# A CLINICAL EXPERIENCE WITH R 2040-CREME*

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## INTRODUCTION

The local use of corticosteroids in the treatment of dermatological complaints has greatly increased in recent years. For many less extensive skin diseases the external application of corticosteroids in the form of lotions and ointments is adequate. Moreover the side effects are absent in local application as the amounts of preparation absorbed are very small. The main action of topical corticosteroid is anti-inflammatory. The relief of inflammation is not always accompanied by relief of pruritus. The antiphlogestic action of these preparations results in a decrease of immunity to infection by reducing migration of blood elements to the site of injury, hence increased susceptibility to bacterial, fungal and viral infection. To prevent bacterial infection and produce anti-pruritic effect various bacteriostatic and anti-pruritic agents have been employed. Eurax-hydrocortisone combination is another such attempt in this direction. Disadvantages of antibiotics is the development of sensitisation. In this paper an attempt has been made to study therapeutic efficacy of eurax-hydrocortisone combination in various types of pruritic dermatoses.

## BRIEF REVIEW OF LITERATURE

Goldman et al[1] (1952) and Sulzberger and Witten[2] (1952) were the first to show the efficacy of topically applied corticosteroids in the various dermatoses. The topical costicosteroids were found to be useful in dermatological conditions associated with local irritation, eczematization, allergic reaction and localised oedema etc. These steroids are of much less value in dermatological conditions associated with lichenification and trophic changes. In 1946, Domenjoz, R[3] used it first as an acaricidal agent. The same year, Burckhardt and Rymarowicz[4] evaluated the clinical usefulness of Crotonyl-N-ethyl-O-toluidine in scabies. Their results showed that it was not only excellent as an acaricidal but also possessed considerable anti-bacterial action and did not irritate eczematized scabietic lesions. It possessed marked anti-pruritic effect.

Lenggenhager, R.[5] (1947) showed that it possessed excellent acaricidal properties. Subsequent studies by Von Roten[6] (1947), Dorner[7] (1949), Couperas, M.[8] (1949), Patterson[9] (1950), Johnson and Bringe[10] (1951), Mehta, T. K.[11] (1954), Majumdar, T. D.[12] (1956), Joshi and Mehta[13] (1963) have shown it to be an excellent anti-scabietic and anti-pruritic and bacteridal agent. Peck and Michelfelder[14] (1950) has shown that Crotonyl-N-ethyl-O-toluidine possessed low sensitizing index.

In 1950, W. Burckhardt[15] showed that a cream containing 0.25% hydrocortisone acetate and 10% eurax ( crotonyl-N-ethyl-O-toluidine ) gave good result in cases of eczema, neurodermatitis and anal and genital pruritis. He has further mentioned that

* Eurax 10% + Hydrocortisone 0.25%.

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the local treatment must of ofcourse be supplemented by further diagnostic, prophylactic and therapeutic measures.

In 1957, Tronstein[16] studied 139 cases with combination of hydrocortisone and eurax. Of this 139 patients, 67 (48%) showed excellent results, 49 responded in "good fashion"; 17 (12%) exhibited "no essential changes" and the remaining six (5%) showed either flares or reaction under therapy. From the results obtained from this series, one sees little, if any great differences in results between eurax 5% with hydrocortizone 0.5%, eurax 10% with hydrocortisone 0.5%. This study did not include a combination of eurax 10% with hydrocortisone 0.5%.

## PHARMACOLOGY

R 2040-creme contains 10% Crotonyl-N-Ethyl-O-toludine (eurax) with 0.25% Hydrocortosone acetate. Crotonyl-N-ethyl-O-toluidine (eurax) has been mentioned as an antipruritic and acaricidal agent. It also possesses antibacterial, fungistatic properties with low senstisation index. It is stable for long periods of time. It is insoluble in water but readily soluble in ether, acetone, alcohol, fat, oils, etc., hence may be used in a number of vehicles. It is colorless, odorless and does not stain. It is readily available, and is a good deal less expensive than are most of the antibiotics. Hence Eurax possesses a superior merit for combination with the steroid for topical therapy.

