CURRENT CLINICAL SOLUTIONS
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HALCINONIDE

A Review of its Clinical Merits

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Clinical Use of Topical Corticosteroids

Glucocorticosteroids act on a wide range of cells and have a wide range of mechanisms of action. They have been successfully applied in many inflammatory skin diseases and are one of the most frequently used drugs in dermatology. Some inflammatory skin diseases such as acute eczema and seborrheic dermatitis are more responsive to corticosteroids than are chronic hyperkeratotic or lichenified eczema, psoriasis, lichen planus, discoid lupus erythematosus, vitiligo, or alopecia areata. Mild atopic dermatitis frequently responds to low- to mid-potent topical corticosteroids, though short-term use of more potent agents can also be used to achieve rapid improvement. Recalcitrant conditions may respond only to high- or very high-potency preparations, sometimes requiring occlusion (though with "recalcitrant" conditions, poor adherence should also be considered).

Halcinonide is one of the available highly potent topical corticosteroids. It is a derivative of hydrocortisone and contains important modifications in its structure that alters its absorption, potency, and adverse effects compared with hydrocortisone. Halcinonide—along with desoximetasone, betamethasone, fluocinonide, and diflorasone diacetate—is classified as a Class II potency corticosteroid. Although similar in strength, halcinonide in Halog (the only topical product available that contains halcinonide) differs from many other compounds of this class in formulation.

Halcinonide cream is formulated in a biphasic base that allows for immediate-release of halcinonide upon application to the skin, followed by a delayed and sustained release of halcinonide over time. This "dual formulation" strategy allows for prolonged halcinonide activity.[1] The formulation of halcinonide cream contains microcrystals of halcinonide. An equilibrium is established between dissolved halcinonide in the cream and non-dissolved halcinonide in the microcrystals. As soluble halcinonide enters the skin, additional quantities of halcinonide from the microcrystals become available as a new equilibrium is established. This dynamic equilibrium serves to maintain a sustained level of halcinonide well beyond the time of application (unpublished data provided by the manufacturer).

Contact dermatitis due to topical corticosteroids is not rare. The prevalence was reported to be in the range of 0.2–6% in contact dermatitis clinics.[2-4] Contact dermatitis may be due to allergy to the steroid molecule or to the ingredients in the vehicle. Halcinonide cream contains a minimal number of inactive ingredients, and lacks preservatives and lanolin.[5]

Effectiveness in Dermatologic Diseases—A Review of the Literature

Use of halcinonide has been studied and reported in the medical literature since the 1970s and as recent as 2011 by Baum. Baum reported the efficacy and patient acceptance of halcinonide 0.1% cream in 216g jars for the treatment of large-area, moderate-to-severe dermatoses affecting an average of 12% body surface area. Dermatoses included psoriasis and dermatitis in the 40 patients who were followed. Improvement was noted for all patients, with nearly half exhibiting a complete or almost complete clearing. Most patients (95%) agreed that they liked the way the product spread on the skin, and more than 80% found that it was neither sticky nor greasy. The authors concluded that halcinonide cream was an effective and convenient treatment for patients with large-area dermatoses.[6]

An early study by Belknap and Dodson examined the efficacy of halcinonide 0.1% in 101 patients with contact dermatitis, atopic dermatitis, nummular eczema, neurodermatitis, stasis dermatitis, and/or dyshidrotic eczema when applied 2 or 3 times daily for 3 weeks. Sixteen patients cleared after two weeks. By the end of three weeks, dermatitis in 46 of the patients had completely resolved, the condition in 39 showed marked improvement, and the condition in 10 had improved moderately. No local or systemic side effects were reported, and more than 9 out of 10 patients rated their acceptance of halcinonide as "excellent" or "good".[7]

