

ORIGINAL PAPER

Importance of the Cytoplasmic Super-oxide Dismutase in the Normal Tissue of the Endometrium and the Endometrium Carcinoma

Nenad Lucic, Zora Antonic, Vesna Ecim, Slobodan Grahovac, Rosanda Jeftovic, Dragica Draganovic, Branka Cancarevic- Djajic, Aleksandra Rodic

Department of Obstetrics and Gynaecology, Clinical Center of Banja Luka, Bosnia and Herzegovina

Objectives: The objective of the study is comparing pathohistological picture and test results of the activity of the enzymes of the anti-oxidative protection –cytoplasmic super-oxide dismutase (CuZnSOD) from the blood and endometrium in the promotion of the progression or regression of the hyperplasia and endometrium carcinoma.

Materials and Methods: The study has been carried out on 70 patients. We have analysed: The age patients, the supersonic test – transvaginal probe, pathohistological diagnosis (PHD) analysis of the curet of the patient—we have gathered the tissue of the normal and the pathologically changed endometrium from the exploratory curet, determining the CuZnSOD in the blood and in the tissue of the normal and pathological endometrium of the uterus. The Group A has been made out of 30 of them who did not have the irregular bleeding from the uterus, and 40 of them represented the Group B with the irregular bleeding, who also had PHD confirmed hyperplasia or malign changes of the endometrium. We have tested if there has been the pathological changes in the small pelvis (the ovary tumor, myoma etc.) in both groups. **Results:** Dominant age in the Group B is 41 – 50 (55%), in Group A, age difference is not that apparent ($p > 0.05$). The results of the arithmetic mean of the CuZnSOD in the blood (19.90%) and (29.05%) in the endometrium which is lower than the Group A (blood-29.95%, endometrium-32.56%). Lower values CuZnSOD in the blood (18,9%) and endometrium (30,09%) we have in the experimental group patients who have had bleeding as well as those beside bleeding had some other gynecological – pathological proces (myoma, cyst on the ovary etc.) **Conclusions:** According to the facts we can see the significance of the activity of the enzymes of the anti – oxidative system in the diagnostic of the hyperplasia and endometrium carcinoma as well as the possibility of their application in the clinical practice. **KEY WORDS:** CYTOPLASMIC, SUPER – OXIDE DESMUTASE, ENDOMETRIUM, CARCINOMA

Corresponding author: ass prof Nenad Lucic, MD, PhD. Clinic for Gynecology and obstetrics, Clinical center of University of Banja Luka, B&H. 12 beba Paprikovac Banja Luka Tel . : 0038765926923, E-mail : nenadi@blic.net

1. INTRODUCTION

In the last decade there has been series of interesting discoveries which are related to the free radicals and their effects in the biological system. It is es-

sential, for the physiology of the healthy organism to keep the dynamic balance between molecular oxygen in its free radicals. The anti – oxidative defence is usually based on the activities of the

enzymes marked as super-oxide dismutase (SOD), which are present in every organism, tissue and cell and they represent our genetic predisposition.

Mc Cord and Fridovich 1969. (1), indicate that SOD are metalloproteins with Cu, Zn, Mn or Fe in the active centre. In the cytosol of the eucaryotic cells CuZnSOD are present and they are characterized by evolutionary stability. In humans, the gene for CuZnSOD is situated on chromosome 21.

According to S. Pajovic (2), the results obtained from the clinical and biochemical studies indicate the presence of the certain correlation between the activity of the SOD and different pathological conditions (inflammatory, ulcerous, convulsive, diabetic and cancerous). In these cases much lower activity of the SOD is also noticeable which causes greater production of the super – oxide anion radicals. When the inefficient functioning of the anti – oxidative system in the protection from the free radicals appears, it will lead to the overcoming of the capacities of the anti – oxidants which will cause the condition known as the oxidative stress (3). Endometrium is a mucous membrane without the submucosa which reaches to the isthmus of the uterus where it is smooth, and to the cervical canal where it is wrinkled (4). There is a surface functional part and deep basis stratum on it. The process of the growth and the regression of the endometrium represents the answer to the cyclic changes during the menstruation, which is pre-

Age	Experimental group		Control group	
	Number	%	Number	%
Up to30	1	2.5	2	6.6
31 – 40	2	5.0	4	13.4
41 – 50	22	55.0	11	36.6
51 – 60	10	25.0	9	30.0
Over 60	5	12.5	4	13.4
Total	40	100.0	30	100.0

TABLE 1. Disposition of the patients according to their age

Control group in general		n	Ar. mean	Std. deviation	Std. error
A. O. Enzymes	CuZnSOD (k)	29	25.95	14.458	2.6848
	CuZnSOD (e)	29	32.56	13.806	2.5637
Experimental group in general		n	Ar. mean	Std. deviation	Std. error
A. O. Enzymes	CuZnSOD (k)	39	19.90	9.908	1.5866
	CuZnSOD (e)	39	29.05	18.850	3.0184

TABLE 2. General descriptive measures - the control and the experimental group: k - blood; e - endometrium

sented by the anatomic and functional changes in glands, vascular and stromal part of the endometrium.

