URINARY 17-KETOSTEROID IN VITILIGO

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Summary

Estimation of urinary 17-ketosteroid was carried out in 42 cases of vitiligo. The cases were divided into 3 clinical varieties; Active, Quiescent and Improving. No significant difference was found in the value of 17 ketosteroid among the 3 varieties. A significantly low 17 ketosteroid value in patients with vitiligo was observed. Since vitiligo is considered to be an auto immune derangement, a cross linked auto-immune reaction between melanocytes and adrenal tissue has been suggested.

Introduction

Vitiligo is a common problem. Its course is enigmatic and aetiology not fully established. Behl et al[1] has investigated and discussed the possible role of copper, nutrition and metabolic factors in the etiology of this disease.

The present investigation deals with hormonal studies in 42 cases of vitiligo. Several workers have claimed the possible role of adrenal cortical hormones in vitiligo[2,3]. Determination of urinary 17-Ketosteroid (KS) serves as an easy parameter for roughly assessing the activity of adrenal cortex. Because of suggestion of auto-immune mechanism and its probable effect on adrenal cortex and reported improvement of vitiligo lesions with corticosteroid ointment[4], the present work was designed to evaluate the possible influence of adrenals on vitiligo.

Material and Methods

42 cases of vitiligo were included in this series. 4 healthy adults served as controls. 24 hour specimen of urine was collected from each patient, in 10 c.c. of conc. hydrochloric acid. The volume of urine was recorded in litres and subjected to estimation of 17-ketosteroid by colorimetric method as detailed in Signa Technical Bulletin 1971. The cases were divided into three clinical varieties; active, quiescent and improving. 'Active' vitiligo is one which has a definite history of development of new lesions, increase in size of the vitiligo patch/patches and a blurred or ill-defined margin. The 'Quiescent' variety has a hyperpigmented border and history of being stationary. The 'Improving' one is characterised by a decreasing size of the lesion and signs of repigmentation. Urinary 17-ketosteroids are excreted as water soluble glucuronides and sulphates. In the test, these derivatives are first hydrolyzed with acid. The liberated steroids are extracted with ethyl ether and extraneous chromogens and estrogenic substances removed from the ether extract with an alkali wash. Final quantitation is based upon the Zimmerman reaction.

Observations

Table one shows the normal values of 17 ketosteroid in different sexes.

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TABLE 1

Normal values of urinary 17 KS (in mg/24 hrs)

Adult Male	10–25 mg
Adult Female	7–20 mg

Eight children were in the study; four from each sex (Table 2). The mean values of 17 KS in children in our series are higher than normal, which may have been due to inclusion of 3 children above the age of 10 years i. e. those approaching puberty.

TABLE 2

Urinary 17 KS (Below 13 years of age)

Sex	No. of cases	Minimum (in mg/24 hours)	Maximum	Mean
Male child	4	4.4	6.0	5.2
Female child	4	3.0	6.4	3.9

34 adult cases were above the age of 13 years. Among them 21 were males and 13 females (Table 3)

TABLE 3

Urinary 17 K S (above 13 years of age)

Sex	No. of cases	Minimum in mg/24 hours)	Maximum	Mean
Male Adult	21	3.0	9.6	5.6
Female Adult	13	4.2	8.8	6.2

Among the 34 cases, 5 (one male and 4 female) had values within normal limits. 29 cases showed a reduced excretion of 17–Ketosteroids.

The cases were further divided into active, quiescent and improving ones to find out if the 17 ketosteroids urinary output bears any relation with these clinical varieties (Table 4). Among the 42 cases studied, 5 (4 active and 1 improving) had normal values. From the above observation, we are unable to establish any correlation between clinical varieties of vitiligo and values of 17–ketosteroids. The only relevant finding is an overall decrease in the urinary 17–ketosteroid excretion.