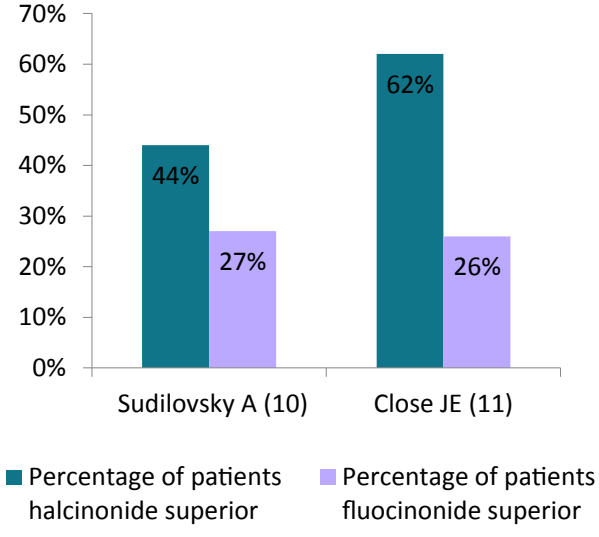
In 1982 Pirozzi evaluated halcinonide cream 0.1% in 100 patients with dermatitis. Ninety-eight percent of the patients showed some degree of improvement, and 85% had complete clearing or marked improvement after two weeks. One case of urticaria was the only side effect noted in this series. Ninety-six percent of the patients rated their acceptance of the formulation as excellent or good.[8] Three years later, Bleeker compared halcinonide cream 0.1% (Class II) with clobetasol propionate cream 0.05% (Class I) in patients with psoriasis or eczema. Over a 14-day period of therapy there was similar efficacy for the two preparations. Minimal number of patients reported side effects—2% with halcinonide and 1% with clobetasol—which were stinging or burning with erythema.[1] However, the results of another comparative trial of clobetasol and halcinonide cream demonstrated a superior efficiency of clobetasol in psoriasis as measured by degree, rate, and duration of healing.[9]

Comparative studies with halcinonide and fluocinonide have yielded results in favor of halcinonide. Sudilovsky and Clewe conducted a multicenter, randomized, double-blind, paired analysis in which they reported on the efficacy of halcinonide 0.1% cream and fluocinonide 0.05% cream in 140 patients with moderate-to-serve psoriasis. Patients had bilateral lesions, in which they applied one cream to one side and the other cream to the other side. Upon study completion, halcinonide produced superior results over fluocinonide in 44% of patients, fluocinonide produced superior results over halcinonide in 27% of patients, both drugs were equal in 26% of patients, and there was no relief in 4% of patients.[10]

In a similar bilateral, double-blind study of halcinonide and fluocinonide, treating 50 patients with moderate-to-severe psoriasis for up to 3 weeks, Close reported that halcinonide

0.1% cream was superior to fluocinonide 0.05% in 62% of patients, fluocinonide was superior to halcinonide in 26% of patients, both were equal in efficacy in 10% of patients, and there was no relief in 4% of patients.[11] Figure 1 compares the results of two clinical trials comparing halcinonide with fluocinonide in treatment of psoriasis. In yet a third double-blind, paired comparison of halcinonide cream and fluocinonide cream in 59 patients with severe psoriasis, significantly more patients treated with halcinonide than with fluocinonide improved to normal or slight inflammation in 4 weeks—56% versus 44%.[12]

Figure 1. Results of two double-blind clinical trials comparing halcinonide with fluocinonide in treatment of psoriasis.



Halcinonide has also been studied in pediatric patients. Six groups of children suffering from widespread atopic dermatitis were treated with six topical steroids of different potency. In this study, halcinonide was less effective than betamethasone dipropionate and difluorocortolone valerianate and more effective than clobetasone butyrate, desonide, and fluocortine butylester in controlling dermatitis. The study showed a clear relationship between clinical efficacy of the steroid treatment and degree of reduced adrenal function.[13]

Using Halcinonide

Halcinonide cream is indicated for the relief of the inflammation in corticosteroid-responsive dermatoses. It is a highly-potent corticosteroid, comparable to Class I products in some studies.[1,9] It exhibits a low irritation potential due to its structure and minimal inactive ingredients in its vehicle. Our review of the literature also found a low incidence of local adverse effects with monitored use over short periods and a high patient acceptance rate.[1,3,4,6,14,15]

The halcinonide 0.1% cream formulation, discussed in this review article, is distributed in the market as 30-g, 60-g and 216-g packages of halcinonide cream. The large 216-g jar is suitable and economical for patients who need a large amount of topical steroid due to diffuse, extensive dermatoses. After an initial control, intermittent application of a thin layer of the cream may be used for maintaining remission in many steroid-responsive diseases. Intermittent or short-term application of a high-potency corticosteroid may have the same risk/benefit ratio of frequent application of a less potent formula, with potentially lower cost and better patient acceptance. Halcinonide cream, with its prolonged period of activity, may help reduce the total amount and frequency of application, which potentially could increase patient acceptance and decrease the cost of therapy.

