

**SUICIDE ATTEMPTS AMONG PATIENTS TREATED
WITH ANTIDEPRESSANTS, MANSOURA EMERGENCY HOSPITAL,
TOXICOLOGY UNIT (2006-2009)**

BY

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ABSTRACT

Suicide attempt includes any self-destructive behavior with the intension of ending one's life. It may or may not result in injuries. Intentional drug overdose is the most frequent method of suicide attempts (parasuicide). Controversy regarding the issue of antidepressants contributing to suicidal behavior continues in the literature. This work aims to (1) determine socio-demographic criteria of parasuicidal patients on current antidepressant treatment presented to Mansoura Emergency Hospital- Toxicology Unit with intentional drug overdose, and (2) highlight the use pattern of different types of antidepressants and their potential risk of suicidal attempts according to patient subgroups. It was found that the commonest intentional drug overdose is the current antidepressant medication with high incidence rate for Tricyclic antidepressants (TCA) followed by selective serotonin reuptake inhibitors (SSRIs). Female to Male ratio was 1.5:1. Further research is essential to identify subpopulations at risk of suicidal behavior to establish preventive strategies against recurrent attempts.

Keywords: Antidepressants, Parasuicide, Intentional Drug Overdose.

INTRODUCTION

There is a considerable debate and uncertainty if antidepressants treatment is associated with a reduction in suicide rate with a specific focus on whether selective serotonin reuptake inhibitors "SSRIs" increase the risk of suicidal behaviours in some young people (Fortune and Hawton, 2007; Rubino et al., 2007).

offer controversy about complete safety of antidepressants in reduction of suicide rates. They have been reported to increase suicidal ideation (Juurlink et al., 2006; Gibbons et al., 2007); the long term treatment may protect against suicidal behavior (Baldessarini et al., 2006; Erlangsen et al., 2008) or have no effect on suicide risk or decrease risk (Beyer, 2007; Simon and Savarino, 2007).

Inconsistent results of available studies

In May, 2007, the FDA ordered that all

antidepressants carry an expanded black box warning incorporating information about an increased risk of suicidal symptoms in young adults 18-24 years of age (Friedman and Leon, 2007; Smith, 2009).

Parasuicide means deliberate self-harm that creates the risk of death with or without a clear intent to die. On the other hand, suicide attempt includes any self-destructive behavior with the intension of ending one's life "cutting, overdosing, hanging, and running into traffic". The action may or may not result in injuries. Intentional drug overdose is considered the most frequent method of suicide attempts (Dieserud et al., 2000; Fortune and Hawton, 2007).

Parasuicide is the strongest risk factor for suicide. Its epidemiology as a suicidal act aiming primarily at drawing attention to the subject's desperate situation is different from that of suicide. However, the majority of studies focus on completed suicides. Hence, identifying patterns associated with parasuicidal behavior is important to establish preventive strategies against recurrent attempts (Maris, 2002).

This is the first study in our locality that aims to (1) determine socio-demographic criteria of parasuicidal patients on current antidepressant treatment presented to Mansoura Emergency Toxicology Unit with drug overdose, and (2) highlight the

use pattern of different classes of antidepressants and their particular types associated with higher risk of suicidal attempts according to patient subgroups.

SUBJECTS AND METHODS

(1) Subjects:

All parasuicide patients with intentional drug overdose who attended the Toxicology Unit in Mansoura Emergency Hospital during the period between January 2006 and December 2009.

• Patients Inclusion Criteria:

- All patients on current treatment (within 3 months) with any type of antidepressants.
- Patients presented with intentional drug overdose either by their antidepressant medication, any drug or by other substances.

• Patients Exclusion Criteria:

- Patients with history of current drug abuse or give positive urine screen for any of the drugs of abuse except those taking benzodiazepines.

(2) Methods:

- a. Thorough history taking was done to evaluate some socio-demographic data of the patients such as age, sex, marital status, educational level and occupation.
- b. Present history for pattern of drug

overdose, type of current antidepressant medication and time of starting antidepressant therapy.

