DÜZCE TIP DERGİSİ
DUZCE MEDICAL JOURNAL

ORİJİNAL MAKALE / ORIGINAL ARTICLE

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Submitted/Başvuru tarihi: 09.01.2013
Accepted/Kabul tarihi: 11.03.2013
Registration/Kayıt no: 13.01.268

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e-ISSN 1307- 671X
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duzcetipdergisi@duzce.edu.tr

Demographic Characteristics of Patients, who Attempted Suicide with Paracetamol in a Research Hospital

Bir Eğitim Hastanesinde Parasetamol ile İntihar Girişiminde Bulunan Hastaların Demografik Özellikleri

ABSTRACT

Purpose: Diversity and widespread availability of paracetamol containing preparations increase the likelihood of their use for suicidal attempts. This retrospective study aimed to provide information regarding the clinical and demographic characteristics of patients with paracetamol intoxication.

Material and Methods: A total of 214 patients attending to the Emergency Unit of the Izmir Bozyaka Training and Research Hospital between 1 January–31 December 2009 with a preliminary diagnosis of paracetamol intoxication were included. Demographic and clinical data have been collected.

Results: Patients younger than 20 years of age represented the majority (78 patients, 36.4%) of the cases. Most of the emergency visits were recorded between 22:00 and 23:00 p.m. and between 00:00 and 01:00 a.m. Proportion of patients was highest in June as compared to other months. Of the whole study population, 55 (26%) ingested only paracetamol, while 159 (74%) were intoxicated with other drugs and/or alcohol as well. Symptoms were present in 174 patients (81%); 40 patients (19%) had no symptoms.

Conclusions: Good knowledge of demographic data of the patients and effective use of poison call centers may help to improve diagnosis and management in paracetamol intoxication.
Key words: Paracetamol, intoxication, suicide, demographic data

ÖZET

Amaç: Parasetamol içeren preparatların çeşitliliği ve yaygın olması, suicid amaçlı kullanılma ihtimalini artırır. Bu retrospektif çalışmada, parasetamol intoksikasyonuyla gelen hastaların klinik ve demografik özelliklerininin ortaya konulması amaçlanmıştır.

Yöntem ve Gereç: Çalışmaya parasetamol zehirlenmesi ön tanısı ile 1 Ocak–31 Aralık 2009 tarihleri arasında İzmir Bozyaka Eğitim ve Araştırma Hastanesi Acil Ünitesine başvuran 214 hasta dahil edilerek hastaların demografik ve klinik verileri toplanmıştır.

Bulgular: Vakaların büyük bir kısmını 20 yaşın altında hastalar oluşturmuştur (78 hasta,%36.4). Başvuruların 22:00-23:00 ve 00:00-01:00 saatleri arasında yoğun olduğu görülürken, Haziran ayında diğer aylara oranla daha fazla vakanın acile başvurduğu görüldü. Olguların 55'i (%26) sadece parasetamol, 159'u (%74) ise parasetamolü diğer ilaçlar ve/veya alkol ile birlikte almıştır. İntoksikasyon semptomları 174 hastada (%81) mevcutken, 40 hastada (%19) herhangi bir intoksikasyon belirtisi yoktu.

Sonuç: Hastaların demografik bilgilerinin iyi bilinmesi ve Zehir Danışma Merkezlerinin etkin kullanımı, parasetamol zehirlenmesinin tanı ve tedavisinin geliştirilmesinde faydalı olabilir.
Anahtar kelimeler: Parasetamol, zehirlenme, intihar, demografik bilgiler

INTRODUCTION

Suicide attempts represent a major medical emergency due to the life threatening nature of the condition requiring immediate medical assistance. Suicide-associated deaths are the 11th and 3rd most common cause of mortality in the general population and among youngsters in the United States (US), respectively (1).

Proven safety profile of the appropriate doses of paracetamol has led to its widespread use for the symptomatic treatment of pain and high fever in many conditions. In addition to those formulations that contain paracetamol as the sole ingredient, many other combination preparations exist in which this agent is combined with opioids, other painkillers, anxiolytics, decongestants, expectorants, and antihistamines (2). Paracetamol toxicity was reported to account for 5% of all drug intoxications and 23% of all deaths due to drug intoxication (3,4).

Table 1. Distribution of the patients by age groups.

