ASSESSMENT OF THE LEVEL OF APOPTOSIS MARKERS IN WOMEN WITH NON-DEVELOPING PREGNANCIES, DEPENDING ON THE ORIGIN

DILNOZA SAIDJALILOVA
Tashkent Medical Academy, Uzbekistan

ABSTRACT

Based on survey of 257 women with non-developing pregnancies of various geneses, it was shown that the level of apoptosis marker P53 in the decidual tissue is increased, and anti-apoptotic protein Bcl-2 simultaneously is reduced, compared with similar data of women with physiological pregnancies. The morphological and histochemical investigation of apoptotic changes during NDP, by means of Bcl-2 and P53, must consider the main marker in early manifestations of the dynamics of the pathological processes.

UDC CODE & KEYWORDS

■ UDC: 618.39-02-076.5 ■ Non-developing pregnancy ■ Factors of apoptosis ■

INTRODUCTION

Non-developing pregnancy (NDP) represents etiopathogenetically different heterogeneous groups, including a number of causal factors of histogenesis, rates of autolytic processes, and clinical course of pregnancy (Zolotukhin, 2003; Milovanov et al., 2008). Despite numerous studies (e.g. Zolotukhin, 2003), the trends to reduce of this pathology, including the effectiveness of diagnosis and prevention of NDP, are still absent. Therefore, understanding the mechanisms involved in NDP formation is one of the possible ways to improve forecasting methods for NDP, and, respectively, its prevention and treatment.

In the last decade, in obstetrics and gynecology significant progress in understanding the molecular biology of the cell has been achieved. Belushkina et al. (2001), Milovanov et al. (2001), Bushtyryova et al. (2007), Gorbachyova et al. (2007), Huppertz et al. (2005) established that the vital activity of cells is the result of several series of successive processes – proliferation, differentiation and death.

In recent years, no protein has been studied as intensively as P53. Over the last quarter century, it has been the subject of roughly forty thousand scientific research papers, and that number continuing to steadily rise (Chumakov, 2000). If reparation of damage is impossible, P53 drives the mechanisms of apoptosis. It is now established that the role of disturbances of the P53 gene in development play a role in not only oncological, but also cardiovascular, neurodegenerative, metabolic diseases, and focal brain ischemia (Sagatov et al., 2010).

There are a lot of reports that determination of the molecular biological markers in the decidual tissue may provide prognostic information. These markers include the proteins P53 and Bcl-2 (Toki et al., 1999; Lomunova et al., 2007; Milovanov et al., 2001; 2007). These proteins were found in the villous and extravillous trophoblasts that during apoptosis are associated with intrauterine fetal pathology, impairment of attachment of the placenta, trophoblastic disease and late gestosis (Dimmeler et al., 2000; Belushkina et al., 2001; Lomunova et al., 2007; Milovanov et al., 2001; 2007).

Today, apoptosis is found to involve multiple intra- and extracellular factors. Many important processes in the organism are dependent on apoptosis. In our case, the development of NDP is apparently due to the influence of etiological factors at the level of initiation and realization of apoptosis that was reported by Milovanov et al. in 2007 and 2008. To test this hypothesis, in separate series of studies we carried out immunohistochemical assessment of apoptosis markers P53 and Bcl-2 in the decidual tissue of women, depending on the pathogenic subtype of NDP.

The purpose of research was to evaluate P53 and Bcl-2 markers of apoptosis in the endometrium of women with non-developing pregnancies, depending on the origin.

Materials and methods

The survey included groups of women with NDP (n = 257), in the genesis of which dominated inflammatory diseases of pelvic organs, hormonal, autoimmune disorders, genetic and associated pathologies. Comparison group included women with spontaneous miscarriages (n = 70). Control group consisted of women with physiological pregnancies who had admitted to the hospital for an abortion (n = 40). P53 and Bcl-2 markers were determined in the scrapings from the uterine cavity by immunohistochemical method by Milovanov et al. (2008). The scrapings were fixed in 12% solution of formalin and after standard histological manipulation, were filled by paraffin. Coloration of preparations was carried out by hematoxylin eosin, using a standard method. Investigation of histochemical reactions was carried out by means of specified sera of Monoclonal Mouse Bcl-2 and P53 in polyeosin glasses. P53 and Bcl-2 markers were accounted in tissues per 100 cells in % ratio. The data obtained were processed by the method of variation statistics.