TABLE 4

Urinary 17 - KS in clinical varieties of Vitiligo

Clinical Varieties	Total No. of cases	Minimum (in mg/24 hours)	Maximum	Mean
Active	20	3.6	8.8	5.8
Quiescent	10	3.1	5.4	4.9
Improving	12	3.0	8.4	5.7

Of the 4 normal adult controls (3 male and 1 female), the males showed K. S. value ranging between 12 and 14.8 mg/24 hours and the female 7.4 mg/24 hrs.

Discussion

The role of hormones in the etiology of vitiligo has been a subject of several studies in the past many decades. The role of pituitary M.S.H. in the dispersion of melanin granules[5], hyperpigmentation of areola and the occurrence of chloasma under the influence of oestrogen and progesterone[6], probable direct inhibition of melanogenesis by adrenocortical hormones[7], are the several evidences of relationship between hormones and melanin. Our attempt is to study the association, if any, of adrenal cortex with vitiligo. It is an attempt to roughly assess the activity of adrenal cortex in patients with vitiligo by the estimation of urinary 17–ketosteroid and explain the possible inter-relationship.

Addison in his first description of eleven or possibly twelve patients with adrenocortical insufficiency, noted that two patients in addition to hyperpigmentation, had vitiligo. Since that time many physicians have cited the simultaneous occurrence of hyperpigmentation and spreading vitiligo in Addison's disease[8]. The problem is to explain this association. In Addison's disease there is decreased urinary 17–ketosteroid excretion and increase of skin pigmentation[9]. Hall et al[10] by reflectance spectrophotometry studies, concluded that cortisone reverses toward normal the pigmentary changes observed in Addison's disease,

but ACTH increases melanin content of the skin in Addison's disease. That adrenal produces depression of melanogenesis has been suggested by various workers. Lerner[2] suggested that adrenal has two ways of action on melanogenesis namely direct and indirect. In an indirect way an increase in corticosteroid may depress liberation of M.S.H. and hence cause decreased pigmentation. Stress factors lead to more adrenal output specially of adrenal and not adrenaline which act directly through a peripheral blocking of the action of M.S.H. on melanocytes causing depigmentation. Administration of cortisone or hydrocortisone prevents darkening of the skin of bilaterally adrenalectomized human subjects or decreases darkening of skin colour in patients with adreno-cortical deficiency[11]. Melanin deposition in hair is also stimulated by adrenalectomy under conditions that ordinarily inhibit its production[12]. Whitaker and Baker[13] observed inhibition of hair growth by certain adrenal cortical preparations applied percutaneously. Thus, adrenal perhaps exerts an inhibitory influence on melanogenesis. Addisonian hyperpigmentation could be then explained on the basis of a lack of adrenal hormone and indirectly as a result of increased output of M.S.H. by pituitary gland[2].

Aggarwal et al[3] found a high value of urinary 17 ketosteroid in patients with vitiligo and suggested that adrenal hyperactivity producing depression of melanogenesis as suggested by Lerner[2] might be the possible explanation. But this does not explain the association of vitiligo with Addison's disease.

It has been suggested that vitiligo may be expected in mature onset diabetes mellitus[14]. Increased incidence of vitiligo has been reported in patients with adrenocortical insufficiency, hyperthyroidism, alopecia areata, pernicious anaemia, melanoma, scleroderma and morphea[8]. All the diseases mentioned above have a probable autoimmune etiology. That autoimmunity might be the underlying etiology in vitiligo has been suggested in recent literature[15]. Organ specific antibodies to adrenal tissue have been found in serum of patients with vitiligo[16]. Serial section studies in 48 cases of vitiligo have suggested the histological evidence of autoimmune factor in the aetiology of vitiligo (under publication). Thus we presume that vitiligo is perhaps an autoimmune disorder. If vitiligo is considered as an autoimmune derangement, could it be that the autoimmune reaction against melanocytes might establish a cross linked reaction with the adrenal tissue, thereby producing a minimal or subtotal depression of adrenal gland and hence the low 17-ketosteroid values ? In that case antigenic similarity between the components of melanocytes and adrenal tissue requires confirmation.

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