Some Mechanisms of Impairments in Rats' Erythrone under Dioxin-Containing Herbicide (2,4-DA) Effect

Alia F.Kayumova*, Asiya A.Baigildina , Felix Kh. Kamilov **, Dinara F. Kayumova***.

Bashkir State Medical University, Lenin str. 3, 450000 Ufa, Russia.
*Department of Physiology, Bashkir State Medical University, Revolutsionnaya str. 28/1 – 31 450077 Ufa, Russia
**Department of Biochemistry, Bashkir State Medical University, Lenin str. 3, 450000 Ufa, Russia
***Republican Clinical Hospital, Dostoyevsky str. 132, 450087 Ufa, Russia

Introduction

The derivatives of 2,4-dichlorphenoxiacetic acid, specifically 40% 2,4- amino salt are widely used as herbicides. While getting into man and animal organism they cause immunity depression[1,2], neutropenia and anemia[3]. The latter is accompanied by erythrocytes osmotic and acid resistance decrease, their hypochromia, erythroblasts maturation delay in the bone marrow[4]. However, the mechanisms of erythrone impairment as well as its biochemical basis is not clear yet.

Material and Methods

The experiments were carried out on 250 male rats weighting 180-200 g. Toxic effect was caused by 40% -D-amino salt injection in the total dose of LD50, 1/2LD50, 1/4LD50,1/10LD50 and 1/20LD50.

The subacute experiment lasted 7 and 30 days, chronic 2 to 3 months. Intact rats of the same weight served as control, they were injected distilled water. Following toxic time expiration the animals were decapitated under ether anaesthisia. Liquid chromatography method was employed to assess 2,4-DA and its derivatives accumulation in tissues (liver, serum). The selection, calculation and classification of erythroblast islets (EI) into 5 maturity classes were carried out according to Yu.Zakharov et.al.[5]. The calculation of CFUe involvement in differentiation into proerythroblasts, the possibility of repeated central macrophage (CM) EI involvement in new erythropoiesis was carried out according to Yu.Zakharov et.al.[6] Fe^{2+} induced chemoluminescence intensity in serum, hepatic tissue (20% homogenate) and bone marrow (20% homogenate) was estimated by Yu. Vladimirov and A. Archakov[7] method, malon dialdehide content was assessed according to L. Stalnaya and F. Garishvili[8] catalase activity using M.Korolyuk and L. Ivanova method[9].

Results and Discussion

The investigation of 2,4-DA metabolism products distribution and accumulation in different organ tissues of rats revealed the presence of 2,4-D acid and general chlororganic compounds in all studied organs following 2,4-DA injection for 2 months, the greatest general chlororganic compounds content being in the liver in case of LD50 and 1/20LD50. Irrespective of the dose injected the concentration of general chlororganic and 2,4-DA acid compounds in serum didn7t show any substancial difference in both groups.

Herbicide caused hemolytic anemia in rats. Anemia degree showed direct dose dependence. Anemia disappearance by the end of the experiment (the 30th day in all groups, the conclusion being made on the basis of erythrocytes and hemoglobin count in 1 litre of blood) suggested that slowed erythropoiesis activation in the bone marrow during the first weeks following 2,4-DA injection was replaced by erythrone adaptation to moderate hemolysis and possibly direct 2,4-DA toxic effect on the drug injection. This made it possible to make up for erythrocyte deficiency in the blood.

The supposition of slowed erythroid sprout regeneration in rats as a result of impaired cellular-cellular interaction in EI bone marrow confirmed the study of erythropoiesis in EI. Reduced EI formation in the rats' bone marrow due to slowed (compared to intact rats) CFUe interaction both with residual done marrow macrophages and EI involuting ones as well as amplification wave inhibition and erythroblasts maturity in the "crown" of EI formed proved to be characteristic features of cellular-cellular interaction impairment in these rats.