Results and discussion

The analysis of results has showed that the content of P53 was higher in a group of women with spontaneous miscarriages in 7.9 times to control, and in 1.8 times compared with a group of women with inflammatory genesis of NDP, in 2.8 times

■ European Medical, Health and Pharmaceutical Journal ■ ISSN 1804-5804 ■
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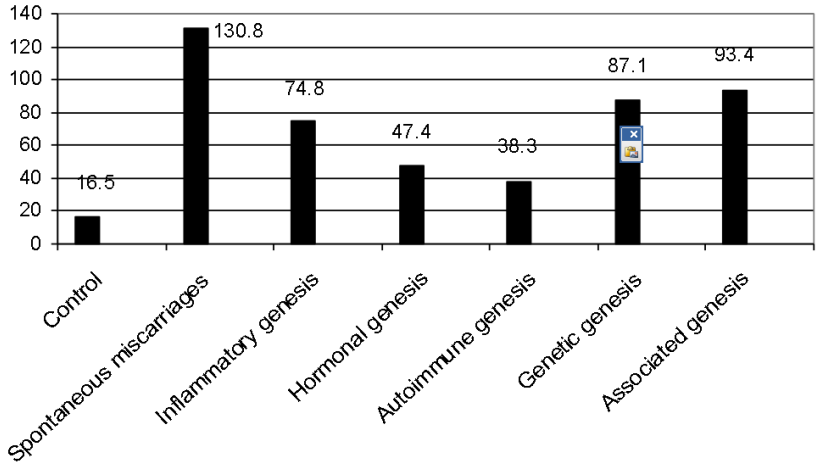
to those with hormonal disorders, in 3.4; 1.5 and 1.4 times to women with autoimmune, genetic and associated pathologies, respectively (Figure 1).

It should be noted that content of P53 protein was significantly higher in the basic groups of women than in control.

Figure 1. The content of wt P53 in the trophoblast and decidual tissue, depending on the genesis of NDP (%).



Source: Author

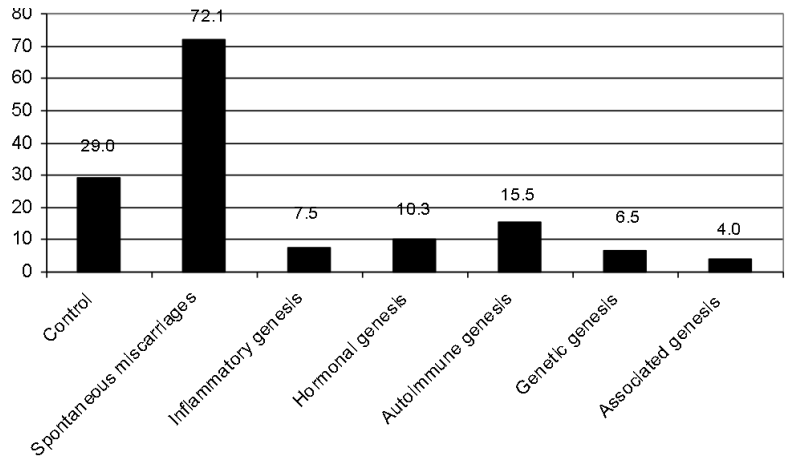
Thus, in women with inflammatory genesis of NDP the level of P53 was higher to control in 4.5 times, whereas in the group of women with hormonal disorders it was higher in 2.9 times, with autoimmune, genetic and associated pathologies in 2.3; 5.3 and 5.7 times, respectively.

Analyzing differences in the content of P53 in the decidual tissue of women in the basic group, we should note that the maximum its level was found in women with spontaneous miscarriages, to a lesser extent on the sequence of decreasing values in women with genetic, inflammatory, hormonal and autoimmune origins of NDP, i.e. changes in the level of P53 depend on the negative effects of etiological factors on the body.

According to recent literature (Belushkina et al., 2001; Bushtyryova et al., 2007; Gorbachyova et al., 2007), changes in the ratio between Bcl-2 and P53 may be a cause of changes in angiogenesis and apoptosis in villous and extravillous trophoblasts and reduction of extravillous trophoblast to invade.

Our studies have shown that in women with spontaneous miscarriages the level of Bcl-2 was 2.5 times higher than in control; whereas in women with NDP this protein was significantly lower (Figure 2). In women with spontaneous miscarriages Bcl-2 protein was also higher than in women with inflammatory and hormonal genesis of NDP in 9.6 and 6.9 times, and in 4.7; 11.1 and 11.08 times higher than in those with autoimmune, genetic and associated genesis of NDP, respectively. At the same time, in women with associated origin of NDP we found low levels of this protein, which further was increasing in women with genetic, inflammatory, hormonal and autoimmune origins of NDP. Consequently, among the underlying reasons for the development of NDP may be factors leading to a decrease of the major anti-apoptotic protein Bcl-2 in trophoblast. In this case, depending on the genesis of NDP were observed varying degrees of reduction of Bcl-2.