- c. Complete medical examination was performed to determine pattern of drug or substance overdose according to the different clinical manifestations of the patients with special attention to anticholinergic, cardiovascular or CNS effects related to antidepressants.
- d. Urine and blood sampling: after having informed consent, forty ml urine and ten ml blood were obtained from each patient at time of admission and prior to giving any treatment. Each sample was collected in a dry, sterile labeled container.
- e. Toxicological analysis:
 - Preliminary drug screen test was achieved using Enzyme Multiplied immunoassay technique (EMIT) "Syva, Solaris S/N 1076 Version 3.00L. Using Emit® d.a.u. Assay". Each urine sample was screened for cannabinoids, opiates, benzodiazepines, barbiturates and ethyl alcohol.
 - Confirmatory Thin Layer Chromatography was done for positive drug screen to exclude patients with positive screen for the drugs mentioned above (except benzodiazepines).
 - EMIT using Vita lab Viva analyzer according to Tricyclic Antidepressant (TCA) assay in Viva manual in toxicological laboratory to detect current

TCA present in serum.

- Therapeutic Drug Monitoring for salicylates, paracetamol and digoxin in serum was performed using TDx analyser (developed by Abbott Laboratories, USA). Drug assay was done according to Abbott manual of Abbott Diagnostic Division in Poison Laboratory in Mansoura Emergency Hospital.

f. Statistical analysis:

Quantitative data were presented as mean \pm standard deviation and qualitative data were presented as number and percentage. Association between different qualitative variables was performed using Chi square test (χ^2). Analysis of data was done using P value significance level. It was considered insignificant if more than 0.05, significant if ≤ 0.05 and highly significant if ≤ 0.01 .

RESULTS

A total of 1015 parasuicide patients attended Mansoura Toxicology Unit and presented with intentional drug overdose during the period between January 2006 and December 2009. Only 150 patients fulfilled the inclusion criteria.

I- Age and gender characteristics of the studied patients (Table 1):

Patients' age ranged between 15-50 years (mean age: 28.7 ± 12.7). The common-

est age for parasuicide is 20-30 years in female and 30-40 years in male. Regarding gender, female represented 60% of cases while male accounted for 40% (Female: Male ratio is 1.5:1). A statistically high significant association was found regarding parasuicide in relation to age and gender of patients ($P = 0.003$).

II-Pattern of intentional drug overdose in the studied patients (Table 2):

According to the clinical manifestations and toxicological analysis, the present work showed that intentional overdose with current antidepressant medication was the most common (46.7%). Other patients on antidepressant treatment try to commit suicide by other drugs in the following manner : organophosphates (24.7%), benzodiazepines (18%) and salicylates (8.6%) and finally digitalis (2%). A statistically significant difference was found as regards parasuicide in association with type of drug overdose ($P=0.004$).

III- Type of current antidepressant medication prescribed in the studied patients (Table 3):

As illustrated in table (3), the commonest prescribed antidepressant was Tricyclic Antidepressants "TCA" (68%) followed by Selective Serotonin Reuptake Inhibitors "SSRIs" (27.3%). Other types or mixed antidepressants represented 4.7%. A highly significant statistical increase in

cases of parasuicide was found in relation to Amitriptyline ($p=0.003$).

DISCUSSION

Are antidepressants considered safe drugs or a threat for patients' lives? This is a controversial issue that exists in the literature. Mixed findings suggest either a very weak relationship or that the risks or benefits differ depending on patient subgroups. Hence, the most important question may not be whether antidepressants increase or decrease suicide risk, but rather which ones, for whom, when, and under what circumstances (Zisook, 2009).

The results of the present work revealed that the commonest age for parasuicide in patients with intentional drug overdose is 20-30 years in female and 30-40 years in male. Regarding gender, Female: Male ratio is 1.5:1. A statistically high significant association was found regarding parasuicide in relation to age and gender of patients ($P \leq 0.001$).

These results coincide with those obtained by Schmidtke et al. (1996) and Bille-Brahe et al. (1997). It was found that gender is an important risk factor for parasuicide with women 2-folds higher than men in samples of parasuicidal subjects (Hawton et al., 2003). Self-poisoning occurs mainly in older adolescents and young

adults particularly under 35 years (Hawton and Harriss, 2007). This could be explained by more prevalence of major depressive disorder in women "twice more than men" (Kessler, 1993) with an earlier age of onset, greater functional impairment and more severity of illness (Kornstein et al., 2000). In addition, gender differences were reported to be related also to variable treatment response (Kornstein and Wojcik, 2000).

The present work showed that intentional antidepressant medication overdose was the most common (46.7%). Other patients on antidepressant treatment try to commit suicide by other substances such as organophosphates (24.7%) and benzodiazepines (18%).

