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STUDIES

INFLUENCE OF LIPOSOMAL DRUG ENTRAPMENT ON THE PERFORMANCE OF CORTICOSTEROID CREAMS

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Skin blanching and clinical efficacy of a liposomally entrapped Triamcinolone acetonide (TRMA) cream was compared with that of the conventional TRMA cream in healthy human volunteers and eczema patients respectively. Both the creams showed equal efficacy in eczema patients. A significant reduction in the skin blanching response with the liposomal TRMA cream as compared to the conventional TRMA cream suggests a decrease in the systemic absorption of the corticosteroid with the former.

Key Words : Liposomes, TRMA, Skin blanching, Clinical profile

Introduction

Prolonged topical application of corticosteroids in dermatitis, psoriasis and other dermatosis is known to cause unintended systemic side effects due to the percutaneous absorption of the drug. A new approach to achieve selective drug delivery to the skin is the use of liposomes as drug localizers.[1] Liposomes are microscopic vesicles composed of phospholipid bilayers which form spontaneously when appropriate composition of phospholipids are hydrated in aqueous media.[2]

Encapsulation of TRMA into liposomes favourably alters the drug disposition in rabbits with lower TRMA levels in the blood stream as compared to conventional TRMA cream.[3]

In the present study, the liposomal TRMA cream was compared with the conventional TRMA cream with respect to its skin blanching potential in healthy human volunteers and its efficacy in eczema patients.

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Meterials and Methods

TRMA liposomes were prepared by Bangham's lipid film rehydration method[4] using TRMA : lecithin : cholesterol in the ratio of 69μM : 190μM : 93μM. A 0.1% w/w liposomal TRMA cream was prepared by incorporating the drug loaded liposomes into aqueous cream base BPC. A conventional 0.1% w/w TRMA cream was prepared in the same base.

A double blind, occluded, skin blanching assay was conducted on forearms of 13 healthy human volunteers of either sex, using 10± 1 mg of the prepared creams. Skin blanching score was assigned after six hours of application by an unbiased observor using a 0-4 scale rating based on the Barry Woodford's method.[5] The blanching scores for the two creams were subjected to a two tailed t-test to study the level of significance.

A double blind clinical trial was conducted at the Skin and VD Department of

Shri Sayaji General Hospital, Baroda, on 10 patients with dry bilateral eczema for 1 month, with weekly assessments by clinical experts.

Results

The blanching scores for all the volunteers, for each formulation, were summed up and expressed as the percentage of the total possible score (%TPS). The histogram (Fig. 1) shows a statistically significant ($p<0.001$) decrease in the %TPS with the liposomal TRMA cream as compared to the conventional TRMA cream suggesting a decrease in the skin blanching response elicited by the former.

The table I shows the results of the clinical trials. No statistically significant difference was observed in the clinical efficacy of the two creams in eczema patients.

Comments

The human skin blanching assay is an excellent model in evaluating the efficacy of topical corticosteroids prior to clinical trials.[6] When corticosteroids from topically applied dosage forms penetrate to the blood vessels of the skin, they cause vasoconstriction of the same and hence the skin gets blanched.

Table I. Results of Clinical Trials

Symptoms	% of patients responding to	
	liposomal TRMA cream	conventional TRMA cream
Exfoliation/ Hyperpigmentation	20	20
Lichenification/ Fissuring	40	40
Pruritis	50	50
Erythema/Itching/ Burning	60	60

Histogram

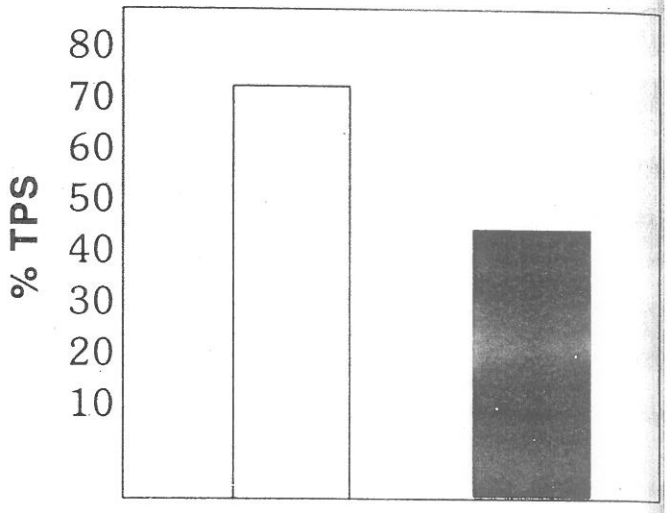

Fig. 1. Comparative skin blanching responses for the liposomal TRMA cream (■) and the conventional TRMA cream (□). ($p<0.001$, $n=13$)

Reduction in skin blanching without adverse effects on the efficacy by the liposomal TRMA cream suggests the following :

(i) incorporation of drug into liposomes limits the drug from reaching the blood stream. The lecithin of the liposomes probably increases the total lipid content of the stratum corneum which leads to formation of a steroid depot in this region from where a controlled delivery of the steroid to the lower skin layers, where blanching takes place, occurs. Hence the use of liposomal cream may reduce the systemic side effects.

(ii) Liposomally entrapped drug, localizes in the epidermis-dermis. Hence the dose of the drug can be reduced making the therapy cost effective.

References

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