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Patients Treated with Antidepressants and the Relative Risk of Suicide Attempt

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Abstract

Tricyclic antidepressants (TCAs) have been approved by the Food and Drug Administration (FDA) specifically to treat depression, with their generic or chemical names. The aim of this study was to characterize patients on antidepressants after self-poisoning with suicidal intent regarding age, sex, type of current antidepressant therapy, and type of substances ingested in order to commit suicide. This study was conducted on patients (n=1283) of different ages, 924 males and 359 female. These patients were attended to poison unit at emergency hospital, Mansoura University during the period from January 2002 to December 2009. During the study period, 175-Para suicide patients were found with current antidepressants therapy and presented with self-poisoning using their antidepressant therapy or other medications. A substantial difference between different types of antidepressants was found. Para suicide risks for selective serotonin reuptake inhibitor were significantly low than those of tricyclic antidepressants, so in suicide prevention, risks and benefits of antidepressant should be taken into account when choosing treatment for depressive patients. At the same time, depressed patients should be under close psychiatric assessment in order to prevent such possible suicidal attempts.

Keywords: Blood samples, antidepressant drug, EMIT

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1. Introduction

The majority of studies focus on completed suicides but, it has to be emphasized that the epidemiology of Para suicide, as a suicide act not aiming at death but primarily at drawing attention to the subject's desperate situation, is different from that of suicide. As most attempted suicides is non-violent, generally involving self-poisoning. Knowledge of the type of substances that are frequently used in Para suicides can help the emergence physician to deal properly with patient [18]. Para suicide is the strongest risk factor for suicide; so, identifying risk factors for suicidal behavior that can be assessed and modified by therapeutic / preventive interventions is a major public health issue [13]. There is no regular population based monitoring of epidemiological data regarding Para suicide, but it is estimated to be 10-25 times more frequent than completed suicide. The strongest correlates of Para suicide relate to the subject's depressive state at around the time of the suicidal behavior [7]. The most frequent method of Para suicide is intentional drug overdose, defined as substance ingestion in excess of the prescribed or generally recognized therapeutic dosage [6]. Several studies have liked the use of antidepressants to increased risks of suicidal behavior. On February 2, 2004, FDA issued a report asking manufactures of antidepressant drugs to include warnings on their drug label about the need to monitor people taking antidepressants for worsening depression and the emergence of suicidal thoughts. During the last ten years, several new antidepressants, including selective serotonin reuptake inhibitors (SSRIs), has been introduced in Egypt. While one of the major problems with TCAs is their toxicity in overdose [12], the new antidepressants have been claimed to be effective as tricyclics [16], and less toxic [9], [5], [13] and [3]. However, [11] assed risks of various antidepressants by relating number of Para suicide to particular drugs; they found higher risks with SSRIs. Fluoxetine represents the prototype of the SSRIs and has been in wide spread use for over a decade [8]. Therefore, the aim of this work is

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to uncover the correlation between continuous intake of antidepressants among depressed patients and tendency to commit suicide and to detect particular types of antidepressants associated with higher risk.

2. Materials and Methods

The study included the entire patients on antidepressants therapy and presented with drug over dose in suicidal intent attending the poison unit in emergency hospital, Mansoura University in the period between Jan 2002 and Dec 2009.

Subjects:

A total number of 1283 patients (924 males and 359 female) of different ages and signs of TCAs poisoning, attended the poison unit. At the time of arrival to hospital, all of the patient were underwent clinical and toxicological evaluation.

History

In this study, data were collected from patients, relatives, friends or paramedics as regards:

- Age, sex.
- Present history of treatment with one of antidepressants.
- Type of current antidepressant therapy.
- Duration of starting antidepressant therapy.

Clinical evaluation

- Physical examinations for findings related to anticholinergic manifestations, CNS signs and other possible drugs taken in suicidal attempts.

Lab investigations

- Detection of drug abuse in blood samples by enzyme multiplying immune assay technique (EMIT):

Blood samples (3 ml) were obtained from all patients after consent, centrifuged and TCA was measured

By enzyme multiplying immunoassay technique (Vita lab viva analyzer, Germany) according to TCA, assay method in the viva manual in poison laboratory at emergency hospital, Mansoura University. Serum TCA levels are not likely to be helpful in the immediate treatment of the patient with TCA poisoning.

