

COMPARISON BETWEEN THE MANAGEMENT AND OUTCOME OF TYPICAL AND ATYPICAL ANTIPSYCHOTIC DRUGS OVERDOSE: A STUDY FROM THE NATIONAL ENVIRONMENTAL AND CLINICAL TOXICOLOGY RESEARCH CENTRE, CAIRO UNIVERSITY HOSPITAL

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Submit Date 2022-11-28.

Revise Date 2023-03-25.

Accept Date 2023-03-25.

ABSTRACT

Objectives: The purpose of this study was to compare between the management and the outcome of typical and atypical antipsychotic drugs overdose in Egypt. **Methodology:** This study was conducted on 75 cases presented to National Environmental and Clinical Toxicology research Centre, Cairo university hospitals with antipsychotic medications toxicity, from April 2018 to September 2018. **Results:** The most common presenting age group was age group B; from 18-40 years (45.3%), females (68%), belonging to urban population (82.7%), educated (96.2%) and not working (89.3%). The majority of cases presented with abnormal CNS manifestation; altered conscious level (97.3%), abnormal pulse; tachycardia (98.7%) and abnormal pupil size; mydriasis or miosis (52%). Most of the cases did not do drug screening (98.7%), neither do decontamination (66.7%) nor receive antidote (100%), but most of them received supportive measures. Most of the cases were admitted (90.7%) and stayed in hospital more than 24 hours and less than one week. Regarding the outcome, most of the cases were cured (92.6%).

Keywords: Typical, Atypical, Antipsychotic, Toxicity, management, Outcome.

INTRODUCTION

Acute poisoning after accidental or intentional ingestion of drug overdose can lead to a high degree of mortality, morbidity and health care cost worldwide (Bulut et al., 2022). Drug overdoses can affect all age groups. The majority of paediatric overdoses are accidental, while that occurring in adolescents are mainly intentional (Azab et al., 2016).

Psychotropic medications are group of medications that include antipsychotics, sedatives, antidepressants, mood stabilizers and attention deficit hyperactivity disorder medications (Solmi et al., 2020).

The first generation of antipsychotic medications was introduced in the 1950s. Before 1990s, antipsychotics were used mainly for adults suffering of severe psychotic disorders. Then, the newer atypical antipsychotics, considered as safer than typical antipsychotics, have changed the landscape of antipsychotic treatment. (Crystal et al., 2009).

Second-generation (atypical) antipsychotics are also effective in the treatment of psychosis. They have less extrapyramidal side effects if taken in therapeutic doses as dystonia, akathisia, parkinsonism, and tardive dyskinesia (Abu-Naser et al., 2021). They are now considered to be the first-line of treatment in cases of schizophrenia in both adults and children, including tic disorders, bipolar disorders, autism, eating disorders and obsessive compulsive disorder (Pedrelli et al., 2015).

Antipsychotics overdose is common in Western society. In 2010, poison control centers in the US received about 43 000 calls complaining of atypical antipsychotics overdose (Evoy et al., 2021). The actual incidence of atypical antipsychotics overdose is greater than announced, due to underreporting. Overdose of an atypical antipsychotic is presented clinically with multiple disorders as

CNS depression, tachycardia and orthostatic hypotension (Van Alphen et al., 2022).

Supportive measures as maintaining patent airway, assessment of breathing, maintaining adequate circulation are necessary before confirmation of intoxication (Mokhlesi et al., 2003). Evaluation and management of antipsychotic drugs toxicities needs high level of suspicion, careful history taking, proper examination, and investigations to improve the outcome of such patients (Rasimas et al., 2012).

The purpose of our study was to compare between the management and the outcome of typical and atypical antipsychotic drugs overdose in Egypt.

SUBJECTS & METHODS

The study was a descriptive prospective study including 75 cases presented to National Environmental and Clinical Toxicology research Centre, Cairo university hospitals from April 2018 to September 2018. Data were analyzed with respect to socio-demographic data, types of drugs, clinical presentations, management, admission rate and outcome. Coding system was used to maintain privacy and confidentiality of data and records.

