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Attempted suicide by acetaminophen ingestion

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Objective : *To study clinical characteristics, mental illness and medical conditions of hepatotoxicity in patients who attempted suicide by acetaminophen ingestion and to determine the relationship between acetaminophen toxicity and severity of depression or anxiety.*

Design : *Descriptive study*

Methods : *This study was conducted at King Chulalongkorn Memorial Hospital in July 2000 to October 2001. A total of 52 patients, whose age was above 15 years old, and who were admitted with suicidal attempt by acetaminophen ingestion were diagnosed and interviewed. Psychiatric diagnosis under DSM-IV criteria, and the details of their self-harm acts were assessed. Hamilton rating scale for depression and Zung self-rating anxiety scale were performed, as well as liver function test and serum acetaminophen level were recorded.*

Results : *80.8 % of the suicidal attempt patients were female; their age ranged between 15 to 25 years old. One-fourth of the patients ingested acetaminophen combined with other drugs. About 15 %of the patients had made a previous attempt; usually they repeated the same method. Most of them had taken less than 40 tablets of acetaminophen and received their treatment within 12 hours after the drug ingestion. About 65 % had no*

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significant change in their liver function test and serum acetaminophen levels were categorized as slight risk. Psychiatric assessment revealed that 80 % had adjustment disorder and their mean score of clinical status for depression and anxiety were in moderate severity. There are statistical significances in some correlation between the number of tablets of ingested acetaminophen and abnormal liver function test and the length of hospitalization; however, no correlation was found between the number of tablet and the severity of depression or anxiety.

Conclusion : *Hepatotoxicity in patients who attempted suicide by acetaminophen ingestion was associated with the number of acetaminophen tablets and duration before receiving treatment. However, it was not correlated with the severity of psychiatric symptoms. Their physician and psychiatrist should collaborate in the treatment. Education on acetaminophen poisoning and detection of patients who have risk of suicidal behavior may be useful for the prevention of suicide.*

Keywords : *Attempted suicide, Acetaminophen.*

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วัตถุประสงค์ : *เพื่อศึกษาลักษณะทางคลินิก การป่วยทางจิตเวช และความรุนแรงของภาวะพิษต่อตับในผู้ที่มีพฤติกรรมพยายามฆ่าตัวตายด้วยวิธีกินยาอะเซตามิโนเฟนและเพื่อประเมินความสัมพันธ์ระหว่างภาวะพิษเนื่องจากยาอะเซตามิโนเฟนกับระดับอาการซึมเศร้าหรือวิตกกังวล*

รูปแบบการวิจัย : *การศึกษาเชิงพรรณนา*

วิธีการวิจัย : *ศึกษาผู้ป่วยที่มารับการรักษาแบบผู้ป่วยในด้วยเรื่องกินยาอะเซตามิโนเฟนหรือพาราเซตามอลเพื่อพยายามฆ่าตัวตายและส่งปรึกษาจิตเวชในช่วงกรกฎาคม 2543 ถึงตุลาคม 2544 จำนวน 52 ราย ผู้ป่วยได้รับการสัมภาษณ์และวินิจฉัยโรคทางจิตเวช,ประเมินความรุนแรงของภาวะซึมเศร้าและวิตกกังวลตรวจผลการทำงานของตับและระดับยาอะเซตามิโนเฟนในเลือด*

