to male ratio was 1.7:1.3. On the contrary to this study Soueif, (1994) found that poisoning was more common among males than females to cope with psychosocial problems or difficult working conditions, as well as at times of studying and examinations. Adejuyigbe et al., (2002) also found that poisoning was more common among males than females.

Males and females comprised the predominance of age group 20-<40 years. This coincides with Batra et al., (2003) who stated that the most affected age group in their study in rural India was 21-30 years, followed by group 31-40 years. Gupta and Vaghela (2005) stated that maximum cases of poisoning in Jamnagar, India belonged to second and third decades of life.

The majority of cases under 10 years old had taken the overdose accidentally it could be due to that this age has increased activities and skills causing more exposure to their environment (Kliegman et al., 2008). Gupta et al., (2003) stated that children lack discrimination between harmful and non harmful things. Infants and small children are closer to the ground than older children; in addition, children have a natural exploratory curiosity and put everything in their mouth. Predominance of males in accidental poisoning due to that males are more active and tend to have more exploratory character than females in childhood (Malangu, 2008).

The results showed that the suicidal mode of poisoning was (66.6%) of cases. The majority of cases were females (75%). These results agreed with Garg and Verma, (2010) who stated that suicidal mode was the most common mode of acute intoxication. Yasan et al., (2008) found that higher suicide attempt rates were observed in females compared to the males. Suicidal attempts in antipsychotic overdose cases can be explained by the presence of depressive symptoms including depressed mood and hopelessness, stressful life events , divorce, separation and presence of delusions and/or auditory hallucinations (Bouhlel et al ., 2012). Other reported reasons of suicide attempts were impulsive suicides which are generally motivated by anger, the desire to get even, the wish to frighten or punish others, or the need to avoid intense shame subsequent to economic crisis, examination failure, love failure, quarrels, or unemployment, and chronic illness (Aslan et al., 2011). In the current study there was only one homicidal case it was for a father in the third decade from urban area was given (risperidal) in his tea by his daughter.

Accidental poisoning was higher in rural areas (89.5%), while suicidal poisoning was found more in urban areas (75%). This result was in accordance with the results reported by Cahfer and Ismail, (2004); Anthony and Kulkarni, (2012). Rural nature of Menoufia governorate and low socioeconomic standards associated with low levels of education and culture, easy availability, extensive use and low cost of the drugs, all make the population more vulnerable for accidental poisoning. The same result was reported by Garg and Verma, (2010). This was against Manzar et al., (2010) who reported that persons in urban areas are more exposed than those in rural areas due to mothers are workers leading to neglect of child.

The results revealed that there was significant relation between severity grades of the studied cases according to PSS and co-ingestion of drugs with antipsychotics. This coincided with Olson (2012) who stated that it is not uncommon for patients to take multiple psychiatric medications and toxicity of antipsychotic medications may be increased by co-ingestion of other agents, particularly drugs with similar metabolic pathways such as lithium, cyclic or other antidepressants and benzodiazepines.

Also there was significant relation between PSS and patients who were on psychic therapy. This result was in accordance with Aslan et al., (2011) who found that (22.5%) of the patients had previous visits to the psychiatry outpatient clinics prior to the admission to the emergency department for intoxication.

Summer represented the commonest season for antipsychotic overdose cases. The rate of cases is higher during summer due to the results of end year examinations appear for secondary schools and universities and suicidal attempts increase due to failure of examinations for fearing of guilt or to escape punishment. Also children on summer holidays are

more likely to be outdoors or to be left at home unattended or in the care of an older child or elderly relatives (Adejuyigbe et al., 2002). This result was in accordance with that published by Oguche et al., (2007) as they stated that highest frequency of admission was recorded during hot and dry months of March to June.

Concerning clinical manifestations, the results revealed vomiting was evident in (100%) of fatal severity grade cases followed by (73%) in minor grade cases. Vomiting can be explained by the anticholinergic effects of antipsychotics (Lackey, 2012). Cases of loss of consciousness were of severe and fatal grades followed by (28%) of cases of moderate grade. This could be explained by the centrally mediated sedation and diminished cerebral perfusion secondary to systemic hypotension and anticholinergic effects contributed to CNS depression caused by antipsychotics (Lackey, 2012). Kwiatkowsk, (2008) stated that mental state changes were the most common manifestation in antipsychotic overdose. Impaired consciousness is a common and dose dependent feature of antipsychotic overdose, ranging from somnolence to frank coma. Concerning dizziness, it was evident in minor grade cases (53.3%) followed by moderate grade cases (8%). Hoffman et al., (2007) found that drowsiness and dizziness were the most common clinical features. Also blockage of peripheral α1 adrenergic leads to decreased vasomotor tone and accounts for it.