Erythroid elements maturation inhibition in the bone marrow and maternal erythroid cells formation (proerythroblasts and first order basophil erythroblasts) appeared to be a characteristic feature of erythropoiesis in rats. EI formation inhibition is likely to be related to (direct or indirect) 2,4-DA effect on bone marrow macrophage quality. It is likely to be related to 2,4-DA ability to impaire adhesive monocytes/macrophages[10] quality which was determined by us during the experiment. The development of EI adhesive receptors of 2 types sialoadhesive and erytroblasts[11] receptor on CM membrane is known to be the basis for EI formation. The "development" or functioning of these EI CM receptors is likely to be impaired in animals due to herbicide or its metabolits effect. The fact that EI erythroid "crown" maturation inhibition in rats is likely to be also related, to some extent, to the impairment of liver function erythropoiesis due to toxic hepatitis development (the impairment of purine derivatives formation necessary for bone marrow erythroid cells formation), liver function disturbance as the principal vitamin B_{12} depot cannot be excluded[12].

The study of peroxide lipid oxidation (PLO) intensity showed marked Fe^{2+}- induced chemoluminescence intensity increase in case of all total 2,4-DA dose in serum and liver. Distinct chemoluminescence increase in the bone marrow tissue was not observed. The accumulation of one of the PLO end product – malone dialdehide – in serum and liver tends to increase while malone dialdehide accumulation in bone marrow tissue fails to occur.

In physiological conditions the system of antioxidant defence resists the impairing effect of lipoperoxidation products. Catalase is one of the enzymes of the system. The enzyme activity in case of chronic herbicide effect in all total doses approaches the index in intact rats, it being significantly greater than in control in liver and bone marrow tissue. Thus, marked PLO intensity increase in bone marrow tissue is not observed where as enzyme activity of antioxidant defence increases. Liver tissue is notably sensitive to 2,4-DA impairing effect: the

changes in the indexes studied are more pronounced in liver tissues compared to other tissues which is probably due to it being the universal protector in the body.

Acknowledgements

Thus, beside the direct 2,4-DA and its metabolits effect on erythrocyte membrane (their content in serum) which increases peroxide lipid oxydation, PLO products accumulate in erythrocytes which leads to the increase in antioxidant blood and tissue activity.

References

1. Konstantinova T.K., Antonenko T.A. p.104-108, in *Essential problems of remote consequences of occupational poisons effect.* **1976**.
2. Konstantinova T.K., Kovalencko A.V., Trubnikova T.I., Kulakov A.E., Yefimenko L.P., Malkova V.B; *Gygiene of Labour in Agriculture.* **1973**,86-88 .
3. Izbavitelev P.V; *Soviet Medicine.* **1962**, 9, 87-91.
4. Karpenko V.N; *Hygiene of Labour.* **1981**, 17, 75-80.
5. Zakharov Yu.M., Melnikov I.Yu., Rassokhin A.G; *Archives of Anatomy, Histology and Embryology.* **1990**, 98, 5, 38-42.
6. Zakharov Yu.M., Vorgova L.B; *USSR Physiological Journal.* **1990**, 76, 2, 200-205.
7. Vladimirov Ya., Archakov A.I. 153 p, *Peroxide Lipid Oxydation in Biological Membranes*, **1972**.
8. Stalnaya I.D., Garishvili T.G. p.66-68, in *Modern Methods in Biochemistry*, **1977**.
9. Korolyuk M.A., Ivanova L.I., Mayorova K.M; *Laboratory Business.* **1988**, 1, 16-19.
10. Imelbayeva E.A., Kayumova A.F., Kamilov F.Kh., Teplova S.N. (*Thesis*), Effect of amino salt 2,4-dichlorphenoxiacetic acid (2,4-DA) on macrophag cells state, Novosibirsk University, **1995**.
11. Wilson J.G., Tavassoli M. Vol. 718, p. 271-284, in *Molecular, Cellular and Developmental Biology of Erythropoietin and Erythropoiesis. Annals of the N.Y. Academy of Sciences*, **1994**.
12. Williams W.J. 1728 p, *Hematology*, 3rd. Edition McGraw, Hill Book Company, N.Y. **1986**.