3. Statistical Analysis

The quantitative data were presented as mean ± standard deviation and the qualitative data were presented as number and percentage. Association between different qualitative variables was performed using Chi square test (x^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

4. Results

The annual number and percentage of positive cases of TCA by EMIT as shown in Table (1) according to the total number of samples. The age of patients ranged between 19–39 years with a mean age 23.52±6.09. To characterize patients, age groups were reported in intervals of 5 years (19-24, 25-29, 30-34 and 35-39). As regards sex, among those were 80 males (45.7%) and 95 females (54.3%) with a sex ratio 1:1.19, the distribution of Para suicides according to age and sex is shown in Table (2). A statistically high significant association was found regarding parasuicide in relation to age and gender of patients (p = ≤ 0.003). A large variety of substances was used to commit suicide.

Table 1. Annual No and percentage of positive cases of TCA according to the total number of samples

Year	No of samples	Negative cases	Positive cases		Males		Females	
			No	%	No	%	No	%
Jan 2002	77	50	27	35.06	15	19.48	12	15.58
2003	252	233	19	7.54	11	4.36	8	3.18
2004	196	164	32	16.32	16	8.16	16	8.16
2005	134	117	17	12.68	9	6.71	8	5.97
2006	119	100	19	15.96	8	6.72	11	9.24
2007	102	85	17	16.66	9	8.82	8	7.84
2008	173	158	15	8.67	-	-	15	8.67
Dec 2009	230	201	29	12.61	12	5.22	17	7.39
Total	**1283**	**1108**	**175**	**13.64**	**80**	**6.23**	**95**	**7.41**

Table 2. Patients with positive antidepressants (n=175) by age and sex

Age group	Male		Female		Total	
	No	%	No	%	No	%
19-24	8	10	29	30.52	37	21.14
25-29	24	30	35	36.85	59	33.72
30-34	36	45	13	13.68	49	28
35-39	12	15	18	18.95	30	17.14
Total	**80**	**100**	**95**	**100**	**175**	**100**
Mean ± SD* of the total No of + ve samples			23.52±6.09	P value = 0.003**		

SD*: Standard Deviation
P **≤ 0.01 is highly significant

Table 3. Different substances taken by Para suicide patients

Substance	Males		Females		Total	
	No	%	No	%	No	%
Antidepressants	38	47.5	37	38.95	75	42.86
Benzodiazepines	24	30	10	10.53	34	19.43
Organophosphorus	10	12.5	29	30.52	39	22.28
Salicylates	5	6.25	16	16.84	21	12
Digitalis	3	3.75	3	3.16	6	3.43
Total	**80**	**100**	**95**	**100**	**175**	**100**

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

The commonest substance taken to commit suicide was the current antidepressants treatment (47.5% for males and 38.95% for females). Males were significantly more likely to take benzodiazepines than females (30% and 10.53%, respectively), whereas females were more likely to take organophosphorus than males (30.52% and 12.5%, respectively), Table (3). A statistically significant difference was found regarding parasuicide in relation to type of drug overdose (p = ≤ 0.004).

Among Para suicides patients (n=175), 63% of patients were treated by TCAs, while SSRIs were taken only by 27% of patients. Amitriptyline was the major drug responsible for Para suicide cases on TCA (25% of cases), then dothiepin (20%) and clomipramine (10%), while citalopram was the major drug responsible for Para suicide cases on SSRIs (11% of cases), then sertaline (7%) and fluoxetine (5%). Mixed TCA and SSRIs were taken only by 2% of cases. Some Para suicides were on antidepressants other than TCA or SSRIs e.g. bupropion (norepinephrine and dopamine reuptake inhibitor), responsible only about 4% of cases, and trazodone (serotonin and norepinephrine reuptake inhibitor), it represented only 4% of cases. Different antidepressants used by the patients as a treatment during study period is shown in Table (4). A highly significant statistical increase in cases of Para suicide was found in relation to Amitriptyline (p = 0.003)

Table 4. Different antidepressants used by the patients As a treatment during study period

Type of antidepressants	Classification	Patients	
		No	%
Amitriptyline	TCA	44	25
Imipramine	"	13	7
Clomipramine	"	19	11
Dothiepin	"	36	20
Citalopram	SSRI	18	10
Fluoxetine	"	8	5
Paroxetine	"	8	5
Sertaline	"	13	7
Bupropion	NDRI	6	4
Trazodone	SNRI	6	4
Mixed	TCA, SSRI	4	2

