Acta Dermatovener (Stockholm) 50: 479–480, 1970

AN ANTIANDROGEN DELTA 1 CHLORMADINONE ACETATE IN ACNE: LACK OF EFFECT TOPICALLY

Robert M. Adams and Kenneth H. Burdick

From the Department of Dermatology, Palo Alto Medical Clinic and the Syntex Research Center, Palo Alto, Calif., USA

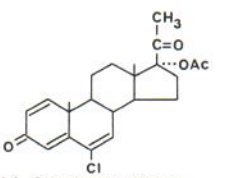
Abstract. Twenty patients with acne were treated topically with creams containing either 0.2% or 5% delta 1 chlormadinone acetate for 7 weeks. These creams were applied b.i.d. to half the face and placebo cream to the other side. No effect on the acne was noted and surface lipids were unchanged.

In recent years many new synthetic steroid hormones have been produced; seemingly minor modifications of their chemical structures have resulted in profound alterations in their biological assays (8). The synthetic molecules which block the effect of normal androgens have been of particular interest to the dermatologist. Although changes in hair growth and sebum levels have been observed following systemic administration of these so-called antiandrogens (4, 6, 7, 9), other hormonal effects preclude their systemic use for treatment of minor diseases (2, 4). Nevertheless, antiandrogens could be very useful therapeutic agents if topical application produced an effective level of the hormone in target organs in the skin, without at the same time resulting in significant systemic absorption.

In one study, Cunliffe et al. (3) using cyproterone acetate in topical DMSO were unable to show an effect on either acne or sebum levels. Large oral doses of chlormadinone acetate were reported by Strauss and Pochi to lower sebum in adult males (7). However, they were unable to demonstrate significant alteration of sebum levels by topically applied 1% chlormadinone acetate cream or 5% delta 1 chlormadinone acetate cream (7). The latter compound (Fig. 1) is a potent antiandrogen (8) which has shown some topical activity on the sebaceous glands of the hamster costovertebral spot (1).

Since Strauss and Pochi's negative studies with delta 1 chlormadinone acetate were done on normal males, it seemed advisable to use this compound in the treatment of acne. Twenty college students with acne were selected (9 males and 11 females).

Two preparations, in concentrations of 0.2% and 5%, were incorporated into a fatty alcohol-propylene glycol base and applied twice daily over a 7 week period to one side of the face. The other side received the base alone. The tubes containing medication and placebo were coded, thus preventing patient and observers from knowing which side received the active medication or the concentration employed. For each application $^1/_4''$ of preparation was extruded from the tubes, representing a topical dose of approximately 0.2 mg and 5 mg respectively. No other therapy was permitted. The patient's observations were recorded, and lesion counts and photography were done weekly over the 7 week period of the study. Surface lipids were measured by the method of Jones, Spencer & Sanches (5) at weekly intervals. Laboratory profiles, consisting of a CBC, PBI, BUN, SGOT, LDH, alkaline phosphatase, cholesterol, bilirubin, protein, albumin, globulin,



Δ1 CHLORMADINONE ACETATE

6 chloro-17 α hydroxypregna-1,4,6 triene-3,20-dione acetate

Fig. 1. Delta 1 chlormadinone acetate.

total lipids, creatinine, glucose and uric acid were done before, during, and at the end of the treatment period.

During the treatment period, none of the patients noted a significant change in their acne, or a consistent difference between the sides of their faces. We agreed with the students and based our opinion on lesion counts and photography. In addition, we were unable to demonstrate any significant change in the surface lipid levels. No changes in laboratory values were noted. Two women using the higher concentrations stated they experienced mild irregularity in their menstrual pattern while on treatment, and it is possible, though unlikely, that systemic absorption may have caused this complaint.

REFERENCES

1. Burdick, K. H. & Hill, R.: Brit J Derm. In press.
2. Caplan, Richard M.: Gynecomastia from a non-estrogenic antiandrogen. J Endocr *27:* 1348, September 1967.
3. Cunliffe, W. J., Shuster, S. & Smith, J. C.: The effect of topical cyproterone acetate on sebum secretion in patients with acne. Brit J Derm *81:* 200, 1968.
4. Hammerstein, J. & Cupceancu, B.: Behandlung des Hirsutismus mit Cyproteronacetat. Deutsch Med Wschr, 18 April 1969.
5. Jones, K. K., Spencer, M. C. & Sanches, A.: The estimation of the rate of sebum secretion in man. J Invest Derm *17:* 213, 1951.
6. Pria, S. D., Greenblatt, R. B. & Mahesh, V. B.: An antiandrogen in acne and idiopathic hirsutism. J Invest Derm *52* (4): 348, 1969.
7. Strauss, J. S. & Pochi, P. E.: The use of human sebaceous glands for assaying androgens and antiandrogens. Brit J Derm. In press.
8. Wiechert, R., von, Steinbeck, H., Elger, W. & Neumann, F.: Wirkungen und Struktur neuer antiandrogener Steroide. Arzneimittel *17:* 1103, September 1967.
9. Winkler, K.: The value of anti-androgens in dermatology. Ann Derm Syph *95:* 147, 1968.

Received May 8, 1970

Robert M. Adams, M.D.
Palo Alto Medical Clinic
300 Homer Avenue
Palo Alto, California 94301
USA