Inclusion criteria:

Patients of all ages and all sexes, who presented to the National Environmental and Clinical Toxicology Research Centre with a history and/or clinical manifestations of antipsychotic drug overdose or toxicity.

Exclusion criteria:

Patients with any pre-existing chronic diseases such as diabetes, cardiac and hepatic. Also, patients with mixed drug ingestion and those who received medical treatment before admission were excluded.

Diagnosis:

Antipsychotic medications poisoning was diagnosed by history taking and/or manifestations of toxicity. A standard sheet was done for each patient including socio-demographic data (age, sex, residence, education and work), clinical manifestations, drug screening, supportive measures, GIT decontamination, specific antidote, admission rate, period of stay and outcome. Patients were divided into 3 age groups: group A; less than 18 years, group B; from 18-40 years and group C more than 40 years. Complete clinical examination was recorded including assessment of level of consciousness by Glasgow coma scale (GCS), vital signs (heart rate, blood pressure, temperature and respiratory rate), general examination and systemic examination. Also drug screening was done for all patients.

RESULTS

Seventy five (75) patients presenting with antipsychotic drugs overdose were included in our study. Antipsychotics drugs category among the studied cases, were divided into 14 cases with typical antipsychotics overdose (18.7%) and 61 cases with atypical antipsychotics overdose (81.3%) as shown in figure (1).

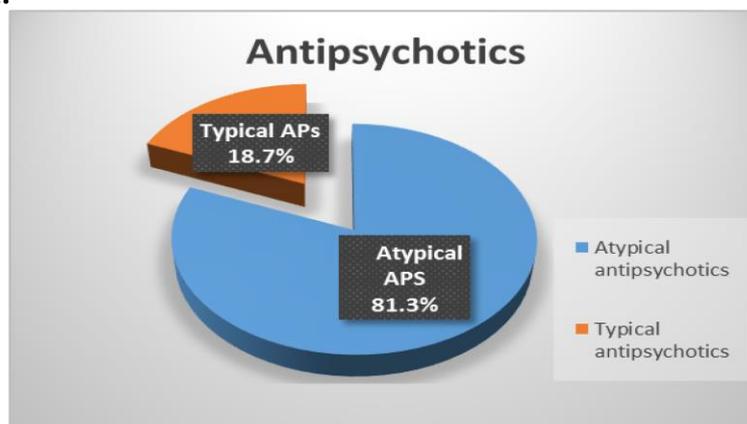


Figure (1): Antipsychotic category among the studied cases

The majority of typical antipsychotics cases are age group A (less than 18 years) 64.3%, females (71.4%), belongs to urban population (71.4%) and with no work (100%), while the majority of atypical antipsychotics cases are age group B (18-40 years) (49.2%),

females (67.2%), belongs to urban population (82.2%) and with no work (86.9%). As shown in Table 1. This means that this table shows non-significant relation between types of antipsychotics and age groups (p 0.237), sex (p 0.76), residence (p 0.218) and work (p 0.152).

Table (1): Comparison between types of antipsychotics regarding age, sex, residence and work.

		Typical antipsychotic (n=14)		Atypical antipsychotics (n=61)		P value
		Count	%	Count	%	
Age group	Group A	9	64.3%	24	39.3%	0.237
	Group B	4	28.6%	30	49.2%	
	Group C	1	7.1%	7	11.5%	
Sex	Female	10	71.4%	41	67.2%	0.76
	Male	4	28.6%	20	32.8%	
Residence	Urban	10	71.4%	52	85.2%	0.218
	Rural	4	28.6%	9	14.8%	
Work	No	14	100.0%	53	86.9%	0.152
	Yes	0	0.0%	8	13.1%	

*n: number, P-value < 0.05 is statistically significant.

