Some Factors Influencing Structural and Functional Properties of Erythrocyte Membranes in Pregnant Women

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Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 123, No. 1, pp. 26-28, January, 1997
Original article submitted October 20, 1995

Study of lipid peroxidation and antioxidant activity of blood serum and the properties of the erythrocyte plasma membrane during pregnancy showed that the level of lipid peroxidation reaches the maximum by delivery. A decrease in serum antioxidant activity at that time is one of the determinants of structural changes in erythrocyte membranes. These changes may be associated with increased membrane permeability for oxytocic substances before delivery.

Key Words: *microviscosity; hydrophilicity; lipid peroxidation; antioxidant activity*

Lipid peroxidation (LPO) is a process essential for any living cell [1,2,11]. During pregnancy, generation of LPO products is associated with the synthesis of prostaglandins and steroid hormones [5,7,9,10].

In this study we measured serum levels of primary and secondary LPO products and examined their effects on structural organization of the erythrocyte plasma membrane in women at different times of uncomplicated pregnancy.

MATERIALS AND METHODS

Structural and functional properties of erythrocyte membranes were examined in blood samples obtained from 132 women at different terms of normal pregnancy. Samples from 30 nonpregnant adult healthy women served as the control. The groups were matched for age and parity.

The intensity of LPO in erythrocyte membranes was evaluated by hydroperoxide (HP) [3] and malonic dialdehyde (MDA) contents using colorimetry with thiobarbituric acid [12]. Blood antioxidant activity was determined as described [4]. Changes in the structure of the erythrocyte plasma membrane were assessed by changes in microviscosity (S) and hydrophobicity (h), which were calculated as the order parameter, and hydrophobicity using electron paramagnetic resonance spectra of spin-labeled stearic acid [6,13] recorded at room temperature.

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RESULTS

As Table 1 shows, the mean serum levels of MDA, a secondary LPO product, increase during pregnancy. During weeks 24-28, MDA levels slightly differed from those in nonpregnant healthy women, while during weeks 29-32 they increased significantly compared with that in the control group ($p<0.001$) and on the 24th-28th week of pregnancy ($p<0.05$). On weeks 29-32, serum MDA in 2/3 of women ranged from 30 to 33 optical density (OD) units *vs.* 24-30 OD units during weeks 24-28.

Serum MDA level increased during weeks 33-37 ($p<0.001$) and 38-40: 36-39 and 39-42 OD units, respectively. A correlation ($r=0.52$, $p< 0.05$) between the MDA level and duration of pregnancy has been established.

The mean serum level of HP during weeks 24-28 of pregnancy did not differ significantly from that in nonpregnant women, but then (weeks 29-32) sig-

0007-4888/97/0001-0021$18.00

TABLE 1. LPO Product Levels at Different Times of Normal Pregnancy ($M \pm m$)

Week of pregnancy	Serum, OD units		Erythrocytes, OD units	
	MDA	HP	MDA	HP
Nonpregnant controls (n=30)	26±2.0	37±4.0	85±4.0	156±10
24-28 (n=10)	25.5±1.1	34.5±1.1	102±6.0	220.5±4.0
29-32 (n=10)	32.0±1.8*	42.7±1.1*	107±5.0**	228±4.1
33-37 (n=12)	35±2.1*	52.0±1.3**	99±5.0	249±11.0
38-40 (n=12)	39±2.7*	51±4.0***	119±6.3***°°	308±6.8**°
Mean normal values	36±2.3	48.0±2.9	110.1±4.3	283.3±14

Note. *p<0.001, **p<0.05, ***p<0.01 compared with the control group; *p<0.001 compared with weeks 29-32; °p<0.001, °°p<0.01 compared with weeks 33-37. MDA = malonic dialdehyde; HP = hydroperoxides; OD units = optical density units.

nificantly rose to 42.7±1.1 OD units (p<0.001). During weeks 33-37, it reached the maximum: 52.0±1.3 OD units, remaining unchanged until delivery. Analysis of individual values showed that in 2/3 of women on the 38th-40th week of pregnancy the HP level varied from 48 to 57 OD units, while on weeks 33-37 of pregnancy HP reached this level in 1/3 of the women.