Age groups (years)	All patients n (%)	Females n (%)	Males n (%)
14-20	78 (36.4)	59 (39.6)	19 (29.2)
20-29	73 (34.1)	52 (34.9)	21 (32.3)
30-39	40 (18.7)	26 (17.4)	14 (21.5)
40-49	15 (7)	8 (5.4)	7 (10.8)
50-59	4 (1.9)	2 (1.3)	2 (3.1)
>60	4 (1.9)	2 (1.3)	2 (3.1)

Table 2. Blood pressure, pulse, AST and ALT values of the patients

	All patients	Female	Male
Systolic (mmHg)	115.7±17.3	114.4±17.6	118.8±16.2
Diastolic (mmHg)	73.3±12.5	73.6±12.9	72.7±11.8
Pulse (/min)	86.7±14.6	88.0±13.5	83.7±16.8
AST (U/L)	24.9+12.7	23.1−9.5	29.0+17.4
ALT (U/L)	20.4±23.1	16.4±10.6	29.6±37.4

Diversity of paracetamol containing preparations and their widespread availability may also be associated with an increased likelihood of its use for suicidal attempts (5)

Patient history, clinical signs, and the blood paracetamol concentration in particular represent the cornerstones of the diagnosis of paracetamol intoxication (6). This study was undertaken to provide information regarding the clinical and demographic characteristics of patients with paracetamol intoxication in the hope of contributing to management strategies. For this purpose, a retrospective analysis on the clinical and demographic characteristics of patients attempting suicide with paracetamol was performed.

METHODS

Patients and Data Collection

Patients attending to the Emergency Unit of the Izmir Bozyaka Training and Research Hospital between 1 January–31 December 2009 with a preliminary diagnosis of paracetamol intoxication were included in this retrospective study.

Patient records were retrieved using a search for the specific ICD-10 diagnostic code (X44) and recollecting the relevant information from the hospital data recording system and forensic registry of the hospital. Patients with missing files or inadequate data were excluded. The study protocol was approved by the local ethics committee.

Demographic characteristics, age, gender, date and time of admission, address, time to admission, initial findings, presence or absence of paracetamol related symptoms, laboratory results, treatment(s) administered, clinical course, requirement for hospitalization, and length of hospital and emergency stay were recorded in the data collection form.

Assessments

Routine blood biochemistry was studied using an auto-analyser (Moduler P800, Roche Diagnostics®, Germany) in the biochemistry laboratory of the emergency unit. Paracetamol levels were determined spectrophotometrically using a MCG-240 device and "DRI Acetaminophen serum Tox Assay" kits (Thermo Scientific®). In order to determine whether toxic doses were ingested and treatment required, Rumack-Matthew nomogram identifying the severity of paracetamol-induced hepatic damage in a single acute intake was used.

Statistical Analysis

Data were analyzed using SPSS 16.0 software for statistical analyses. Descriptive statistics were used to present demographic data. Kolmogorov-Smirnov test was used to test normal distribution of blood pressure, pulse, and enzyme levels. Between-group comparisons for variables without normal distribution were performed using Mann-Whitney U test. Categorical variables were compared with chi-square test, p value less than 0.05 was considered significant.

RESULTS

A total of 214 patients between 14 and 84 years of age (149 female,70%; 65 male,30%) attending to the emergency unit with a diagnosis of paracetamol intoxication were identified. The average age was 26.1±11.8 years, mean age was 25.0±10.9 and 28.6±13.4 years in female and male patients, respectively. Comparison between age groups showed that the patients younger than 20 years of age represented the majority (78 patients, 36.4%) of the cases, followed by patients between 20-29 years of age (73 patients, 34.1%). Table 1 shows the age distribution across groups and sexes.

Most of the emergency visits were recorded between 22:00 and 23:00 p.m. and between 00:00 and 01:00 a.m., while number of patients attending to the emergency unit was lowest between 08:00 and 09:00 a.m. (Figure 1). Monthly distribution analysis showed that proportion of patients attending to the emergency unit due to paracetamol intoxication was highest in June as compared to other months for male patients (n=35, 16.4%), female patients (n=24, 16.1%), and for the overall group (n=11, 16.9%) (Figure 2).