Regarding the clinical manifestations of cases in the present study, all typical antipsychotics (100%), and most atypical antipsychotics (98.4%, 90.2%) cases did not show any GIT manifestations as (nausea, vomiting or change on bowel habits) and respiratory manifestations as abnormal breathing or saturation respectively. Most typical antipsychotic cases (85.7%, 92.9%) and atypical antipsychotic cases (68.9%, 91.8%) did not show abnormalities in blood pressure as (hypotension and temperature) and fever respectively. On the other hand, the majority of typical (100%, 100%) and atypical (96.7%, 98.4%) antipsychotics cases presented with abnormal CNS manifestation in the form of

disturbed conscious level or drowsiness and abnormal pulse in the form of tachycardia. Also, the majority of typical (71.4%) antipsychotics cases presented with constricted pupils, while the majority of atypical (52.5%) antipsychotics cases presented with normal pupils.

This is shown in **Table 2**, concluding that there was non-significant relation between types of Antipsychotics and vital signs (pulse, blood pressure, temperature) with non-significant p values (p 1, p 0.324, p 1) respectively. There was also non-significant relation between types of antipsychotics and (pupil, GIT, respiratory and CNS manifestations) with non-significant p values (p 0.107, p 1, p 0.755, p 0.682) respectively.

Table (2): Comparison between types of antipsychotics regarding clinical manifestations among studied cases (n=75).

		Typical antipsychotics (n=14)		Atypical antipsychotics(n=61)		P value	
		Count	%	Count	%		
GIT manifestations	No	14	100%	60	98.4%	1	
	Yes	0	0%	1	1.6%		
Respiration	Normal	14	100%	55	90.2%	0.755	
	Abnormal	0	0%	6	8.8%		
CNS manifestation	Normal	0	0%	2	3.3%	0.682	
	DCL	9	64.3%	35	57.4%		
	Drowsy	5	35.7%	24	39.3		
Vital signs	Pulse	Normal	0	0%	1	1.6%	1
		Tachycardia	14	100%	60	98.4 %	
	Blood pressure	Hypotension	2	14.3%	19	31.1%	0.324
		Normal	12	85.7%	42	68.9%	
	Temperature	Fever	1	7.1%	5	8.2%	1
Normal		13	92.9%	56	91.8%		
Pupils	Constricted	10	71.4%	29	47.5%	0.107	
	Normal	4	28.6%	32	52.5%		

*GIT: Gastrointestinal tract, *CNS: Central nervous system, *DCL: disturbed conscious level, *n: number, P-value < 0.05 is statistically significant.

Table 3 shows comparison between types of antipsychotics regarding investigations and drug level. The majority of typical (100%) and atypical (98.4%) antipsychotic drugs overdose shows sinus tachycardia in the ECG. Minority of the typical (14.3%, 28.5%) and atypical (1.7%, 3.3%) antipsychotic drugs overdose cases show metabolic acidosis and respiratory acidosis

respectively. All the typical (100%) and most of the atypical (98.4%) antipsychotic drugs overdose did not do drug screening. As a conclusion, there is non-significant relation between types of antipsychotics with ECG and drug screening with non-significant p value (p 0.63, p 0.675) respectively. While there is statistically significant relation between types of antipsychotics with ABG results with significant p value (p 0.002).

Table (3): Comparison between types of antipsychotics regarding investigations and drug level.

		Typical antipsychotics (n=14)		Atypical antipsychotics (n=61)		P value
		Count	%	Count	%	
ECG	Normal	0	0%	1	1.6%	1
	Sinus tachycardia	14	100%	60	98.4 %	
ABG	Normal	8	57.2%	58	95%	0.002*
	Metabolic acidosis	2	14.3%	1	1.7%	
	Respiratory acidosis	4	28.5%	2	3.3%	
Drug screening	No	14	100 %	60	98.4%	0.675
	Yes	0	0 %	1	1.6%	

*n: number, P-value < 0.05 is statistically significant.

All cases were given activated charcoal (100%), all typical (100%) antipsychotic drugs overdose did not undergo gastric lavage, while the majority of atypical (58.3%) antipsychotics overdose cases did not undergo gastric lavage.

