Accumulated ecological damage to the health of workers in the production of vinyl chloride

G.M. Bodienkova¹,² and S S Timofeeva¹

¹ Irkutsk National Research Technical University, Russia
² East-Siberian Institute of Medical and Environmental Research, Russia

E-mail: sstimofeeva@mail.ru

Abstract. With prolonged exposure of workers in the production of VC to adverse factors, an increase in immunity stress (over time after 5 years) in healthy workers and an imbalance in the system of pro-anti-inflammatory cytokines in individuals with initial manifestations of neurotoxication with VC were recorded. Reduction in the degree of manifestation of compensatory and protective reactions that do not allow for the full implementation of protective mechanisms under the continuing chronic exposure to VC, contributes to the accumulation of ecological damage to the health of workers. The results obtained necessitate the timely detection of initial functional changes, indicate high informative value of biomarkers (IL-1β, TNFα, INFγ, IL-4, S-100, NF-200, MBP) and the possibility of using them to monitor the degree of manifestation of the pathological process. Identification of the leading immunopathogenetic factors of neurological deficit increase can be the basis for developing a method for predicting the individual risk of developing occupational neurointoxication.

1. Introduction

The production of vinyl chloride (VC) is one of the largest in terms of the volume of produced organic semi-products in the global chemical production, whose consumption is growing rapidly, and according to predicted estimates, IHS will be growing by 2020 at a rate of 4.2% per year [1]. VC is one of the most common highly hazardous (hazard class 1) chemicals polluting both the industrial and natural environment. It is known that when exposed to high concentrations of VC and its derivatives under production conditions, it is possible to damage the central, peripheral nervous, immune, cardiovascular and other systems [2,3,4,5]. The results of studies carried out in previous years by a number of authors [6,7] indicate that the maximum allowable concentrations of VC in the air of industrial premises are exceeded by a factor of 10-30. In emergency situations, these values reached 800-1500 mg/m³. High values of average annual levels of the toxicant continued to persist for a long time, and the highest values (7.1 ± 2.1 to 13.5 ± 1.6 mg/m³) were identified in 1994-2000. In recent years, the working conditions of workers generally comply with hygienic standards. However, it is impossible to exclude ecological damage accumulated over a long period of time, both to the environment and to the health of workers. In this regard, it was of certain interest to analyze the dynamics of changes in the functional reserves of the body of long time workers.

The aim of this work is to analyze the ecological damage to the health of workers with prolonged exposure to production factors based on the assessment of changes in inflammatory mediators over time in long time workers without signs of health problems and individuals with initial manifestations of vinyl chloride neurointoxication.
2. Material and methods

The object of the study were long time workers who were examined in a coherent sample at one of the largest VC production facilities in Eastern Siberia. The study group at presentation included 55 men with an average level of a priori occupational risk, mainly due to exposure to VC and 1,2-dichloroethane (1,2 DCE). Including: 36 - long time workers with no signs of health problems from exposure to industrial toxicants aged 36.9 ± 1.2 years, work period of 12.2 ± 0.7 years, and 19 - with initial manifestations of neurointoxication with vinyl chloride, identified during an in-depth neurophysiological examination by physicians of the clinic in the East-Siberian Institute of Medical and Environmental Research. All the same individuals were examined 5 years after continued contact with adverse production factors. The comparison group included 47 conditionally healthy men of representative age and total work period, who do not have contact with hazardous substances in their occupational route.

Using the method of enzyme immunoassay on Alisei Q.S., an automated high-speed analyzer (Italy), we determined inflammatory mediators - cytokines (IL-1β, IL-4, IL-6, IL-2, TNF-α, INF-γ) in the serum of the examined workers by means of test systems of Vector Best CJSC (Novosibirsk).

Statistical processing of the results was carried out using the STATISTICA 6.0 application package in the Windows environment. The significance of differences was assessed using the non-parametric Mann-Whitney tests, taking into account the Bonferroni adjustment (with a distribution different from the standard).

The work does not infringe upon any rights and does not endanger the well-being of the examined workers in accordance with the requirements of biomedical ethics approved by the World Medical Association's Declaration of Helsinki (2000). The studies were performed in the clinic of the Institute with the informed consent of the patients.

3. Results of research

In previous studies, we have shown that the level of occupational risk for workers in the main occupations in the production of vinyl chloride is regarded as medium, for operators and administrative staff - as low, which is generally consistent with the working conditions of these specialists [8]. Whereby the occupational health risk is due to exposure mainly to vinyl chloride and 1,2 dichloroethane. This study focuses on the changes in the dynamics of long-term effects of these toxicants on the immune system whose dysfunction may be one of the possible risk factors for the development of occupational health disorders of workers. Thus, relying on numerous facts speaking for the interrelation of the route of entry, duration of work and immune response [9,10], we found it necessary to analyze changes over time in inflammatory mediators (cytokines) under the continuing exposure to the priority pollutants, as they ensure the development of a full and adequate immune-mediated reaction in the body. Table 1 presents the results of the analysis of serum concentrations of inflammatory mediators in long time workers without signs of health problems from exposure to occupational hazards, and individuals with initial manifestations of neurotoxication with VC compared to the control group and after 5 years of work under exposure to the toxicants.

