

INTERMITTENT THERAPY WITH CORTICOTROPHIN IN VITILIGO

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Summary

Fundamental factors influencing formation and subsequent behaviour of melanin are enumerated. Three most favoured hypotheses regarding etiology of vitiligo are :-

1. vitiligo is an autoimmune disorder.
2. vitiligo is a neurogenic disorder.
3. vitiligo is caused as the result of self destruction of melanocytes.

Steroids have proved very effective in acute phase of autoimmune diseases and have anti-inflammatory action. On the assumption that these factors might be operative in some vitiligo cases, ACTH therapy was instituted in 27 cases. Effective of treatment and untoward reactions have been discussed as also some case reports. It is concluded that the treatment is effective and duration of therapy considerably reduced.

Loss of normal colour due to absence of melanin pigment is the main visible change encountered in the vitiliginous skin. The cycle of melanin production is apparently in a state of physiochemical equilibrium capable of being altered by either local or systemic changes. However identification of precise nature and location of the various factors in the cycle resulting in manifest disease are difficult to locate, because faults at different stages can result in the same visible effect and different agents may

interfere with the cycle at the same point. Thus unsettled functional, structural and metabolic defects in the melanocyte unit result in defective melanin formation, leading to manifest vitiliginous patches.

Fundamental factors influencing formation and subsequent behaviour of melanin pigment are total body mechanisms. Many factors, e.g. humoral, inflammatory, nutritional, enzymatic, genetic, infectious, trophoneurotic, immunological etc. have been considered to play some etiological roles in these mechanisms. A genetic predisposition is well recognized. Only some vitiligo patients give a family history of the disease. (35% Fitzpatrick¹ 38%, Lerner²). There are three favoured hypotheses regarding the pathogenesis of vitiligo :-

(1) It is an autoimmune disorder resulting from formation of an

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antimelanocyte antibody³. Vitiligo is associated with diseases believed to be of autoimmune origin⁴. Increased incidence of autoantibodies to thyroid, gastric parietal cells and adrenal tissue have been demonstrated by Brostaff, Bur., Feiwel⁵.

(2) A neurogenic factor is involved. There is some evidence to suggest that the loss of pigment could be attributed to the failure of neural or neurochemical control of melanocytes, resulting from damage to nerve fibres⁶.

(3) Lerner⁷ has proposed a hypothesis that the melanocytes destroy themselves by formation and accumulation of toxic melanin precursors.

It is likely that these etiologic factors may be operative at least in some of the cases where no hereditary background can be traced. It was considered worthwhile to study the effects of corticotrophin (ACTH) in such cases because of the beneficial effects in acute phases of autoimmune diseases on the basis of its antiinflammatory action.

Hormone are important regulators of skin pigmentation. ACTH increases formation of melanin pigment. It stimulates the growth of the adrenal gland and the production and release of hormonal steroids by adrenal cortex. It also increases blood flow through the gland to some extent. In addition, corticotrophin has a melanocyte stimulating activity. There are few reports on clinical use of ACTH in dermatology⁸. In the present study, ACTH was preferred to oral steroids, because some of the side effects are less severe with ACTH⁹ & ¹⁰ and the problem of withdrawal crisis can be avoided. Corticotrophin therapy rather than oral corticoids was preferred in children since the latter has the undesirable effect of growth suppression.

As against these advantages are some factors which restrict its use. One such factor is the development of antibodies to specific portion of the corticotrophin molecule¹¹. Sensitization reactions varying in severity from mild fever to anaphylaxis are possible. Synthetic corticotrophin is preferable, to corticotrophin of animal origin which is more antigenic in man. Since the synthetic formulation was not available in this country, the natural product had to be used. Suppression of the hypothalamus-pituitary axis can occur with ACTH. Intermittent therapy can obviate some of these side effects. Long acting formulation was used because the effect of a single injection of ACTH is short lived, lasting for about 90 minutes only¹².

