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Pharmacology

CHRONOLOGICAL APPROACH OF SEQUENTIAL DRUG UTILISATION IN CHRONIC ECZEMA: DATA ANALYSIS

KEY WORDS: Atopic dermatitis, Topical antimicrobials, Topical steroids.

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ABSTRACT

Pharmacovigilance survey for prescriptions of chronic eczema revealed prescription of irrational cluster of drugs which at the outset seemed to not offer relief. Hence we assessed the therapeutic efficacy of standard drugs scientifically with reference to the pathology and mechanism of drug action. Data collected of 320 adult men with chronic eczema (< 5 yr. duration) between age 25-44 yr. and analysed for sequential efficacy. Patients were treated in two stages over 16 weeks. The initial stage of topical antimicrobial application (gentian violet, mercurochrome, povidone-iodine) was done every fourth day. Wound healing was recorded weekly. From first week onwards, the healing of small size and superficial wounds was observed and gradually the other wounds healed over 16 weeks. In the second stage, those showing healing were prescribed ointment clobetasol and salicylic acid. Within subsequent one to two months there was satisfactory post-healing repair without any skin thickening and pigmentation.

INTRODUCTION

World Allergy Organization published a consensus statement supporting the use of the term eczema, instead of Atopic Dermatitis (AD) or atopic eczema (AE), with atopic and nonatopic subtypes.¹ A variety of different terms are still used as AD, AE, eczema, infantile eczema, atopiform dermatitis, flexural eczema, and atopic neurodermatitis.²

Eczema and dermatitis indicate the inflammatory lesions of epidermis. Acute eczema involves epidermal edema (spongiosis) with predominant intra-epidermal vesiculation; while chronic type presents with marked epidermal thickening (acanthosis)³. There is infiltration of mononuclear cells (T-cell lymphocytes) around dermal capillaries leading to vasodilatation⁴. The subtypes of eczema has varied aetiology and presenting features. However presence of ulcer, oozing, bleeding and pruritus are common symptoms which are responsible for denial of healing. There is epidermal proliferation leading to chronicity in the form of acanthosis.

Prescriptions include dermal steroids with or without topical and systemic antimicrobials⁴. However, we observed prescription of dermal steroid with topical antimicrobials, with +/- salicylates and H₁ antihistaminics etc. Such combination therapy is irrational, delays healing, and leads to chronicity of disease. In pharmacotherapy of dermatitis, steroids are withheld until healing takes place; since owing to local immunosuppressive action, infection may flare up, with added impairment of fibrogenesis⁴. Topical corticosteroids are recommended for individuals who have failed to respond to good skin care and regular use of emollients alone.⁵ Topical drugs like salicylate and steroids have a rationale and justified role in promoting the repair of lesion, provided they are used following complete healing of existing ulcerative focus⁴. Recently, more attention is given to a proactive therapeutic by regular intermittent application of low potency steroids or topical calcineurin inhibitors to prevent new flares.⁶

MATERIALS AND METHOD

Data of 320 adult male of 25-44 yrs. age group attending Dermatology OPD of chronic eczema was pooled to study the sequential efficacy of various topical antimicrobials, dermal steroids and other drugs in healing of eczema lesions. History

of duration and chronology of sites affected, any other allergic illness to the participant, drug used for eczema and systemic diseases was noted. Dermal examination were recorded. Swab for culture of lesions and finding of other investigations advised were noted.

Exclusion criteria:-

- Eczema > 5 yrs.,
- Age above 44 yrs.,
- Evidence of diabetes mellitus,
- History suggestive of drug allergy,
- Presence of concurrent chronic disease.

The enrolled patients were divided into age groups of 25-34 (group A) and 35-44 yrs. (group B). Debridement was carried with normal saline followed by irrigation with hydrogen peroxide and subsequent removal of debris/crust/pus. At the start and every fourth day application of topical antimicrobial (Gentian-violet-1%, Mercurochrome- 1% and Povidone iodine-5%) was done in sequential order, finally sterile occlusive dressing was done. All participants were prescribed tablet Cefixime 200mg OD, Vitamin C 500 mg OD and Multivitamin. At each review, the notes on morphology of lesions were recorded. Wound dressing was done till healing; after which topical steroid with salicylic acid were recommended.

RESULTS

In this study, 320 adult men, clinically diagnosed to be suffering from chronic eczema by dermatologist were enrolled. The age distribution as per site of eczema is shown in table 1.

Table 1 Location of eczema lesion as per age groups.

Site of Lesion	Age 25-34 yr.	Age 35-44 yr.	Total
Face/Neck	32	28	60 (12.50 %)
Hands	92	106	198 (41.25 %)
Legs	104	118	222 (46.25%)
	228 (47.5%)	252 (52.5%)	480*

* due to more than one lesion in some, total n= exceeds sample size of 320

Table 1 shows the distribution of eczema lesions as per age group A and B. Lesion on neck, face were seen in 32 from group A, and 28 from group B, total (12.5%) had superficial lesions on face/neck, without any oozing.

Patients with upper limb lesions are 92 and 106 (41.25%) had scanty oozing, crust formation. while patients with lower limb lesions are 104 and 118 total(46.24%); affecting dorsum of feet, periankle region few had deep lesions, some oozing/crusts and unhealthy granulation base.

Eczema lesions as a whole found prevalent in group-A in 228 (47.5%) and gr B 252(52.5%) patients. Some patients had more than one site affected, so total 480 wounds were recorded in sample size of 320.

