Activity of Glucose-6-phosphate 1-Dehydrogenase in Hair Follicles with Male-pattern Alopecia

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Note

Activity of glucose-6-phosphate 1-dehydrogenase (G6PDH) in human hair follicles was measured. A good relationship has been demonstrated between the activity and the ratio of the number of the anagen hairs to that of all the plucked hairs in the frontal-parietal region of the scalp with male-pattern alopecia. As the ratio becomes lower so that the advancing degree of alopecia is higher, the G6PDH activity becomes lower.

Key words: alopecia; glucose 6-phosphate 1-dehydrogenase; hair follicle; pentose phosphate pathway

It is thought that male sex hormones and genetic factors are closely related with the crisis of male-pattern alopecia. However, its mechanism has not been clear.1) Enzymes in hair follicles of animals and human beings have been studied from various aspects, such as male sex hormone metabolism,2) keratinization,3) and energy metabolism.4,5) In these studies, enzyme activities between resting (telogen) and growing (anagen) phases of the hair cycle, and those in hair follicles in the growth step of hairs have been examined. Although the histological changes occurring during the growing, regressing (catagen), and resting phases have been described in detail, the mechanistic basis underlying the cessation and reactivation of follicular growth has remained obscure.6,7) When the hair cycle of guinea-pig changes from the telogen to anagen phase, both ATP content and activity of glucose-6-phosphate 1-dehydrogenase (G6PDH, EC 1.1.1.49) in follicles increase quickly, followed by an increase in DNA content and the size of the follicles.8) The ATP content in the follicles of telogen phase increases by the addition of glyceraldehydes of odd-numbered fatty acids, especially pentadecanoic acid.9) These observations suggest that energy metabolism in the follicles might be increased during the transition from the telogen to anagen phase. In this paper, the G6PDH activity in human hair follicles plucked from the scalp is measured to investigate the relevance of the crisis of male-pattern alopecia to energy metabolism in the follicles.

The subjects were 25 volunteers (male, 20-49 years old) with male-pattern alopecia with various degrees. Hairs of the scalps were collected from the frontal-parietal region and the occipital-temporal region by plucking with a needle-carrier for surgical operations.5,6) Ten to twenty hairs were collected from the respective regions individually. Immediately after plucking hairs, they were grouped into anagen and telogen hairs by the previously described method10) using a 16-power loupe. The ratio of the anagen hairs to all the plucked hairs was measured in each of the regions. Hair samples were preserved at −25°C until use. The G6PDH activity was measured by the method described previously11,12) with some modification. NADPH produced in the reaction was detected by fluorescence.13,14) Hair samples collected were homogenized by 0.5 ml of 125 mM Tris-HCl buffer, pH 8.8 (buffer A). The reaction was started by adding the homogenate to 0.25 ml of buffer A containing 2.0 mM glucose-6-phosphate, 2.5 mM MgCl2, 0.5 mM EDTA, 0.3 mM NADP+, and 0.05% bovine serum albumin (BSA). After the incubation at 38°C for 60 min, the reaction was stopped by adding 0.25 ml of 80 mM NaOH. The resultant solution was incubated at 60°C for 15 min, followed by adding 0.5 ml of 12 M NaOH, and the solution was incubated at 60°C for 30 min. Thereafter, 4.0 ml of water was added to the solution, and fluorescence emission at 460 nm with an excitation at 360 nm was measured at 25°C. The enzyme activity producing one mole of NADPH per min was defined as one unit. Hair samples collected from scalps were homogenized by 3.0 ml of buffer A, followed by centrifugation at 3,000 × g for 15 min. The protein in the supernatant was analyzed by the Lowry method with BSA as the standard.

The amount of soluble protein in the hairs of the anagen phase was in the range of 2.3-4.4 μg/hair (the average value: 3.1 μg/hair). A clear relationship between the protein content in the hair follicles of anagen hairs and the advancing state of alopecia was not recognized. The protein content of the telogen hairs was 1.1-1.8 μg/hair (the average value: 1.3 μg/hair), significantly lower than that of the anagen hairs. The protein content of the telogen hairs was independent of the degree of alopecia. Thus, the G6PDH activity was evaluated as the amount of NADPH produced during the assay reaction for 1 min per hair. Relationship between the ratio of the anagen hairs to all the plucked hairs and the G6PDH activity of all the plucked hairs from the in

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individual subject was examined for the hairs collected from the frontal-parietal region and those from the occipital-temporal region. Concerning the hairs from the frontal-parietal region, the ratio varied greatly from 0.08 to 0.85 depending on the subjects (the average: 0.51), and the average G6PDH activity of the anagen hairs was $4.0 \times 10^{-11}$ units/hair. A clear tendency was observed between them (Fig. 1). With a decrease in the ratio of the anagen hairs, the activity decreased with the correlation coefficient, $r = 0.688$ ($p < 0.01$). The enzyme activity of the telogen hairs was $(0.3-1.2) \times 10^{-11}$ units/hair (the average: $0.6 \times 10^{-11}$ units/hair), suggesting that the activity in the telogen hairs was almost negligible in comparison with that in the anagen hairs. On the other hand, the average ratio of the anagen hairs to all the hairs collected from the occipital-temporal region ranged from 0.63 to 1.00 (the average: 0.90). The average enzyme activities in the anagen and telogen hairs were $6.9 \times 10^{-11}$ and $0.6 \times 10^{-11}$ units/hair, respectively. The correlation coefficient, $r$, between the anagen-hair ratio and the enzyme activity in the anagen hairs was 0.151 (Fig. 2), indicating that there is no clear relationship between the anagen-hair ratio and the activity.

In anagen hairs, hair matrix cells are dividing without interruption so as to cause the hairs to grow. Glucose, as an energy source of hair matrix cells, reaches cell membranes through blood, to be converted to phosphate derivatives. Part of glucose is preserved as glycogen in the outer root sheaths of hairs and the like, and most of the remaining glucose is metabolized through glycolysis, the pentose phosphate pathway, and the TCA cycle. G6PDH is a rate-limiting enzyme of the pentose phosphate pathway, and is related with biosynthesis of fatty acids, steroids, and nucleic acid. It is known that one of the main symptoms of male-pattern alopecia is a decrease in the ratio of the number of hairs in the anagen phase. The decrease is caused by the fact that the period of the anagen phase of a hair cycle is shortened with the advance of the symptom. Several patterns of hair loss in male-pattern alopecia are known. In all patterns, it starts from the frontal or parietal regions of the scalp and does not arise easily in the occipital or temporal regions. The average ratio of the number of the anagen hairs to all the plucked hairs was 51% in the frontal-parietal region and was 90% in the occipital-temporal region. This result may support the above-mentioned known fact. Concerning the G6PDH activity in the hair follicles in the frontal-parietal region, it showed a good relationship with the ratio of the number of the anagen hairs to that of all the plucked hairs. In other words, it was made sure that the G6PDH activity decreases when the ratio of the anagen hairs decreases so that the advancing degree of alopecia increases. The energy metabolism done by G6PDH in hair follicles of male-pattern alopecia may be related to the hair growth, and activation of the energy metabolism may be a new strategy to prevent and cure male-pattern alopecia. G6PDH could be a suitable marker for diagnosis of alopecia, and enzyme immunoassay of G6PDH might be applicable for this purpose with higher sensitivity and more convenience than the G6PDH activity assay used in this study.

References


