Pediatric Pharmacotherapy

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Topical Corticosteroid Preparations

Pharmacology Literature Reviews

Formularly Update

Nearly fifty years ago the first topical corticosteroid preparation, hydrocortisone, was introduced in the United States, making a dramatic impact on the management of pediatric dermatologic conditions. Since that time, a wide spectrum of products has been developed in an effort to maximize anti-inflammatory properties while minimizing mineralocorticoid activity and adverse effects.

Topical corticosteroid preparations have become a cornerstone in the treatment of children with a variety of skin conditions, including atopic dermatitis, psoriasis, eczema, seborrheic dermatitis, contact dermatitis, and some types of burns. They are useful adjunctive therapy in other dermatologic conditions, such as porphyria, lupus, epidermolysis bullosa, and severe cases of diaper dermatitis in infants.[1] This brief review will focus on issues related to potency and drug selection, differences in vehicles, toxicities, and the use of combination corticosteroid products.[2-5]

Comparing Potency

The most common method for comparing topical corticosteroid products is relative potency. Potency is determined by the degree of tissue penetration of a product (bioavailability) and the resulting vasoconstriction (skin-blanching) that is produced. It may not be relevant to efficacy in treating specific skin conditions. Testing to determine potency is conducted by pharmaceutical manufacturers and reflects a particular name brand product. Generic products with the same ingredients may not have the same potency.

In addition to potency classifications, many products are available in more than one strength, reflecting a difference in the amount of active drug present in a given amount of ointment, cream, or lotion.[1-3]

A comparison of potencies is provided below. Common brand names are in parentheses. It should be noted that none of the very high potency agents carry an FDA-approved indication for use in children.

Very High Potency (* on UVA formulary)

- Augmented betamethasone dipropionate (Diprolene AF®)
- propionate (Temovate®)*
- Diflorasone diacetate (Florone®, Maxiflor®)
- Halobetasol propionate (Ultravate®)

High Potency

- Amcinonide (Cyclocort®)
- Betamethasone dipropionate (Diprosone®)
- Betamethasone valerate (Valisone®)
- Desoximetasone (Topicort®)
- Fluocinolone acetonide (Synalar®)*
- Fluocinonide (Lidex®)*
- Halcinonide (Halog®)
- Triamcinolone acetonide (Kenalog®)*

Moderate Potency

- Betamethasone benzoate (Uticort®)
- Clocortolone pivalate (Cloderm®)
- Flurandrenolide (Cordran®)
- Fluticasone propionate (Cutivate®)*
- Hydrocortisone valerate (Westcort®)
- Mometasone furoate (Elocon®)

Low Potency

- Aclometasone dipropionate (Aclovate®)

- Desonide (Tridesilon®)
- Dexamethasone sod. phosphate (Decadron®)*
- Hydrocortisone (Cortizone®)*
- Hydrocortisone acetate (Cortaid®)*

Most pediatric patients respond well to mild or moderately-potent agents. In patients with refractory dermatologic conditions requiring long-term therapy, a high or moderately high-potency product is recommended for initial use. This preparation can be replaced with lower potency products as the condition resolves.[3]

Selecting a Vehicle

All topical products consist of an active ingredient and a vehicle (or solvent). In addition to being a carrier for the corticosteroid, the vehicle serves other functions including hydrating the skin and enhancing drug penetration. Most topical corticosteroid preparations are available in several forms, including ointments, creams, gels, aerosols, and lotions.

When selecting a vehicle, the severity of the dermatologic condition should be considered. For serious conditions, ointments may provide delivery of greater amounts of drug into the epidermal and dermal tissues. Ointments typically contain petrolatum, waxes, paraffin, propylene glycol, or mineral oil. They provide hydration of the stratum corneum by acting as an occlusive barrier to prevent evaporation, and therefore, enhance drug penetration. Ointments are particularly useful for dry, scaly lesions.

Creams contain a water-soluble base (up to 50% water). While more acceptable than ointments to most patients, creams do not provide significant skin hydration and do not enhance drug penetration. Lotions and gels are similar to creams, but contain even greater amounts of water.[5,6] The higher water content of these vehicles promotes drying of the skin through evaporation. Creams, lotions, and gels are are useful for weeping or blistered lesions where additional hydration is not desired. These products also are more easily applied to hair-covered skin than ointments. Lotions and creams may be preferred by parents since they are easier to apply and clean up than greasy ointments and less likely to stain their children's clothing.[2,3]

In addition to the corticosteroid potency and vehicle, the choice of dressing also will affect drug penetration. A potent corticosteroid, in an ointment form, used in combination with an occlusive dressing, can provide a high degree of drug penetration, but also may result in greater systemic absorption and a greater risk of adverse effects. Occlusive dressings should be used only for those children with serious conditions and should not be left in place for periods longer than eight hours per day. [3]

Evaluating Toxicity

The greatest risk associated with the topical use of corticosteroids is systemic absorption leading to adrenal axis suppression. While this event is rare, the use of large amounts of high potency preparations or the use of any topical corticosteroid for a prolonged period is known to increase the risk. In addition, occlusive dressings for prolonged periods or the use of topical products on inflamed or broken skin can predispose the patient to systemic toxicity.[1-3]

Local reactions to topical corticosteroids are much more common. These include atrophy and striae of the skin as well as purpura, acneiform eruptions, telangictasia, and discoloration of the skin. While many of these reactions are reversible once therapy has been discontinued, the presence of atrophy and striae are usually permanent. The mechanism for these effects appears to be related to the ability of high-potency agents to induce epidermal thinning and interruption of collagen synthesis. The same risk factors cited for adrenal suppression also apply to the likelihood of developing local reactions. It is recommended that moderately-high, high, and very high-potency agents not be used on the face due to the risk of these local reactions.[1]

In addition to reactions caused by the corticosteroid itself, patients also may exhibit reactions to the vehicle. A thorough patient history which includes any prior sensitivity to creams or ointments is helpful prior to prescribing these products. Patients with chronic conditions, such as psoriasis, should be counseled that sudden discontinuation of their medication may result in a flare-up of their condition.[1,5]

Selecting Combination Products

There are a number of corticosteroid preparations which contain other active ingredients, such as antibiotics and antifungals. Neomycin sulfate is the most common antibiotic used in these products and is available in combinations with several corticosteroids including hydrocortisone (Cortisporin®), fluocinolone (Neo-Synalar®), and dexamethasone (Neodecadron®). Clinoquinol and pramoxine are other antibiotics used in corticosteroid combination products.

