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Hair Cortisol Analysis - A Potential Biomarker in Research and Clinical **Applications**

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Introduction

Cortisol is the most common glucocorticoid in humans and has a wide spectrum of physiological effects throughout the human body including glucose, lipid and protein metabolism, body composition, immunosuppressive and anti-inflammatory actions. The experience of chronic stress and endocrine disorders, such as Cushing's syndrome and Addison's disease, are well-known to be associated with a range of negative effects of cortisol on health. The crucial neuroendocrine axis involved in mediating these effects is the hypothalamuspituitary-adrenal (HPA) axis leading to the secretion of the glucocorticoid.

To date, the majority of studies have investigated cortisol responses using samples of serum, saliva or urine. Both saliva and serum samples provide a measurement of the cortisol concentration at a single point in time. They can therefore be used to test short-term changes, but are subject to major physiological daily fluctuations, making the assessment of overall long-term systemic cortisol exposure difficult without multiple repeated measures. Hence, a single measurement cannot adequately reflect a long-term cortisol exposure over several weeks or months. To help overcome this challenge, most contemporary studies typically obtain multiple salivary samples from the time of waking until sleep, but this is experimentally complex. The compliance of individual participants with the sampling schedule may vary and it is logistically difficult to apply to larger populations. In addition, the act of obtaining a serum sample via venipuncture could by itself be a source of stress and falsely increase cortisol levels [1]. Another approach that has been used is 24 h urine collections to provide a measure of free cortisol concentrations, thus overcoming the issue of its diurnal rhythm [2]. However, the collection is labor intensive for participants, and it reflects cortisol level only up to 24 h.

Hair analysis has been used for decades as an accurate method to monitor exposure to exogenous compounds, with particular emphasis on detecting drugs of abuse [3]. It was the first reported in 2000 that ten corticosteroids including cortisol and cortisone in human hair were identified using high performance liquid chromatography-ionspray spectrometry [4]. As average hair growth rate is approximately

one centimeter per month with the most uniform growth rates in the posterior vertex region [5,6], a measurement of cortisol concentration in 1 cm of hair segment proximal to the scalp may reflect retrospective changes in cortisol concentration over previous month.

More recently there has been a growing interest in assessment of cortisol in hair which may be a retrospective biomarker for cortisol exposure and offers the possibility to show the long-term activity of the HPA axis. Patients with adrenal insufficiency (AI), in which the adrenal glands fail to produce sufficient corticosteroid hormones, require lifelong replacement therapy with exogenous glucocorticoids. Gow et al. [7] explored the measurement of hair cortisol as a biomarker of long-term systemic cortisol exposure in patients with AI treated with hydrocortisone (HC). They found the significant correlation between daily HC dose and hair cortisol content suggesting hair cortisol may become a useful monitoring tool for long-term cortisol exposure in patients treated with glucocorticoids. Hair cortisol assessment had provided a retrospective record of cortisol levels in Cushing's syndrome (CS) [8]. The severity of CS depends on the duration and extent of the exposure to excess glucocorticoids. In Thomson's study, hair cortisol had been measured and revealed that hair cortisol levels were significantly higher in patients with CS than in healthy control subjects and the levels decreased following successful therapy. Another study about CS had also demonstrated that hair cortisol timelines of patients with CS and cyclic CS corresponded with clinical course and suggested that hair cortisol analysis as a new diagnostic tool may contribute to early recognition of patients suffering from cyclic CS [9].

As a potential biomarker, hair cortisol is becoming more widely accepted as a measure in the assessment of chronic psychological stress and applied in many biopsychology studies. Several studies had demonstrated that hair cortisol concentrations were indeed elevated in subjects undergoing significant stress compared with matched controls. Human studies of hair cortisol and stress include individuals suffering from chronic pain [10], individuals who were unemployed for at least 12 months compared with those who had jobs [11], alcohol-dependent individuals undergoing withdrawal compared with abstinent alcoholics or control subjects [12],

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individuals consigned to shift work compared with day workers [13], endurance athletes who undergo severe physical stress [14]. For example, Steudte's study revealed that hair cortisol levels of participants with posttraumatic stress disorder (PTSD) were significantly higher than those of traumatized controls [15]. Their study also showed a positive association between hair cortisol levels and the number of lifetime traumatic events.

Measurement of hair cortisol offers a number of advantages. The most important one is that the approach provides a biomarker of integrated cortisol levels over periods of time (weeks to months) that is uninfluenced by the time of day when samples are collected. Therefore, it can assess dynamic systemic cortisol exposure and provides unique retrospective information on variation in cortisol. In addition, hair sampling is a noninvasive procedure which can be performed by non-health care workers at any time of the day. The collected samples can be stored at room temperature and sent by mail. Some limitations for hair cortisol analysis have to be considered since many factors could influence the results of the measurement. These may include hair growth rate for each individual, gender, age, hair color (cosmetic treatment), hair washing frequency, environmental exposure (UV) and others. Further studies are needed to address these issues and to further validate this measure as a biomarker for research and clinical applications.

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