The least controversial type of the hyperplasia of the endometrium is the cyst hyperplasia, while the adenoma is accepted as the precursor of the carcinoma endometrium. Atypical hyperplasia shows great affinity towards the progression in the adenocarcinoma. The more complex hyperplasia has greater chances for the emergence of the invasive carcinoma (5).

2. THE AIM OF WORK

The objective of the research is comparing the pathohistological picture with the tests of the activity of the enzymes of the anti – oxidative protection in the promotion of the progression or the regression of the malign changes of the endometrium.

3. METHODS AND MATERIAL

The material in this research was collected from the Department of the Obstetrics and Gynecology in Banja Luka. The study has been carried out on 70 patients. The control group has been made out of 30 of them who did not have the irregular bleeding from

Experimental group combined diagnoses		n	Ar. mean	Std. deviation	Std. error
A.O. Enzymes	CuZnSOD (k)	20	18.91	10.012	2.2398
	CuZnSOD (e)	20	30.09	19.258	4.3062
Experimental group bleeding		n	Ar. mean	Std. deviation	Std. error
A.O. Enzymes	CuZnSOD (k)	19	20.95	9.959	2.2847
	CuZnSOD (e)	19	27.96	18.873	4.3298

TABLE 3. Descriptive measures for the experimental group - combined diagnoses and bleeding

the uterus, and 40 of them represented the experimental group both the irregular bleeding, who also had pathohistological diagnosis (PHD) confirmed malign changes of the endometrium.

In the range of the study we have analysed:

- **The age** (patients were organised in five categories)
- **The supersonic test** – using the transvaginal probe, we have tested

if there has been the pathological changes in the small pelvis (the ovary tumour, myoma etc.) in both groups.

- **PHD analysis** - we have gathered the tissue of the normal and the pathologically changed endometrium from the exploratory curettage of the patients, and the results that we have got from the curettage were analysed with the optical microscopy – pathohistological diagnostic.
- **Determining the anti – oxidative enzyme** in the blood and endometrium has been carried out in The Institute For The Nuclear Science Vinca in Belgrade. In our research we have been stipulating the activities of the cytoplasmic SOD – CuZnSOD, which activity is present in the tissue of the

normal and pathological endometrium of the uterus. The testings were carried out using the methods given from Misra and Fridovich (6, 7). These methods are based on the capability of the SOD to inhibit the autooxidation of the adrenaline into the adrenochrome.

The results of the tests were presented as the specific enzyme activity (unit/mgprotein).

4. RESULTS AND DISCUSSION

According to their age, patients were organised into five categories. In the Table 1 has been presented that dominant age group was 41-50 years.

General note:

The extreme values (Outlier) have been excluded as well as those who can lead to the wrong conclusions. The criterion of the exclusion of the specific values of the testings was that those values were out of the interval (2SD) so they were left out from the sample.

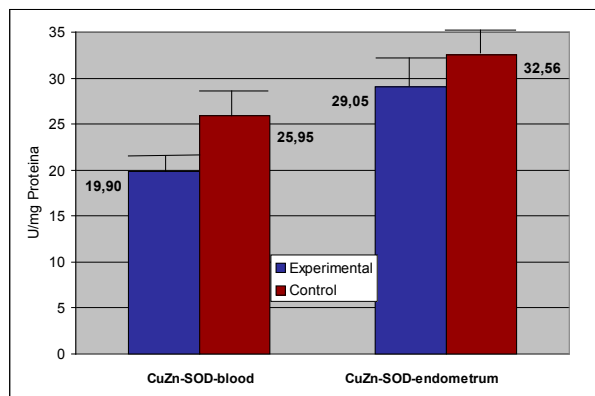


FIGURE 1. CuZn - SOD in the blood and endometrium - the experimental and the control group in general

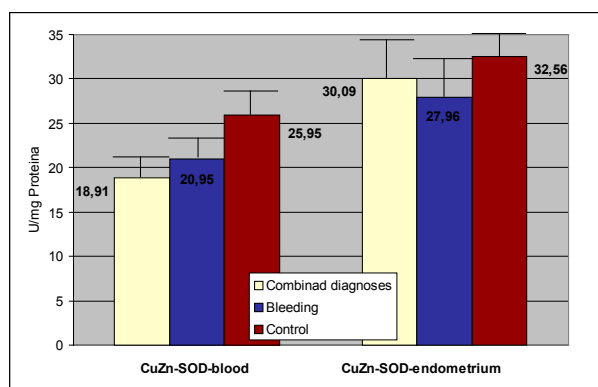


FIGURE 2. CuZnSOD in the blood and endometrium in cases of combined diagnoses and bleeding - the experimental and the control group

The results of the arithmetic mean of the CuZnSOD were 19,90% in blood and 29,05% in endometrium of the experimental group, while in the control group were 25,95% in blood and 32,56% in endometrium (Table 2, Figure 1).