ผลการศึกษา : *ผู้ป่วยส่วนใหญ่เป็นหญิง อายุอยู่ในช่วง 15 ถึง 25 ปี หนึ่งในสี่ใช้ยาอื่นร่วมด้วย, ร้อยละ 15 เคยพยายามฆ่าตัวตายมาก่อนด้วยวิธีเดียวกัน ผู้ป่วยส่วนใหญ่กินยาพาราเซตามอลน้อยกว่า 40 เม็ด และมารับการรักษาภายใน 12 ชั่วโมง ประมาณร้อยละ 65 มีผลการทำงานของตับอยู่ในเกณฑ์ปกติและระดับยาอะเซตามิโนเฟนในเลือดเป็นแบบมีความเสี่ยงเล็กน้อย ส่วนใหญ่ได้รับการวินิจฉัยว่าเป็น Adjustment disorder (ร้อยละ 80) และมีอาการซึมเศร้าอยู่ระดับปานกลาง อย่างไรก็ตามพบว่า จำนวนเม็ดยาที่กินมีความสัมพันธ์กับระดับ SGOT SGPT PT และจำนวนวันที่อยู่โรงพยาบาล แต่ไม่พบความสัมพันธ์กับความรุนแรงของภาวะซึมเศร้า หรือวิตกกังวล*

สรุปผลการศึกษา : *ภาวะพิษต่อตับเนื่องจากยาอะเซตามิโนเฟน มีความสัมพันธ์กับจำนวนเม็ดยาที่กินและระยะเวลามารับการรักษา โดยไม่พบความสัมพันธ์กับความรุนแรงของอาการทางจิตเวช อย่างไรก็ตาม จิตแพทย์และอายุรแพทย์ควรให้การช่วยเหลือผู้ป่วยควบคู่กันไป และการให้ความรู้ความเข้าใจที่ถูกต้องถึงอันตรายของยาอะเซตามิโนเฟนเกินขนาด และการเฝ้าระวังผู้ที่มีความเสี่ยงต่อการฆ่าตัวตาย คงมีส่วนช่วยลดปัญหา การพยายามฆ่าตัวตาย*

คำสำคัญ : *การพยายามฆ่าตัวตาย, ยาอะเซตามิโนเฟน*

The national strategy for the prevention of suicide of the National Institute of Health (NIH) sets specific goals and objectives to reduce suicide. Some of these measures include the raising of public awareness that suicide is a preventable health problem, and the reduction of access to lethal means and methods of self-harm.[1]

Individuals who attempt suicide in contrast to those who complete suicide are distinctive, but overlapping populations. There are eight to ten times of cases of suicide attempts than that of completed suicides.[2] However, the rate of attempted suicide is estimated to be somewhere between 10 and 50 times the rate of completed suicide[3,4], because many attempts were unreported. Statistically, more than 10 % of all adults have thought about committing suicide, and nearly 3 % have attempted suicide at some point in their life.[4] Depression is the most common diagnosed psychiatric disorder that comprises of the most significant risk factor of suicide.[3,5] While making an attempt, a person is also engaged in a major risk factor for completed suicide[6]; within this large group of suicide attempters, the risk of completed suicide is highly variable.[7-9] Among the characteristics of suicide attempt, the medical severity of the attempt, measured in a number of ways, have been associated with both high suicidal intent [6,10,11]and subsequent completed suicide.[12]

Ingestion of drugs or chemical agents resulting in self-poisoning was the most common method of suicidal attempt.[1,4] Regarding the type of drug used, in both North American and Western European clinics, most attempts are by overdose, nearly always of a non-narcotic analgesic or psychotropic drug.[13,14] In Thailand, however, some studies[15,16] reported that insecticides and agents used in agriculture were common; so far analgesic drugs especially acetaminophen has been increasingly reported, particularly in urban areas.

Acetaminophen is generally thought to be safe analgesic when used within its therapeutic doses. In the cases of its overdose, liver damage is a toxic effect which is present in most patients who ingested more than 15 g of acetaminophen. Although it may be counted as a nonviolent method of suicide, acetaminophen overdose may cause hepatotoxicity which leads to other serious complications. A few studies have looked into attempted suicide with acetaminophen ingestion and its consequence. This research was aimed to study the clinical characteristics, mental illnesses and medical conditions of hepatotoxicity in patients who attempted suicide with acetaminophen ingestion and to determine the relationship between acetaminophen toxicity and the severity of psychiatric conditions.

