Effect of Glucocorticoids and Gestagens on Glutathione Redox-System in Rat Skin Involved in Dermatitis

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In the model of experimental dermatitis the effect of hydrocortisone and two gestagens (endogenous progesterone and synthetic mecygestone) on the level of glutathione redox-system components (reduced glutathione, glutathione reductase, and glutathione peroxidase) in rat dermis and epidermis is characterized by different degree of activation of this system.

Key Words: *skin; dermis; epidermis; allergic dermatitis; hydrocortisone; progesterone; mecygestone; gestagens; glutathione*

Long-term and intensive hormonal therapy of skin diseases even with local drugs is often accompanied by complications and relapses after discontinuation [6], which can be due to insufficient knowledge about the effects produced by hormones on the skin.

The antiinflammatory effect of glucocorticoids is probably related to their capacity to inhibit lipid peroxidation (LPO), which is maintained at a certain level due to the action of prooxidant and antioxidant systems. Hydrocortisone inhibits LPO in tissues due to antioxidant activity [1,5]; however, the mechanisms of this effect are poorly understood.

Steroid hormones can regulate the antiperoxidation defense due to their effect on the glutathione redox-system expressed in almost all tissues [4]. However, we found no published data on the effect of glucocorticoids on the state and activity of its components in the skin. Apart from the antioxidant effect similar to that of hydrocortisone [8], progesterone also produces an antiproliferative effect in dermatoses.

Our aim was to compare the effects of hydrocortisone and two gestagens (endogenous progesterone and synthetic mecygestone) on the content of reduced glutathione (GSH) and activity of glutathione reductase (GR) and glutathione peroxidase (GPx) in rat dermis and epidermis in experimental dermatitis.

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MATERIALS AND METHODS

Experiments were performed on female rats (150 g) in the diestrus phase [3]. Five to seven rats were used in each experiment. The rats were sacrificed under light ether narcosis. Skin homogenates were prepared as described previously [7]. The content of GSH, GR, and GPx was determined spectrophotometrically [2]. Contact allergic dermatitis (CAD) was induced by nitrobenzene chloride [9]. Test hormones in 20% alcohol were injected subcutaneously in doses of 30-300 μg/100 g body weight for 5 days after dermatosis development. The rats were killed 30 min after the last injection. Protein was estimated according to the method of Lowry [10]. The data were processed statistically using Student's *t* test.

RESULTS

The content of GSH and activity of GR and GPx in the dermis and epidermis of intact rats were taken as the control (Table 1).

In rats with experimental dermatitis the content of GSH in the dermis and epidermis decreased by 5 and 1.4 times in comparison with those in intact rats. Activity of both examined enzymes also decreased (Table 1): GPx activity similarly to the content of GSH most markedly decreased in the dermis, while GR activity decreased mainly in epidermis. These changes

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TABLE 1. Effect of Hormones on Parameters of Glutathione Redox-System in Rat Skin Involved in Dermatitis ($M \pm m$)

Conditions	Tissue	Parameters of redox-system		
		GSH, nmol/mg protein	activity, μmol/min/mg protein×10²	
			GR	GPx
Control	Epidermis	3.1±0.25	1.9±0.2	3.4±0.1
	Dermis	3.7±0.20	2.2±0.2	3.7±0.1
Dermatitis	Epidermis	0.6±0.01*	1.2±0.1*	2.6±0.2*
	Dermis	2.6±0.2*	1.7±0.1*	2.4±0.1*
Hydrocortisone				
2 μg/100 g	Epidermis	0.5±0.01*	1.0±0.1*	2.5±0.2*
	Dermis	2.1±0.03*	1.5±0.2*	2.4±0.1*
200 μg/100 g	Epidermis	3.0±0.4	1.8±0.2	3.6±0.2
	Dermis	3.6±0.2	2.3±0.2	3.6±0.2
Progesterone				
2 μg/100 g	Epidermis	1.1±0.1*	1.7±0.1	5.3±0.2*
	Dermis	3.4±0.1	4.2±0.1*	7.0±0.3*
200 μg/100 g	Epidermis	3.4±0.2	2.1±0.1	4.8±0.2*
	Dermis	3.6±0.1	4.7±0.2*	5.4±0.2*
Mecygestone				
2 μg/100 g	Epidermis	3.1±0.2	2.0±0.2	3.2±0.2
	Dermis	3.5±0.15	2.1±0.2	3.5±0.1
200 μg/100 g	Epidermis	3.8±0.1*	2.8±0.1*	2.9±0.1*
	Dermis	4.1±0.2*	3.5±0.1*	2.8±0.1*

Note. *$p<0.05$ compared to the control value.

can depend on abnormalities in GR and GPx or result from hormonal regulation disturbed of the glutathione redox-system.

Subcutaneous injection of hormones along the apparent boundary of skin lesion in dermatitis changed functional activity of the glutathione redox-system starting from a dose of 2 μg/100 g. Hydrocortisone in this dose produced further decrease in the content of GSH and GR activity in comparison with untreated dermatitis without changing significantly GPx activity in both tissues. When applied in a dose of 200 μg/100 g, it increased all examined parameters of the glutathione redox system practically to normal both in the dermis and epidermis.

Progesterone increased in a dose-dependent manner both the content of GSH (to a greater degree in the epidermis) and activity of the enzymes. Activities of GPx in both tissues and GR in the dermis surpassed the normal (Table 1).

Synthetic gestagen mecygestone, a 17-β-oxopentaran derivative, produced a normalizing effect in a dose of about 3 μg/100 g (Table 1) and brought the examined parameters to normal values more closely than progesterone. In a dose of 300 μg/100 g it increased GSH and GR activity above normal values, but decreased GPx activity.

Therefore, activity of the glutathione redox system in the skin involved in dermatitis decreases, which is probably responsible for activation of LPO in the dermis and epidermis. Similarly to hydrocortisone, gestagens promote reactivation of the glutathione redox-system in contact dermatitis and probably in other inflammatory processes in the skin. This effect is dose-dependent. The positive effect is observed at a dose of 2-3 μg/100 g. To achieve the same effect with hydrocortisone, a 100-fold dose is required.

Our data indicate that similarly to glucocorticoids, gestagens can be used in local treatment of allergic dermatitides as components of the complex therapy in doses affecting glutathione redox-system.

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