The results of the arithmetic mean of the CuZnSOD in the blood and endometrium in the experimental group were lower comparing to the control group. This shows that there are changes in the activity of the dismutase, that can lead to the quantitatively and qualitatively changes of the enzymes created during the process of the hyperplasia, as well as, malign transformation of the endometrium. The results of Punnonena and Sar,1993. (8), show the lower values of the SOD in the carcinoma endometrium compared with the normal endometrium in the results of Finland's and Japan's women.

The changes in the anti-oxidative protective system were explained as changes combined with the changes of the biochemical paths. Dach and all 1983. (9), explain that the activity of the SOD in tumours as well as the older tissues is reduced compared with the normal tissues or the tissues of the younger organism. While the normal cells are capable to induce different forms of the anti-oxidative enzymes which can reduce relative radicals and prevent damages of the cell in the conditions of the oxygen stress, tumour cells mainly lose that capability and can not induce these enzymes so their concentration and activity are reduced (10).

In our research we have also exam-

ined patients in the experimental group who have had bleeding confirmed with pathohistological diagnosis of malign changes of the endometrium as well as those who beside that had some other gynecological - pathological process (myoma, cyst on the ovary etc.). We have noticed lower values CuZnSOD in the blood (18,91%) and endometrium (30,09%) in

experimental group patients who have had bleeding caused by malign changes of endometrium, as well as those bleeding had some more gynecological pathological process (myoma, cyst of the ovary et.) (Table 3, Figure 2). The presence of these pathological conditions is confirmed with the supersonic test. We have compared these results with the results of the control group in order to verify if some other gynecological - pathological condition can affect the values of the anti - oxidative enzymes in patients who have had irregular bleedings.

According to the results of the arithmetic means of the CuZnSOD in the blood and endometrium in both tested groups we can draw the conclusion that there are visible lower values of the enzymes in the blood and endometrium in the experimental group compared with the control group. Ishikawa and all indicate that anti - oxidative enzymes in the endometrosis as well as the adenomyosis are constantly higher during the menstruation (11). Testing the informational RNK in the peritoneal liquid of women, the mentioned authors have shown that the expression of the CuZnSOD is greater in the patients' suffering from the adenomyosis

5. CONCLUSION

In the diagnosis of the pathology of the endometrium of the uterus, besides the explorative curettage, the new screening methods can be considered.

The results that we have come up with in our research indicate the lower

activities of the SOD in the blood and endometrium of the patients who have the hyperplasia and endometrium carcinoma of the uterus.

We have also registered the lower activity of the SOD in the blood and endometrium with the patients who have some other processes as well (myoma, cyst on the ovary etc.). Based on the shown results we can see the significance of the detection and modulation of the activity of the enzymes of the anti - oxidative system in the diagnostic of the carcinoma endometrium, as well as the possibility of their application in clinical practice.

REFERENCES

- McCord JM, Fridovich I. Superoxide dismutase. An enzymatic function for erythrocuprein (hemocuprein). *J Biol Chem.* 1969; 244: 6049- 6055.
- Pajovic S. Superoksid dismutaza kao biomarker patoloških stanja. *U: Savremena biofizika.* Velarta, Beograd, 2000: 115-153.
- Sies H. Oxidative stress. *U: Oxidative stress II: Oxidants and antioxidants.* Ed. H. Sies. Academic Press New York 1991: XV-XVII.
- Popovic D. Patologija cerviksa i endometrija, Beograd, 1999: 81-105.
- Gore H, Hertig A T. Carcinoma in situ of endometrium. *Am J Obstet Gynecol.* 1966; 94: 134.
- McCord JM. Free radicals and inflammation: protection of synovial fluid by superoxide dismutase. *Science.* 1974; 185: 529-531.
- Mistra HP, Fridovich I. The role of superoxide anion in the autooxidation of epinephrine and a simple assay for superoxide dismutase. *J Biol Chem.* 1972; 247: 3170-3175.
- Punnonen R, Kudo R, Punnonen K, Hietanen E, Kouppala T, Kainulainen H, Sato K, Ahotupa M. Activities of antioxidant enzymes and lipid peroxidation in endometrial cancer. *Eur J Cancer.* 1993; 29 A,(2): 266-269.
- Dach HC, Benedetti MS, Dostert P. J. *Neurochem.* 1983; 40: 1003.
- Oberley LW, Oberley TD. Free radicals cancer, and aging. In: *Free Radicals, Aging and Degenerative Diseases* (JE. Johnson, R. Walford, D. Harman, J. Miquel editors). Modern Aging Research, AR. Liss, Inc., New York 1986; pp.325-371.
- Ishikawa M, Nakata T, Yaginuma Y, Nishiwaki K, Goishi K, Saitoh S. Expression of superoxide dismutase (SOD) in adenomyosis. *Am J Obstet Gynecol.* 1993; 169: 730-734.