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Research Article

The Effects of Acute Intoxications with 1,2-Dichloroethane, Tetrachloromethane and Trichloroethylene on Innate Immunity Parameters

Pavel F Zabrodskii[1]*, Vladimir G Lim[2] and Vladimir K Parfenyuk[3]

[1]*Saratov Medical University "REAVIZ", Saratov, Russia*

[2]*I.M. Sechenov First Moscow State Medical University, Moscow, Russia*

[3]*Saratov State Medical University named after V. I. Razumovsky, Saratov, Russia*

***Corresponding Author:** Hitoshi Miyasaka, Department of Applied Life Science, Sojo University, Nishiku, Japan.

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Abstract

Chlorinated hydrocarbons (ChH) - 1,2-dichloroethane (DchE), tetrachloromethane (TChM), and trichloroethylene (TChE) are widely used in industry as solvents for oils, fats, rubber and resins etc. Despite the low frequency of acute intoxication with these compounds (up to 5%), they are characterized by very high lethality (32-96%). Experiments on random-bred albino rats showed that chlorinated hydrocarbons acute intoxications (DchE, TChM, TChE) a single dose of 0.8 LD_{50} causes a reduction the integral state of the innate immunity (increased mortality of rats from experimental infection by 27.8-41.9% caused by *P. vulgaris*, decreased LD_{50} *P. vulgaris* by 1.58-1.68 times, mean effective lifetime of animals (Et_{50}) by 1.70-2.08 times ($p < 0.05$). ChH acute intoxications decreased the parameters of innate immunity (bactericidal activity of blood serum by 1.43-1.60 times, serum concentrations of lysozyme by 1.70-2.27 times and platelet cationic protein by 1.38-1.62 times, activity of natural killer cells (NK) by 1.73-2.20 times, increases the contents of *P. vulgaris* in peripheral blood by 1.96-2.37 times and spleen by 1.70-1.98 times in the modeling of an experimental infection ($p < 0.05$). No significant differences were found between parameters of the integral state of the innate immunity and the parameters of innate immunity after various chlorinated hydrocarbons acute intoxications ($p > 0.05$).

Keywords: Chlorinated Hydrocarbons; Immunotoxicity; Innate Immunity; NK; *P. vulgaris*

Introduction

Chlorinated hydrocarbons (ChH) - 1,2-dichloroethane (DChE, ethylene dichloride), tetrachloromethane (TChM, carbon tetrachloride, perchlormethane, methane tetrachloride, Freon-10, Halon-104) and trichloroethylene (TChE, 1,1,2-Trichloroethylene, 1-chloro-2,2-dichloroethylene, 1-chloro-2,2-dichloroethylene, ethylene trichloride, trilene) are widely used in industry as solvents for oils, fats, rubber and resins, for dry-cleaning clothes etc. [1]. These chlorinated hydrocarbons can affect virtually all body organs and systems [1,2] and, if intoxicated, can enter the body through the respiratory tract (less commonly through the skin and digestive tract), they have allergic [3], mutagenic and carcinogenic properties [1,4], affect kidneys [1,3,5] and liver [1,3,6], cause autoimmune diseases [1], and have immunotoxic [1] and psychotropic effects [1,3]. Common in toxicokinetics of ChH is their ability to metabolize with the formation of more toxic compounds ("lethal synthesis") [1,7]. Acute group poisonings of ChH are possible in case of violations of safety precautions when handling them, as well as in emergency situations at chemical plants. Consumption of ChH as an alcohol surrogate or for suicidal purposes cannot be excluded [1,7]. In recent years, the frequency of acute intoxication with ChH and the mortality rate from intoxications have not decreased. Despite the low frequency of acute intoxication with these compounds (up to 5%), they are characterized by very high lethality (32-96%) [1,7].

One of the causes of lethality after CHG acute intoxications may be infectious complications and diseases associated with reduced innate immunity as a result of the immunotoxic effects of both CHGs and their highly toxic metabolites. A study of the effect of ChH on innate immunity parameters is necessary to substantiate the correction of post-intoxication disorders in order to prevent various infectious complications [1].

Aim of the Study

The aim of the study was a comparative assessment of changes basic parameters of innate immunity after acute intoxication with chlorinated hydrocarbons (1,2-dichloroethane, tetrachloromethane and trichloroethylene).