Method

The patients were recruited when they were hospitalized for suicidal attempts with acetaminophen ingestion and received psychiatric consultation in July 2000 to October 2001. The total cases of fifty-two patients, aged over 15 years, were brought in for clinical diagnostic interview in which the psychiatrist established a good rapport and completed DSM-IV criteria to determine axis I diagnosis. Data on suicidal behaviors were obtained. Thai version of Hamilton rating scale for depression (HAM-D) was used to measure the severity of depression. Zung self-rating anxiety scale was performed by the patients to assess their level of anxiety.

Laboratory investigations that measure medical severity were collected. The peak values of plasma aspartate (SGOT), plasma alanine (SGPT) and prothrombin time were used to evaluate the degree of liver damage or liver function. Serum acetaminophen level between 4 and 24 hours after ingestion was recorded as well as the patient's length of hospitalization. The basic risk category assignment was determined based on the level of serum acetaminophen. A nomogram was used as a tool to determine the risk which was categorized as follows.[17]

Risk assignment	Predicted serum Acetaminophen level (μg/ml)				
	4 hr	or	8 hr	or	12 hr
Slight risk	≤ 120		≤ 60		≤ 30
Possible risk	>120, <200		>60, <100		>30,<50
Probable risk	≥ 200		≥100		≥50

From Rumack BH, Peterson RG, Koch GG, Amara IA: Acetaminophen overdose : 662 eases with evaluation of aral acetylcysteine treatment. Arch Intern Med 141: 380; 1981

The data were analyzed by SPSS for Windows version 10. Descriptive statistics were reported. The levels of statistical significance of the relationship between various possible risk factors of the patients and laboratory measurements of hepatotoxicity were evaluated in terms of chi-square test or t-test. The strength of association is summarized by correlation coefficient.

Results

The results showed that of the 52 patients of suicidal attempt, 42 were female (80.8 %) and 10 male (19.2 %), shown in Table 1. Their mean age was 23.37 years (SD = 6.3) and 33 cases (63.5 %) were in the age group of 15-25 years. Thirty-two patients were single; 21 cases were employed and 15 cases were students. Nearly half of them were university graduate or received college education. 7.7 % of all the subjects (n = 4) had history of physical illness, but no one had liver disease; 7.7% had history of psychiatric illness. There were 23.1 % (n =12) who had history of alcohol use. Family history of suicide was found in 13.5 % of the cases. Nine cases (17.3 %) had earlier episode of suicide attempt, and most of them repeated the same method. One-fourth of the patients (n = 13) attempted suicide by ingestion of acetaminophen combined with other drugs such as chlorpheniramine and anxiolytic drugs. Psychiatric interviews and assessment revealed that 80.8 % of the patients in the study group (n = 42) met the DSM-IV criteria for diagnosis of adjustment disorder; 7.7 % (n = 4) for major depressive disorder; and 7.7 % (n = 4) for depressive disorder not otherwise specified (Table 2). The mean score of clinical status of depression from HAM-D scale was 15.46 (SD=2.97); and 57.7 % (n = 30) were of moderate severity. The mean score of anxiety symptom from Zung self-rating anxiety scale was 39.5 (SD = 4.8) (Table 3). Most patients reported their psychosocial problems, particularly with their families and personal relationship.

Table 1. Characteristics of patients who attempted suicide by acetaminophen ingestion (N = 52).