There is non-significant relation between types of antipsychotics with activated charcoal administration and GIT decontamination (gastric lavage) with non-significant p value (p 0.63, p 0.675). As shown in **table 4**.

Table (4): Comparison between types of antipsychotics regarding decontamination.

		Typical antipsychotics (n=14)		Atypical antipsychotics (n=61)		P value
		Count	%	Count	%	
Activated Charcoal	No	0	0 %	0	0%	0.63
	Yes	14	100 %	61	100%	
GIT Decontamination (gastric lavage)	No	15	100 %	35	58.3%	0.675
	Yes	0	0 %	25	41.7%	

*n: number, P-value < 0.05 is statistically significant.

Regarding the rate of admission and period of stay, **Table 5** stated that most of the typical (92.9%) and atypical (90.2%) antipsychotics overdose cases were admitted with non-significant relation between antipsychotic overdose and admission with non-significant p value (p 0.755). Also, the majority of typical

(92.9%) and atypical (76.7%) antipsychotic overdose cases stayed in hospital more than 24 hours and less than one week, with non-significant relation between antipsychotic overdose and period of stay with non-significant p value (p 0.175).

Table (5): Comparison between types of antipsychotics regarding admission rate and period of stay.

		Typical antipsychotics (n=14)		Atypical antipsychotics (n=61)		P value
		Count	%	Count	%	
Admission	No	1	7.1%	6	9.8%	0.755
	Yes	13	92.9%	55	90.2%	
Period of stay	<24 hrs	1	7.1%	14	23.3%	0.175
	>24 hrs	13	92.9%	46	76.7%	

*n: number, P-value < 0.05 is statistically significant.

All typical (100%) and most atypical (90.9%) antipsychotics drugs overdose were cured (92.6). Also, this table shows non-significant relation between types of

antipsychotics and the outcome with non-significant p value (p 0.575). As shown in **table 6**.

Table (6): Comparison between types of antipsychotics regarding the outcome among admitted cases (n=75).

		Typical antipsychotics (n=13)		Atypical antipsychotics (n= 55)		P value
		Count	%	Count	%	
Outcome	Cured	13	100%	50	90.9%	0.575
	complicated	0	0%	5	9.1%	

*n: number, P-value < 0.05 is statistically significant.

DISCUSSION

Antipsychotics overdoses are considered the most common poisoning each year. That's why providing prevention programs and instruction plan to educate patients, psychiatrists and health care staff is extremely important (**Esmaily et al., 2016**).

This prospective study was conducted on antipsychotics overdose who presented at National Centre for Clinical & Environmental Toxicology (NECTR), Cairo university hospitals during six months period from the beginning of April to the end of September 2018. The study included 75 cases (51 females and 24 males).

Regarding types of antipsychotics in the present study, most of them were atypical antipsychotics (81.3% of cases), while typical antipsychotics were (18.7% of cases). This agrees with **Berling et al., (2016)** study, stating that there was a dramatic rise in atypical antipsychotics overdose (79% of cases) and explained this by the toxicity profile of antipsychotics has been changed due to the introduction of the newer 'atypical' antipsychotics and subsequent changes in prescription patterns.

Regarding age groups, the majority of the atypical cases presenting in our study were in group B; age group from 18-40 years, followed by age group A less than 18 years, then age group C more than 40 years, differing from typical antipsychotics cases, the majority were in group A followed by group b then group C. In agreement with our findings, the result from Menoufia Poison and Dependence Control Center (MPCC) (2012 to 2013) on antipsychotics poisoning, age group 20 to less than 40 years represented (42.5%) of cases followed by age less than 20 years (32. 5%) then

age more than 40 years (25%) (**Hammad et al., 2016**).