Material and Methods

This study reports clinical results of treatment of vitiligo with parenteral long acting corticotrophin. Patients attending dermatology outpatients department, K. E. M. Hospital, Rasta Peth, Poona, and a private clinic were studied. No attempt was made at any special pattern of selection; they were picked up as they presented for treatment. All of them have been treated as ambulatory cases. Their histories were recorded and routine clinical examinations were carried out. A note of their complexion and reaction to exposure to the sun was made. Stools were examined for cysts, ova, etc. Urine was examined for sugar, albumin, bile salts and bile pigments. Microscopic examination of urine was also done. Blood was examined for colour index; R. B. C., W. B. C. and differential counts were done. Blood was submitted to serological test for syphilis. Regular periodic check up during the course of treatment was carried out with particular reference to signs and symptoms of diabetes, peptic ulcer, psychosis etc. Any abnormality detected

in the light of laboratory reports was adequately treated.

Twenty seven patients who were otherwise in normal health have been studied. None of them had diabetes. Their ages ranged from 10 to 32 years. Sixteen patients were males and eleven females. Duration of disease varied from 2 to 12 years.

The patients were categorised into two groups :-

(1) 16 cases were treated at the clinic conventionally with psoralens and other adjunctive drugs like anthelmintics, heamatinics, etc., but did not give satisfactory results. These patients were therefore given corticotrophin treatment.

(2) Encouraged by the results of corticotrophin treatment in the first group, some patients were treated with corticotrophin right from the day they presented at the clinic for treatment. Before visit to our clinic some of them had received some sort of treatment with unsatisfactory results. However, none of them had received any form of treatment for vitiligo for at least 4 months prior to this trial.

Long acting ACTH* was administered intramuscularly twice a week in doses of 25 to 40 I. U. depending on the age of the patient. Ten to twelve such injections were given followed by a break of 2 to 4 weeks. Such courses were repeated as required; the maximum given being 4 courses.

Patients treated with conventional treatment (psoralens etc.), when transferred to corticotrophic (ACTH) regime reported quicker and better response. Mostly the pigmentation was follicular but in some cases it was

* Action Prolongatum. Frederiksberg Chemical Laboratories Limited, Copenhagen.

† In this country (India) the sunshine is present for 9 months of the year, almost throughout the day time.

effected by encroachment of pigment from the margin. In some cases signs of repigmentation manifested in three weeks time. On the whole it was felt that the duration of treatment was considerably shortened and that many resistant patches reacted favourably. However, it must be made clear that some of the patches on the shins, dorsa of fingers, feet etc., took long time to repigment while some others proved resistant. Lesions on the parts exposed to the sun† reacted more quickly and favourably compared with covered parts (Fig. 7). No special regime of exposure to the sun was advised or followed by the patients. None of the patients were given artificial ultra violet exposures. It was noted that patches on the face pigmented quickly and deeply. Whether this is due to natural exposure of the face to sunlight, peculiarity of its nerve distribution or the density, its melanocyte population is difficult to say at this stage. Response to treatment was better in dark skinned subjects. In each case the results were evaluated at the end of six months. Pigment developed up to 80% in 16 cases; 50% in 6 cases; 20% or less in 4 cases. One case did not react at all to the treatment. In general the results of the treatment have been encouraging.

Side Effects

About 10% patients developed moon facies. One female patient developed downy hair on her face. One patient developed acne. Two patients complained of aggravation of existing acne lesions. In some fair patients generalised melanoderma was easily noticeable. Even during the course of treatment or during a break period, a few depigmented lesions in the form of specks appeared, affecting the moral of the patients.

