Imbalance of lipid peroxidation, antioxidant defense system and the cytokine system in the blood of women with postpartum purulent- septic complications

Shahlo Abduzhabarova[1, 2], Ubaidilla Datkhayev[3], Raisa Abdullabekova[4]

[1] Department of Obstetrics and Gynecology, Kyrgyz-Russian Slavic University, Kyrgyzstan, Bishkek
[2] Department of Pathological Physiology, Kyrgyz Scientific Center of Human, Kyrgyzstan, Bishkek
[3] Kazakh National Medical University named after S.D. Asfendiyarov, Kazakhstan, Almaty
[4] Medical Rehabilitation and Sports Medicine Course of CPDF, Karaganda State Medical University, Kazakhstan, Karaganda
kairat_phd@mail.ru

Abstract: Physiological course during the postpartum period is characterized by the intensification of lipid peroxidation processes and system of anitoxsidant protection. Purulent- septic complications are accompanied by an avalanche growth of radical formation processes due to the lowering of antioxidant content and significant depletion of the antioxidant defense system at the development of sepsis. Sepsis is a particular pathological condition that develops due to inadequate course of the infectious process in a weakened organism. In sepsis the pathological process due to virtue of insolvency of protective organism forces is manifested by a generalized dissemination of infectious onset in conditions of increasing general immunosuppression, which further leads to the development and deepening of multiple organ dysfunction syndrome. The development of septic process begins with the appearance and the sharp increase in the systemic circulation of immunological competent cells capable of cytokine production - mediators of sepsis. Further, the situation is evolving according to the scenario of uncontrolled systemic crisis, in the genesis of which the significance the immune system is obvious.
[Abduzhabarova Sh, Datkhayev U, Abdullabekova R. **Imbalance of lipid peroxidation, antioxidant defense system and the cytokine system in the blood of women with postpartum purulent- septic complications.** *Life Sci J* 2014;11(12s):22-25]. (ISSN:1097-8135). http://www.lifesciencesite.com. 4

Keywords: Endometritis; puerperal sepsis; cytokines; lipid peroxidation; antioxidants; medium- molecular peptides

1. Introduction

People health is one of major factors of development of any state [1, 2, 3]. The modern health system has to meet the new requirements of all concerned parties: population, health service and state [4, 5].

Despite advances of modern medicine in the fight against purulent- septic diseases, sepsis remains one of the most difficult and insufficiently studied problems [6].

In the world sepsis annually is diagnosed in 1.5 million patients, and in the most technologically advanced country - the United States of America- in 750 thousand people [7]. In Russia, the actual number of patients with sepsis is 10 times higher than the data of official statistics and corresponds to the frequency of sepsis in leading hospitals around the world [8].

Obstetric surgical sepsis as the dominant form is characterized by high mortality. Today, in the world 500 thousand of patients die annually from sepsis, in the European Union countries - about 135 thousand, in the USA - about 250 thousand of people, the tendency of increase in mortality is typical for the technologically advanced countries of Europe and North America [7]. Extensive use of modern means of causal therapy in the treatment of patients with purulent -septic diseases do not safeguard against the risk of death [6].

Extremely important is the development of new approaches to the diagnosis and treatment of sepsis, which will contribute to the recognition of the key role of immune disorders in its pathogenesis [9, 10]. The variety and depth of immune disorders observed in patients with sepsis suggest considering them as important pathogenetic link of sepsis [10]. In connection with the above mentioned we defined the objective of the research: to study the pathophysiological and clinical responses of implementation of purulent-septic complications of lipid peroxidation and antioxidant defense system, to assess the immunological reactivity of the cytokine system in puerperants with physiologic course of puerperial period and purulent- septic complications.

2. Material and Methods

We examined 81 patients in the postpartum and postoperative periods, which were divided into appropriate groups: group 1 consisted of 23 women in childbirth, postpartum period of which is complicated by obstetric sepsis, group 2 consisted of 30 women in childbirth, postpartum period of which was complicated by acute endometritis, the third group - control one consisted of 28 parturients with

physiological course (puerperiya) of postpartum period.

