Brief Communication

Effects of maternal bilateral adrenalectomy on skin development

Mehmet Kilinc, PhD, *Sennur Ketani*, PhD, *Mustafa Deniz*, PhD.

The adrenal gland is important in producing steroids, both corticosteroids and mineral corticoids. If the adrenal gland does not produce these hormones, the loss leads to devastating effects in nearly every organ system, and eventually death. Patients may first experience weight loss, muscle weakness, fatigue, low blood pressure, and sometimes darkening of the skin. Some critical functions of the steroids include maintenance of blood pressure, regulation of insulin, and regulation of the breakdown of proteins, carbohydrates, and fats. Chronically elevated glucocorticoids, either because of increased endogenous secretion (such as in psychogenic amenorrhea, anorexia nervosa, Cushing's syndrome and marathon runners) or exogenous administration, have adverse effects on the reproductive system.[1] In this study, our purpose is to investigate the effects of adrenalectomy (maternal adrenal hormones deficiency) on the skin of puppy rats.

Ten fertile Wistar albino female rats were obtained from the University of Dicle, Medical Science and Application Center (DUSAM). Ten adult Wistar albino female rats were maintained and fed with an standard pellet food ad libitum during the study. All animals received human care according to the criteria outlined in the 'Guide for the Care and Use of Laboratory Animals'' prepared by the National Academy of Sciences and published by the National Institutes of Health. The experiments were approved by the Committee on Experimental Animal Ethics of University of Dicle. The ambient temperature (22°C) and relative humidity (45%) were maintained throughout the experiments. The rats were divided randomly into 2 groups: Group I: the animals served as control (n=5). Group II: under ketamine HCl (50 mg/kg) and xylazine (10 mg/kg) anesthesia, the bilateral adrenal glands were removed (ADX) (n=5). The rat were given 20 g/day saline and 1.1% calcium drink water ad libitum after surgery to prevent dehydration - Addison crisis.

The rats were allowed 21 days of recovery, following which they were fertilized. The control and experimental group produced 65 puppy rats. Twenty-four, 7-day-old puppy rats were selected randomly, and sacrificed with ketamine HCl.

The abdominal skins were pinned out on dental wax to their length and placed immediately in a 10% phosphate-buffered formalin solution at pH 7.4 for 4 hours. Tissue pieces were chosen at random, and washed with tap water and dehydrated in graded ethanol series. Sample tissues were embedded in paraffin. Sections were cut into 4-5 µm and stained with hematoxylin and eosin, and Masson Tipple. The specimens were examined and photographed using light microscope (Nikon-Ellipse 400).

In group I (control), we observed that the epidermal structure of the puppy rats were normal in appearance. It was seen that the epidermal layer and keratinization layer was of normal appearance and stratum basal cells were mitotic figures. We showed that the stratum corneum of epidermis were normally keratinization, normal epidermis and dermis together with dermal adnexa. The stratum reticulare of dermis showed regular collagen fibers.

In group II, (adrenalectomy-ADX) when compared with the control groups, the changes occurred in the epidermis and dermis. At histological evaluation, the removal of maternal adrenal glands greatly decreased the keratinization and this was accompanied by epidermis and dermal atrophy. Atrophic sebaceous gland and atrophic follicle pili were also seen. Loss of stratum reticulare was observed, with the absence of this layer. Stratum reticulare of dermis showed irregular collagen fibers and absence of the subcutis layer **(Figure 1).**

Whole tissue analysis by atomic absorption spectrophotometer indicated that zinc and copper levels were affected after adrenalectomy and hydrocortisone treatment, leading to pathological changes in the testis.[2] Bilateral adrenalectomy has separate effects on somatic, neural and endocrine growth and these distinct impacts may reflect the varied distribution of glucocorticoid receptors in organs and tissues. In the central nervous system, the cerebral cortex, cerebellum and hippocampus are known to express high numbers of corticoid receptors.[3] In postnatal life, administration of these hormones has a 2-edge impact on the adult brain, causing both neuroprotection and neurodestruction.[3] High-dose corticosteroids are known to cause specific malformations of cleft palate and wavy ribs during fetal development in rats. Although reports have indicated that adrenocortical hormones have a range of effects on different body systems. Our study revealed microscopic evidence of underdevelopment skin due to ADX.