Representative Case Reports

Case 1. A 19 year old married female had wide spread vitiliginous lesions



Fig. 1 Case No. 1 Before treatment



Fig. 2 Case No. 1 After treatment

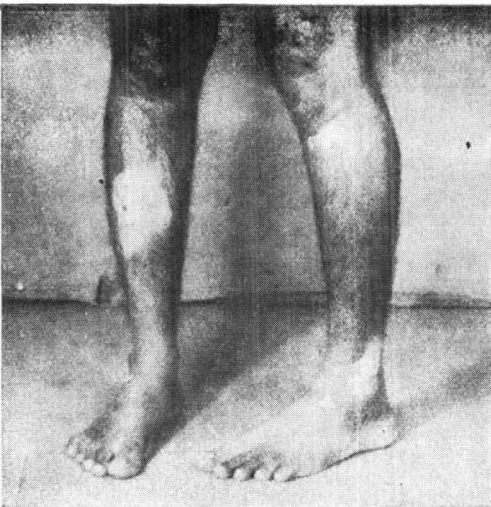


Fig. 3 Case No. 2 Before treatment



Fig. 4 Case No. 2 After treatment



Fig. 5 Case No. 2
Before treatment

over the body, face, both sides of waist and between breasts. The patches started appearing at the age of 14 years. She was put on ACTH treatment. Within 16 weeks there was complete repigmentation of the face lesions, 70% repigmentation on the waist and about 50% repigmentation on the chest wall.

Case 2. (Fig. 3 & 4; 5 & 6) An unmarried male aged 25 years presented with depigmented patches on both legs and forearms. These patches had developed about four years earlier. Patient had unsuccessfully undergone some treatment. He had wheat complexion. He received three courses of ACTH injections. There was no sign of repigmentation after two courses. Four weeks after the third course his patches started repigmenting rapidly.

Case 3. (Fig. 7) A housewife aged 48 started developing depigmented patches all over the body and face. According to her a large number of patches started appearing after enteric fever in 1974. She had three courses of ACTH. Patches on the face started showing signs of repigmentation about 6 weeks after the initiation of the ACTH treatment. She wears saree in Indian

style exposing the right arm while the left arm remains covered by saree. The relatively more exposed right arm became better pigmented than the left.

Case 4. (Fig. 8 & 9) A girl of 16 years presented with widely distributed patches in the inguinal and gluteal regions, both shins and back of the left elbow. The lesions had first appeared at the age of 9 years. She started to repigment after three courses of ACTH.

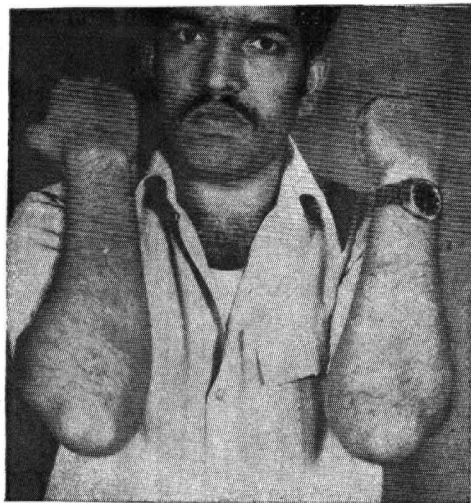


Fig. 6 Case No. 2 After treatment



Fig. 7 Case No. 3 Better pigmentation of the exposed forearm than the covered forearm

Case 5. (Fig. 10) A young male of 19 years of very dark complexion, otherwise in good health had depigmented lips, vitiliginous patches on dorsa of both hands and front of both legs. These patches were noticed first after a traumatic injury to his right thigh but they had continued to spread. No other person in the family had vitiligo. He had four courses of ACTH injections without any effect.

Concluding Remarks

Cases in group one had failed to react satisfactorily to psoralen treatment. On administration of ACTH there was good response. Cases in group two also reacted favourably.