The material for this study was the blood of parturients with sepsis and acute endometritis and also the blood of women with physiological course of postpartum period, which was taken from a peripheral vein in an amount of 5-7 ml. The obtained blood was decanted and subjected to further centrifugation at 1500 rev / min for 30 minutes.

Determination of lipid peroxidation products in the blood plasma was carried out by spectrophotometric method. Principle of the method is based on the intensive ultraviolet absorption of blood lipid extracts: NL - in the field of 212-220 nm, HPL -232-234 nm, DK -272 - 275 nm. The measurement results were expressed in relative optical density units per 1.0 ml of blood plasma, since the calculation for the molar concentration of the peroxide for complex of lipid mixture was practically unfeasible. Oxidative index was calculated by ratio of content of HPL to NL.

Determination of the concentration of the medium- molecular peptides in blood plasma was performed by spectrophotometric method and was based on the detection of blood plasma which was freed of coarse dispersive proteins with 10% of trichloroacetic acid solution and dilution with distilled water by measuring the optical density of the plasma in the ultraviolet light at a wavelength of 254 nm.

Determination of content of total antioxidants in blood plasma was determined by enzyme immunoassay on analyzer «Multiskan» by sets of firm «Randox». Principle of the ABTS method is in incubating (2,2 -Azino-di [3 – ethylbenzthiazoline sulphonate]) with peroxidase (metmyoslobin) and hydrogen peroxide with forming the radical ABTS R +. The obtained solution has a relatively stable blue-green coloring which was measured at 600 nm. Antioxidants contained in the test sample inhibit the color development in proportion to their concentration in the sample. The results are expressed in mmol/l.

Determination of IL -1β, IL- 6, IL -8, TNF - α, IL -4 content in blood plasma was determined by enzyme immunoassay on agent kits of Multiscan apparatus of firm «Vector- Best» (Russia).

3. Results

Study of lipid peroxidation showed that puerperants with physiological course of puerperial period (IInd group), compared with healthy non-pregnant women of reproductive age (Ist group), in indices of lipid peroxidation there was observed the tendency to intensification of the processes of lipid peroxidation, manifesting in a slight increase of plasma levels of lipid hydroperoxides (HPL) ($p < 005$), a significant increase of dienketons (DK) ($p < 001$), which have resulted in a slight increase in the content of neutral lipids (NL) and to a statistically significant increase in the value of oxidative index (OI) ($p < 005$).

In women-puerperants with purulent - septic complications these processes significantly went out beyond the steady state. So, in parturients with obstetric sepsis (IIId group) there is a pronounced activation of lipid peroxidation processes as compared to the indices of the Ist and IInd groups of parturients. Thus, the content of neutral lipids increased slightly, but they were reliably significant as compared with the indices of the group I ($p < 005$), but compared to indices of Group II it tended to increasing, but did not reach significant values ($p < 005$). Lipid hydroperoxide content increases significantly in 4 and 3 -fold ($p < 0001$) in parturients of the group III. Dienketon's content rises as compared with the group I for 20 times ($p < 0001$) compared to indices of Group II in 5 times ($p < 0001$). Accordingly, the value of OI increases to the coefficient 1.342 ($p < 0001$) and is associated with a large increase in the concentration of lipid hydroperoxides relatively to neutral lipids.

In women, with postpartum endometritis (IVth group) there was observed a similar pattern in levels of lipid peroxidation indices change compared with those groups I and II, and as compared to women of group III the content of lipid hydroperoxides and dienketons was somewhat lower ($p < 005$), while this value didn't reach significant changes ($p> 005$).

Excessive activation of the process of lipid peroxidation in purulent septic complications contributes to precipitous growth of radical generation processes with forming the initial – lipid hydroperoxides, and the final products - dienketons (Figure 1).

Figure 1 – Indicators of lipid peroxidation processes in blood plasma in healthy women of reproductive age, in parturients with physiological course of postpartum period and puerperiants with purulent- septic complications.