Regarding sex distribution in the present study, female cases (68%) represented the majority of studied cases in comparison with male cases who represented (32%), also the majority received atypical antipsychotics. This agrees with a study conducted by **El-Gharbawy (2018)** who stated that in antipsychotic overdose, females represented (65.1%) of cases while males represented (34.9%). Also, this agrees with **Hammad et al., (2016)** study who stated that female cases (58.3%) are more than male cases (41.7%).

Regarding residency distribution in the present study, cases came from urban areas represented (82.7%), while cases came from rural areas represented (17.3%), also the majority received atypical antipsychotics. This agrees with the following study: **Hammad et al., (2016)** who stated that the majority of cases came from urban areas. This may be explained by presence of (NECTR) at great Cairo, which is closer to most of urban areas where a lot of patients can seek medical advice there.

Regarding the work, most of the cases were not working (89.3%), and the majority received atypical antipsychotics. This may be explained by the lower rate of employment with predominance of social problems or emotional stress problems.

Regarding clinical manifestations of the cases in the present study, most of the cases presented with tachycardia without hypotension, and the majority received atypical antipsychotics. This agrees with a study conducted by **Borg, et al (2016)** that stated that tachycardia was found in most cases. **Rasima and Liebelt (2012)** also stated that after antipsychotic drugs overdose, the most

common cardiovascular manifestations were tachycardia, mild hypotension, and prolongation of the QT interval that may predispose the patient to torsades.

Also, most of the cases presented with disturbed conscious level and the majority received atypical antipsychotics). Constricted pupils were found in most of typical antipsychotic cases, while normal pupils were found in most atypical antipsychotic cases. This can be explained by **Yanagawa (2007)**, who stated that antipsychotic drugs overdose drugs induce an inhibitory action on the central nervous system. Also, **Rasima and Liebelt (2012)** stated that adults and children may manifest with toxic sedation, confusion, cardiovascular dysfunction and metabolic disturbances.

Regarding other manifestations in the present study, most of the cases did not show any GIT manifestations, respiratory manifestations, and temperature abnormality as hypothermia or hyperthermia. This disagrees with **Rasima and Liebelt (2012)**, they stated that antipsychotics toxicity can present with nausea, vomiting, dry mouth, impaired peristalsis, hepatic toxicity, hypothermia, or hyperthermia.

Regarding ECG results in the present study, most of the cases showed sinus tachycardia, and the majority of cases were atypical antipsychotics. This agrees with a study conducted by **borg L et al (2016)**, who stated that tachycardia was the most frequent ECG abnormality (49% of cases), while QRS interval prolongation represented (2% of cases).

Regarding ABG results, typical antipsychotics cases showed more acidosis than those cases presenting with atypical antipsychotics cases. This is explained by the abnormal CNS manifestations of all typical antipsychotic cases in comparison to those presenting with atypical antipsychotics cases.

Regarding drug screening in the present study, all of the typical and most of the atypical antipsychotics cases did not do drug screening. Furthermore, **Rasima and Liebelt, (2012)** stated that routine urine screening of drug of abuse, do not detect atypical antipsychotics. That's why it is not considered to be helpful in acute management, except in the case of false-positive cross-reactivity with tricyclic antidepressant immunoassays that can be seen with quetiapine and olanzapine.

Regarding GIT decontamination in the present study, all cases received activated charcoal, all typical and most atypical antipsychotic cases did not do gastric lavage. This agrees with a study conducted by **Hori, (2016)**, who stated that GIT decontamination was done in 50.9% of cases.

Regarding antidote use in the present study, no (0%) cases received antidote. This agrees with the following study that stated that treatment of acute antipsychotics poisoning is based mainly on good supportive measures, in absence of specific antidote (**El-Gharbawy, 2018**).

Regarding the admission rate and period of stay, most of the cases were admitted, and stayed at hospital for more than 24 hours and less than one week, with the majority of cases received atypical antipsychotics. This agrees with a study conducted by **Hori, (2016)**, who stated that the average days of hospital stay were 3.4 days.