General Characteristics	Cases (%)	Characteristics of illnesses	Cases (%)
Sex		History of physical illness	4 (7.7)
Male	10 (19.2)	History of psychiatric illness	4 (7.7)
Female	42 (80.8)	History of alcohol use	12 (23.1)
Age group		Current status of alcohol use	
15 to 25 years	33 (63.5)	Always	2 (3.8)
>25 to 50 years	19 (36.5)	Seldom	8 (15.4)
Marital status		No	42 (80.8)
Single	32 (61.5)	Previous suicidal attempt	9 (17.3)
Married	20 (38.5)	Repeated the same method	8 (15.4)
Religion		Suicidal attempt by ingestion of	
Buddhism	51 (98.1)	acetaminophen	
Islam	1 (1.9)	Alone	39 (75)
Residence province		Combined with other drugs	13 (25)
Bangkok	33 (63.5)	Reported psychosocial stress	50 (96.2)
Central	13 (25.0)	Interpersonal relationship	33 (63.5)
Other	6 (11.5)	Family	17 (32.7)
Education		Work	7 (13.5)
Primary or	28 (53.8)	Financial	4 (7.7)
secondary school		Health	1 (1.9)
College or graduated	24 (46.2)	Learning	1 (1.9)
Occupation		Family history of suicide	7 (13.5)
Employee	21 (40.4)		
Student	15 (28.8)		
Unemployed	9 (17.3)		
Other	7 (13.5)		
Income (Bahts/month)			
None	19 (36.5)		
5,000 or lower	16 (30.8)		
5,001 to 10,000	2 (3.8)		
More than 10,000	15 (28.9)		

Table 2. DSM-IV Axis I diagnosis among patients (N = 52).

Diagnosis	Cases	Percent
Major depressive disorder	4	7.7
Depressive disorder not otherwise specified	4	7.7
Adjustment disorder with depressed mood	31	59.6
Adjustment disorder with mixed emotion	11	21.2
Mixed anxiety depression	2	3.8

Table 3. Score on severity of depression and anxiety level and data about acetaminophen number among patients.

	Mean	S.D.	Min	Max
HAM-D	15.46	2.97	10	25
ZAS	39.5	4.8	26	51
Number of tablets of ingested acetaminophen	41.8	68.14	6	500
Number of hours before receiving treatment	9.07	6.35	4	24
Number of days for admission	3.48	3.29	1	21

HAM-D ; Hamilton rating scale for depression, ZAS ; Zung self-rating anxiety scale

Most patients (n = 41; 78.9 %) took less than 40 tablets or 20 grams of acetaminophen. However, the number of tablets in this study varied from 6 to 500. Gender was found associated with the number of ingested acetaminophen (x^2 = 6.18; p = .025). Average number of tablets taken in male and female are 86.8 and 31.1, respectively. It was found that one-third of the patients had threefold abnormal level of SGOT, SGPT ; and serum acetaminophen levels were categorized in possible or probable risk (Table 4). Their length of hospitalization varied from 1 to 21 days with the mean of 3.48 days (SD = 3.29). There are statistically significant correlations between the number of ingested acetaminophen tablets and abnormal prothrombin time (r = .7; p = .0001), SGPT (r = .36; p =.008), SGOT (r = 0.28: p = 0.044), length of hospitalization (r = 0.33; p = 0.015) (Table 5). We did not find any association between the severity of psychiatric symptoms (i.e. depression or anxiety) and the number of ingested acetaminophen tablets or acetaminophen toxicity.

Nevertheless, it was found that patients who had abnormal liver function test (SGOT, SGPT) had longer duration before recieving treatment than those whose LFT were normal (Table 6).

Table 4. Number and percentage of patients by severity of depression, anxiety, number of acetaminophen, number of hours before receiving treatment, SGOT, SGPT and serum acetaminophen level.

	Male	Female	Total	%
HAM-D				
Mild	1	8	9	17.3
Moderate	6	24	30	57.7
Severe	3	10	13	25.0
ZAS (75^{th} percentile = 42)				
≤ 42	9	31	40	76.9
>42	1	11	12	23.1
Number of ingested acetaminophen (tablets)				
≤ 20	3	18	21	40.4
21-40	2	18	20	38.5
> 40	5	6	11	21.2
Number of hours before receiving treatment				
< 6	2	21	23	44.2
6-12	5	12	17	32.7
> 12	3	9	12	23.1
SGOT				
Normal	7	28	35	67.3
Three-fold abnormal	3	14	17	32.7
SGPT				
Normal	7	27	34	65.4
Three-fold abnormal	3	15	18	34.6
Serum acetaminophen level				
Slight	4	29	33	63.5
Possible	4	5	9	17.3
Probable risk	2	8	10	19.2

Table 5. Correlation between number of acetaminophen and medical toxicity or severity of psychiatric symptoms.

