Clofazimine Ointment in the Treatment of Trophic Ulcers*

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**SUMMARY**

A small series of patients suffering from trophic ulceration of various aetiologies, successfully treated with clofazimine 1% ointment, is reported. The healing time achieved in this uncontrolled series was sufficiently remarkable to warrant further investigations and assessment.


Clofazimine (Lamprene, Ro663, G30320) is one of a large series of rimino-compound of structure I synthesized originally as a potential antimycobacterial agent. These are orange-red phenazine derivatives, whose colour is related to their quinone-imine character. Given orally in the micromized form, 70-90% of the drug is absorbed and serum levels on a dosage of 600 mg/day reach 3 - 4 μg/ml in man; while skin and lymph nodes may contain 40 μg/g.

Excretion is extremely slow, only a few milligrams per day being excreted by the kidneys, while in addition a small amount is eliminated in the sweat and sebum.

The low plasma and tissue levels are due to the active take-up of the drug by the reticulo-endothelial system.

The first clinical trial of the drug was undertaken by Browne and Hogerzeil who reported favourable therapeutic response in leprosy. They suggested additionally that the drug may exert a suppressive effect on the development of acute exacerbations in lepromatous leprosy, and reported a reduced incidence of erythema nodosum leprosum compared with corresponding groups of patients on conventional therapy.

This observation has subsequently been confirmed by numerous workers and has been explored.

Pigmentation of the skin of patients on clofazimine therapy has been noted by many workers. It occurs particularly in the peri-orbital and perinasal regions and in thick, hairless, hypopigmented skin of the palms and soles.

A further effect is ichthyosis and drying effect on the skin with manifestations of a mosaic pattern.

Vischer reported that clofazimine was not only active against some strains of mycobacteria, but also against other strains of the families Corynebacteriaceae, Bacillaceae, Micrococaceae, Actinomycetaceae and Streptomycetaceae, and speculated whether this was of practical importance in infections involving these micro-organisms.

Finally, the effect of systemic clofazimine in leprosy ulcers and other mycobacterial skin ulcers led us to consider the possible efficacy of a topical application in ulceration due to various aetiologies.

**MATERIALS AND METHODS**

A bland base was used to incorporate the active ingredient at an empirically selected 1% strength. The ointment was made by expressing the capsule contents directly into the base. The active ingredient itself is suspended in the capsule in a vegetable oil with the addition of minor amounts of beeswax, soya lecithin and partially hydrated vegetable oils. Butylhydroxytoluene is added as a stabilizer.

Patients were selected on the basis of suitability, failed previous therapy and intractability. Suitability criteria included tissue and bone damage of the type encountered in leprosy, tissue damage over large areas (bedsores and burns), and necrotic sinus formation due to trauma (dog and snake bites, and abscesses).

Previous therapy included antibiotics, formal desloughing, topical cleansing, a variety of specific ointments and creams over long periods, and skin grafting.

The method of treatment was standard throughout the trial period—after swabbing for culture purposes, the ulcer was carefully cleansed with a mixture of Hibitane 2% and acetic acid 0.5%. The trial ointment was spread over and into the ulcer with a spatula; sinuses were filled using a syringe to ensure full-depth filling. The area was covered with layers of gauze, a crepe bandage firmly applied and left in situ for 4 - 7 days. No antibiotics or other antiseptics were prescribed during treatment, except in cases 1 and 2.

Surgical intervention involved formal desloughing and/or sequestrotomy when necessary before and during treatment.

Immediately the dressings were opened after the requisite contact period repeat cultures were taken, and the whole cleansing/dressing procedure started again until the area was healed or considered ready for skin grafting.

As this series was uncontrolled the criterion of success had to be gauged against previous therapy/surgical failure and our experience with other topical preparations used in similar cases over a number of years.

The most striking observation early in our experience with clofazimine ointment was that profuse microbacterial infection was not detrimental, and although repeated cultures showed continued presence of the initial pathogens, there was good epithelialization and granulation, with...
It has been well documented and demonstrated that clofazimine is a multifactorial drug, having antibacterial and anti-inflammatory properties, and as our preliminary investigations have shown, has also possible topical healing properties in a variety of aetiologies. Repeated cultures during topical treatment show the continued presence of pathogens, yet the healing process continued. This observation leads to the speculation whether topical clofazimine exerts an inhibitory action on the toxic activity of the infecting pathogens, thereby limiting or preventing tissue and bone necrosis.

Another unusual aspect was that the resultant healed area had a feeling of smoothness best described as peau de soie, which belied its toughness.

**DISCUSSION**

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**REFERENCES**