Glucocorticoids are proven factors in the control of mitosis and maturation in the prenatal rat cerebral cortex and hippocampus.[4,5] Our observations on skin development in the ADX group concur with the findings of Trejo et al.[4]

Glucocorticoid hormones and glucocorticoid analogues possess marked anti-inflammatory and antiproliferative effects, and these effects have been correlated with their potency in the inhibition of tumor promotion. It has been show that

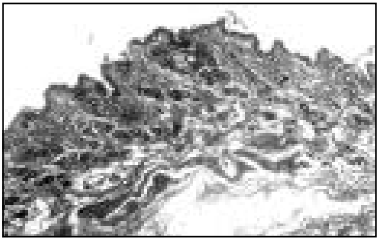

Figure 1 - Histological appearance of exposed maternal adrenalectomy. Loss of stratum reticular was observed with decreasing collagen fiber. e - epidermis, ed - dermal adnexa, Sc - subcutis, follicle piles (arrow). (Mason triple, original magnification x 10).

glucocorticoid hormones can suppress the growth of certain cancers and inhibit hyperplasia and neoplasia in a number of systems including several types of leukemia and lymphoma.[6] The adrenal gland has been implicated as a mediator of the beneficial effects of dietary energy restriction in a number of studies.[7] Adrenalectomy stimulated carcinogen-induced mammary tumor growth and the tumor-inhibitory effect of food restriction in skin carcinogenesis models were reversed by ADX.[7]

Our findings clearly show that ADX causes negative effects in the epidermis and thickening of each dermal layer, as well as the developing skin as a whole, in the puppy rat.

Received 8th February 2005. Accepted for publication in final form 5th March 2005.

From the Department of Anatomy (Kilinc), Medical Veterinary, Department of Biology (Ketani), Education Faculty University of Dicle, Diyarbakir and the Department of Anatomy (Deniz), Medical Faculty, University of Harran, Sanliurfa, Turkey. Address correspondence and reprint requests to Dr. Mehmet Kilinc, Department of Anatomy, Medical Veterinary Faculty, University of Dicle, Diyarbakır 21280, Turkey. Tel. +90 (412) 2488020. Fax. +90 (412) 2488021. E-mail: mkilinc@dicle.edu.tr

References

1. McGivern RF, Redei E. Adrenalectomy reverses stress-induced suppression of luteinizing hormone secretion in long-term ovariectomized rats. ***Physiol Behav*** 1994; 55: 1147-1150.
2. Nair N, Bedwal RS, Mathur RS. Effect of adrenalectomy and adrenalectomy + hydrocortisone treatment on histopathological, biochemical and zinc and copper profiles in rat testes. ***Indian J Exp Biol*** 1995; 33: 655-663.
3. Trejo JL, Rua C, Cuchillo I, Machin C. Calbindin –D28k- and astrological protein-immunoreactivities and ultrastructural differentiation in the prenatal rat cerebral cortex and hippocampus are affected by maternal adrenalectomy. ***Developmental Brain Research*** 1998; 108: 161-177.
4. Trejo JL, Machin C, Arahuetes RM, Rua C. Influence of maternal adrenalectomy and glucocorticoid administration on the development of rat cerebral cortex. ***Anat Embryol*** (Berl) 1995; 192: 89-99.
5. Rua C, Trejo JL, Machin C, Arahuates RM. Effects of maternal adrenalectomy and glucocorticoid administration on the development of rat hippocampus. ***J Hirnforsch*** 1995; 36: 473-483.
6. Smets LA, Salomons G, Van Den Berg J. Glucocorticoid induced apoptosis in leukemia. ***Adv Exp Med Biol*** 1999; 457: 607-614.
7. Pashko LL, Schwartz AG. Reversal of food restriction-induced inhibition of mouse skin tumor promotion by adrenalectomy. ***Carcinogenesis*** 1992; 13: 1925-1928.

Treatment of vitiligo with topical 15% lactic acid solution in combination with ultra violet-A

Khalifa E. Sharquie, *MBChB, PhD,*
Media S. Abdulla, *MBChB.*

There are many topical therapies reported for treatment of vitiligo such as topical steroids, phototherapy, psoralen ultraviolet A (PUVA), topical iodine tincture 5%,[1] and topical calcipotriol, each has advantages and side effects, none are universally effective. Most recently, topical 15% lactic acid solution has been used successfully in treatment of vitiligo.[1] The present work has been arranged to evaluate topical 15% lactic acid solution with or without ultraviolet A (UVA) exposure.

This study included 46 patients with vitiligo. Seventeen patients completed the study, 14 were females and 3 were males. Their ages ranged between 3-30 years with a mean ± SD of 17.29 ± 6.64 years. All patients included in this study had localized vitiligo in the non exposed area with at least 4 patches. The study was carried out in the out patient Department of Dermatology and Venereology in Baghdad Teaching Hospital, Baghdad, Iraq, during the period between November 2001 to March 2003. The size of patches ranged between 0.25-46 cm^2 with a mean ± SD of 6.48 ± 10.52 cm^2. The out line of each patches was drawn on transparent paper, and the surface area measured with graph paper before treatment, and every 2 months for 6 months. The patches were divided to 4 groups randomly according to the type of treatment: Group I: was treated with topical 15% lactic acid solution. Group II: was treated with UVA. Group III: was treated with combination of 15% lactic acid solution and UVA. Group IV: control (treated by tap water). In each patient, some of the patches were treated by lactic acid and some