Composition of the **R 2040-Creme (10 grams Cream)

| | |
|---|---|
| Crotonyl-N-ethyl-O-toluidine .. .. | 10 grams |
| Hydrocortisone acetate .. .. | 0.25 grams |
| Base .. .. .. .. | 100 grams |

*(Eurax 10% + Hydrocortisone 0.25%)

## CLINICAL MATERIAL AND METHODS

Forty cases of pruritic dermatoses of varied aetiology were selected for trial with R 2040-Creme. This constituted group I. Simultaneous study was done in another forty cases with Eurax 10% alone, constituting group II. Care was taken to include those cases in the control study (Group II) with more or less identical nature and extent of lesion. The duration of treatment was adjusted according to the site, extent and duration of disease. Types of cases included in Group I and Group II were 1. Infected scabies with eczematoid dermatitis—8 cases; 2. Impetiginised pediculosis capitis—8 cases; 3. Tinea pedis with eczematoid change—8 cases; 4. Pompholyx—6 cases; 5. Impetigo contagiosa—8 cases; 6. Seborrhoeic eczema—8 cases-7. Nummular eczema—4 cases; 8. Atopic Dermatitis—4 cases; 9. Contact Dermatitis—6 cases; 10. Localised neurodermatitis—8 cases; 11. Ano-genital pruritus—6 cases; 12. Lichen planus—4 cases; 13. Fox-Fordyce's disease—2 cases. Total number of cases included in Group I and II was 80 cases.

** The medicine was supplied by Messrs J. R. Geigy S. A. Basle, Switzerland. The material was packaged in 10 grams tubes bearing the number R 2040-Creme.

Mode of application. The treatment consisted of application of the cream 2-4 times daily to the involved sites after cleaning the area by means of compresses, soap, and spirit.

In classifying results as to being " Excellent ", " Good ", " no essential changes ", and " worse under treatment and reaction " it was felt that to be considered as excellent, the results would have to be better than those obtained from the usual preparation of hydrocortisone alone or eurax alone. Further more to be considered as " excellent ", results had to be both subjectively and objectively of high order, and for as long a time as one had a reasonable right to expect it of them.

## CLINICAL OBSERVATION AND RESULT

Eighty cases, including forty cases for control study, were observed during the trial. Group I consisted of forty cases studied with R 2040-Creme and Group II consisted of another forty cases studied with Eurax 10% alone. Group II constituted as control group.

The results are tabulated below.

I. Age and Sex:—Group I included 21 males, 19 Females; their age varied from 1-42 years. Group II included 22 males, 18 females; age varied from 1½-60 years.

II. Types of Diseases.

TABLE I.

| S. No. | Type of Disease | Group I No. of cases | with percentage | Group II No of cases | with percentage |
|---|---|---|---|---|---|
| 1. | Infected scabies with Eczematoid Dermatitis | 4 | 10% | 4 | 10% |
| 2. | Impetiginised Pediculosis Capitis | 4 | 10% | 4 | 10% |
| 3. | Tinea pedis with eczematoid change | 4 | 10% | 4 | 10% |
| 4. | Pompholyx | 3 | 7.5% | 3 | 7.5% |
| 5. | Impetigo contagiosa | 4 | 10% | 4 | 10% |
| 6. | Seborrhoeic Eczema | 4 | 10% | 4 | 10% |
| 7. | Nummular Eczema | 2 | 5% | 2 | 5% |
| 8. | Atopic Dermatitis | 2 | 5% | 2 | 5% |
| 9. | Contact Dermatitis | 3 | 7.5% | 3 | 7.5% |
| 10. | Localised Neurodermatitis | 4 | 10% | 4 | 10% |
| 11. | Ano-genital Pruritus | 3 | 7.5% | 3 | 7.5% |
| 12. | Lichen Planus | 2 | 5% | 2 | 7.5% |
| 13. | Fox-Fordyce's disease | 1 | 2.5% | 1 | 2.5% |
| | Total | 40 | | 40 | |

III. Extent of Disease:—The Extent of disease is graded from one to four plus. The number of cases is shown against each grade in the table No. 2 below.

TABLE 2

| Extent of Disease | Group I No. of cases with | percentage | Group II No. of cases with | percentage |
|---|---|---|---|---|
| 1. Slight+ | 4 | 10% | 4 | 10% |
| 2. Moderate++ | 23 | 57.5% | 24 | 60% |
| 3. Extensive ++++ | 13 | 32.5% | 12 | 30% |

IV. Duration of illness.

| | Group I | Group II |
|---|---|---|
| Maximum | 12 weeks | 14 weeks |
| Minimum | 2 days | 3 days |
| Average | 4.07 weeks | 3.5 weeks |

The duration of illness with number of cases is tabulated below in Table 3.