Of the whole study population, 55 (26%) ingested only paracetamol, while 159 (74%) were intoxicated with other drugs and/or alcohol as well. Symptoms were present in 174 patients (81%); 40 patients (19%) had no symptoms. Symptomatic patients were more likely to have been intoxicated with additional drugs and/or alcohol, such that only three patients were symptomatic among those with sole paracetamol toxication. The most common symptoms were nausea, vomiting, palpitations and malaise. Two patients (0.9%) were intubated, one with a history of additional ingestion of tricyclic antidepressant and one with benzodiazepine; none of these two patients had toxic blood paracetamol levels.

Table 2 shows physical examination findings such as blood pressure and pulse, as well as AST and ALT levels. Despite absence of any gender difference in blood pressure and pulse, males had significantly higher levels of AST and ALT ($p < 0.05$). Paracetamol levels were measured in 166 patients (78%), with 38% of the measurements being performed within four hours of intoxication and 62% at a later timepoint than that. Toxic levels were determined in 46 (28%) patients, with 21 (13%) of the patients having non-toxic levels despite a measurement before 4 hours. A third measurement was performed in 19 (8.9%) patients, all of whom were admitted.

A poison center call was made for 153 patients (71.5%); 130 patients (61%) received activated charcoal after gastric lavage and 76 patients (35.8%) were given N-acetylcysteine (NAC) (through

Figure 1: The distribution of patients according to the hours per day

i.v. route in 93.7%). No gender differences were noted in terms of the proportion of patients for whom a poison-center call was made and in terms of the proportion of patients who were given activated charcoal and NAC.

The average length of stay in the emergency room was 7.1±6.6 hours (min. 2 hours, max. 24 hours). Forty-five percent of the patients (n=96) were admitted and 1% (n=2) were referred. Of the patients who were admitted, 29% (n=28) were admitted to the intensive care unit and 71% (n=68) were admitted to a normal inpatient service. The maximum length of stay (in a psychiatric unit) in the hospital was 7 days, with no mortality.

DISCUSSION

According to 2005 US data, a total of 70.000 cases of paracetamol intoxication were recorded with 300 patients dying from the condition (7). Although similar data for Turkey has traditionally been limited, a recent increase in the number of publications and studies conducted by centers where specialist training is provided for emergency medicine has led to an accumulation of epidemiologic data regarding drug poisoning (8).

The present results showed that 26% had sole paracetamol intoxication, while 74% also ingested other medications or alcohol. Similarly, in the study by Gunnel et al. (9) and a retrospective study by Hocaoglu et al. from Poison Call Center, Dokuz Eylul University encompassing a 12-year period showed that paracetamol was the most frequently overdosed agent (10). This is in contrast with the study by Karabulut et al.'s study, antidepressants have been the most frequently used agents for suicidal purposes (11).

In this study, most cases of paracetamol overdose occurred in June both for the overall group and for both sexes. This finding is in line with study by Uyanikoglu et al., (12) Gunnel et al.(9) and UZEM, Emergency Unit of Marmara University and datas (13). UZEM data suggests that 44% the drug intoxications were due to suicide attempts and most of the emergency visits occur between 00:00 and 01:00 a.m.. These are similar to our observations where the number of emergency visits was highest between 22:00 and 23:00 p.m. and between 00:00 and 01:00 a.m.. Our data for female patients (70%) is similar to those reported a study from Adnan Menderes University and Emergency Unit of Marmara University (8,13). Although our data is similar, it should be remembered that our study population consisted of patients with paracetamol intoxication only.

In our study the average age was 26.1±11.8 years. Similar average age for patients with intoxication was 27.65±11.12 years in the study by Uyanikoglu et al. (12). The latter study found that the average age for females was slightly higher and the average age for males was slightly lower than the overall average age. In contrast with these findings, males had a higher average in our study. In a study by Deniz et al. from the Emergency Unit of Kirikkale Hospital, majority of the patients were between 1 and 20 years of age (61.5%), while most of the patients (72.6%) with a suicide attempt were between 11 and 25 years of age (14). In their study, the average age is considerably lower, compared to other studies. These authors evaluated a total of 497 intoxication cases. The average age for the overall group, female patients and male patients were 19.20±17.3, 18.01±17.8 and 20.31±16.8 years, respectively. However, it should be noted that the proportion of patients between 0 and 10 years of age were higher in that study as compared to other studies (n=196) and that the age range was relatively wide (1-88 years), as reflected by the high standard deviation.