With parallel change in the intensity of lipid peroxidation there occurs the change of activity of the antioxidant defense system. As it is seen from Figure 2, the dynamics of the content of total antioxidants in groups III and IV tends to a significant reduction compared with the data of Ist and IInd groups ($p < 001$). The concentration of middle molecular peptides (MMP) has a reverse tendency, i.e. a significant increase ($p < 005$ - < 001), but the concentration of MMP in the group III is slightly higher than in the group IV ($p < 005$). It

should be noted that the values of common antioxidants and middle molecular peptides in groups I and II are practically at the same level and have no significant changes (p> 005) (Figure 2).

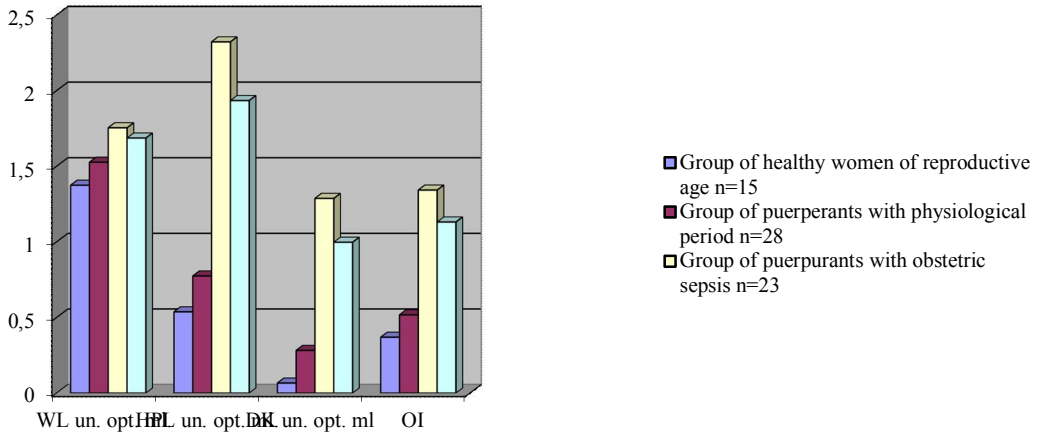

Figure 1. Indicators of lipid peroxidation processes in blood plasma in healthy women of reproductive age, in parturients with physiological course of postpartum period and puerperiants with purulent- septic complications

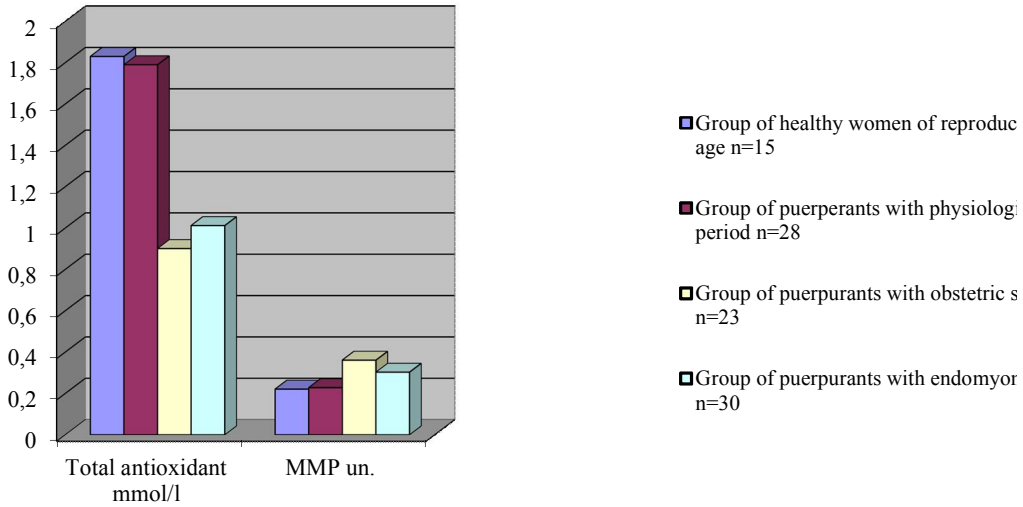

Figure 2. Indicators of content in blood plasma of total antioxidants and MMP concentration in healthy women of reproductive age, in puerperants with physiological course of postpartum period and in women with purulent- septic complications

