CASE REPORT

S. K. Lee · K. Ameno · S. W. In · J. Y. Yang · K. U. Kim K. S. Koo · Y. C. Yoo · S. Ameno · I. Ijiri Levels of paraguat in fatal intoxications

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Abstract We describe here fatal levels of paraquat in plasma of victims due to the ingestion of the herbicide, paraguat, and the relationship between those levels and survival times after ingestion. We determined paraquat levels in plasma of 106 paraquat poisoning cases in Korea between June 1992 and December 1996 using a visible spectrophotometric method based on the alkali-dithionite reaction. Among 55 cases with known survival times, plasma paraquat levels of victims who died within one day of ingestion ranged from 2.3 to 636.6 μ g/ml (average 127.6 μ g/ml) while those of the victims who died between 1~4 days ranged from 0.9 to 25.1 µg/ml (average 7.0 μ g/ml). Since preparations containing 24.5% paraquat dichloride are still used in Korea, our data for Korean victims who died within one day were 8.5 times higher than those in Baselt and Cravey's report for the same survival times. Our data also suggest that victims in whom a plasma paraquat concentration of more than 30 μ g/ml was detected are likely to have died within 24 h after ingestion.

Key words Toxicology · Paraquat · Plasma or serum concentration · Survival times

Introduction

Paraquat (1.1'- dimethyl-4,4'-bipyridylium ion), a nonselective contact herbicide, is used widely throughout the world. It has high toxicity since an oral dose of only $1\sim2$ g is fatal to most adults [1, 2] and there have been many

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reports about accidental and suicidal ingestion [1, 3–9]. An assessment of the severity of paraquat poisoning using a toxicological index of paraquat to separate the survival and fatal cases has also been reported [10]. In Korea, many fatal cases involving its ingestion mainly for suicidal purposes have also been observed since its sale in 1970 and paraquat poisoning is responsible for about 35% of fatalities due to pesticide poisoning [11].

In most countries, commercial paraquat preparations contain below 10% but in Korea preparations containing 24.5% paraquat dichloride are generally available. Therefore, fatal levels of paraquat are suspected to be higher than those of previous reports [1, 3–8].

We describe here the fatal levels of paraquat in the plasma of Korean victims and, based on the relationship between paraquat levels and survival times after ingestion, we also estimate whether survival time after ingestion is within one day or more.

Materials and methods

The study consisted of a total of 106 Koreans who died following ingestion of paraquat between June 1992 and December 1996 in Korea. There were two subcategories within the study population; those found dead prior to receiving medical treatment and those who died in hospital while receiving medical treatment such as gastric lavage, hemodialysis and forced diuresis. From the results of police investigations, we could identify the survival times in 55 of the 106 investigated cases and of these, 27 survived more than 16 h died in hospital. At autopsy which was conducted within one day after death, we collected heart blood and gastric contents for toxicological screening.

Quantitation of paraquat in plasma was performed by the visible spectrophotometric method based on the alkali-dithionite reaction after SepPak C_{18} extraction according to Maruyama and Ide [12] and Lee et al. [11].

Results

Table 1 shows the paraquat concentrations in plasma according to survival times and medical treatment of the 106 Korean victims. In cases where death occurred within one

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Table 1Plasma or serumparaquat concentration in fatalcases according to survivalperiod and medical treatment(+: received medical treatment;-: not received medical treat-ment)

Survival period (days)	Conc. (µg/ml) range	No of cases	Conc. (µg/ml) average	Medical treatment
0~1	2.3~636.6	38	127.6	
	2.3~30.0	14		+10/-4
	30.1~636.6	24		_
1~4	0.9~25.1	15	7.0	+
8	4.5	1	4.5	+
12	0.8	1	0.8	+
Unknown	2.5~1023.5	51	170.8	
	2.5~30.0	14		_
	30.1~1023.5	37		_