	Correlation	P
Number of acetaminophen tablets and PT	.7	<.0001*
Number of acetaminophen tablets and SGPT	.36	.008*
Number of acetaminophen tablets and SGOT	.28	.044*
Number of acetaminophen tablets and length of hospitalization	.33	.015*
Number of acetaminophen tablets and score on HAM-D	.17	.22
Number of acetaminophen tablets and score on ZAS	.08	.583
SGOT and SGPT	.90	.0001*
Serum acetaminophen level and SGOT	.31	.025*
Serum acetaminophen level and SGPT	.32	.019*
HAM-D and ZAS	.28	.014*

Table 6. Difference of duration before receiving treatment between the groups.

	Mean of hours before receiving treatment (SD)		p
SGOT			
Abnormal	12.94	(8.14)	<.0001*
Normal	7.2	(4.3)	
SGPT			
Abnormal	13.06	(7.9)	<.0001*
Normal	6.97	(4.11)	

Discussion

The general characteristics of patients who attempted suicide with acetaminophen ingestion were mostly similar to those who attempted by other nonviolent methods.[1] Most of the them were female with their age between 15 to 25 years. In recent years, there have been a growing concern over the increasing rate of young people particularly in developed countries.[13,18-19] In this study it was found that some patients had history of previous suicidal attempt; nearly all of them repeated the same method of drug ingestion. Studies show that about 40 percent of depressed patients who committed suicide had made a previous attempt. A history of suicide attempt is perhaps that the best indicator that a patient has increased risk of suicide.[1] Goldstein *et al.*[20] noted that not only a history of prior suicide attempt but also the number of attempts is critical as the risk of suicide increases with each subsequent suicidal attempt. Prospective studies of clinical cases have shown that between 0.1 to 11% of adolescent suicide attempters eventually commit suicide.[21] The likelihood of later suicide is increased in older teenagers, in male, and in those who have been hospitalized. In Otto's study, 70 % of the attempters who ultimately completed suicide died by the methods similar to those used in their initial attempt, and the remainders used a more lethal method.[22] Family history of suicide was found in 13.5% of the patients. Studies in psychiatric patients show that a family history of suicide raises the risk of suicidal behavior.[23] However, Roy[24] and Linkowski[25] reported that a family history of suicide was found significantly higher among depressed patients who had made a violent suicidal attempt in comparison with patients who had made a nonviolent attempt. Therefore the development of appropriate follow-up and treatment of the people who are known to be of high risk of further suicidal behavior, including those who have made previous suicide attempts, is important.

Most patients had adjustment disorder and reported psychosocial problems particularly about their family and personal relationship. These findings are consistent with other studies.[26-28] Stresses commonly precede a suicide or attempted suicide.[29-30] Honkanen *et al.*[31] noted that life dissatisfaction has a long-term effect in the risk of