Materials and Methods

The experiments were performed on random-bred albino rats of both sexes weighing 180-240 g. ChH (Sigma-Aldrich) was administered intragastrically (per os) a single dose of 0.8 LD_{50} in an olive oil solution. LD_{50} of 1,2-dichloroethane (DchE), tetrachloromethane (TChM) and trichloroethylene (TChE) for rats after intragastrically administration was 0,75±0,10; 6,1±0,3 and 4,7 ±0,4 mg/kg, respectively). Control animals received per os equal volume of olive oil. Four groups of rats (control, rats injected with DchE, TChM, TChE) were injected with *P. vulgaris* 1 day after administration of olive oil (control) and ChH. The integral state of the innate immunity was determined by the indices of the experimental infection course caused by intrapulmonary injection of P. vulgaris daily culture suspension in a single doses of 1.5×10^9, 2.0×10^9 and 3.0×10^9 CFUs in 1.5-3.0 ml of saline (three groups of rats, with 7 animals in each group) [8,9].

The integral state of the innate immunity was evaluated by mortality of rats (P. *vulgaris* intrapulmonary) during 36 h from experimental infection, as well as by mean lethal doses (LD_{50}) of *P. vulgaris* and mean effective lifetime of animals (Et_{50}) in experimental and control groups calculated by probit analysis [8].

The bactericidal activity of blood serum (BABS) of rats, serum concentrations of lysozyme and platelet cationic protein (PCP), activity of NK, and contents of *P. vulgaris* in peripheral blood (CFUs in 0.05 ml) and spleen (CFUs x 10^2) of surviving mice was determined after intrapulmonary injection of the P. vulgaris daily culture suspension in a single doses of 1.5×10^9 CFUs in 1.5 ml of saline by conventional methods [1,10]. These parameters of innate immunity were evaluated 48 h after ChH administration.

The data obtained were processed statistically using the Student's t-test. Differences between the parameters were considered reliable at $p < 0.05$.

Results

Under the influence of DchE, TChM, TChE acute intoxications at dose of 0.8 LD_{50} the mortality of rats from experimental infection increased in comparison with the control, respectively, by 41,9% ($p < 0.05$), 32,4% ($p < 0.05$) and 27,6% ($p < 0.05$); decreased LD_{50} *P. vulgaris* by 1.58 ($p < 0.05$), 1.62 ($p < 0.05$), 1.68 times ($p < 0.05$) and Et_{50} of rats - by 1.85 ($p < 0.05$), 2,09 ($p < 0.05$), and 1.70 times ($p < 0.05$), respectively, indicating the integral state of the innate immunity suppression (table). No significant differences were found between parameters of the integral state of the innate immunity after DchE, TChM, TChE acute intoxications ($p > 0.05$).

Parameters	Control	DhE	TChM	TChE
Mortality, %	20,0 ± 5,2 (60)	61,9 ± 10,6* (21)	52,4 ± 10,9* (21)	47,6 ± 9,0* (21)
LD_{50} P. vulgaris, 10^9 CFUs	2,54 ± 0,08 (60)	1,61+0,16* (21)	1,57+0,18* (21)	1,51+0,19* (21)
Et_{50}, h	19,2 ± 1,3 (60)	10,4 ± 2,4* (21)	9,2 ± 2,3* (21)	11,3 ± 2,4* (21)
BABS, %	80,1 ± 8,8 (20)	55,2 ± 6,1* (8)	50,0 ± 6,2* (9)	56,1 ± 7,0* (10)
Lysozyme, mg/l	7,5 ± 0,4 (20)	3,1 ± 0,6* (8)	4,4 ± 0,7* (9)	3,3 ± 0,5* (10)
PCP, %	62,0 ± 2,9 (20)	43,0 ± 4,6* (8)	38,3 ± 4,4* (8)	45,0 ± 4,7* (9)
NK activity, %	26,4 ± 3,1 (20)	13,1 ± 4,0* (8)	12,0 ± 3,8* (9)	15,3 ± 4,5* (10)
Content of P. vulgaris of peripheral blood (CFUs in 0.05 ml)	37,2 ± 6,4 (7)	85,5 ± 8,2* (7)	73,0 ± 6,5* (7)	88,1 ± 9,7* (7)
Number of P. vulgaris in spleen, CFUs x 10^2	90,0 ± 15,2 (7)	169,0 ± 19,7* (7)	178,0 ± 18,8* (7)	153,0 ± 17,9* (7)

Table: Effect of chlorinated hydrocarbons acute intoxication (0,8 LD_{50}) on integral state of the innate immunity and parameters of innate immunity of albino rats (M ± m)

* -p <0,05 as compared to control; in parentheses - the number of animals.

