Paracetamol Overdose in Suicidal Attempt Patients

Paitoon Narongchai MD*,
Siriphun Narongchai MS*

** Department of Forensic Medicine, Faculty of Medicine, Chiang Mai University*

Twenty one suicidal attempt patients of paracetamol overdose were studied at Maharaj Nakorn ChiangMai Hospital between 2000-2002. Most of them were females (16 or 76%), students (8 or 38%) and employees (7 or 33%). The average age was 22 years old and the majority of cases were single (18 or 86%) and had problems with their partner (9 or 43%). The number of paracetamol tablets (500 mg/tablet) were ingested between 10-90 tablets. Blood levels of paracetamol were 0.12-8.3 gm/L at 72-2 hours which did not correlate significantly with oral doses. These were caused by vomiting after ingestion of large doses and the efficacy of individual absorption or properties of ingradient and mixed vehicles in each tablet. Nausea and vomiting occurred in all cases. However, a few victims suffered from liver intoxication in the present study, but all of them survived and recovered completely.

Keywords : *Paracetamol, NAPQI, Hepatotoxicity*

J Med Assoc Thai 2004; 87(4): 423-6

The toxicity of paracetamol (or acetaminophen) overdoses has been recognized since 1966[1] and paracetamol accounts for most cases in the USA and worldwide[1,2]. The most serious toxicity of paracetamol overdose is hepatic failure and it is the main reason for most of the liver transplantations in Great Britian and United States[3]. Toxicity of paracetamol may be delayed in many conditions such as co-ingestion with propoxyphene and other opioids and also in extended release preparation. The plasma paracetamol level will peak 16 hours after ingestion[4]. The toxic metabolite, N-acetyl-p-benzoquinone-imine (NAPQI) is formed when it is metabolized by mixed-function oxidase system[5,6]. It attaches to the hepatic cell membrane and damages the lipid bilayer. Glutathione in the liver and blood is the primary anti-oxidant which conjugates and neutralizes NAPQI[7,8]. When glutathione is depleted to less than 70% of normal levels as in paracetamol overdose or alcoholic intoxication, in NAPQI cannot be detoxified resulting in injury to hepatocytes, arylation of macromoleculs and cell death, respectively. A single oral dose of more than 7.5 grams for adults or 150 mg/kg for children is considered toxic[1]. The clinical manifestations commence with gastro-intestinal upset such as nausea, vomiting and increasing transaminase activity within one day[9]. The serious toxicities will normally start up after 3 days with liver cell injury, prolonged prothombin time, renal insufficiency and right upper quandrant pain[12]. About 3.5% of the patients will develop severe hepatotoxicity and less than half of the patients with fulminant liver failure die[10,11]. But in the survivors the liver recovers completely with no evidence of fibrosis within 30 days[12]. However, in the case of chronic alcoholic patients there is a higher risk for development of hepatotoxicity than in normal patients after paracetamol overdose[13].

Correspondence to : Narongchai P, Department of Forensic Medicine, Faculty of Medicine, Chiang Mai University, Thailand

Material and Method

The authors studied 21 victims between 2000-2002 at the Maharaj Nakorn Chiang Mai, Thailand. Most of them had a brief history of paracetamol ingestion and were confirmed by blood levels of paracetamol by spectrophotometry.

Inclusion criteria:

1. Prompt history of paracetamol ingestion.
2. Acute onset of clinical manifestations a few hours after ingestion.
3. Detection of paracetamol in stomach or gastric lavage and also in the blood.

The history and general information of the

patients was collected including sex, age, status, profession, motivation, oral dosage of paracetamol ingestion, clinical laboratory manifestation and paracetamol blood level.

Results

There were 21 victims, 16 females (76%) and 5 males (24%) between 2000-2002. Most of them were students (8) and employees (7). The average age was 22 years and the age of 16-20 (48%) and 21-25 years old (38%) was the most common range. Almost all of them were single (86 %). The motivation for para-cetamol abuse was quarrelling with a boy or girl friend (43%). The amount of paracetamol intake was 10-90 tablets (500 mg/tablets) or 5-45 gm or an average of 30 tablets.

Vomiting and nausea were the most common clinical manifestations occurring in all cases. They were 3 cases who suffered liver injury during the first day of abuse.

Blood from all the victims was collected at the time of visiting. The levels of blood paracetamol were detected by spectrophotometry at a wavelength of 250 nm. None of the patients died and the average time of treatment was 3-4 days.

Discussion

Paracetamol is the most common drug in attempted suicide, but almost all of the victims survive. Only a few cases die, but severe liver cell injury requires proper treatment. However, the victims who have little or no liver cell injury will recover completely. Sometimes the toxicity dissolves by itself because large doses of paracetamol make all victims vomit, thereby pushing paracetamol in the stomach out of the body. That is probably the most likely reason. The oral dosages were not correlated with blood levels of paracetamol and hepatotoxicity was uncommonly developed in these victims owing to plasma concentrations lower than the toxicity level. However, absorption, bioavailibity and volume of distribution of paracetamol preperation or different production companies can make plasma paracetamol concentration lower than the real concentration.