Methods used for parasuicide have been reported to display great regional variation (Nordentoft and Branner, 2008). In our society, the wide use and prescription of antidepressants reflects the higher prevalence of intentional antidepressant overdose. However, other substances like organophosphates are readily available, cheap and easy to be obtained. Moreover, benzodiazepines are sometimes prescribed with no respect to drug legislation policy or bought from some pharmacies in absence of medical prescription.

Findings of this work suggest that certain antidepressants used in treatment of

some psychiatric illnesses notably TCAs might be associated with a potential risk for increased suicidal behavior similar to other reports (Maris, 2002; Bertolote et al., 2003; Markowitz and Cuellar, 2007). A highly significant statistical increase of suicide attempts is noticed in relation to amitriptyline followed by dothiepin. This may be attributed to a higher prescription rates for these drugs in our community.

However, Isacson et al. (1997) found high risks and tendency to commit suicide with SSRIs. Alternatively, Hotopf et al. (1997) did not find any significant difference between SSRIs and TCAs.

Most of the patients in the current study presented with suicide attempts within the first month of starting treatment with antidepressants. A possible explanation is that people tend to begin taking antidepressants when they are at their most depressed state, and several weeks have to be passed to experience the benefits of their medications. Alternatively, antidepressants would worsen depression before it is alleviated or they might reinforce patients' motivation to act destructively before elevating their mood which needs several weeks of therapy (American Psychiatric Association, 2003).

Limitations:

The first limitation of this work is absence of a precise diagnosis of the type of

depressive illness in the studied patients. This is attributed due to the fact that our patients were presented to the Toxicology Unit because of an emergency overdose and not because of their depressive illness and there is no written document about their condition, besides the culture of Egyptian community, particularly those of low socioeconomic standards who still deny and refuse accepting the fact that mental or psychiatric diseases need psychological therapy along with medical treatment. Another big obstacle is lack of follow up and close monitoring of those patients to avoid potential risks associated with antidepressant use. The second limitation is the small study population which necessitates further larger researches in collaboration with psychiatric clinics to identify the real magnitude of the problem.

CONCLUSIONS AND RECOMMENDATIONS

Controversy over the issue of antidepressants contributing to suicidal behavior continues in the literature. The legal and ethical responsibility of physicians in clinical management of depression is to treat rather than be a threat to the mental health of patients. Several important guidelines were concluded: First, the prevalence and pattern of parasuicide should be monitored to identify populations at risk of recurrent

attempts and to prevent completed suicide.

Second, when prescribing antidepressants, physicians must identify vulnerable patients and warn their families of possible risk of suicidal thoughts or behavior after starting the treatment and dangers of abrupt discontinuation of therapy.

Third, physicians should provide depressed patients with written instructions about their antidepressant as stressed or anxious patients poorly retain verbal information or may remember them incorrectly. Information must include common false beliefs such as taking the medication only on those days when feeling depressed. This could achieve better response to the drug, more adherence to treatment and decrease incidence of suicide attempts.

Fourth, close patient monitoring is recommended in the first 12 weeks immediately following antidepressants therapy for worsening depression or emergence of suicidal behavior.

Fifth, psychological therapy and problem solving are effective in reducing depression, lowering risk of suicidal ideation and repetition of self-harm. Finally, reduced access to toxic amounts of pharmaceutical agents is effective in reducing the dangers of a self-poisoning act.

Table (1) : Age and gender of patients presented with drug overdose (n=150)

Age group	Male (60)		Female (90)		Total (150)		P value
	No	%	No	%	No	%	
< 20	7	11.6	30	33.3	37	24.7	
20-30	16	26.7	35	38.9	51	34*	
30-40	29	48.3	10	11.1	39	26	
> 40	8	13.4	15	16.7	23	15.3	
Mean± SD	29.6±11.6		25.4±8.8		28.7±12.7		0.003*

*P ≤ 0.01 is highly significant

Table (2) : Prevalence rates for pattern of intentional drug overdose in the studied group (n=150).