After DchE, TChM, TChE acute intoxications decreased BABS in comparison with the control, respectively, by 1,45 ($p < 0.05$), 1.60 ($p < 0.05$) and 1.43 ($p < 0.05$) times, serum concentrations of lysozyme with the control by 2,42 ($p < 0.05$), 1.70 ($p < 0.05$) and 2.27 ($p < 0.05$) times, PCP - by 1,44 ($p < 0.05$), 1.62 ($p < 0.05$) and 1.38 ($p < 0.05$) times, activity of NK - by 2,02 ($p < 0.05$), 2.20 ($p < 0.05$) and 1.73 ($p < 0.05$) times, while the content of *P. vulgaris* in peripheral blood (CFUs in 0.05 ml) increased by 2.30 ($p < 0.05$), 1.96 ($p < 0.05$) and 2.37 ($p < 0.05$) and the number of *P. vulgaris* in spleen (CFUs x 10^2) increased by 1.88, 1.98 ($p < 0.05$), 1.70 ($p < 0.05$) times ($p < 0.05$), respectively (table). There were no statistically significant differences ($p>0.05$) between the investigated parameters of innate immunity after acute intoxications with different ChH.

Discussion

The suppression of the integral state of the innate immunity (mortality of rats, LD_{50} of *P. vulgaris*, Et_{50}) after acute ChH intoxication is caused by a decrease in the bactericidal activity of blood serum of rats, serum concentrations of lysozyme and platelet cationic protein, activity of NK) [1].

The mechanism of suppression of innate immunity parameters is due to the damage of almost all organs and systems of the body, in particular, the immune system organs and blood cells as a result of interaction with sulfhydryl and amino groups enzymes and highly toxic products of ChH biotransformation, leading to disruption of numerous biochemical processes in the body's cells, including inhibition of tissue respiration and oxidative phosphorylation [1,7]. Many products of ChH metabolism are known to be more toxic than DChE (2-chloroethanol, chloroacetic aldehyde, monochloroacetic acid) [1,7,11,12,13]. TChM (chlorine, phosgene, carbon monoxide, and free radicals - carbon dichloride; CCl^{+}_{3}; O-O-CCl; HO-$OCCCl_3$; HO-CCl_3), TChE (dichloroacetyl chloride, dichloroacetic acid, trichloroacetaldehyde, trichloroacetic acid, trichloroethanol, N-(hydroxyacetyl) ethanolamine, trichloroethanediol) [1,4].

Conclusions

- Chlorinated hydrocarbons acute intoxications (1,2-dichloroethane, tetrachloromethane, trichloroethylene) a single dose of 0.8 LD_{50} causes a reduction the integral state of the innate immunity (increased mortality of rats from experimental infection, caused by *P. vulgaris* by 27.8-41.9%; decreased LD_{50} *P. vulgaris* by 1.58-1.68 times, mean effective lifetime of animals (Et_{50}) by 1.70- 2.08 times. No significant differences were found between parameters of the integral state of the innate immunity after various chlorinated hydrocarbons acute intoxications.
- Acute intoxications of 1,2-dichloroethane, tetrachloromethane, trichloroethylene reduced the parameters of innate immunity (bactericidal activity of blood serum by 1.43-1.60 times, serum concentrations of lysozyme by 1.70-2.27 times and platelet cationic protein by 1.38-1.62 times, activity of NK by 1.73-2.20 times, increases the contents of *P. vulgaris* in peripheral blood by 1.96-2.37 times and spleen by 1.70-1.98 times in the modeling of experimental infection. There were no statistically significant differences between the investigated parameters of innate immunity after acute intoxications with different chlorinated hydrocarbons.

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