Antifungal combinations include such products as Lotrisone® (betamethasone and clotrimazole) and Mycolog-II® (triamcinolone and nystatin). Many UVA health care professionals are familiar with "Greer's goo," a compounded mixture consisting of hydrocortisone, nystatin, and zinc oxide for diaper rash used in our nurseries.

Instructions for Parents

Parents are often concerned about the proper application of these products on their children. It is difficult to easily convey the amount of medication that should be used and the extent of the area to be covered. In an effort to minimize variation in the amount of product applied, Long and Finlay[7] devised a simple method termed the "finger-tip unit." The authors instruct patients to squeeze the medication from its tube in a ribbon-like fashion from the upper joint skin crease of the index finger to the tip. Multiples of this

amount are then used to determine the proper dosage. The authors have developed a chart listing the number of units needed for specific areas. For example, covering one foot of an adult with ointment should require approximately two finger-tip units.

It has been suggested that this method may be useful in helping parents determine how much medication to apply to their children's bodies. To approximate the difference in size, an infant will require only one-fourth the amount recommended for adults and a child between one and four years of age will require one-third of the adult amount. Children over four years of age may be treated as adults.[5]

In addition to addressing the amount of medication to be applied, specific information should be provided on the frequency and duration of cream or ointment use and whether or not an occlusive dressing should be used.

The frequency of application varies with the product used and the condition being treated. Most topical corticosteroid products should be applied no more than two to four times daily. More frequent application is usually not needed, since these lipophilic compounds form a reservoir in the skin. It has recently been suggested that a single application of 0.05% betamethasone dipropionate applied in the late afternoon to take advantage of the body's cortisol circadian rhythm will provide sufficient penetration of drug for most dermatologic conditions.[8] Some clinicians recommend more frequent use of the topical corticosteroids initially in the treatment course, then reducing the number of applications as the condition improves.

The variety of topical corticosteroid preparations available may seem overwhelming at first glance, but offers the health care provider a useful array of selections based on differing potencies, strengths, and vehicles. A basic knowledge of these properties is key to selecting the optimal product for each patient.

References

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Pharmacology Literature Review

Placental Drug Transfer

As more research is conducted on the transfer of medications across the placenta, the complexity of this dynamic system becomes more apparent. These authors have studied the effects of alterations in maternal and fetal blood flow on the transfer of medications across isolated, perfused human placentas. Antipyrine was chosen to represent a high degree of drug transfer, diclofenac as a moderately transferred compound, and cimetidine as the low permeability medication. When maternal flow rate was altered and fetal rate held constant, the amount of study compound transferred varied up to fivefold. This significant change in the potential exposure of the fetus demonstrates the highly complex nature of this relationship and calls into question many of our current concepts of placental drug transfer. Bassily M, Ghabrial H, Smallwood RA et al. Determinants of placental drug transfer: Studies in the isolated perfused human placenta. **J Pharmaceut Sci 1995;84:1054-60.**

Antiepileptic Pharmacokinetics

This is the second of the two-part series reviewing pharmacokinetic studies performed in children receiving antiepileptics. Section II includes: phenytoin, carbamazepine, lamotrigine, felbamate, and three drugs not currently marketed in the U.S., sulthiame, vigabatrin, and oxcarbazepine. The article incorporates information from 139 clinical trials published since 1969. Battino D, Estienne M, Avanzini G. Clinical pharmacokinetics of antiepileptic drugs in paediatric patients. Part I. Clin Pharmacokinet 1995;29:341-69.

Gentamicin in Children with Cancer

In this study, the authors evaluated the pharmacokinetics of gentamicin in three groups of children: 29 with cancer receiving nephrotoxic chemotherapy, 23 with cancer receiving chemotherapy not known to be nephrotoxic, and 25 control patients without cancer. Children receiving nephrotoxic chemotherapy had a lower mean clearance than the other groups, but this difference achieved statistical significance only when clearance was normalized for body surface

area. Comparing clearance normalized by weight (as typically calculated) revealed no difference among the groups. There were no differences among the groups in either volume of distribution or elimination half-life. The authors concluded that no change in dosing is required in pediatric patients with cancer. Evaluation of the patients by age revealed the expected decline in dosing requirement with increasing age. Ho KK, Bryson SM, Thiesen JJ et al. The effects of age and chemotherapy on gentamicin pharmacokinetics and dosing in pediatric oncology patients. Pharmacotherapy 1995;15:754-64.

Formulary Update

The following actions were taken by the Pharmacy and Therapeutics Committee at their meeting on 12/15/96:

1. Alendronate (Fosamax®), a biphosphate indicated for the treatment of osteoporosis in postmenopausal women, was added to the formulary.
2. A quarterly summary of the Adverse Drug Reaction (ADR) Reporting System was presented. These reports are used to assess the frequency of serious, rare, or unusual adverse effects. They are of particular importance for new therapies. If you have questions about the program or would like to report an ADR, please contact the Drug Information Center at (804) 924-8034.

If you have comments, questions, suggestions, or would like
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