TABLE 3

| Duration of illness | Group I No. of cases with | percentage | Group II No. of cases with | percentage |
|---|---|---|---|---|
| Less than 1 week | 4 | 10% | 5 | 12.5% |
| 1–2 weeks | 11 | 27.5% | 15 | 37.5% |
| 3–4 weeks | 11 | 27.5% | 9 | 22.5% |
| 5–6 weeks | 5 | 12.5% | 5 | 12.5% |
| 7–8 weeks | 4 | 10% | 2 | 5% |
| 9–10 weeks | 3 | 7.5% | 2 | 5% |
| 11–12 weeks | 2 | 5% | 1 | 2.5% |
| 13–14 weeks | – | – | 1 | 2.5% |

V. Duration of Topical Therapy:—R 2040 and Eurax alone.

The table 4 shows the duration of Local treatment in Group I with R 2040-Creme and Group II with eurax alone.

| | Group I | Group II |
|---|---|---|
| Maximum | 13 weeks | 12 weeks |
| Minimum | 1 day | 6 days |
| Average | 3.92 weeks | 2.95 weeks |

TABLE 4

| Duration of Topical Therapy | Group I No. of cases with | percentage | Group II No. of coses with | Percentage |
|---|---|---|---|---|
| Less than 1 week | 3 | 7.5% | 1 | 2.5% |
| 1—2 weeks | 13 | 32.5% | 23 | 57.5% |
| 3—4 weeks | 11 | 27.5% | 10 | 25% |
| 5—6 weeks | 7 | 17.5% | 3 | 7.5% |
| 7—8 weeks | 2 | 5% | – | — |
| 9–10 weeks | 1 | 2.5% | 2 | 5% |
| 11–12 weeks | 2 | 5% | 1 | 2.5% |
| 13–14 weeks | 1 | 2.5% | – | — |

VI. Result of Therapy: The result of therapy was assessed in terms of disappearance of signs and symptoms. Accordingly the result was graded clinically (i) Excellent, (ii) Good (iii) Failure and (iv) Flare/Reaction.

TABLE 5

| Result | Group I Number of cases with percentage | | Group II Number of cases with percentage | |
|---|---|---|---|---|
| Excellent | 23 | 57.5% | 4 | 10% |
| Good | 16 | 40% | 31 | 77.5% |
| Failure ( No essential change ) | 1 | 2.5% | 5 | 12.5% |
| Flare up/Reaction | *1 *(reaction) | 2.5% | 3<br>*1 *(reaction) | 7.5%<br>2.5% |

## DISCUSSION

Crotonyl—N-Ethyl-O-Toluidine was first used by Domenjoz, R[3] as a new acaricidal remedy in 1946. In the same year, Burckhardt and Rymarowicz[1] evaluated its usefullness for scabies. Later it was described in the American writings by Tronstein[16]. These workers found this compound to be an excellent antipruritic, antibacterial and fungistatic agent with low sensitization index.

Subsequent studies were made by Von-Roton[6] in 1947, Dorner[7] (1949) Couperas, M.[8] (1949), Patterson[9] (1950), Peck and Michelfelder[14] (1950), Johnson and Bring[10] (1951), Mehta, T. K.[11] (1954), Majumdar[12] (1956), Joshi and Mehta[13] (1963).

This substance is marketed in a 10% concentration in a vanishing cream base under the trade name of Eurax. In an attempt to supplement anti-inflammatory and anti-pruritic effect of cortisone, a combination of eurax with hydrocortisone was later introduced. In 1950 W. Burckhardt[15] used a combination of eurax 10%. hydrocortisone 0.25% in 300 cases of neurodermatitis and ano-genital pruritus. He found this combination to be very effective and superior to either of eurax or hydrocortisone when used alone. His published study makes no mention of its use in various other pruritic dermatosis as included in the present study. Tronstein[16] studied the effect of varying concentrations of hydrocortisone and eurax combination in 139 cases. He did not find any great difference in results between eurax 5%, eurax 5% with hydrocortisone 0.5%. eurax 10% with hydrocortisone 0.5%. His study did not include a combination of eurax 10% with hydrocortisone, 0.25% as reported in the present study.

