Changes in Hematologic Parameters with Acute Exposure to 1, 1, 1-Trichloroethane

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Abstract: By acute exposure of dogs to 1,1,1-trichloroethane and observing the changes in hematologic parameters during and after exposure, the following results were obtained.
A marked but temporary decrease in leukocytes was noted 30 minutes after the start of exposure, but no change was observed in the erythrocytes, hematocrit values or thrombocytes. According to leukocyte differential counts, all types of leukocytes showed a decrease. The decrease in neutrophils was particularly prominent. A dose-response relationship was seen between the exposure concentrations of 1,1,1-trichloroethane from 200 to 700 ppm. and the grade of decrease in leukocyte counts.

Key words: 1,1,1-trichloroethane—Hematologic parameter—Leukocyte differential count—Exposure—Dog

INTRODUCTION

The development of the modern chemical industry has brought about a rapid increase in the amount of organic solvents produced and consumed. Consequently, the chance of exposure to these solvents has been increased for a large number of people, and many studies on the hazards and toxicity of these substances have been reported.1-4) The blood plays an important role as a carrier for absorption and excretion of solvents, and a number of observations on the toxicity to the blood have been made.5-7) In this study, the effects of 1,1,1-trichloroethane (1,1,1-TCE) on the hematologic parameters were examined in dogs.

1. Experimental animals
Fifty mature cross-bred dogs weighing from 8 to 12 kg were used.
2. *1,1,1-TCE exposure and injection*

The dogs were anesthetized by intravenous injection of sodium-pentobarbital (25–30 mg/kg). The respiratory tract was assured by tracheal intubation, and the dogs were connected to the exposure apparatus described in our previous paper. Five dogs each were exposed to 200, 500, 700, 1,000, 1,500 and 2,000 ppm of 1,1,1-TCE for one hour. In addition to this, five dogs were exposed to 700 ppm of 1,1,1-TCE for four hours. The remaining animals served as the control group.

The intravenous injection of 50 mg/kg was undertaken at the rate of approximately 1 ml/min. through the right femoral vein. 1,1,1-TCE of special grade (Katayama Chemical Co., Inc.; purity 99%) was used. The concentration of 1,1,1-TCE in the inspired air was determined by an FID gas chromatograph with a gas sampler apparatus (Shimadzu GC-7AG). The conditions of gas chromatography were as follows: column, glass 3.0 mmφ × 2.0 m; temp., 150°C; packing, 20% polyurethylene glycol; support, Celite 545 AW, DMCS, 60–80 M.; carrier, N₂ 60 ml/min.; detector, FID; temp., 170°C.

3. *Blood sampling and methods for determining hematologic parameters*

Arterial blood samples were obtained repeatedly from the right femoral artery. The volume of blood withdrawn was set at 3 ml each time. Leukocytes and erythrocytes were counted by the Bürker-Türk type plate count method, hematocrit values by the capillary method and thrombocytes by the Brecker-Cronkite method. Leukocyte differential counts were obtained by microscopic observation of blood smear samples following May-Giemsa staining.

**RESULTS**

1. *Changes in hematologic parameters by one-hour exposure to 1,1,1-TCE*

Five dogs inhaled 1,1,1-TCE at 700 ppm for one hour. Blood sampling was performed nine times, once before exposure, at 5, 10, 30 and 60 minutes exposure and at 5, 10, 30 and 60 minutes after the termination of exposure. Leukocyte counts, leukocyte differential counts, erythrocyte counts, hematocrit values and thrombocyte counts were measured with the samples.

Fig. 1 shows the change in the ratio of leukocyte counts compared with before-exposure counts. The ratio values of the leukocyte count began to decrease instantly following the start of exposure and, at the end of exposure, reached the minimum value, i.e., a decrease of 69%. After the end of exposure, the values gradually recovered, and, at 60 minutes, the ratio reached 35% as compared with the before-exposure count. The controls, which were ventilated with fresh air, showed no significant changes in leukocyte counts at any time.

In Fig. 2, time-responses of the leukocyte differential counts (%) are indicated. Along with the decrease in leukocyte counts, the neutrophil percentage declined
markedly and the lymphocyte percentage increased rapidly, whereas eosinophils and monocytes rose slightly. These changes, similar to the leukocyte count decrease, reached a peak at the end of exposure and tended to return to before-exposure conditions thereafter.
2. Changes in hematologic parameters by four hours' exposure to 1,1,1-TCE

Five dogs inhaled 1,1,1-TCE at 700 ppm. for four hours, and blood sampling was performed six times, i.e., once before exposure and at 60, 90, 120, 180 and 240 minutes following the start of exposure.

Fig. 3 shows the time-response in the ratio of leukocyte counts as compared with before-exposure counts. At the initial stage following the start of exposure, leukocyte counts began to decrease, reaching a minimum at 90 minutes and beginning to increase thereafter. The minimum value observed at 90 minutes of exposure was only 25% as compared to the before-exposure value, and, by four hours, the percent decrease had recovered to 40%. Change in leukocyte differential counts was similar to the results observed with one-hour exposure. No significant change was observed in erythrocyte counts, hematocrit values or thrombocyte counts.