Figure 2. The content of Bcl-2 protein in the decidual tissue and trophoblast of women, depending on the genesis of NDP (%)



Source: Author

According to evaluation of P53 and Bcl-2 in the decidual tissue, among women with spontaneous miscarriages P53 protein was increased on the background of simultaneous increased Bcl-2 expression, compared with those in control. In control group low level of P53 was characterized by high content of Bcl-2. In the groups of women with inflammatory, hormonal, autoimmune, genetic and associated origins of NDP we determined high levels of P53 protein, compared with the values of control, which was associated with reduction in anti-apoptotic protein Bcl-2.

Conclusion

According to our data, in women with different genesis of NDP the level of apoptosis protein P53 in the decidual tissue is increased, and the level of anti-apoptotic protein Bcl-2 is simultaneously reduced, compared with similar data in control. At the same time, in women with spontaneous miscarriages increase of P53 in the decidual tissue is associated with increased Bcl-2 expression to a greater extent than in women with NDP. Consequently, in women with NDP the levels of P53 in the decidual tissue have the same directions, whereas the contents of Bcl-2 have different directions, compared with women with spontaneous miscarriages: in women with spontaneous miscarriages they are increased, and in NDP, by contrast, are reduced. The morphological and histochemical investigations of apoptotic changes during NDP, by means of Bcl-2 and P53, must consider the main marker in early manifestations of the dynamics of the pathological processes.

References

1. Belushkin, N.N., Severin, S.E., 2001. “Molecular basis of pathology of apoptosis”, [Arhiv Patologii], in Russian, No.1, pp.51-60.

2. Bushtyryova, I.O., Mikashinovich, Z.I., Shestopalov, A.V., Borisenko, O.V., 2007. “The role of apoptosis in placental development”, [Zhurnal ROAG], in Russian, No.7, pp.49-53.

3. Chumakov, P.M., 2000. “Function of gen p53: choice between the life and death”, Biochem., Vol.65, No.1, pp.34-47.

4. Dimmeler, S., Zeiher, A.M., 2000. “Endothelial cell apoptosis in angiogenesis and vessel regression”, Circ. Res., Vol.87, pp.434-439.

5. Gorbachyova, Y.V., Voloshchuk, I.N., Paltsev, M.A., 2007. “Apoptosis in the trophoblast cells in normally developing pregnancy”, [Molekulyarnaya Meditsina], in Russian, No.2, pp.3-8.

6. Huppertz, B., Herrler, A., 2005. “Regulation of proliferation and apoptosis during development of the preimplantation embryo and the placenta”, Birth Defects Res. Embryo Today, Vol.75, No.4, pp.249-261.

7. Lomunova, M.A., Talayev, V.Y., 2007. “Trophoblast cells of human placenta: the ways of their maturation and interaction with the immune system”, [Immunologiya], in Russian, No.1, pp.50-58.

8. Milovanov, A.P., Boltovskaya, M.N., Fokina, T.V., 2008. “Non-developing pregnancy: histological and immunohistochemical markers of endocrine disruption in endometrial scrapings”, [Arhiv Patologii], in Russian, No.6, pp.22-25.

9. Milovanov, A.P., Fokina, T.V., Starosvetskaya, N.A., 2007. “Decidualization of the endometrium as a factor regulating cytotrophoblastic invasion during the first trimester of pregnancy”, [Arhiv Patologii], in Russian, No.5, pp.31-34.

10. Milovanov, A.P., Kirichenko, A.K., 2001. “Molecular mechanisms of regulation of cytotrophoblast invasion in uteroplacental region”, [Arhiv Patologii], in Russian, No.5, pp.63.

11. Sagatov, D.R., Rasulova, H.A., Madjidova, Y.N., 2010. “Morphological insight into new opportunities using Bcl-2 and P53 in studies of neurotrophicity, neuroprotection and neuroplasticity in brain ischemia”, International Journal of Applied and Fundamental Research, No.4, pp.31-38.

12. Toki, T., Horluchi, A., Ichikava, N. et al., 1999. “Inverse relationship between apoptosis and Bcl-2 expression in syncytotrophoblast and fibrin-tipe fibrinoid in early gestation”, Mol. Hum. Reprod., Vol.5, No.3, pp.246-251.

13. Zolotukhin, T.V., 2003. “Clinical and pathogenetic aspects of non-developing pregnancy”, [Rossiyskiy Vestnik akushera-ginekologa], in Russian, Vol.3, No.2, pp.40-44.