Table 2. Healed wound status on follow up every fourth day.

Group	Status of healed wound at week																Total healed Wound
	1	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	
A	19	20	27	24	35	39	35	26	39	26	39	26	39	26	39	26	264
B	12	13	19	26	32	39	26	28	21	21	21	21	21	21	21	21	216
Total	31	33	46	50	67	78	61	54	60	60	60	60	60	60	60	60	480

Table 2 shows the number of wounds healed as noted on case sheets on weekly review. The wounds which healed during initial follow up were superficial and mostly on the upper limb, and neck. Deeper wounds in lower limbs healed later until 16 weeks. Thus total 16 weeks cumulative span was required to achieve healing of all the wounds.

In age group-A, healing of wounds was early and more in number in comparison to group-B, except week 6, 14 (less) and equal cases at week 10 (39 each). Age gr. A showed maximum healing at week 10 and 16 (39 each); age gr. B subjects showed maximum healing at week 10(n=39). Overall both age gr. had healing in most subjects at week 10 (n=78). Subsequently those who showed healing of wound were found to have been prescribed clobetasol cream (0.05%) + salicylic acid ointment (10%). The healed superficial eczema wounds were healthy without scar/ thickening or pigmentation following one month of topical steroid + salicylate application. The deep wounds of lower limbs healed by second intension with overlying skin thickening and mild pigmentation; both resolved after two months of clobetasol and salicylate application. Culture of swab revealed growth of staphylococci isolates, which were sensitive to all antimicrobials. No adverse effects of drug was seen in any patient.

DISCUSSION

Topical steroids are most useful for the treatment of eczema⁴. Most of the eczema wounds which are oozing and secondarily infected⁴, needs appropriate management of the primary target, followed by topical steroids and keratolytic drugs⁵. Topical steroids are classified as per potency (anti-allergic, anti-inflammatory and anti-proliferative)⁷ as mild (Hydrocortisone acetate 1%, Clobetasole butyrate), moderate(Fluticasone, Mometasone), potent (Betamethasone, Fluocinolone, Triamcinolone) and super-potent (Clobetasol propionate, betamethasone).

Many topical antimicrobials are available, the much needed is one which has antimicrobial action and also controls oozing so that the wound can heal early; however deep seated wounds with unhealthy granulation base and pyogenic focus have delayed healing despite appropriate debridement, but heal with second intension; may lead to scar, hyper-squamation and pigmentation⁷. Gentian violet, mercurochrome are dyes, which discolour the skin and overlying cloths; not much used these days. Povidone iodine is topical iodine preparation; all have germicidal, disinfectant and antiseptic actions⁸. These agents dry up the wound, therefore oozing, itching and secondary infection is controlled, and so healing is promoted. Topical steroids should be used only after healing, else the laying down of fibrous tissue is impaired which delay healing^{3,4}.

In this study the data shows that scientific approach was

adapted for controlling oozing, infection by use of topical and systemic antimicrobials, subsequent repair by using topical clobetasol propionate with salicylic acid. Since eczema lesions were chronic, clobetasol use after healing is justified being super-potent anti-inflammatory drug⁷. Ointments, creams, gels causes logging and retention of oozing fluid in deep seated lesions, so healing is halted and secondary infection may flare up. Therefore the topical preparation that makes wound dry could be helpful in healing of wound, initiating use of gentian violet, mercurochrome and povidone iodine appears to be beneficial. The mechanism of action of topical salicylate is described as^{4,7,9}

- **Local vasodilatation** that improves healing process of damaged tissue at the site of application, arrests apoptosis of healthy cells.
- **Hyperaemia** provides local warmth, thereby improves metabolic rate; nutritional uptake and growth of healing tissue.
- **Keratolytic action** so epilates thick and dead tissue debris, paving regeneration base for laying new cells.
- **Antiseborrhoeac** action- reducing the secretory activity of sebaceous glands, secreting scanty, thinner sebum that provides utilisable nutrition, hydration, lubrication and promotes growth of new cells. Salicylates act as adjuvant to steroid (keratolytic effect); induces synergistic effect on regeneration and restructuring of growing skin overlying wound.

The age group B patients were found to be having more prevalence of eczema lesions (52.5%) suggesting upper age specific vulnerability of developing the disease. Most vital aspect of this study was unpredictable duration required for healing. The three types of topical antimicrobials applied on wound surface, were effective in healing small sized, superficial wounds within one week which include neck and upper limb. From second week onward there was gradual healing in deep wounds. At peri-terminal period (12-16 weeks) pyogenic wounds were found to have healed. We observed that the younger age group-A exceeded in healing wounds early except (week 6, 14). Until ahead 16th week, remaining wounds were seen to have healed. Following healing of wound these patients were prescribed ointment Clobetasol and salicylic acid. There was satisfactory response in the form of regression of thick skin and pigmentation. Healed wound surface was moist with natural glow. Thus morphology restructured within one and two months regarding superficial and deep wounds respectively.

CONCLUSION

The age group B patients were found to be having more prevalence of eczema lesions (52.5%) suggesting upper age specific vulnerability of developing the disease.

Total 16 weeks of therapy is required to achieve healing of all the wounds.

In this study the Pharmacotherapeutic description of drugs used and the sequential chronology of therapy seen justified e.g. topical antimicrobials → healing → topical clobetasol + salicylic acid → regained morphology. Any deviation in the sequence of drug and procedure would therefore be irrational, unethical and unscientific.

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