Convulsions were found in (100%) of severe and fatal grades and (48%) for moderate grade. Levine and Ruha, (2012) stated that the typical and atypical antipsychotics have the ability to lower seizure threshold. As regard palpitation, it was presented in (60%) of moderate grade cases. Palpitation may reflect the anti cholinergic effect of the drug and reflex tachycardia can be due to hypotension, patient's pain and anxiety (Minns and Clark, 2012).

Abnormal movements were found in (60%) of moderate grade cases. Levine and Ruha, (2012) reported that Extrapyramidal syndromes can occur with either typical or atypical antipsychotics. Patients who had no complaints were recorded in (100%) of "none" grade cases. This was in accordance with Zakaria et al., (2012) who reported that although overdose and poisoning by antipsychotics are common, most cases with pure overdose manifest no symptoms or only mild toxicity. This finding can be explained by allegation of taking the drug or the patients come within one hour of ingestion or the parents may doubt their children taking the drug and they bring them for assurance or the patients may had induced vomiting by parents, friend or one of their relatives.

In the present study, cases admitted to ICU were of the severe and fatal grades (100%) and (32%) of moderate grade. These cases had one or more of the clinical criteria for ICU admission in poisoned patients; these criteria are: PCO2 >45 mmHg., need for emergency intubation, the presence of post ingestion seizures, unresponsiveness to verbal stimuli, a non-sinus cardiac rhythm, second- or third-degree AV block, systolic blood pressure less than 80 mmHg, or QRS duration ≥ 0.12 S (Steven, 2006). Regarding the need for emergency stabilization, the study showed that all severe and fatal grades cases and (40%) of moderate grade needed emergency stabilization. Hoffman et al., (2007) stated that indication of emergency stabilization in the form of supplemental oxygen should be administered if hypoxia is present, and patients with altered mental status should receive thiamine, naloxone, and parenteral dextrose as needed. Intubation and ventilation are rarely required, but may be necessary for patients with very large overdoses of antipsychotics or ingestion of other CNS depressants.

The results showed that (100%) of cases of severe and fatal grades toxicity had hypokalemia. Alfonzo et al., (2006) stated that potassium disorders are common and may precipitate cardiac arrhythmias or cardiopulmonary arrest. Liver functions levels were elevated in (100%), (26.7%), and (20.0%) of severe, minor and moderate grades toxicity cases respectively. This was due to co-ingested drugs such as acetaminophen, benzodizapines and antidepressants. This is in accordance with Pratt and Kaplan, (2000). Elevation of renal functions levels in (10%) from all studied cases in this study could be explained by the fact that elder population on antipsychotics was susceptible to diminished renal function; thus having high intoxication risk. The results showed that increased CPK level in all cases of severe and fatal toxicity grades and in (12 %) of cases of moderate grade. This is in agreement with Saltik and Basgul, (2012) who reported that numerous cases of Neuro Malignant Syndrome (NMS) have been reported with atypical antipsychotic medications including clozapine, olanzapine, quetiapine, and risperidone in recent years. On contrary to Strawn et al., (2007) ; Seitz and Gill, (2009) reported that NMS most often associated with typical high-potency neuroleptics e.g. haloperidol, fluphenazine.

The results showed that the frequency of ECG changes of studied cases was sinus tachycardia (20%) followed by wide QRS and prolonged QT and depressed ST segment (6.7%) for each. This result was in agreement with Minns and Clark, (2012) who reported that the most common cardiovascular effects that occur after atypical antipsychotic overdose are tachycardia, mild hypotension, and prolongation of the QT interval. There was a highly significant relation between PSS and ECG changes, Zareba and Lin, (2003) stated that the risk of QT prolongation and resultant torsades de pointes is dose dependent and slightly increased in overdose. The study showed that all the studied cases received activated charcoal, Vernon and Gleich, (1997) reported that activated charcoal remains the gastrointestinal decontamination method of choice. Repeated doses of activated charcoal every 6 hours without cathartics may increase clearance of some neuroleptics that undergo enterohepatic circulation (Bond, 2002). Sedatives were used in 28.3% of cases to control convulsions, this in accordance with Wills and Erickson, (2005) who stated that multiple or refractory seizures can be treated with benzodiazepines. The cardiotoxic effects of antipsychotic were treated with sodium biocarbonate in