Conclusion

Halcinonide cream is a strong Class II steroid with low irritation potential, very little local adverse effects with proper use, prolonged period of activity, and high patient acceptance rate. It can be used for a wide variety of steroid responsive inflammatory skin diseases such as eczema, psoriasis, lichen planus, discoid lupus erythematosus, vitiligo, and alopecia areata. A wise selection of amount, vehicle, frequency and length of use of potent topical corticosteroids and good communication with patient can lead to a high success rate, low rate of adverse effects, and a reasonably low cost.

Disclosure

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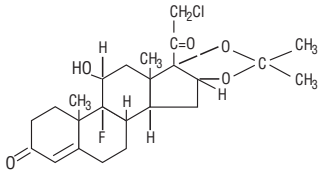
HALOG®
(Halcinonide Cream, USP) 0.1%

Rx only

FOR TOPICAL USE ONLY.
NOT FOR OPHTHALMIC, ORAL, OR INTRAVAGINAL USE.

DESCRIPTION

The topical corticosteroids constitute a class of primarily synthetic steroids used as anti-inflammatory and antipruritic agents.
The steroids in this class include halcinonide. Halcinonide is designated chemically as 21-Chloro-9-fluoro-11β,16α, 17-trihydroxypregn-4-ene-3,20- dione cyclic 16,17-acetal with acetone. Graphic formula:



$C_{24}H_{32}ClFO_5$, MW 454.96, CAS-3093-35-4

Each gram of 0.1% HALOG (Halcinonide Cream, USP) contains 1 mg halcinonide in a specially formulated cream base consisting of cetyl alcohol, dimethicone 350, glyceryl monostearate NF XII, isopropyl palmitate, polysorbate 60, propylene glycol, purified water, and titanium dioxide.

CLINICAL PHARMACOLOGY

Topical corticosteroids share anti-inflammatory, antipruritic and vasoconstrictive actions.

The mechanism of anti-inflammatory activity of the topical corticosteroids is unclear. Various laboratory methods, including vasoconstrictor assays, are used to compare and predict potencies and/or clinical efficacies of the topical corticosteroids. There is some evidence to suggest that a recognizable correlation exists between vasoconstrictor potency and therapeutic efficacy in man.

Pharmacokinetics

The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle, the integrity of the epidermal barrier, and the use of occlusive dressings.

Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin increase percutaneous absorption. Occlusive dressings substantially increase the percutaneous absorption of topical corticosteroids. Thus, occlusive dressings may be a valuable therapeutic adjunct for treatment of resistant dermatoses (see **DOSAGE AND ADMINISTRATION)**."

Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. Corticosteroids are bound to plasma proteins in varying degrees. Corticosteroids are metabolized primarily in the liver and are then excreted by the kidneys. Some of the topical corticosteroids and their metabolites are also excreted into the bile.

INDICATIONS AND USAGE

HALOG (Halcinonide Cream, USP) 0.1% is indicated for the relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses.

CONTRAINDICATIONS

Topical corticosteroids are contraindicated in those patients with a history of hypersensitivity to any of the components of the preparations.

PRECAUTIONS

General

Systemic absorption of topical corticosteroids has produced reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients.

Conditions which augment systemic absorption include the application of the more potent steroids, use over large surface areas, prolonged use, and the addition of occlusive dressings.

Therefore, patients receiving a large dose of any potent topical steroid applied to a large surface area or under an occlusive dressing should be evaluated periodically for evidence of HPA axis suppression by using the urinary free cortisol and ACTH stimulation tests, and for impairment of thermal homeostasis. If HPA axis suppression or elevation of the body temperature occurs, an attempt should be made to withdraw the drug, to reduce the frequency of application, substitute a less potent steroid, or use a sequential approach when utilizing the occlusive technique.

Recovery of HPA axis function and thermal homeostasis are generally prompt and complete upon discontinuation of the drug. Infrequently, signs and symptoms of steroid withdrawal may occur, requiring supplemental systemic corticosteroids. Occasionally, a patient may develop a sensitivity reaction to a particular occlusive dressing material or adhesive and a substitute material may be necessary.

Children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity (see **PRECAUTIONS: Pediatric Use**).