Thus, both MDA and HP levels gradually increase during normal pregnancy and reach the maximum by delivery.

Since all erythrocyte lipids occur in the plasma membrane, changes in the LPO level can be regarded as an indirect indicator of structural perturbations in the erythrocyte plasma membrane. As shown in Table 1, the mean MDA content of erythrocytes, unlike that of serum, was significantly higher in all the women (>93 OD units) during the 24th-28th weeks of pregnancy compared with the control. It slightly increased to 107±5 OD units during weeks 29-32, decreased to 99±5 OD units during weeks 33-37, and reached the maximum (119±6.3 OD units) during weeks 38-40 (Table 1).

The HP levels in erythrocytes also increased, reaching the maximum value (twice that in the controls, p<0.001 and 1.4-fold higher than that on the 24th-28th week of pregnancy) by delivery. A strong correlation (r=0.63, p<0.01) was established between the HP content of erythrocytes and duration of pregnancy. Consequently, both serum and erythrocyte contents of LPO products gradually increase during pregnancy.

TABLE 2. Order Parameter (S) and Hydrophobicity (h) of the Erythrocyte Membranes at Periods of Pregnancy

Week of pregnancy	S, rel. units	h, rel. units
24-28	0.670±0.001	0.83±0.03
29-32	0.671±0.001	0.79±0.01
33-37	0.671±0.001	0.76±0.02
38-40	0.675±0.002	0.73±0.01
Nonpregnant controls	0.671±0.001	0.80±0.002

Lipid peroxidation and antioxidant activity are the factors that determine the state of the erythrocyte plasma membrane. Lipid peroxidation is regulated by the antioxidant system. The state of this system was assessed by measuring the antioxidant activity of blood serum. The results obtained show that serum antioxidant activity remains low during the entire period of during pregnancy.

Biochemical tests were paralleled by determination of two parameters characterizing the structure of the erythrocyte membrane (Table 2). The microviscosity of erythrocyte membranes up to the 37th week of pregnancy was 0.670±0.001 *vs.* 0.671±0.001 rel. units in the control. However, analysis of individual values in the course of pregnancy revealed a tendency toward an increase. During the last three weeks of pregnancy, the microviscosity of erythrocyte membranes increased to 0.675±0.002 rel. units (p< 0.05), ranging from 0.674 to 0.677 rel. units in 3/4 of the women during the 38th-40th week of pregnancy. Consequently, a statistically significant increase in the microviscosity of the erythrocyte plasma membrane occurs in full-term pregnancy, when the intensity of LPO processes in the blood increases against the background of a low antioxidant activity of the serum.

During weeks 24-28 of pregnancy, the mean hydrophobicity was close to that in the control group (in 2/3 of the women it ranged from 0.82 to 0.85 rel. units) and then progressively decreased to 0.76± 0.02 rel. units during weeks 33-37 (p<0.05, a 0.77-0.81 rel. unit in 2/3 of the women) and to 0.73±0.01 rel. units during weeks 38-40 (p<0.05) (Table 2). Consequently, hydrophobicity of the erythrocyte plasma membrane is minimal immediately before delivery. The hydrophobicity of erythrocyte membranes negatively correlated with duration of pregnancy (r= -0.66, p<0.01).

We have compared some LPO parameters with antioxidant activity of blood sera and the parameters characterizing structural organization of erythrocyte membranes. A correlation was established between serum MDA content and the order parameter (r= 0.64, p<0.01), between serum MDA and the erythrocyte membrane microviscosity (r=-0.52, p<0.05), between HP content and membrane microviscosity (r=0.54, p<0.05), and between erythrocyte HP and serum antioxidant activity (r=0.57, p<0.05). Thus, the intensity of free-radical processes and antioxidant activity correlate with the state of the erythrocyte plasma membrane.

In conclusion it should be emphasized that the LPO level in healthy pregnant women reaches the maximum by the time of delivery. The lowered serum antioxidant activity at that time is one of the factors determining changes in cell structure. These changes may be associated with increased permeability of biological membranes for the oxytocic compounds before delivery.

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