3. Relationship between leukocyte counts and exposure concentrations of 1,1,1-TCE

Five dogs each were exposed to 200, 500, 700, 1,000, 1,500 and 2,000 ppm. of 1,1,1-TCE for one hour. Arterial blood samples were obtained repeatedly from the right femoral artery. Sampling was carried out three times, once before exposure and at 30 and 60 minutes following the start of exposure.

Fig. 4 shows the change in the ratio of leukocyte counts at each exposure.

Fig. 3. The ratio of leukocyte count in the arterial blood with four hours exposure to 1,1,1-trichloroethane at 700 ppm.
concentration as compared with before-exposure counts. No significant leukocyte decrease was observed with exposure to 200 ppm of 1,1,1-TCE, at either 30 or 60 minutes. However, with exposure to more than 500 ppm, a significant decrease was observed. At 700 ppm, the value reached a minimum, and, from there to 2,000 ppm, no significant change was observed.

Fig. 4. Change in the ratio of leukocyte count with exposure to 1,1,1-trichloroethane at various concentrations.

Fig. 5. The ratio of leukocyte count in the arterial blood after injection of 1,1,1-trichloroethane.
4. Changes in hematologic parameters by intravenous injections of 1,1,1-TCE

In order to clarify the effects of high concentrations in acute exposure, 50 mg/kg of 1,1,1-TCE were intravenously injected into five dogs. Blood sampling was performed five times, once before injection and at 30, 60, 90 and 120 minutes after injection.

Fig. 5 shows the change in the ratio of leukocyte counts as compared with before-injection counts. The ratio(s) of leukocyte counts reached a minimum at 30 minutes after the injection and gradually increased thereafter. The percent decrease at 30 minutes after injection was 61%; this recovered to 20% by 120 minutes. The changes in leukocyte differential counts were similar to exposure cases. No significant changes were observed in erythrocyte counts, thrombocyte counts or hematocrit values before or after injection.

DISCUSSION

The effects of chronic exposure to organic solvents on hematologic parameters have been studied in detail. The fact that a large number of solvents cause impairments to hemopoietic tissues has been known. There have been several reports concerned with the toxicity of 1,1,1-TCE. In these reports, impairment in hemopoietic tissues has not been shown, and no study involving a detailed investigation of the acute toxicity and its relation to hematologic parameters has been carried out.

In this study, one-hour exposure to 700 ppm. of 1,1,1-TCE caused a significant decrease of leukocytes from the initial stage of exposure, reaching minimum value at the end of exposure and recovering gradually thereafter. With four hours of exposure, the minimum value was reached at 90 minutes after the beginning of exposure, and recovery began thereafter. The decrease in leukocyte counts may result from destruction of leukocytes by contact with 1,1,1-TCE or by pinocytosis of 1,1,1-TCE, or from the leukocytes being trapped in specific tissues, resulting in their decrease in the peripheral blood. In the leukocyte differential count (%), neutrophils decreased significantly, while lymphocytes, acidophils and monocytes increased. The leukocytes differential counts showed no peculiar reaction, such as a shift to the right or left, either during or after exposure compared to before-exposure counts. From these results, it seems that the decrease of leukocytes with 1,1,1-TCE exposure is not due to the destruction of neutrophils, but rather to the trapping of neutrophils from the peripheral blood in other tissues.

In the relationship between exposure concentrations and the decrease of leukocyte counts, a dose-response relationship was found in the concentrations of 1,1,1-TCE from 200 to 700 ppm. Furthermore, based on pulmonary absorption values calculated from exposure concentrations and exposure duration time by the authors, it is assumed that the leukocyte decrease is related to exposure concentrations of 1,1,1-TCE, but not to pulmonary absorption values. A similar
phenomenon was reported by Tani et al.10) According to their report, 1,1,1-TCE was injected into the intraperitoneum of mice and guinea pigs, and a leukocyte decrease was observed one day later in both animals. After 93 hours to two weeks of exposure, a leukocyte decrease was observed in the mice. The grade of leukocyte decrease is extremely small compared with the results of our study. Furthermore, Tani et al. reported only a lymphocyte decrease and no decrease in neutrophils. This discrepancy could be ascribed to the differences in the animals, the experimental procedures, including the time and condition of measurement, and other factors.

The change in leukocyte counts may be a temporary reaction considering the following results. The leukocyte decrease begins immediately at the start of exposure and recovers even during the exposure. The leukocyte differential counts showed no peculiar reaction, such as a shift to the right or left, either during or after exposure. It is apparent that inhaled 1,1,1-TCE is rapidly taken up by the tissues from the blood, and it is quite possible that, as a result of the defensive mechanism of the body, leukocytes in circulation are gathered into the tissues. There may be many factors related to changes of leukocyte distribution in the peripheral blood. One of them may be an increase in leukocytes trapped in the capillary beds of the organs. These reactions may probably cause the decrease of leukocytes in the peripheral blood. This problem will be investigated in future studies.

REFERENCES