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Acute Drug Poisoning at Critical Care Departments in Japan

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During 1996, 1188 patients with acute drug poisoning were admitted to 59 critical care departments in Japan. The patients were predominantly female (68.4%) and relatively young (69.2%, under the age of 40). Further analysis of the 1188 patients indicated that the majority (77.9%) were admitted as a result of deliberate self-poisoning, while 15.1% of the cases were admitted due to accidental poisoning (unknown cause : 7%). A total of 2517 drugs was taken by these patients. The most common group of drugs involved were benzodiazepines (32.1%), followed by neuroleptics (12.2%), antidepressants (10.2%), analgesics (9.1%), antihistamines (7.3%) and barbiturates (6.2%).

An important difference observed in the pattern of acute drug poisoning, when compared with that in other countries, was the preferential use of bromvalerylurea by young individuals for deliberate self-poisoning. This drug has not been used in any other country recently.

There were twelve cases of fatal drug poisoning in the 59 critical care departments during 1996, including nine women. Four patients had taken barbiturates and six patients had taken a combination of benzodiazepines. In order to treat patients with acute drug poisoning, it is important to provide physicians with essential information on the incidence, mechanism of poisoning, and metabolism of the drug involved. In the case of rare drug poisoning, however, as it would take considerable time for any one critical care department alone to amass enough admissions for generating a reliable information database regarding management and prognosis, we therefore believe that a national approach is required to address the issue of management of patients with acute drug poisoning.

Key words — critical care departments, accidental poisoning, deliberate self-poisoning, benzodiazepines

Introduction

Acute drug poisoning is a common problem confronting every hospital in European countries, accounting for 5 to 7% of all acute medical admissions¹⁾. We also have many patients with acute

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drug poisoning, but there is little information in the literature concerning the frequency or the pattern of acute drug poisoning in Japan²⁾. This study details the magnitude of the problem of acute drug poisoning in Japan based on the number of acute medical admissions to 59 critical care departments (45% of all critical care departments) in Japan during 1996.

Subjects and Methods

A retrospective analysis of 1188 cases was performed. All patients admitted from January to December in 1996, to 59 critical care departments (**Fig. 1**), with acute drug poisoning were included in this study. These patients were identified by reviewing the admission and hospital records of each of the 59 critical care departments.

A standard data form was used for all admissions, to collect data on the patients, such as demographic data (age, gender), data on all drugs ingested and the ingested doses, data on co-ingested substances, and details of the management and complications of the drug poisoning. The diagnosis concerning accidental poisoning or dliberate self-poisoning was mainly based on anamnesis and clinical observation. At discharge, further data (including the time spent in the critical care department, serial plasma drug concentrations and final diagnosis) was collected. The hospital records of

Fig. 1. Catchment Area in This Study (● : 59 critical care departments)

these patients were then reviewed by the medical doctors and clinical pharmacists in these institutions. Only some patients had undergone plasma or urinary drug-screening tests. When drugs ingested by the patients could not be precisely identified, the nature of the drugs were determined from the patients' medical histories and clinical features. Cases with allergic reactions to drugs were excluded.

Data collection

The survey population was the all critical care departments in Japan; the names and addresses were provided by the Japanese Association for Acute Medicine.

The initial questionnaire regarding acute drug poisoning was mailed to all critical care departments in Japan (n=131) at the end of December, 1996. A follow-up mailing was sent to nonrespondents at the end of January, 1997. Data collection was completed by the end of March, 1997.

Data analysis

Demographic data and information regarding diagnosis, causes of poisoning, agents used, treatment, and outcome were entered into a computerized database.

Results

From January to December 1996, 231292 patients were admitted to the 59 critical care departments (as determined from the response to the questionnaire of 45%) in Japan as medical and surgical emergencies. During this period, 1188 patients were admitted with acute drug poisoning, of which 179 patients (15.1%) were accidental drug poisoning. The majority of patients (925, 77.9%) were admitted after deliberate self-poisoning with drugs.

Five hundred and eighty-four patients (49.2%) suffered from psychiatric illnesses, as indicated by their past medical histories or formal psychiatric assessment. However, only 35 of the patients who had been accidentally poisoned with drugs had a history of psychiatric illness (**Table 1**).