Type of drug overdose	Men (60)		Female (90)		Total	
	No	%	No	%	No	%
Antidepressants	32	53.3	38	42.2	70	46.7*
Organophosphates	7	11.7	30	33.3	37	24.7
Benzodiazepines	17	28.3	10	11.1	27	18
Salicylates	3	5	10	11.6	13	8.6
Digitalis	1	1	2	2	3	2

*P= 0.004 (P ≤ 0.01 is highly significant)

Table (3) : Type of current antidepressant medication prescribed in the studied patients (n=150)

Class of antidepressant	Antidepressant Prescribed	Patients	
		No	%
TCA	<i>Amitriptyline</i>	41	27.3*
	<i>Dothiepin</i>	34	22.7*
	<i>Clomipramine</i>	18	12
	<i>Imipramine</i>	9	6
SSRI	<i>Citalopram</i>	16	10.7
	<i>Sertraline</i>	13	8.7
	<i>Fluoxetine</i>	6	4
	<i>Paroxetine</i>	6	4
NDRI	<i>Bupropion</i>	3	2
SNRI	<i>Trazodone</i>	2	1.3
TCA, SSRI	<i>Mixed</i>	2	1.3

Tricyclic Antidepressants (TCA), Selective Serotonin Reuptake Inhibitors (SSRIs), Norepinephrine and Dopamine Reuptake Inhibitor (NDRI), Serotonin and Norepinephrine Reuptake Inhibitor (SNRI).

P= 0.003*

* P ≤ 0.01 is highly significant

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محاولات الانتحار بين المرضى الذين يعالجون بمضادات الاكتئاب - مستشفى الطوارئ بالمنصورة - وحدة علاج السموم (٢٠٠٦ - ٢٠٠٩)

المشركون في البحث

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محاولات الإنتحار تتضمن أي سلوك لتدمير الذات أو إنهاء الحياة. وقد لا يسفر ذلك عن وقوع اصابات. ويعتبر تناول جرعات زائدة من الأدوية هو الأسلوب الأكثر شيوعاً لمحاولات الانتحار. وقد تزايد الجدل بشأن استخدام مضادات الاكتئاب والتي يمكن أن تسهم في استمرار السلوك الانتحاري. ويهدف هذا العمل إلى تحديد الخصائص الاجتماعية للمرضى الذين يعالجون بمضادات الاكتئاب وحضروا إلى مستشفى الطوارئ، الجامعي بالمنصورة، وحدة السموم بسبب تناول المتعمد لجرعة زائدة من الأدوية، كذلك إلقاء الضوء على نط استخدام الأنواع المختلفة من مضادات الاكتئاب والمخاطر المحتملة لحدوث محاولات الانتحار. وقد تبين أن أكثر الأدوية استخداماً في الإنتحار بين مرضى الاكتئاب هو الدواء المضاد للاكتئاب والذي يعالج به المريض مع ارتفاع معدل تناول مضادات الاكتئاب ثلاثية الحلقات (TCAs) يليه مثبطات السيروتونين الاختيارية (SSRIs) وكانت نسبة الإناث إلى الذكور 1:1.5.

ونستنتج من البحث أن هناك مسؤولية قانونية وأخلاقية تقع على عاتق الأطباء في تدبير العلاج الأمثل للاكتئاب والحرص على ألا تشكل مضادات الاكتئاب تهديداً للصحة العقلية للمرضى المصابين بالاكتئاب. لذلك يجب مراعاة التالي في علاج هؤلاء المرضى ينبغي رصد مدى انتشار ونمط محاولات الإنتحار لتحديد المجموعات الأكثر عرضة للمحاولات المتكررة، كما يجب على الأطباء عند وصف مضادات الاكتئاب، تحذير أسر المرضى بخصوص احتمال حدوث محاولات الانتحار بعد البدء في العلاج ومخاطر التوقف المفاجئ للدواء. ولذلك ينبغي توفير تعليمات مكتوبة عن الأدوية المضادة للاكتئاب متضمنة تلك المعتقدات الخاطئة الشائعة مثل تناول الدواء فقط في تلك الأيام عندما تشعر بالاكتئاب. وبهذا يمكن تحقيق أفضل استجابة للدواء، والحد من محاولات الانتحار. ويوصى أيضاً بمراقبة المرضى في الأسابيع الثانية عشر الأولى التي تعقب مباشرة بداية استخدام مضادات الاكتئاب لمتابعة ظهور السلوك الانتحاري. مع التأكيد على أهمية العلاج النفسي وحل المشكلة للحد من مرض الاكتئاب، وخفض مخاطر التفكير في الانتحار.