References

1. Haddad LM, Shannon. MW and Winchester JF. Chemical Management of Poisoning and Drug overdose 3rd edition, W.B. Saunders company, Philadelphia USA 1998. 664-742.
2. Litovitz TL, Felberg L, Soloway RA, et al. 1994 An-

Table 1. The general situation of paracetamol overdosed patients during 2000-2002

Sex		Status		Age(years)					
				15	16-20	21-25	26-30	31-35	≥ 36
Male	5(24%)	single	18(86%)	2	11	4	2	0	2
Female	16(76%)	couple	3(14%)	(9.5%)	(52%)	(19%)	(9.5%)	(0%)	(9.5%)
Profession						Motivation			
student	employee	trader	monk	agriculture	unknown	Friend	Family	stress	
8	7	3	2	1	1	9	5	7	

Table 2. The actaul corelation between number of paracetamol tablets and blood concentrations

No.	No. of acetaminophen tablets (500 mg/tablet)	Blood acetaminophen concentration (mg%)	Hours after ingestion (hrs)	No.	No. of acetaminophen tablets (500 mg/tablet)	Blood acetaminophen concentration (mg%)	Hours after ingestion (hrs)
1	30	1.56	1	12	15	0.12	12
2	13	2.18	2	13	39	6.6	12
3	30	8.3	2	14	15	2.68	12
4	20	1.7	2	15	24	2.3	15
5	20	2.2	3	16	90	0.3	24
6	6	0.24	4	17	50	0.13	72
7	40	1.56	4	18	24	2.3	15
8	20	1.8	4	19	10	0.3	9
9	70	1.9	7	20	10	1.7	12
10	50	1.2	8	21	30	0.8	24
11	24	3.2	9	X	30.48	1.98	12.48
SD	19.90	2.03	15.47	SD	19.90	2.03	15.47

Table 3. The detail situations of paracetamol overdose in suicidal attempt patients

Case	Sex	Age	Profession	Status	Motivation	Oral dose (gram)	S/S	Hour after ingestion	Serum conc.(mg%)	LFT							Duration of Rx (dose)	NAC	S/S Rx	
										GOT/GPT	ALP	TB/DB	Na	K	BUN/Cr				
1	F	55	Emp.	W	family	15	N/V	1	1.56	15/19	41	0.34/0.15	141	3.6	14/0.8	2	+	+	F = Female,
2	M	19	Std.	S	friend	8	N/V	4	0.24	15/10	56	0.71/0.23	143	4.2	15/1.1	4	+	+	M = male,
3	F	30	Emp.	S	friend	6.5	N/V	2	2.18	28/30	43	1.02/0.39	142	3.7	11/0.9	2	+	+	C = couple,
4	M	20	monk	S	stress	7.5	N/V	12	0.72	25/30	45	1.1/.4	140	4.1	10/1	2	+	+	S = single,
5	F	14	Std.	S	friend	35	N/V	7	1.9	232/439(D3)	77(D4)	4.02/1.43(D4)	138	3.9	18/1.2	4	+	+	C = couple,
6	F	20	Emp.	S	family	19.5	N/V	12	6.6	34/10	70	0.65/0.18	144	3.8	12/0.7	2	+	+	S = single,
7	F	17	Std.	S	stress	25	N/V	8	1.2	27/21	62	0.58/0.22	137	4.1	13/0.9	3	+	+	N = nausea,
8	M	17	monk	S	stress	20	N/V	4	1.56	19/28	99	0.83/0.29	139	3.7	11/1.3	3	+	+	V = vomiting,
9	M	18	trade	S	family	10	N/V	3	2.2	17/9	67	0.86/0.42	138	4.3	15/1.5	2	+	+	+ = yes,
10	F	22	Std.	S	friend	45	N/V	24	0.3	115/287	76	2.21/1.14	142	3.9	19/1.3	8	+	+	- = no,
11	F	17	Emp.	S	family	7.5	N/V	12	2.68	16/12	50	0.73/0.25	143	4.2	20/1.0Na	2	+	+	std = student,
12	F	40	trade	C	stress	15	N/V	2	8.3	25/30	70	.9/.25	139	3.6	21/1.3	1	+	+	fam.= family
13	F	20	Emp.	S	stress	12	N/V	9	3.2	13/7	50	0.82/0.35	145	4.1	18/1.3	3	+	+	str. = stress,
14	F	29	trade	C	stress	25	N/V	72	0.13	39/226(D8)	190(D1)	9.54/6.43(D1)	138	5.1	41/1.1	17	+	+	na = non detect
15	F	21	Std.	S	friend	10	N/V	2	1.7	40/35	50	1.5/.2	139	4.3	25/1.2	2	+	+	
16	F	22	Std.	S	friend	10	N/V	4	1.8	15/8	55	0.72/0.31	140	4	12/0.7	2	+	+	
17	F	15	Std.	S	friend	12	N/V	15	2.3	40/53	60	1.73/0.78	139	3.9	22/1.2	5	+	+	
18	M	22	Emp.	S	family	20	N/V	24	0.24	25/30	68(D1)	1.59/0.21	140	4.3	20/1.2	6	+	+	
19	F	19	Std.	S	friend	5	N/V	9	0.3	30/25	70	1.2/.5	140	4.2	15/1.0	1	+	+	
20	F	16	Emp.	S	friend	5	N/V	12	1.74	15/8	46	0.52/0.38	138	3.6	8/0.7	3	+	+	
21	F	16	Std.	S	stress	15	N/V	24	0.8	35/30	80	.5/.3	137	4.1	15/.5	1	+	+	
Average		22.33				15.62		12.48	1.98							3.57			
SD		9.57				10.22		15.47	2.03							3.53			