From the medical literature published in India, no reference is available on this subject. This fact stimulated me to undertake a clinical trial of eurax 10% with hydrocortisone 0.25% on a number of pruritic dermatoses of varying aetiology. Age and Sex:—The present study in group I included 21 males, 19 females with age varying from 1–42 years. Group II included 22 males, 18 females, age varried from $1\frac{1}{2}$ to 60

years of age. Treatment with eurax-hydrocortisone was not influenced by age and sex. Previous studies by Burckhardt[15] (1950) and Tronstein[16] (1957) do not make any mention of the age group included.

## TYPE OF DISEASE

The types of cases included in Group I and Group II were more or less identical. The effect of eurax-hydrocortisone did vary with the type of disease. Maximum effect was seen in cases with infected scabies with eczematoid dermatitis where the drug acted on the etiojogical agent as well. The diseases with eczematous changes responded better to eurax hydrocortisone (group I) rather than eurax alone (group II). Burckhardt's[15] study included mostly cases of neurodermatitis and anogenital pruritus whereas the presesent study included pruritic dermatoses of varried aetiology as mentioned in material and methods.

## EXTENT OF DISEASE

Group I included 10% of cases with slight extent, 57% with moderate lesion, and 32.5% with extensive disease. Group II included 10% of cases with slight disease, 60% with moderate and 30% with extensive disease. It has been concluded that the length of treatment with topical treatment varied with the extent of disease; being longer in cases with extensive disease, shorter with slight to moderate extent of disease. Previous studies have not commented upon the extent of disease.

## DURATION OF ILLNESS

Maximum duration of illness was 12 weeks in Group I and 14 weeks in group II; minimum duration was 2 days in group I and 3 days in group II. Average duration was 4.07 week in group I and 3.5 weeks in group II. Studies made by Burckhardt[16] and Tronstein[16] are silent regarding the duration of illness visa vis length of local treatment.

It has been concluded from the present study that the duration of topical therapy varied with duration of illness also. The longer the duration of illness, the longer the period of treatment with topical therapy.

## DURATION OF TOPICAL THERAPY

In this study the minimum duration of treatment in Group I was 6 days, maximum 13 weeks and average 3.92 weeks. Most of the cases required treatment from 1 to 4 weeks. The duration of treatment varied with factors like chronicity, type and extent of disease. No such mention has been made by Burckhardt[15] and Tronstein[16].

It has been observed that treatment with topical therapy was longer in cases with longer duration of illness.

## RESULTS OF TOPICAL THERAPY

In this study, in Group I, 57.5% had excellent result, 40% good, 2.5% without any effect and 2.5% with side effects. Group II showed 10% with excellent effect, 77.5% with good, 12.5% without any effect, 7.5% showed flare up of the lesion and 2.5% with reaction. These results are in general agreement with those of Burckhard[15] (1950); Trodstein[16] (1957). Although proportion of cases with excellent effect is less in the

present study than those of Tronstein, this could be explained due to the fact that a higher concentration of hydrocortisone 0.5% was used by Tronstein as compared with 0.25% hydrocortisone used in the present study. Tronstein by using varying concentration of hydrocortisone noted a significant rise in efficiency when the hydrocortisone concentration is raised from 0.5% to 1%. The present study agrees with the observations made by Tronstein.

It has been concluded from the present study that eurax–hydrocortisone combination is far superior to eurax alone. eurax–hydrocortisone combination is of great value in cases with eczematoid changes. This drug is most effective in cases like infected scabies with eczematoid change, impetiginised pediculosis capitis, seborrhoeic eczema, numular eczema, atopic dermatitis, contact dermatitis, localised neurodermatitis and ano-genital pruritus. It is of moderate value in cases with Tinea pedis with eczematoid change and Impetigo contagiosa. It has been further concluded that this combination is quite safe but in very rare cases flare up or reaction may occur.

In the present study the incidence of flare up and reaction was higher in Group II, consisting of eurax alone, than Group I ( with eurax + hydrocortisone combination ).

## SUMMARY AND CONCLUSION

1. Forty cases of Common pruritic dermatoses with or without eczematoid changes were treated with Eurax 10%—Hydrocortisone 0.25% combination. A control study group II was done in another forty cases of more or less identical nature with eurax 10% alone.
2. Eurax–hydrocortisone seems to be have a remarkable effect in pruritic dermatoses with eczematoid changes.
3. Results show that a combination of Eurax 10%—hydrocortisone 0.25% ( R 2040–Creme ) is better than eurax alone.
4. Side effects were noted in one out of forty cases in group I and 4 out of 40 cases in Eurax group II.

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