Establishment of three National Poisoning Call Centers (UZEM) has been a major step toward management of poisoning in Turkey. These centers not only provide guidance on the management strategies for health facilities, but also deal with personal calls and generate valuable statistical data for the detection, evaluation and prevention of drug poisoning. Thus, a call to poison centers was made by emergency doctors for 71.5% of the cases in our study.

Symptoms were present in 81% of our cases, while 19% were asymptomatic, and simultaneous ingestion of other drugs or alcohol was more likely to be associated with a symptomatic course. However, in the study by Hocaoglu et al. examining intoxication not only with paracetamol but also with other analgesics, 54.7% of the cases were asymptomatic (10). Yesil et al. observed symptoms such as abdominal pain, vomiting, drowsiness, and diarrhea in 21.1%, 20.4%, 15%, and 7.5% of their cases, respectively (9). Confusion, hypotension, nausea, palpitations, and nausea were reported in 44.6%, 39.7%, 27.3%, 26.4%, and 24% of the patients in the study by Karabulut et al. (11). Our patients had similar symptoms.

Of our study subjects, gastric lavage and activated charcoal were administered in 61%, while observation only was preferred for 39%. This is in contrast with the study by Hocaoglu et al. from Poison Call Center, Dokuz Eylul University, in that study both treatments were given to 33.2% (10). N-acetylcystein was given to 35.8% of our participants, intravenously in 93.7% of them. In the study by Hocaoglu et al. an advice for the administration of a specific antidote was given in 2.7%. In the same study, paracetamol and salicylates emerged as the two agents most commonly associated with mortality among analgesics, with two

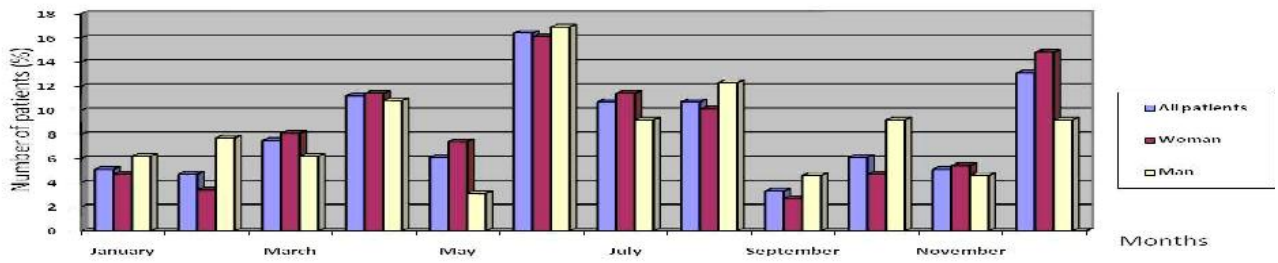

Figure 2: The distribution of patients by month

patients ingesting paracetamol only and one patient with simultaneous ingestion of paracetamol and salicylate dying (10). In our study, two patients were intubated, one with simultaneous intake of tricyclic antidepressant and one with benzodiazepine, and these two patients had non-toxic paracetamol blood levels and were discharged with complete cure. These data suggest unnecessary use of N-acetylcystein in our study population, probably due to a lack of adequate knowledge on toxic levels, failure to use a nomogram, inadequate inquiry about patient history, and a general lack of information on drug intoxication. Also, intravenous route of administration was preferred even if oral use was possible. This might be associated with time constraints limiting the ability to communicate with the patient and unawareness or ignorance regarding the adverse effects of intravenous administration.

Toxic levels of paracetamol was detected in 28% of our study cases, and 13% were considered to have non-toxic levels although the measurement was performed in the first 4 hours. None of the toxic levels resulted in hepatotoxicity. Contrary to these observations, paracetamol toxication is the leading cause of acute liver failure in the United Kingdom and US (15). In a Canadian study, Kozer et al. found a more beneficial effect with the intravenous treatment (5). Interestingly, this latter observation may be associated with the absence of hepatotoxicity in our study where N-acetylcystein was administered to a higher proportion of patients and intravenous route was more commonly preferred in comparison with most of the other studies.

In our study 47% of the patients in our study were hospitalized, while 1% were referred to another center due to the lack of available inpatient beds. This is similar to the percentage (1.3%) of patients in Hocaoglu et al.'s study who were referred to another center after stabilization (10). In the study by Deniz et al. and Karabulut et al., 57.4% and 29.8% of the patients visiting the emergency unit with drug intoxication were hospitalized. (11,14). In two other studies by Kavalci et al. (16) and Kaygusuz et al. the corresponding figures were 20.8% and 11% (17). As these figures suggest, there is a great discrepancy between studies both in terms of hospitalization rates and routes. A possible explanation is the difference between patient populations with regard to general health status.