Table 1. Number and Proportion of Patients with Psychiatric Illnesses Admitted for Acute Drug Poisoning

Patients	Deliberate	Accidental	Unidentified	Total
with psychiatric illnesses	505(42.5%)	35(2.9%)	44(3.7%)	584(49.2%)
without psychiatric illnesses	378(31.8%)	136(11.4%)	36(3.0%)	550(46.3%)
Unknown	42(3.5%)	8(0.7%)	4(0.3%)	54(4.5%)
Total	925(77.9%)	179(15.1%)	84(7.1%)	1188(100.0%)

Gender and age distribution

The subjects were predominantly female (68.4%) and relatively young (69.2% under the age of 40, see **Fig. 2**). The female : male ratio was 1.1 : 1 for patients accidentally poisoned and 2.7 : 1 for those deliberately self-poisoned. The majority of patients with acute drug poisoning of both sexes were aged between 20 and 29 years.

Seasonal incidence

Cumulative data from January to December 1996 show that the maximum number of admissions (n=121) for acute drug poisoning was in June, and the lowest number (n=64) was in December (**Fig. 3**).

Fig. 2. Gender and Age Distribution of 1167 Patients with Acute Drug Poisoning Admitted to Critical Care Departments in Japan in 1996 (There was no record about gender or age in 21 patients.)

Fig. 3. Monthly Admissions Due to Acute Drug Poisoning (There was no record about admission date in 28 patients.)

Drugs used

A total of 2517 drug administration was recorded for the 1174 patients (there were no records about drugs used in 14 patients). Two or more agents were involved in 529 cases (44.5%). The most common groups of drugs used were the benzodiazepines (32.1%), followed by neuroleptics (12.2%), antidepressants (10.2%), analgesics (9.1%), antihistamines (7.3%) and barbiturates (6.2%) (**Fig. 4**). These drug groups accounted for 77.1% of the drugs taken.

One of the main agents used by the group with accidental poisoning was stimulants (9.1%) taken in an overdose by drug abusers (**Table 2**). For the group with deliberate self-poisoning, the individual agents ingested and the frequency of their ingestion are depicted in Table 3. In total, 72.0% of patients took legitimately prescribed medications, of which 5 patients (0.8%) had pre-

Fig. 4. Substance of Intoxication for 1188 Patients (some of whom used two or more compounds)

Table 2. Agents Involved in 179 Patients Admitted for Accidental Poisoning

Pharmaceutical category	Number and proportion of patients
Benzodiazepines	69 (27.3%)
Analgesics	25 (9.9%)
Stimulants/street drugs	23 (9.1%)
Neuroleptics	20 (7.9%)
Antihistamines	19 (7.5%)
Antidepressants	13 (5.1%)
Barbiturates	10 (4.0%)
Others	74 (29.2%)

179 patients (some of whom used two or more compounds and there was no record about drug used in 1 patient)

scribed the drugs themselves, while 20.6% bought over-the-counter (OTC) preparations. Bromvalerylurea was used on 78 occasions.

Only 180 patients (15.2%) had undergone plasma or urinary drug-screening tests by means of Triage® (n=112), REMEDI® (n=49), FPIA (n=29), Toxilab® (n=19), HPLC (n=10) or GC/MS (n=10). Some of the patients were tested using two or three methods.

Treatment

886 patients (72.9%) received gastrolavage and 155 patients (13.0%) received specific antidotes; flumazenil (n=135), acetylcysteine (n=17), glucose (n=2) and naloxone (n=1). Ninety-three patients (7.8%) were subjected to blood purification procedures; direct hemoperfusion (n=80), continuous hemodiafiltration (n=6), hemodialysis (n=4), plasma exchange (n=2) and peritoneal dialysis (n=1).

Duration of stay in critical care department

The average length of stay in the critical care departments was 3.8 days (S.D. 2.9, range 1 to 164 days) (see **Fig. 5**). The majority of patients (84.3%) made a complete recovery and were discharged from the critical care departments.

Deaths in hospital

During 1996, twelve deaths (1%) occurred in the critical care departments as a result of acute drug poisoning (**Table 4**). The age of the twelve patients, nine of whom were women, ranged from 20 to 47 years (mean: 32.3 years). Four patients had taken barbiturates and six had taken a combination of benzodiazepines.

Discussion

The main aim of this study was to investigate the trend of serious accidental poisoning and deliberate self-poisoning with drugs, in Japan. Furthermore, we also aimed to explore the sources of the drugs taken by subjects who had attempted suicide.

Climate variation

In this study, most of the patients were admitted in the heat of June, and the lowest number of admissions was in the cold of December. This is interesting when one considers that in the Newcastle area in Australia, most of the admissions for acute drug poisoning were in the heat of December and the lowest number was in the cold of June³. In general, our observations with regard to the gender and age distribution of patients with deliberate self-poisoning agree with those of other investigations⁴⁻⁶. However, it may be necessary to carry out further analysis to clarify the relationship between suicidal tendencies and climate variation.