The examination of the cytokine system state has shown that in women with physiological course of postpartum period compared with a group of healthy women in the content of mediators in blood plasma IL -1β, IL-6, TNF -α, IL-8 there were not observed significant values (p> 005), the content of IL -4 insignificantly increased (p < 005). In puerperants of Group III there was observed a significant activation of proinflammatory cytokines, IL -1β content as compared with the indices of groups I and II increased 10 times (p < 0001), the contents of IL -6 and TNF -α increased 3-fold (p < 0001).

There was less pronounced increase in content of blood plasma IL -8 (p < 005). The content of anti-inflammatory cytokine IL- 4 has a reverse tendency, i.e. there was observed its double decrease (p < 005 - p < 001). In women of IVth group there was observed a similar pattern in the dynamics of the activity of mediators compared with data of groups I and II. As for indices, the content of IL -1β, IL-6 in group III was reliably lower (p < 005) , and IL-4 - higher (p < 005) (Fig. 3).

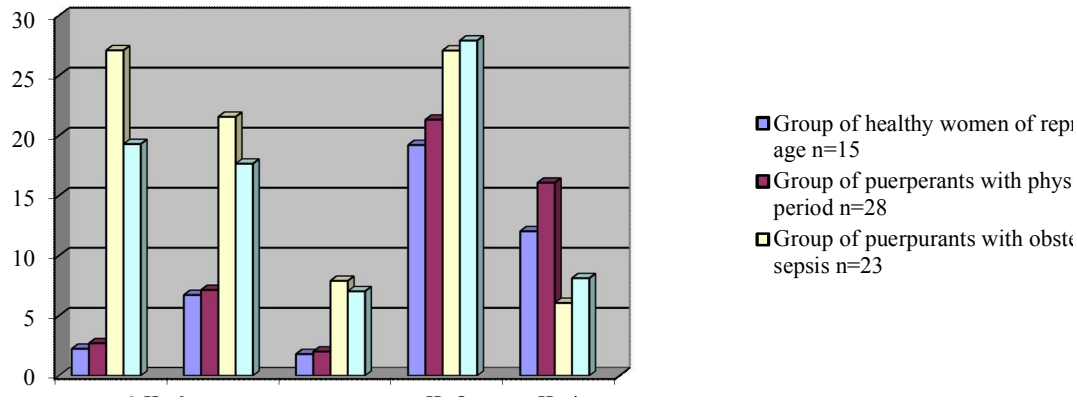

Figure 3. Indicators of cytokine concentration in blood plasma in healthy women of reproductive age, in puerperants with physiological course of postpartum period and in women with purulent- septic complications

4. Discussions

Thus, purulent- septic complications in women-puerperants of postpartum period, of women are characterized by complex pathophysiological mechanisms of development. In response to intensive microbial load and intoxication by bacterial toxins in the organism of puerperants there occurs a cascade of metabolic changes with the position of studied phenomena. It is characterized by the development of oxidative stress phenomena, disturbances in the functioning of the cell membranes, which in turn leads to release of a large number of proinflammatory cytokines, damage to the vessel endothelium and the development of immunopathological reactions. All this eventually leads to malfunctioning on the organ, system, organism level. Lipid peroxidation processes, antioxidant defense system and mediators of the acute phase response in the blood may give indirect and fairly accurate picture of the dynamics of the processes of metabolic adaptation on whole organism level, as well as universal information in biochemical transformations.

Corresponding Author:
Dr. Abduzhabarova
Department of Obstetrics and Gynecology, Kyrgyz-Russian Slavic University, 44, 720000, Kievskyi street, Bishkek, Kyrgyzstan.
E-mail: kairat_phd@mail.ru

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7/10/2014