Psoralen therapy of vitiligo is an important mile stone in the history of treatment of vitiligo. However psoralen treatment does not give satis-

factory results in every case. Therefore a search for improvement in therapy has continued. Farah, Kurban Chaglasian¹³ reported better results with psoralen therapy by addition of oral Triamcinolone. Kandil¹⁴, reported favourable results with intradermal injections of triamcinolone acetone. Koopmans-Van Dorp et al¹⁵, had used betamethasone-17 valerate in dimethyl sulfoxide cream base with good results. Since trophineurotic and autoimmune factors are considered possible etiologic factors in vitiligo and since steroids & corticotrophin are known to influence these two factors and as spontaneous cure in vitiligo is uncommon, it is surmised that ACTH therapy has promoted the process of pigment formation in the two groups.

Efficacy of a therapeutic agent is doubtful in absence of studies on control series. However planning such a study is a vexing problem in vitiligo, because so many factors like location, duration, age, family history etc. influence the prognosis of this malady. This preliminary work is reported with the hope that it will stimulate similar

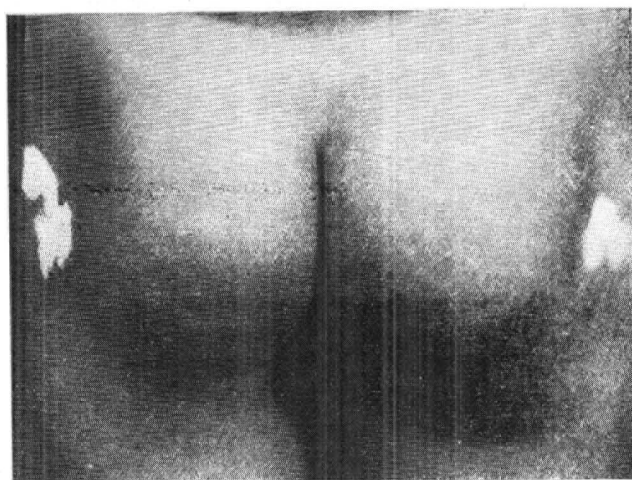


Fig. 8 Case No. 4 Before treatment

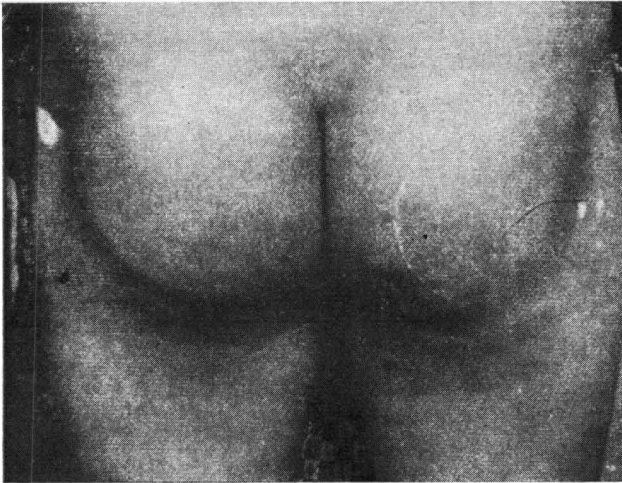


Fig. 9 Case No. 4
After treatment

studies at other centres, enabling a fair evaluation of the therapy by accumulation of larger data.

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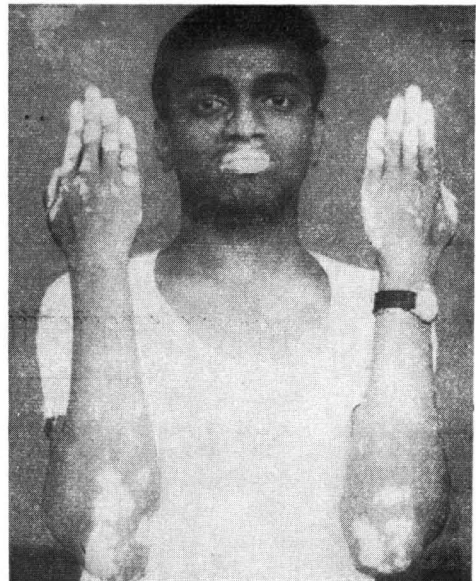


Fig. 10 Case No. 5 No effect of ACTH treatment

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