Our study has several limitations. Firstly, inadequate data were retrieved from patient files in certain patients due to omissions. In addition, blood paracetamol levels were measured in the first four-hour period, most likely due to incorrect information obtained from the patient, leading to false non-toxic results. Furthermore, absence of standard diagnostic and therapeutic strategies could have jeopardized the statistical significance of the results.

In conclusion, widespread availability of paracetamol containing pharmaceutical products is associated with frequent use of these agents for suicidal purposes and a good knowledge of demographic data in such patients and effective use of poison call centers may help to improve diagnosis and management.

REFERENCES

1. Shaffer D, Craft L. Methods of adolescent suicide prevention. J Clin Psychiatry 1999;60 Suppl 2:70-74; discussion 75-76,113-116.
2. Linden CH. Acetaminophen; in Tintinalli JE (4th ed): Emergency medicine. 1995, 787-792.
3. Mert E, Bilgin NG. Demographical, aetiological and clinical characteristics of poisonings in Mersin, Turkey. Hum Exp Toxicol 2006, 25; 217-223.
4. Litovitz T, Klein-Schwartz W, White S: 2000 Annual Report Of The American Association Of Poison Control Centers Toxic Exposure Surveillance System. Am J Emerg Med 2000;19:337.
5. Kozer E, Koren G. Management of paracetamol overdose: Current controversies. Drug Saf 2001; 24:503-512.
6. Ashbourne JF, Olson KR, Khayam-Bashi H. Value of rapid screening for acetaminophen in all patients with intentional drug overdose. Ann Emerg Med 1989;18: 1035-1038.
7. Lai MW, Klein-Schwartz W, Rodgers GC, et al. 2005 Annual Report of The American Association of Poison Control Centers National Poisoning and Exposure Database. Clin Toxicol (Phila) 2006;44: 803-932.
8. Kurt I, Erpeg AG, Kurt MN, Gurel A. Poisoning cases followed at Adnan Menderes University. ADU Tıp Fak. Dergisi 2004;5: 37-40.
9. Gunnell D, Murray V, Hawton K. Use of paracetamol (acetaminophen) for suicide and nonfatal poisoning: Worldwide patterns of use and misuse. Suicide Life Threat Behav 2000;30:313-326.
10. Hocaoglu N, Kalkan S, Akgun A, Capar S, Tuncok Y. A retrospective evaluation of analgesic exposures from Izmir, Turkey. Hum Exp Toxicol 2007;26:629-636.
11. Karabulut N, Celik Z, Atalay C. Retrospective analysis of poisoning cases admitting to Artvin State Hospital. EAJM 2007; 39:198-201.
12. Uyanikoglu A, Zeybek E, Cordan I, Avcı S, Tukek T. Evaluation of intoxication cases. Nobel Medicus 2007; 3(2):18-22.
13. Yesil O, Akoglu H, Onur O, Guneysel O. Retrospective analysis of posioning cases admitting emergency department. Marmara Medical Journal 2008;21:26-32.
14. Deniz T, Kandis H, Saygun M, Buyukkocak U, Ulger H, Karakus A. An analysis of poisoning cases admitting the emergency department of Kırıkkale University Medical Faculty. Düzce Tıp Fakültesi Dergisi 2009;11:15-20.
15. Morgan OW, Griffiths C, Majeed A. Interrupted time-series analysis of regulations to reduce paracetamol (acetaminophen) poisoning. PLoS Med April 2007;4(4):e105.
16. Kavalci C, Durukan P, Cevik Y, Ozer M, Ikizceli I. Analysis of poisoning cases: A 1-year experience of a new hospital. Turkiye Acil Tıp Dergisi 2006;6:163-166.
17. Kaygusuz K, Gursoy S, Kilicoglu F, Ozdemirkol I, Mimaroglu C. Retrospective analysis of acute medicinal poisoning cases followed at cumhuriyet University Medical Faculty Hospital intensive care unit between 1998-2004). Cumhuriyet Universitesi Tıp Fakültesi Dergisi 2004;26:161-165.