TCA: Tricyclic Antidepressants
SSRI: selective serotonin reuptake inhibitors
NDRI: Norepinephrine and dopamine reuptake inhibitor
SNRI: Serotonin and norepinephrine reuptake inhibitor
P** = 0.003 (P **≤ 0.01) is highly significant

5. Discussion

Mixed findings suggest that a very weak relationship or that the risks or benefits differ depending on patient subgroups. Hence, the most important question may not to be if antidepressants increase or decrease suicide risk, but rather which ones for whom when and under what circumstances [19]. In this study, 175-Para suicide

patients were found with current antidepressants therapy and presented with self-inflected poisoning using their antidepressant therapy or other medications, Table (1). The incidence of cyclic antidepressant poisoning is higher in female than in male. This most likely reflects a higher rate of suicide attempts among female. Males to females' ratio are 1:1.19, a ratio that is in contrast to the distribution of completed suicides, where males are at higher risk than females [1]. Para suicides were most frequent in the young females' i.e. 67.37% before 30 years old and 60% for males after 30 years old, Table (2), these findings that are in line with previous cross-sectional data [4]. In our society, which are regionally defined, mainly current antidepressants therapy then benzodiazepines is most probably due to its wide use and availability and organophosphorus, which is also very, cheep, available while salicylates and digitalis represented a small percentage of Para suicide attempts, Table (3). Methods used for Para suicide have been reported to display great regional variation [15].

TCAs were detected in blood samples of patients using EMIT while the toxicological laboratory is lacking of measuring apparatus needed for detection of other types of antidepressants e.g. SSRIs so, diagnosis of current treatment with types of antidepressants other than TCAs depended only on history taking and patient clinical condition. Overall, patient-taking TCAs, of which amitriptyline and dothiepin that are usually prescribed were responsible for the majority of cases, committed 63% of Para suicides. While, about 27% was committed by patients taking SSRIs of which citalopram accounted for the majority of Para suicides, Table (4). Therefore, the present study revealed a decline in Para suicides among those taking SSRIs that are tolerable with fewer side effects. Most of the patients of our study was presented with Para suicide attempts within the first month of starting treatment with antidepressants, so the most explanation is that people tend to begin taking antidepressants when they are at their most depressed condition, and do not experience the benefits of the medications until several weeks have passed. Alternatively, it is possible that antidepressants cause depression to worsen before it is alleviated. This study highlights the importance of closely monitoring people who are taking antidepressants especially during the fist month for worsening depression or emergence of suicidal thoughts or behaviors [2]. Adequate treatment with antidepressants is often useful in the treatment of moderately and severely depressed patients. Many recent studies, however, have revealed unidentification and under treatment of depression among suicide victims, and in suicide prevention, therapeutic failure rather than toxicity of antidepressants have been emphasized [14]. Therefore, much attention has been paid to the recognition of depressive disorders and the education of general practitioners, who have great responsibilities for identifying suicide risk, and who prescribe the majority of antidepressants [17]. The present results are in consistency with findings from several studies [14], [9], [5], [13] and [3]. However, [11] in contrast to our results, found high risks and tendency to commit suicide with SSRIs. Whereas, [10] did not find any significant difference between SSRIs and TCAs in committing such Para suicide attempts.

6. Conclusion

The present study suggests that the use of certain antidepressants is indeed related to suicidal behavior with a substantial difference between different types of antidepressants. Para suicide risks for SSRIs were significantly lower than those of TCAs. TCAs accounted for a major part of Para suicides by antidepressants.

7. Recommendations

- In Para suicide prevention, risks and benefits of antidepressants should therefore be taken into account with choosing treatment for depressive patients. Careful prescription of potentially lethal drugs is emphasized, and favoring drugs with a low risk is recommended whenever it is reasonable according to the patient's clinical condition.
- The key principle of Para suicide prevention is increasing public awareness about the treatment of psychiatric disorders related to suicidal behavior.
- The toxicological laboratory must be equipped with advanced apparatus essential for detection of recent drugs and other types of antidepressants e.g. SSRIs.
- Children with unintentional overdose should be admitted if inadequate supervision in the home is suspected or if adequate follow-up cannot be assured.

Further outpatient care:

Patients may be discharged from the emergency department (ED) if the ingestion was accidental, if no signs or symptoms of CA toxicity are evident during a

minimum observation of 6-8 hours, if the parents are reliable, and if appropriate follow-up is assured.

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9. Conflict of Interest

None Declared

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