If irritation develops, topical corticosteroids should be discontinued and appropriate therapy instituted.

In the presence of dermatological infections, the use of an appropriate antifungal or antibacterial agent should be instituted. If a favorable response does not occur promptly, the corticosteroid should be discontinued until the infection has been adequately controlled.

This preparation is not for ophthalmic, oral, or intravaginal use.

Information for the Patient

Patients using topical corticosteroids should receive the following information and instructions:

1. This medication is to be used as directed by the physician. It is for dermatologic use only. Avoid contact with the eyes.
2. Patients should be advised not to use this medication for any disorder other than for which it was prescribed.
3. The treated skin area should not be bandaged or otherwise covered or wrapped as to be occlusive unless directed by the physician.
4. Patients should report any signs of local adverse reactions especially under occlusive dressing.
5. Parents of pediatric patients should be advised not to use tight-fitting diapers or plastic pants on a child being treated in the diaper area, as these garments may constitute occlusive dressings.

Laboratory Tests

A urinary free cortisol test and ACTH stimulation test may be helpful in evaluating HPA axis suppression.

Carcinogenesis, Mutagenesis, and Impairment of Fertility

Long-term animal studies have not been performed to evaluate the carcinogenic potential or the effect on fertility of topical corticosteroids.

Studies to determine mutagenicity with prednisolone and hydrocortisone showed negative results.

Pregnancy

Teratogenic Effects: Category C

Corticosteroids are generally teratogenic in laboratory animals when administered systemically at relatively low dosage levels. The more potent corticosteroids have been shown to be teratogenic after dermal application in laboratory animals. There are no adequate and wellcontrolled studies in pregnant women on teratogenic effects from topically applied corticosteroids. Therefore, topical corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Drugs of this class should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.

Nursing Mothers

It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in breast milk. Systemically administered corticosteroids are secreted into breast milk in quantities not likely to have a deleterious effect on the infant. Nevertheless, caution should be exercised when topical corticosteroids are administered to a nursing woman.

Pediatric Use

Pediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced HPA axis suppression and Cushing's syndrome than mature patients because of a larger skin surface area to body weight ratio.

HPA axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include linear growth retardation, delayed weight gain, low plasma cortisol levels, and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches, and bilateral papilledema.

Administration of topical corticosteroids to children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of children.

Geriatric Use

Of approximately 3000 patients included in clinical studies of 0.1% HALOG CREAM, 14% were 60 years or older, while 4% were 70 years or older. No overall differences in safety were observed between these patients and younger patients. Efficacy data have not been evaluated for differences between elderly and younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

ADVERSE REACTIONS

The following local adverse reactions are reported infrequently with topical corticosteroids, but may occur more frequently with the use of occlusive dressings (reactions are listed in an approximate decreasing order of occurrence): burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae, and miliaria.

OVERDOSAGE

Topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects (see **PRECAUTIONS: General**).

DOSAGE AND ADMINISTRATION

Apply the 0.1% HALOG (Halcinonide Cream, USP) to the affected area two to three times daily. Rub in gently.

Occlusive Dressing Technique

Occlusive dressings may be used for the management of psoriasis or other recalcitrant conditions. Gently rub a small amount of cream into the lesion until it disappears. Reapply the preparation leaving a thin coating on the lesion, cover with a pliable nonporous film, and seal the edges. If needed, additional moisture may be provided by covering the lesion with a dampened clean cotton cloth before the nonporous film is applied or by briefly wetting the affected area with water immediately prior to applying the medication. The frequency of changing dressings is best determined on an individual basis. It may be convenient to apply HALOG under an occlusive dressing in the evening and to remove the dressing in the morning (i.e., 12-hour occlusion). When utilizing the 12-hour occlusion regimen, additional cream should be applied, without occlusion, during the day. Reapplication is essential at each dressing change.

If an infection develops, the use of occlusive dressings should be discontinued and appropriate antimicrobial therapy instituted.

HOW SUPPLIED

HALOG® (Halcinonide Cream, USP) 0.1% is supplied as tubes containing 15 g (NDC 10631-094-15), 30 g (NDC 10631-094-20), and 60 g (NDC 10631-094-30); and jars containing 216 g (NDC 10631-094-76) of cream.

Storage

Store at room temperature; avoid excessive heat (104º F).

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