Patterns of drug

Efforts to decrease the morbidity and mortality related to acute drug poisoning should target frequently-prescribed drugs or those taken frequently in lethal overdoses. This study confirmed that benzodiazepines, neuroleptics, antidepressants, analgesics, antihistamines and barbiturates are the main agents involved in patients with acute drug poisoning admitted to critical care departments in Japan. Together these drugs account for 77.1% of acute drug poisoning cases. We observed an almost similar pattern of drug intake in cases of accidental poisoning and deliberate self-poisoning. In both groups, benzodiazepines were the most commonly ingested drugs (**Table 2, 3**).

Duration of stay in cases with benzodiazepines and acetaminophen poisoning

With the use of flumazenil (the antidote for benzodiazepines⁷⁾), the average stay in the critical care department was 4.0 days, and with the use of acetylcysteine (the antidote for acetaminophen⁸⁾), the average stay was 5.9 days in cases with benzodiazepine and acetaminophen poisoning, respectively. The time needed to ensure that delayed hepatotoxicity did not occur after an overdose of acetaminophen is probably reflected in an average stay of 5.9 days.

Psychotropic drugs and prescribing

Most drugs used for self-poisoning had been prescribed by physicians (72%). Nearly 50% of patients with self-poisoning in our study suffered from specific psychiatric illnesses (**Table 1**). Therefore, it is not surprising that psychotropic drugs were the most commonly used drugs. Thus, physicians should be more cautious when prescribing psychotropic drugs, and pharmacists should be more cautious with respect to the compliance when dispensing psychotropic drugs.

Antihistamines

It may be surprising that antihistamines were the commonly used drugs in our study. We observed that there are three facts. Firstly promethazine and chlorpromazine have some common properties⁹⁾, although they belong to different drug categories. Second, among the neuroleptics, chlorpromazine was involved at a relatively high rate (52.0% of neuroleptics) in accidental poisoning and deliberate self-poisoning. Third, promethazine was also involved at a significantly high rate (82.5% of antihistamines) in accidental poisoning and deliberate self-poisoning. These observations led us to conclude that antihistamines are commonly used drugs for poisoning.

Tricyclic Antidepressants

Overdoses of tricyclic antidepressants (TCA) could be fatal, especially an overdose of amitriptyline¹⁰⁾. In this study, there were two cases of fatal amitriptyline poisoning. There was a tendency for amitriptyline to be used more often than other antidepressants in deliberate self-poisoning (32.1% of TCA).

Analgesics

Analgesics were used in 191 (9.1%) cases (**Fig. 4**). Younger people attempting suicide used analgesics more often (88.2% under the age of 30), usually purchased without a prescription from pharmacies¹¹⁾, than any other type of drug. Acetaminophen alone, or in combination with other drugs, was the most commonly used drug, followed by aspirin.

Bromvalerylurea

In Japan, the use of bromvalerylurea has recently become the preferred method for deliberate self-poisoning by young persons who attempt suicide¹²⁾. This probably reflects the recommendation in "The complete manual of suicide"¹³⁾. The main risks associated with an overdose of this drug are loss of consciousness, respiratory failure and complicated aspiration¹²⁾. It is surprising that young persons who attempt suicide can purchase bromvalerylures without a prescription from pharmacies, and it may be one of the causes for increase in the morbidity, and even mortality related to acute drug poisoning (**Table 3, 4**).

Fatal toxicity

The patients admitted to the hospitals rarely died as a result of drug poisoning alone. Most of them either had cardiac arrest before arrival, or died of complications such as pneumonia or organ failure. However, we should focus on the fatal toxicity of barbiturates (mortality in this study : 2.3

%), the ingestion of which resulted in death (Table 4).

Lack of drug identification and overdose information

The majority (84.8%) of patients with acute drug poisoning had not undergone plasma of urinary drug-screening tests. The lack of facilities for drug identification may pose problems for the admitting physicians when treating their patients¹⁴⁾. In the United States of America, the Food and Drug Administration requires drug manufacturers to provide overdose information, including management guidelines for new drugs¹⁵⁾. We believe that, in Japan too, there is a need for overdose information to be supplied. In order to treat patients with acute drug poisoning, it is important to provide physicians with the much needed information on the incidence, mechanism of poisoning and metabolism of drugs. However, in the case of rare drug poisonings, it would take long time for any one critical care department alone to have enough admissions for generating reliable information regarding management and prognosis. We believe, therefore, that a national approach to address the issue of management of patients with acute drug poisoning is required.

Our expectation

This study will provide a useful model for those doctors interested in identifying risk factors associated with acute drug poisoning. Moreover, with a national approach, territory-wide studies of continuous surveillance are needed to provide physicians with the much needed information on the incidence and pattern of acute drug poisoning.

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