Regarding the outcome in the present study, all typical and most of atypical antipsychotics cases were cured. This agrees with a study conducted by **El-Gharbawy, (2018)**, who stated that (93%) of cases were cured, while (7%) were complicated. Also, this may be due to the dramatic rise in atypical antipsychotics overdose and introduction of newer 'atypical' antipsychotics, which makes the number of cases receiving atypical antipsychotics higher than those receiving typical antipsychotics (**Berling et al., 2016**).

CONCLUSION

Atypical antipsychotics were common than typical antipsychotics. The most common manifestation was altered conscious level, tachycardia, and abnormal pupils. All typical antipsychotics cases manifested with abnormal CNS manifestations in comparison to those presenting with atypical antipsychotics. Typical antipsychotics cases presented with acidotic ABG more than those presenting with atypical antipsychotics. All cases did not do toxicological screening, nor receive antidote as there is no specific antidote. Most of cases received supportive, symptomatic treatment, activated charcoal, and did not undergo gastric lavage. Most of cases were admitted and their admission period was less than one week. The majority of case were cured. We concluded that 'atypical' antipsychotics are more commonly used, more prevalence, with less manifestations

of toxicity than typical antipsychotics. Good proper clinical assessment, supportive and symptomatic treatment with activated charcoal administration improves the outcome of both types of antipsychotic patients overdose.

RECOMMENDATIONS

Early detection of cases of antipsychotic overdose, with proper diagnosis and treatment especially early supportive, symptomatic treatment and activated charcoal administration can improve their outcome and decrease the morbidity and mortality. Atypical antipsychotics should be prescribed instead of typical antipsychotics as they show less manifestations of toxicity. Antipsychotic medications should be given by pharmacies only with prescriptions. Availability of poison control centre and treatment protocols in governorates other than Giza and Cairo will help in early management and improve outcome of poisoned patients in these areas. Better documentation of data to cases presented to poison centre is needed which help to study epidemiology and management of different antipsychotic drugs overdose in community. It is important to provide prevention programs and instruction plan to educate patients, psychiatrists, and health care staff.

CONFLICTS OF INTEREST

The authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

SOURCE OF FUNDING

None

ETHICAL APPROVAL

The study was approved by local ethical committee of Kasr Alainy faculty of medicine

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الملخص العربي

المقارنة ما بين تلقي جرعات زائدة من أنواع مضادات الذهان النمطية و الأنمطة من خلال خطة التشخيص و العلاج و نتائج العلاج في المركز القومي للسموم

الإكلينيكية والبيئية

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تهدف الدراسة الحالية إلى المقارنة ما بين علاج تلقي جرعات زائدة من أنواع مضادات الذهان والنتائج المترتبة عليها في مصر.

أجريت هذه الدراسة المستقبلية على خمس وسبعين من المرضى الذين تم إدخالهم المركز القومي للسموم الإكلينيكية والبيئية بعد تناولهم جرعات سامة من أنواع مضادات الذهان، خلال فترة ستة أشهر من بداية أبريل وحتى نهاية سبتمبر 2018.

تم جدولة النتائج وتحليلها إحصائياً وكانت غالبية الحالات في الفئة العمرية ما بين 18 إلى 40 سنة (45.3%) ، سيدات (68%)، متعلمين (96.2%)، وليس لديهم مهنة حالية (89.3%). كانت غالبية الحالات تعاني من اضطراب في درجة الوعي (97.3%)، وسرعة في ضربات القلب (98.7%)، وتغير في حجم حدقة العين (52%). معظم الحالات لم تخضع للفحص الدوائي (98.7%)، ولم يتم عمل غسيل معوي لها (66.7%)، ولم تحصل على مضاد للدواء (100%)، لكن معظمهم تلقوا اسعافات وعلاجات داعمة من الأكسجين والمحاليل، وكل الحالات تلقت فحم نشط. تم حجز معظم الحالات (90.7%)، ومكثوا في المستشفى أكثر من 24 ساعة وأقل من أسبوع. أما فيما يتعلق بالنتيجة، فقد تم علاج معظم الحالات (92.6%).