ACTION OF HYDROCORTISONE ON DNA SYNTHESIS BY SEBACEOUS GLAND EPITHELIAL CELLS

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It was shown by autoradiography that after a single injection of hydrocortisone (10 mg/100 g body weight) transition from the G_1 to the S period is delayed and the duration of the S period is increased for epithelial cells in the acinar part of the sebaceous gland (sebocytes) and the stratified squamous epithelium of the efferent ducts. Later, after the proliferative processes have subsided, their intensity increases again and proliferative activity exceeds the initial level. Hydrocortisone has a more powerful action on the proliferative activity of the stratified squamous epithelial cells of the efferent ducts of the sebaceous gland than on proliferative activity of the acinar sebocytes.

KEY WORDS: sebocytes; epithelium of efferent ducts; hydrocortisone; proliferative activity.

Proliferative activity of sebaceous gland cells has now been shown to depend on sex hormones – androgens [9, 12] and estrogens [6, 7, 12] – and also on ACTH [11].

The object of this investigation was to study how activity of sebaceous gland cells depends on corticosteroids.

EXPERIMENTAL METHOD

The diurnal rhythm of proliferative processes was investigated in the sebaceous gland epithelium of the external auditory meatus [13] of 44 male albino rats weighing 150-180 g. Hydrocortisone (Richter) was injected intraperitoneally into 24 rats at 8 a.m. in a dose of 10 mg/100 g body weight. The animals were sacrificed in groups of four at a time, 4, 8, 12, 16, 24, and 48 h after injection of the hormone. Groups of four control rats (total 20) also were sacrificed at the same times.

Thymidine-H^3 was injected into all the animals 1 h before sacrifice in a dose of 0.5 μCi/g (specific activity 4.1 Ci/mmole). The sebaceous gland was fixed in Bouin's fluid. Paraffin sections 7 μ thick were stained with hematoxylin–eosin or azure II–eosin and some of them were coated with type M emulsion and exposed for 31 days. The mitotic coefficient (MC), index of labeled nuclei (ILN), and number of grains of reduced silver in the epithelium of the acinar part and efferent ducts of the gland were calculated. Mitoses and cells synthesizing DNA were counted in 3000 cells of the basal layer. The data were subjected to analysis by the Fisher–Student method.

EXPERIMENTAL RESULTS

As the writer showed previously [3] the proliferative activity of cells in both parts of the sebaceous gland fluctuates during the 24-h period, with a maximum at night or in the early morning and a minimum in the afternoon and evening. The mean diurnal value of MC for cells of the acinar part was 16.3‰ and for cells of the efferent duct 13.0‰ the mean diurnal value of ILN was 76.0 and 65.5‰ respectively.

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TABLE 1. Action of Hydrocortisone on Proliferative Activity of Epithelial Cells of Sebaceous Gland (M ± m)

Group of animals	Duration of action of hydrocortisone (in h)	Acinar part			Efferent ducts		
		ILN (in ‰)	number of grains per nucleus	MC (in ‰)	ILN (in ‰)	number of grains per nucleus	MC (in ‰)
Control	—	62,3±5,6	11,1±0,7	11,0±2,0	69,7±5,2	8,0±0,4	12,0±1,3
Experimental	4	38,8±5,5*	8,6±0,4*	11,5±4,0	42,0±4,9	6,0±0,5*	4,6±0,8
Control	—	55,0±6,0	10,2±0,8	11,8±1,5	45,0±5,0	9,6±0,5	8,3±1,0
Experimental	8	17,8±4,2‡	7,3±0,6*	5,3±1,5†	22,4±6,8*	7,2±0,8*	4,2±0,9*
Control	—	47,3±3,0	11,0±0,6	10,3±1,6	38,0±3,3	10,6±0,4	7,3±1,2
Experimental	12	65,4±6,9	9,0±0,6	4,0±1,1†	14,0±4,4†	7,2±0,6†	2,7±1,1*
Control	—	101,7±11,4	10,5±0,6	20,3±2,2	71,7±5,2	9,1±0,7	13,0±2,0
Experimental	16	135,2±33,1	12,1±0,7	21,3±3,4	58,3±13,0	10,3±1,2	6,9±1,6*
Control	—	95,7±4,8	9,9±0,3	20,0±2,4	65,0±5,4	7,6±0,6	20,3±1,9
Experimental	24	79,8±5,2	11,7±0,7	20,6±3,9	119,8±9,4‡	10,8±0,7†	35,5±9,2
Control	—	95,7±4,8	9,9±0,3	20,0±2,4	65,0±5,4	7,6±0,6	20,0±1,9
Experimental	48	144,7±12,2†	11,2±0,9	23,1±2,7	158,5±22,0	9,7±0,6	37,3±5,6*

Note. P shown relative to control: * < 0.05, † < 0.02; ‡ < 0.01.

As Table 1 shows, 4 h after administration of the hormones a statistically significant decrease in the number of DNA-synthesizing cells and in the number of grains per nucleus was observed; the effect continued for 8 h. The decrease in the number of cells synthesizing DNA was connected with delay in their transition from the G_1 period into the S period, and the decrease in the amount of thymidine-H^3 incorporated was connected with changes in the intensity of DNA synthesis, leading to an increase in duration of the S period. A decrease in the number of cells synthesizing DNA naturally leads to a subsequent decrease also in the number of mitotically dividing cells in the acinar part of the sebaceous gland. The results are in agreement with those of Laguchev [4, 5], who found an increase in duration of the various periods of the mitotic cycle under the influence of hydrocortisone, with a disturbance chiefly of the initiation of DNA synthesis at the end of the G_1 period [1, 10]. After 16 h the number of mitotically dividing cells regained its initial level.

Analysis of the table shows that after 4 h not only were the number of DNA-synthesizing cells and the quantity of thymidine-H^3 incorporated into them reduced, but the number of mitotically dividing cells also decreased. Hydrocortisone probably not only delays the transition of basal cells of the stratified squamous epithelium of the efferent ducts from the G_1 period, but it also has an inhibitory effect on the later stage of the mitotic cycle. Later a statistically significant increase in the number of DNA-synthesizing cells was observed, followed (after 48 h) by an increase in the number of mitoses. This increase was probably due to the transition of cells held up in the G_1 period by hydrocortisone earlier into the S period. The mechanism of this phenomenon requires further study in different tissues. Hydrocortisone had a stronger action on proliferative activity of the cells of the stratified squamous keratinizing epithelium of the efferent duct than on proliferative activity of the sebocytes. Transition of the cells from the G_1 into the S period and their passage through the later stages of the mitotic cycle were delayed. In addition, the decrease in the number of DNA-synthesizing and mitotically dividing cells in this part of the sebaceous gland lasted longer than in the acinar part and the increase in the number of dividing cells was observed sooner. At the same time the results confirm earlier observations [2] of differences in the sensitivity of the proliferative processes of some epidermal tissues to the action of hydrocortisone.

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