suicide and this seems to be partly mediated through poor health behavior. In this study, the mean score of clinical status for depression from HAM-D scale showed moderate severity as well as anxiety level from Zung self-rating anxiety scale. Although the patients might have moderate degree of depression or anxiety, suicidal attempt could occur. Therefore suicidal precaution should be given event to those who use non-violent method such as drug ingestion. Paracetamol or acetaminophen is a widely used and a relatively safe antipyretic analgesic; nevertheless, there is an increasing incidence of acute acetaminophen poisoning including overdose by suicidal attempt. The major complication of paracetamol poisoning is liver damage. The sequence of event following acute over dosage is anorexia, nausea, vomiting and epigastric pain due to direct irritant effect of durg within few hours and may be delayed for 24 hours due to hepatic damage. Maximum liver damage, as assessed by alanine transaminase level, occurs between two and four days from ingestion, the degree of liver damage is as greater as the larger dose. Jaundice may appear after two to sex days; death may occur at any time from two to seven days after ingestion. Most patients in this study took fewer than 40 tablets (20 g). However, one-third of them had abnormal liver function test and their serum acetaminophen levels were categorized as possible or probable risk. Most of the cases took acetaminophen at home and they knew that overdose of the drug is dangerous, but they did not understand the details of its toxicity or affected organs. Number of ingested acetaminophen tablets taken at the time of attempt that were reported by the patients correlated with the degree of abnormality of SGOT, SGPT, PT and their length of hospitalization. This reflects that data of suicidal behavior and the dose of the drug the patients took are reliable and should be concerned by physicians. Male used acetaminophen tablets in their attempted suicide higher than female, but it was not found in association with the increase of abnormal liver function test or risk of acetaminophen toxicity. This may be due to the fact that men had higher body weight or because they hardly showed any longer period for treatment or because of the limitation in this study that there were small number of recruited male patients. However, access to the method employed in the attempt is also important particularly in youth suicide, because it is often impulsive. It is reasonable to expect that limiting access to the commonly used methods could prevent its occurrence under some circumstances.[32] Recent British experience has been the effect of limiting the packaging size of acetaminophen on the assumption that this will reduce the impulsive ingestion of potentially lethal quantities of the medication. This appear to have resulted in a significant reduction in suicidal deaths attributable to acetaminophen, and also to a striking reduction in liver transplants performed on survivors of toxic ingestions.[13,33] This correlation was not found with the severity of psychiatric symptoms; it may because most patients had symptoms of depression and anxiety level of moderate severity. Some persons who had more severe psychiatric symptoms may use other violent methods in attempted suicide. Therefore medical management of acetaminophen overdose in suicidal attempt should be focused on interviewing data on suicidal behavior, the number of ingested acetaminophen tablets and laboratory findings.

Acetylcysteine is an effective the treatment of acetaminophen overdose. It has been clearly shown that treatment with N-acetylcysteine (NAC) should be initiated within the first 16 hours post-ingestion.[17] Since in many cases, the patients are entirely accurate about the time of ingestion. It is acceptable to treat patients during the first 24 hours post-ingestion. However, it is most effective to start the medication as early as possible. Smilkstein *et al.*[32] found that hepatotoxicity developed in 6.1% of the patients at a probable risk when N-acetylcysteine was started within 10 hours of acetaminophen ingestion and in 26.4% of the patients when the therapy was begun 10 to 20 hours after ingestion. Among the patients of high-risk who were treated 16 to 24 hours after an acetaminophen overdose, hepatotoxicity developed in 41%. In this study, however, we found that most of the patients received their treatment within 12 hours with their mean of 9 hours and the patients who had abnormal liver function test had longer duration before receiving treatment than those who had normal LFT. And, all patients recovered.

This study was conducted at a hospital in Bangkok and in the context of an inpatient setting who were consulted for psychiatric evaluation in which the severity of illness may limit generalization to experience with outpatients. However, there are reports that among attempted suicides by drugs or substance ingestion, overdose of acetaminophen in particular has potential liver toxicity which is likely to result in admission. Medical condition following acute acetaminophen ingestion focus on liver damage or hepatotoxicity that was common and major complication. Herein, we did not include other events that might occur in severe poisoning of acetaminophen such as profound hypoglycemia or metabolic acidosis. Nevertheless, all patients recruited in this study recovered with their average length of admission of 3.48 days.

Conclusion

The availability of non-violent methods, particularly acetaminophen overdose, should be of more concern for suicide prevention, particularly in female who has adjustment disorder and moderate depression.

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