28.3% of cases. Its efficacy has been attributed to counteracting the sodium channel blockade. Serum alkalization favors dissociation of the drug from myocardial Na+ channels and the extra cellular Na+ load improves Na+ channel function (Alkatib et al., 2003). Vasopressors were used in 13.3% of cases who sustained hypotensive and manifested with signs of cardiogenic shock. Vasoconstrictor agents stimulate beta1- and alpha-adrenergic receptors, which, in turn increases cardiac muscle contractility, heart rate, and vasoconstriction. As a result, systemic blood pressure and coronary blood-flow increases (Shy and Rund 2011). Cases (26.7%) were treated with Diphenhydramine, anticholinergic medications help restore balance between dopaminergic and cholinergic neurotransmission (Goldfrank et al., 2007).

The study showed that mortality is relatively rare with overdose of antipsychotic medication as it was (1.6%) of total number of cases. This concurred with the result of Huybrechts et al., (2012) who reported that ingestions fatalities remain quite uncommon, with a case fatality rate of approximately 0.02% of all reported exposures because of the high toxic-therapeutic ratio.

Conclusion

Significant relation was found between PSS and poison history as regard co-ingestion and patients on antipsychotic therapy. Cases with moderate severity toxicity had palpation and abnormal movements. Acute antipsychotic overdose seldom results in death.

Recommendation

Increasing physician awareness regarding appropriate pharmacologic treatment of psychiatric problems and patient education about the benefits and possible side effects of antipsychotic medication.

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الملخص العربى

دراسة مستقبلية لمقياس خطورة السمية في حالات التسمم بمضادات الذهان التي ادخلت مركز علاج السموم بجامعة المنوفية خلال عام

سامي عبد الهادي حماد و نيرة فهمي جرجس وصفاء عبد الظاهر أمين و عزة وجيه زناتي و هايدي مصطفى ابو حطب[1]

المقدمة: تصنف مضادات الذهان من أكثر خمس مواد يتعرض لها الإنسان. من الشائع زيادة جرعة أدوية مضادات الذهان.

الهدف من البحث: دراسة حالات التسمم بمضادات الذهان الواردة الى مركز السموم بجامعة المنوفية من حيث النمط الديموجرافي الإجتماعي, الأعراض الإكلينكية, الفحوصات, والنتيجة وعلاقة ذلك بدرجة خطورة السمية.

المرضى و الطريقة: شملت الدراسة المرضى المصابون بجرعة زائدة من دواء مضاد الذهان و الواردة إلى مركز علاج السموم بجامعة المنوفية في الفترة من أول أكتوبر ٢٠١٢ إلى ٣٠ سبتمبر ٢٠١٣. تم جمع البيانات الخاصة لكل مريض في استمارة خاصة بالسموم من حيث البيانات الديموجرافية الإجتماعية و الإكلينكية. تم تقسيم الحالات بالنسبة لدرجة خطورة السمية.

النتائج: شملت الدراسة ستون مريضا. فاق عدد الإناث عدد الذكور. كانت الحالات الأقل عمرا من عشر سنين (٣٣،٣%) من الذكور بينما الأكثر عمرا من أربعين من الإناث (٥٠،٢%). كان التسمم العرضي في الذكور في الفئة العمرية أقل من عشر سنين من المناطق الريفية بينما تعرض (٧٥%) من الإناث من الحضر الى تسمم انتحاري . بالنسبة لدرجة خطورة السمية فإن أغلب الحالات كانت من الدرجة المتوسطة الخطورة و الأقل من الدرجات الخطيرة و المميتة. وجد أن خفقان القلب و الحركات الغير طبيعية من أكثر الأعراض شيوعا. وجد أن الزيادة في سرعة ضربات القلب من أكثر التغيرات في رسم القلب الكهربائي (٢٠%) من الحالات. وجد أن (١٦،٧%) من الحالات دخلت العناية المركزة . تحسنت (٤٠%) من الحالات بينما توفيت حالة واحدة فقط.

الخلاصة و التوصية: وجدت علاقة ذو دلالة بين درجة خطورة السمية و تعاطي أدوية أخري وكذلك المرضى االمعالجون بمضادات الذهان. وجد أن خفقان القلب و الحركات الغير طبيعية كانت في الحالات متوسطة خطورة السمية و أن التسمم الحاد بمضادات الذهان نادرا مايسبب الوفاة . ولذلك نوصي بتوعية الأطباء بوصف الدواء المناسب لعلاج المشاكل النفسية.

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