Analysis of the data presented in the table during the initial examination revealed more pronounced changes in the cytokine profile in individuals with initial manifestations of neurointoxication with VC. Thus, in healthy workers compared with the control group, there is an increase in pro-inflammatory IL-1β (p = 0.006), with a simultaneous pronounced decrease in IL-2 (p = 0.00001) and a tendency to decrease in TNFα (p = 0.036). Evaluating changes in the content of IL-1β, it should be noted that it reflects the functional activity of cells of the monocyte-macrophage link of the immune system and is one of the first activators of nonspecific resistance, and then of the specific immune response [6]. The data obtained in our study on the pronounced tendency to a decrease in the concentration of TNFα in healthy workers can be explained by the inhibitory effect of IL-1β on its production. In workers with initial manifestations of neurointoxication with VC, our attention was attracted by the pronounced hyperproduction of IL-1β against the background of a decrease in anti-inflammatory IL-4 (p = 0.00006) and IL-2 (p = 0.0001).
Table 1. Dynamics of changes in inflammatory mediators after 5 years with chronic exposure to VC and 1,2 DCE, Me (Q25-Q75).  

| Indicator, pg/ml | Control, n=47 | Long time workers, n=36 | Individuals with initial manifestations of vinyl chloride neurointoxication, n=19 |
|------------------|---------------|-------------------------|----------------------------------------------------------------------------------|
|                  | First examination | Second examination | First examination | Second examination |
| IL-1β 0.01 (0.01-1.17) | 0.1(0.01-0.10) | 0.09(0.01-2.28) | 2.58(0.1-6.67) | 0.01(0.01-2.85) |
|                        *p=0.006 |                        *p=0.0003, |                        *p=0.013 |
| IL-6 1.0 (0.01-2.50) | 0.01(0.01-1.35) | 1.31(0.75-3.66) | 0.31(0.01-1.8) | 2.44(0.48-5.52) |
|                        p=0.0007 |                        *p=0.04, |
| TNFα 0.89 (0.12-2.40) | 0.01(0.01-5.60) | 0.24(0.01-1.56) | 0.01(0.01-6.65) | 0.60(0.01-3.93) |
|                        *p=0.0063 |                        *p=0.00001, |
| INFγ 0.2 (0.18-0.20) | 0.01(0.01-4.31) | 0.01(0.01-0.1) | 4.86(0.01-7.15) | 0.01(0.01-0.01) |
|                        *p=0.00001, |                        *p=0.00001, |
| IL-4 0.10 (0.10-8.80) | 0.18(0.01-9.45) | 0.01(0.01-0.44) | 0.01(0.01-0.06) | 0.01(0.01-0.01) |
|                        *p=0.039 |                        *p=0.00007 |                        *p=0.00006 |
| IL-2 12.3 (9.50-14.90) | 1.39(0.2-6.44) | 2.26(0.99-4.0) | 0.46(0.35-0.56) | 1.55(0.72-3.54) |
|                        *p=0.00001 |                        *p=0.00001, |                        *p=0.019 |

Note: * - differences between the 1st and 2nd examination of healthy workers; ** - differences between the 1st and 2nd examination of individuals with initial manifestations of vinyl chloride neurointoxication; ● - differences compared to the control are statistically significant at p <0.01.

The second examination of healthy long time workers after 5 years revealed a compensatory increase in IL-6 level relative to the first examination (p = 0.0007) since an important aspect of its action is the ability to control the adaptive immune response by regulating functions and differentiating T-lymphocytes [11]. At the same time, the level of INFγ decreased (p = 0.006), which may indicate an increase in the immune stress. Analyzing the results obtained during the second examination of individuals with initial manifestations of neurointoxication with VC, we established a regular aggravation of the cytokine imbalance characterized by a decrease in levels of IL-1β (p = 0.01) and INFγ (p = 0.0002), which may contribute to immunosuppression. It should be noted that the enhanced production of cytokines in the initial stages of immunocompromising contributes to the protective reaction of the organism, however, with prolonged exposure, the degree of activation ceases to be adequate and the protective mechanism develops into a pathological process.

4. Conclusion

Thus, with prolonged exposure of workers in the production of VC to adverse factors, an increase in immuno stress (over time after 5 years) in healthy workers and an imbalance in the system of pro-anti-inflammatory cytokines in individuals with initial manifestations of neurointoxication with VC were recorded. Reduction in the degree of manifestation of compensatory and protective reactions that do not allow for the full implementation of protective mechanisms under the continuing chronic exposure to VC, contributes to the accumulation of ecological damage to the health of workers. The results obtained necessitate the timely detection of initial functional changes, indicate high informative value of biomarkers (IL-1β, TNFα, INFγ, IL-4, S-100, NF-200, MBP) and the possibility of using them to monitor the degree of manifestation of the pathological process. Identification of the leading immunopathogenetic factors of neurological deficit increase can be the basis for developing a method for predicting the individual risk of developing occupational neurointoxication.
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