nual report of the American Association of Poison Control Centers Toxic Exposure surveillance System. Am J Emerg Med 13: 1995; 551.

3. Lee WM. Acute liver failure. Am J Med as (Supple iA): iA, 1994.
4. Bizovi K, Keys N, Rivas J, et al. Tylenol ER, late rise in APAP level after overdose. Abstract. J Toxicol Clin Toxicol 33 : 1995; 51.
5. Mitchell JR, Jollow DJ, Gillette JR. et al. Drug metabolism as a cause of Drug toxicity. Drug Metab Dispos I: 1973; 481.
6. Potter WZ, Davis DC, Mitchell JR, et al. Acetaminophen induced hepatic necrosis. Cytochrome P-450-mediated covalent binding in vitro. J Pharmacol Exp Ther 187: 1973; 203.
7. Mitchell Jr, Thorgiersson SS, Potter WZ, et al. Acetaminophen induced hepatic injury: Protective role of glutathione in man and rationale for therapy. Clin Pharmacol Ther 19: 1976; 284.
8. Miners JO, Drew R, Birkett DJ. Mechanism of action of paracetamol protective agents in mice in vivo. Biochem Pharmacol 33: 1984; 1995.
9. Singer AJ, Carracio TR, Mofenson HC. The temporal profile of creased transminase levels in patients with acetaminophen induced liver dysfunction. Ann Emerg Med. 26: 1995; 49.
10. Hamlyn AN, James O, Douglas AP. The spectrum of paracetamol (acetonminophe) overdose: chinical and epidemiological studies. Postgrad Med J. 54: 1978; 400.
11. O'Grady JG, Alexander GJM, Hyllar KM, et al. Early indicators of prognosis in fulminant hepatic failure. Gastroenterology. 97: 1989; 439.
12. Hamlyn AN, Douglas AP, James OFW, et al. Liver structure and function in survivors of acetaminophen poisoning. AM J Dig Dis. 22: 1997; 605.
13. Wright N, PrescoftLF. Potentiation by previous drug therapy of hepatotoxicity following paracetamol over dosage. Scot Med J. 18: 1973; 56.

ยา Paracetamol เกินขนาดในผู้ที่พยายามฆ่าตัวตาย

ไพฑูรย์ ณรงค์ชัย, สิริพันธ์ ณรงค์ชัย

ผู้ที่ได้รับยา paracetamol เกินขนาดเพื่อใช้ฆ่าตัวตายที่เข้ามารับการรักษาในโรงพยาบาลมหาราชนครเชียงใหม่ ระหว่างปี พ.ศ. 2544-2546 จำนวน 21 ราย ซึ่งอยู่ในเกณฑ์การศึกษา พบว่าเป็นเพศหญิงร้อยละ 76 เพศชายร้อยละ 24 อายุเฉลี่ย 22 ปี สถานะทางครอบครัวเป็นโสด ร้อยละ 85.7 และเป็นเด็กนักเรียน และอาชีพรับจ้างทั่วไป ร้อยละ 70 จากการศึกษาพบว่าปริมาณยา paracetamol ขนาดเม็ดละ 500 มิลลิกรัม ที่รับประทาน มีปริมาณตั้งแต่ 10-90 เม็ด ตรวจวัดระดับยาในเลือด ระหว่าง 0.12-8.3 กรัมต่อลิตร ซึ่งระดับยาในเลือดไม่มีความสัมพันธ์กับปริมาณยาที่ได้รับประทานอย่างมีนัยสำคัญทางสถิติ ทั้งนี้น่าจะเกิดจากการอาเจียน หลังจากรับประทานยาปริมาณมาก อย่างไรก็ตาม พบผู้ป่วย 3 ราย ที่มีการทำลายตับอย่างชัดเจน แต่จากการรักษา ไม่พบว่ามีผู้ใดเสียชีวิต จากการได้รับยา paracetamol เกินขนาด