Table 2 Distribution of fatal cases by age and sex (*M* male; *F* female)

Age (years)	Sex		Total	Percentage
	М	F	number	of total
4~ 9	1	1	2	1.9
10~19	3	3	5	4.7
20~29	7	16	23	21.7
30~39	16	13	29	27.4
40~49	7	7	14	13.2
50~59	7	0	7	6.6
60~69	5	4	9	8.5
70~88	0	7	7	6.6
Unknown	6	4	10	9.4
Total	52	54	106	100

day and those with unknown survival times after ingestion, we also subdivided into two groups at a concentration of 30 µg/ml. This arbitrary level was used because among those who received medical treatment and died within one day, the highest plasma paraquat concentration was about 30 µg/ml and in almost every victim who died within one day without medical treatment the plasma paraquat concentration was more than 30 µg/ml. Except for a 4-year-old girl who was forcibly administered paraquat by her mother and died within one day with a concentration of 5.8 µg/ml without medical treatment, all other cases were suicidal or accidental ingestion. The plasma paraquat concentrations ranged from 0.8 to 1023.5 μ g/ml (average 127.0 μ g/ml) and no ethanol or other compounds were detected in any of the known cases. The known survival times of 55 cases from police investigation ranged from 2 h to 288 h (12 days), but others were unknown. The average paraquat level of victims who died within one day was much higher than that of victims who died between 1~4 days, after 8 days and 12 days, but slightly lower than those with an unknown time of death. Of the 106 cases, 49.1% (52 cases) were males and 50.9% (54 cases) were females and ages ranged from 4 to 88 years, with the largest number of cases recorded among the 30~39, 20~29 and 40~49 age groups (Table 2).

Discussion

Baselt and Cravey [1] reported paraquat concentrations in 32 fatal cases and they subdivided paraquat concentrations according to the survival time. The average blood concentration found in nine cases who died within one day was 15 μ g/ml. In our study, the average concentration of paraquat in the plasma of victims who died within one day was 8.5 times higher. This indicates that the victims in our cases ingested massive amounts of paraquat preparation with a high concentration (24.5% of paraquat dichloride) and in most cases the victims were found dead prior to receiving medical treatment. In Korea, paraquat preparations are generally sold in 500 ml bottle, and in some cases we estimated that ingestion volumes were more than 200 ml because residues of less than 300 ml were found in the bottle on site. From the data presented in Table 2, we know that paraquat has been used as a suicidal or accidental agent among all ages in Korea without discrimination by sex.

In fatalities due to toxic substances, the estimation of survival time after ingestion is useful for the medico-legal investigation. However in paraquat poisoning cases, an accurate estimation of survival time after ingestion is quite difficult if dependent only on the measured paraquat concentration in the plasma. Our data and that of Proudfoot et al. [13] suggest that in cases in which a paraquat concentration of more than 30 μ g/ml is detected in the plasma, the victim is likely to have died within 24 h after ingestion in the absence of medical treatment. Therefore, we can estimate that almost all our cases involving unknown survival times will have died within 24 h of ingestion.

The plasma or serum paraquat concentrations of our 27 cases who died in hospital were similar to those reported by Baselt and Cravey [1] within the same survival times and our data regarding fatal levels are also in accordance with the survival curves with respect to paraquat concentrations of Proudfoot et al. [13]. It has been reported that when the plasma levels exceeded 0.3 mg/l 15 h after ingestion, a fatal outcome could be expected, regardless of treatment [14]. Therefore in our 106 cases, the primary cause of death was paraquat poisoning.

In conclusion, paraquat levels of our fatal cases died within one day after ingestion were relatively higher than that of previous reports observed in another countries. This is due to the ingestion of massive amounts of paraquat preparation with high concentration. In cases involving unknown survival times with a paraquat concentration of more than $30 \,\mu g/ml$, the victims is likely to have died within 24 h after ingestion in the absence of medical treatment.

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